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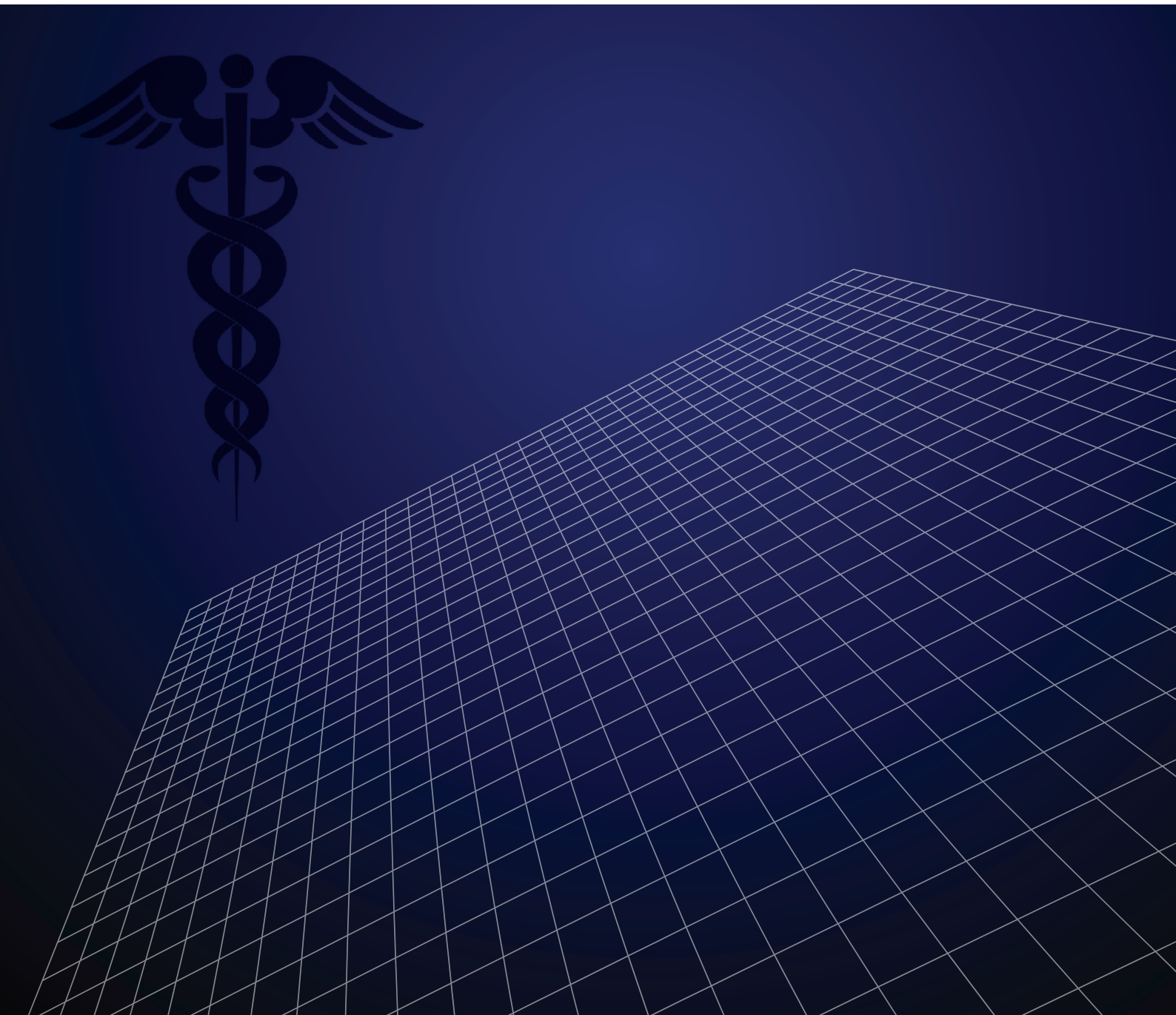

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Orjinal Makale

Çocuklarda sevofluran ile nitröz oksit veya kaudal blok uygulamasının gözlemsel karşılaştırılması

Observational comparison of sevoflurane and nitrous oxide or caudal block in pediatric patients

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Öz

Amaç: Sevofluran çocuklarda anestezi indüksiyonu ve idamesinde en sık tercih edilen volatil anestezik ajandır. Çalışmamızda genel anestezinin analjezik komponentini N2O veya kaudal blok ile sağlayarak ve anestezi süresince bisepektral indeks (BIS) monitörizasyonu ile anestezi derinliğini sabit tutarak; bu iki uygulama şeklinin minimal alveolar konsantrasyon (MAK) ve hemodinami üzerindeki etkilerini gözlemsel olarak karşılaştırmayı amaçladık.

Gereç ve Yöntemler: Genel anestezi altında günübirlik operasyon geçirecek 40 çocuk hastaya; %40 O2/hava (grup K) veya %40 O2/N2O (grup N) karışımı içinde %8 sevofluran kullanılarak inhalasyon indüksiyonu uygulandı. Gurup K'daki çocuklara yan yatar pozisyonda, 22 G kaudal iğneyle 0.7 mL/kg, % 0.2 bupivakain solüsyonu kullanılarak kaudal blok uygulandı. Operasyon süresince her iki grubun hemodinamik parametreleri, BIS ve MAK değerleri takip edilerek kaydedildi.

Bulgular: Her iki grubun hemodinamik parametreleri benzer bulunmuştur. Sevofluranın, N2O katkısı olmaksızın kaudal blok yapılan grupta istatiksel yönden anlamlı olmamakla birlikte daha düşük MAK değerlerinde sürdürülebildiği tespit edilmiştir.

Sonuç: İntraoperatif ve postoperatif analjezi sağlamanın yanı sıra çevre kirliliğini azaltması yönünden de bir avantaj sağladığı için kaudal bloğun, anestezi sırasında uygun koşullarda N2O'e göre daha öncelikle tercih edilmesi gerektiği düşüncesindeyiz.

Anahtar Sözcükler: sevofluran anestezisi; nitröz oksit; kaudal blok

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Abstract

Aim: Sevoflurane is the most preferred volatile anesthetic agent for the induction and maintenance of anesthesia in children. In our study, the analgesic component of general anesthesia was provided by N2O or caudal block and during anesthesia, the depth of the anesthesia was kept constant by means of the monitoring of bispectral index (BIS). We aimed to make an observational comparison the effects of these two methods on minimal alveolar concentration (MAC) and hemodynamics.

Material and Methods: Forty pediatric patients scheduled to undergo on day case based surgery under general anesthesia were included in the study. Inhalation induction using 8% sevoflurane in a mixture of 40% O2/Air (group K) or 40% O2/N2O (group N) were used in all children. Then, patients in Group K received caudal block in lateral decubitus position with 0.7 mL/kg, 0.2% bupivacaine solution using 22 G caudal needle. Hemodynamic parameters, BIS and MAC values were recorded during the operation in all patients.

Results: Hemodynamic parameters were similar in both groups. It was determined that sevoflurane was not statistically significant in the caudal block group without the contribution of N2O, but could be maintained in lower MAC values.

Conclusion: We recommend use of caudal block since it ensures adequately satisfactory intraoperative and postoperative analgesia without any harm to atmosphere in comparison to N2O during general anesthesia in the presence of no medical contraindications.

Keywords: sevoflurane anesthesia; nitrous oxide; caudal block

Giriş

Sevofluran çocuklarda anestezi indüksiyonunda oldukça sık tercih edilen bir volatil anestezik olup, nitröz oksit (N2O) ile birlikte uygulandığında anestezi düzeyine daha hızla ulaşılabilmektedir. Ancak N2O'nun metabolik hastalıklara ve gelişme geriliklerine neden olabilme riski bulunduğu ve ayrıca çevre kirliliği yönünden de sakıncalı olduğu bildirilmiştir [1-3]. Çocuklarda inguinal herni, sünnet ve inmemiş testis gibi operasyonlarda güçlü intraoperatif ve uzun süren postoperatif analjezik etkisi nedeniyle tercih edilen kaudal blok sıklıkla genel anestezi altında uygulanmaktadır [4]. Anestezi derinliğini ölçmek için geliştirilen bisepektral indeks (BIS) monitörü ile yapılan çalışmalarda, BIS ölçümlerinin çocuklarda da anestezinin hipnotik komponentiyle uyumlu olduğu gösterilmiştir [5].

Bu klinik araştırmada, genel anestezinin analjezik komponentini N2O veya kaudal blok ile sağlayarak ve anestezi süresince BIS monitorizasyonu ile anestezi derinliğini sabit tutarak; bu iki uygulama şeklinin minimal alveolar konsantrasyon (MAK) ve hemodinami üzerindeki etkilerini gözlemsel olarak karşılaştırmayı amaçladık.

Gereç ve Yöntemler

Bu klinik araştırma üniversite etik kurul izni (21.02.2005-05) ve ebeveynlerin gönüllü olur formu alındıktan sonra gerçekleştirildi. Çalışmaya genel anestezi altında ASA I-II risk grubunda 1-12 yaş aralığında; inmemiş testis, inguinal herni, hidrosel gibi günübirlik operasyon geçirecek 40 çocuk dahil edildi.

Çocukların alın bölgesi alkollü pamukla silinip kurulandıktan sonra alınlarına uygun problar yerleştirildi (ASPECTTM,Inc Medical Systems P/N REF 186-0110). BIS Monitörü (A-2000, ASPECT Medicak Systems) kullanılarak BIS verileri, XP hiperterminal program yüklenen bilgisayara kaydedildi.

Hastalar kapalı zarf yöntemi kullanılarak, her grupta 20 çocuk olacak şekilde iki gruba ayrıldı. Gruplara %40 O2/Hava (grup K) veya %40 O2/N2O (grup N) karışımı içinde %8 sevofluran kullanılarak inhalasyon indüksiyonu uygulandı. Kirpik refleksinin kaybolduğunda sevofluran %5'e düşürüldü. Daha sonra end tidal sevofluran (ETsev) % 2.2-2.3 aralığında 5 dakika sürdürüldü ve daha sonra uygun laringeal maske (LMA) yerleştirildi. İdame döneminde BİS değerleri 40-60 sınırlarında olacak şekilde ETsev konsantrasyonu ayarlandı.

Grup K'da çocuklar yan pozisyona getirildi, 22 G kaudal iğneyle (Epican® Paed, B Braun Melsungen AG) 0.7 mL/kg, % 0.2 bupivakain solüsyonu yavaş enjekte edilerek kaudal blok uygulanıp hasta sırtüstü pozisyona alındı ve cerrahi hazırlığı takiben operasyon başladı. İntraoperatif olarak kalp atım hızı (KAH), noninvasiv arter kan basıncı (NAKB), periferik oksijen satürasyonu (SpO2) ve end tidal CO2 (ETCO2) monitorize edilerek (Draeger, PM 8060) izlendi. Kaudal blok yapılmayan grupta (grup N), postoperatif analjezi sağlamak için operasyon bitiminde paracetamol 10 mg/kg IV olarak verildi. Kontrol, indüksiyon, LMA yerleşimi öncesi (lmayö),

LMA yerleşimi sonrası (lmays), ilk insizyon, cerrahi stimülasyon (periton gerilmesi), cerrahinin 5, 10, 15, 20, 25 ile 30. dakikaları, kapanma dönemi (ET 1), anestezi bitişi/ LMA çıkarılması öncesi (lmaçö), LMA çıkarılması sonrası (lmaçs) ve uyanma (spontan göz açma, ağlama ve hareket etme) evrelerinde her iki grupta; KAH, ortalama arter basıncı (OAB), MAK değerleri ve BIS ölçümleri kaydedildi. Çalışma için yerel etik kurul onayı alındı. Hasta onam formları imzalatıldı.

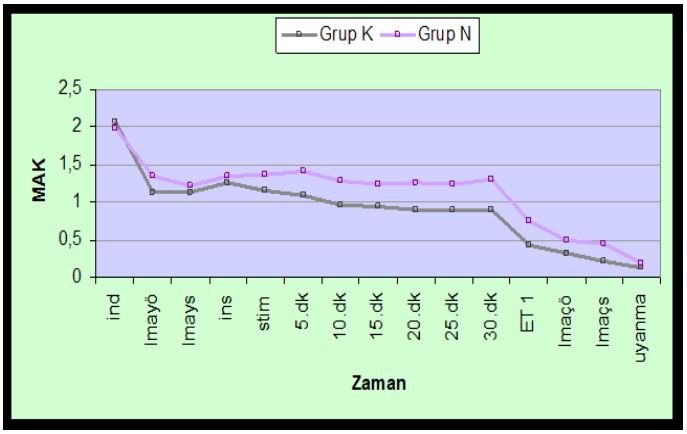
Bulgular

Çalışmaya dahil edilen 40 hastanın demografik özelliği ve cerrahi süresi açısından gruplar arasında fark bulunmadı. Anestezi süresi yönünden ise grup K'nın grup N'ye göre istatistiksel olarak anlamlı olarak daha uzun olduğu belirlendi (p <0.05) (Tablo).

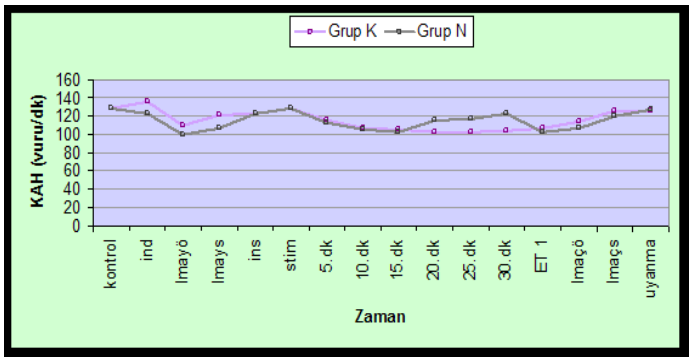
Tablo. Demografik veriler ve anestezi-cerrahi süreler (Ort ± SS)

	Grup K (n=20)	Grup N (n=20)	P değeri
Yaş (yıl)	3.9 ± 2.9	5.3 ± 3.4	-
Ağırlık (kg)	16.5 ± 7.8	20.8 ± 9.2	-
Cinsiyet(K/E)	0 / 20	1 / 19	-
Anestezi süresi	65.6 ± 15.1	54.80 ± 23.1	< 0.05
Cerrahi süresi	43.6 ± 14.1	42.30 ± 21.6	-

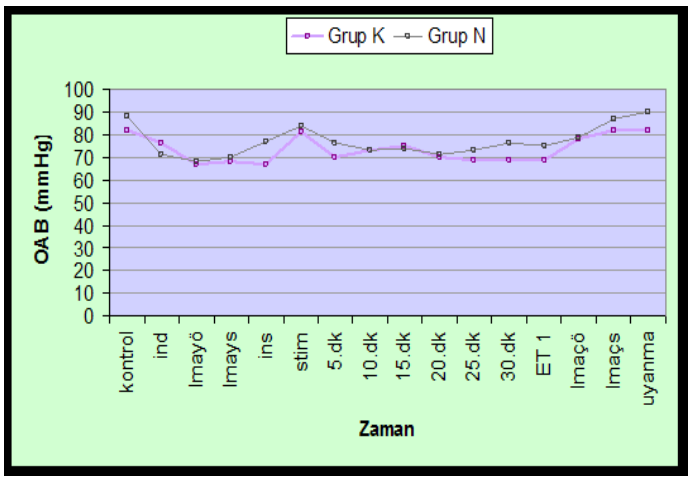
Her iki grupta anestezi indüksiyonuna %8 sevofluran ile başlandığından, başlangıçta MAK değerleri her iki grupta aynı düzeyde tespit edilmiştir. Ancak LMA yerleştirilmesi öncesi, sonrası ve bütün anestezi idamesi süresince, BIS değerleri 40-60 değerleri arasında sabit tutulduğunda, Grup K'da MAK değerleri Grup N'e göre daha düşük ve birbirine paralel olarak seyretmiştir (Şekil 1). Hemodinamik parametreler incelendiğinde ise her iki grubun hem KAH hem de OAB değerleir normal sınırlar içinde birbirine paralel bir seyir göstermiştir (p>0.05) (Şekil 2 ve 3).



Şekil 1. Grupların minimum alveolar konsantrasyon (MAK) değerleri
İnd: indüksiyon, lmayö: LMA yerleşimi öncesi, lmays: LMA yerleşimi sonrası, ins: ilk insizyon, stim: cerrahi stimülasyon, ET 1:kapanma dönemi, lmaçö: LMA çıkarılması öncesi, lmaçs: LMA çıkarılması sonrası



Şekil 2. Grupların kalp atım hızı (KAH) değerleri
İnd: indüksiyon, lmayö: LMA yerleşimi öncesi, lmays: LMA yerleşimi sonrası, ins: ilk insizyon, stim: cerrahi stimülasyon, ET 1:kapanma dönemi, lmaçö: LMA çıkarılması öncesi, lmaçs: LMA çıkarılması sonrası



Şekil 3. Grupların ortalama arter basıncı (OAB) değerleri
İnd: indüksiyon, lmayö: LMA yerleşimi öncesi, lmays: LMA yerleşimi sonrası, ins: ilk insizyon, stim: cerrahi stimülasyon, ET 1:kapanma dönemi, lmaçö: LMA çıkarılması öncesi, lmaçs: LMA çıkarılması sonrası

İstatistiksel Analiz

İstatistiksel analizler SPSS (version 20.0 for windows) programında yapıldı. Tüm veriler ortalama ± standart sapma (Ort ± SS) veya n olarak sunuldu. Tamamlayıcı istatistikler yapıldıktan sonra tekrarlayan ölçümler (repeated measures) ANOVA ile analiz edildi. Gruplar arası karşılaştırmalar için; parametrik verilerde one-way ANOVA, nonparametrik verilerde ise Ki-kare testi kullanıldı ve p<0.05 istatistiksel olarak anlamlı kabul edildi.

Tartışma

Çalışmamızda; genel anestezinin hipnotik komponenti sevofluran ile analjezik komponenti ise N2O veya kaudal blok ile sağlanarak ve anestezi süresince BIS monitorizasyonu ile anestezi derinliği sabit tutularak, bu uygulamaların MAK ve hemodinamik parametreler üzerindeki etkileri takip edilmiştir.

Sevofluranın N2O katkısı olmaksızın kaudal blok yapılan grupta, istatiksel yönden anlamlı olmamakla birlikte diğer gruba göre daha düşük MAK değerlerinde sürdürülebildiği, bununla birlikte hemodinamik açıdan incelendiğinde her iki gruptaki sonuçların birbirine benzer olduğu tespit edilmiştir.

Çocuklarda ağrıya maruz kalmanın davranış değişikliklerine yol açtığı gösterilmiştir. Bu sebeple cerrahi işlemlerde ağrının etkin bir şekilde giderilmesi önem arz etmektedir [6,7]. Kaudal blok çocuk hastalarda göbek altındaki cerrahi işlemlerde güvenli ve etkili bir analjezi yöntemidir [4]. Bunun yanında postoperatif dönemde güçlü analjezik etki sağlaması, hastanın hızla mobilize olması, dolaşımda stres hormon düzeyinin normal sınırlarda kalması ve ek analjezi gereksinimin azalması gibi birçok fayda sağlamaktadır. Genel anestezi ile birlikte yapılan kaudal bloğun intraoperatif inhalasyon ajan tüketimini ve opiod gereksinimini azalttığı saptanmıştır [8,9]. Bu nedenlerle günümüzde çocuklarda genel anesteziyle birlikte yapılan bölgesel veya santral blok uygulamalarına ilgi gittikçe artmaktadır [10]. Özellikle fıtık, sünnet, inmemiş testis gibi operasyonlarda güçlü ve uzun süreli analjezi etkisi nedeniyle tercih edilen kaudal blok sıklıkla genel anestezi altında uygulanmaktadır [4].

Nitröz oksit ikincil gaz etkisi ile volatil anestiziklerin konsantrasyonlarını hızla yükseltmesinin yanı sıra intraoperatif analjezik etkisi nedeniyle de genel anestezide kullanılmaktadır [2]. Keskin kokulu olmaması, hızlı ve yumuşak inhalasyon indüksiyonu sağlaması nedeniyle çocuk hastalarda sıkça kullanılan bir volatil anestezik olan sevofluran, N2O ile birlikte uygulandığında, LMA yerleştirilmesine oluşan yanıtın daha iyi baskılandığı görülmüştür [11]. Bunun yanı sıra N2O; maruziyet süresinin artması oranında postoperatif bulantı ve kusma olasılığının artması, özellikle intraabdominal operasyonlar sırasında batın içi basıncın yükselme riskinin oluşması ve vitamin B12 bağımlı metiyonin sentaz ile timidilat sentaz enzimlerinin inhibisyonu gibi istenmeyen etkilere de yol açabilmektedir [12,13]. Ayrıca N2O kullanılan hastalarda DNA hasarının arttığı ve daha çok postoperatif yara yeri enfeksiyonları ile karşılaşıldığı tespit edilmiştir [14]. Opere olan hastaların yanı sıra özellikle ameliyathanede çalışanlar için de N2O maruziyeti önemli bir sorun teşkil etmektedir [1,3].

Anestezi sırasında kortikal aktivite seviyeleri, hem anestezik maddenin kortikal konsantrasyonu hem de subkortikal uyaran veya uyarılma derecesi ile belirlenir. Rejyonel anestezi subkortikal uyarılma derecesini etkiler. Çocuklarda kaudal bloğun BIS ile ölçülen uyarılma düzeyini azalttığı bulunmuştur [5]. Bununla birlikte epidural bloğun sevofluranın MAK değerini, dolayısıyla hedeflenen BIS değerine (< 50) ulaşmak için gerekli olan sevofluran dozunu azalttığı da gösterilmiştir (15,16). Biz de çalışmamızda BIS monitörizasyonu kullanarak anestezi derinliğini sabit bir düzeyde tutarken, sevofluran ile birlikte yapılan iki değişik uygulama şeklinin MAK ve hemodinami üzerindeki etkilerini tespit etmek istedik.

Kaudal blok ile intraoperatif ve postoperatif etkin analjezi sağlanabilmesi için seçilen lokal anestezi ile kullanılan volüm ve konsantrasyonun önemli olduğu bilinmektedir. Çocuklarda artmış kardiyak output; lokal anesteziklerin dokulardan vaskuler emiliminin artmasına, hızla yüksek başlangıç plazma konsantrasyonlarına ulaşmasına dolayısıyla etki süresinin azalmasına ve sistemik toksisite yaratma ihtimalinin artmasına sebep olmaktadır [17]. Bu nedenle daha yüksek bazal kalp hızı nedeniyle kardiyak toksisite riski artmış olan özellikle 2 yaşından küçük çocuklarda lokal anestezik dozları azaltılmalıdır. Çocuklarda yapılan rejyonel anestezi çalışmalarında kaudal blokta kullanılan lokal anestezikler ve dozları oldukça değişkendir. Kaudal blok uygulamasında; 2 mg/kg'ı geçmemek koşuluyla %0,2 ropivakain, 2,5 mg/kg'ı geçmemek koşuluyla %0,25 levobupivakain / bupivakain önerilen dozlardır [18]. Rejyonel anestezi sonrası motor bloğun uzun sürmesi hem ailelerde endişe yaratmakta, hem de geç taburculuk nedeniyle operasyon sonrası bakım ünitelerinin daha fazla meşgul olmasına neden olmaktadır. Bu nedenle lokal anestezik ajanının konsatrasyon ve volümünün özenle seçilmesi önemlidir. Biz de çalışmamızda; kaudal blok için lokal anestezik olarak güçlü ve uzun süreli analjezik etkisi nedeniyle bupivakaini tercih ettik. Kliniğimizde ilk uygulamalarda bupivakain % 0.25 konsatrasyonda ve 0,5 mL/kg volümünde kullanılırken, zaman içinde daha düşük konsantrasyon (%0,2) ve daha yüksek volüm (0,7mL/kg) tercih edilerek uzun süreli blok riski giderilmiştir. Bu şekilde yapılan uygulamayla analjezik yarar korunarak, motor blok önlenebilmekte veya şiddeti azaltılabilmektedir. Volümü arttırmanın diğer bir yararı da, daha yüksek seviyelerde blok oluşması ve dolayısıyla bloğun geriye dönüş süresinin uzaması, böylece postoperatif analjezinin daha uzun süre devam etmesinin sağlanmış olmasıdır.

Çalışmamızda her iki grup hemodinamik açıdan incelendiğinde; KAH ve OAB yönünden birbirine benzer sonuçlar bulunmuştur. Bununla birlikte sevofluranın, N2O katkısı olmaksızın kaudal blok yapılan grupta, hedeflediğimiz BIS değerinde, istatiksel yönden anlamlı olmamakla birlikte diğer gruba göre daha düşük MAK değerlerinde sürdürülebildiği, bundan dolayı

sevofluran tüketiminin de diğer gruba göre daha az olduğu tespit edilmiştir. Kaudal blok uygulamasının belli bir zaman alması nedeniyle, bu grupta anestezi süresi diğer gruba göre istatistiksel olarak belirgin bir şekilde daha uzun bulunmuştur. Ancak yaklaşık olarak 10 dakika olan bu farkın, uygulamanın sağladığı postoperatif analjezi avantajı düşünüldüğünde, çok da önemli olmadığı görüşündeyiz.

Sonuç

İntraoperatif ve postoperatif analjezi sağlamanın yanı sıra çevre kirliliğini azaltması yönünden de bir avantaj sağladığı için kaudal bloğun, anestezi sırasında uygun koşullarda N2O'e göre daha öncelikle tercih edilmesi gerektiği düşüncesindeyiz.

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Kaynaklar

1. Lew V, McKay E, Maze M. Past, present, and future of nitrous oxide. Br Med Bull 2018; 125: 103-19.
2. Peyton PJ, Chao I, Weinberg L, Robinson GJ, Thompson BR. Nitrous oxide diffusion and the second gas effect on emergence from anesthesia. Anesthesiology 2011; 114: 596-602.
3. Baum VC. When nitrous oxide is no laughing matter: nitrous oxide and pediatric anesthesia. Paediatr Anaesth 2007; 17: 824-30.
4. Silvani P, Camporesi A, Agostino MR, Salvo I. Caudal anesthesia in pediatrics: an update. Minerva Anestesiol 2006; 72: 453-9.
5. Davidson AJ, Ironfield CM, Skinner AV, Frawley GP. The effects of caudal local anesthesia blockade on the bispectral index during general anesthesia in children. Paediatr Anaesth 2006; 16: 828-33.
6. Kain ZN, Mayes LC, Caldwell-Andrews AA, Karas DE, McClain BC. Preoperative anxiety, postoperative pain, and behavioral recovery in young children undergoing surgery. Pediatrics 2006; 118: 651-8.
7. Taddio A, Katz J, Ilersich AL, Koren G. Effect of neonatal circumcision on pain response during subsequent routine vaccination. Lancet 1997; 349: 599-603.
8. Tobias JD. Postoperative analgesia and intraoperative inhalational anesthetic requirements during umbilical herniorrhaphy in children: postincisional local infiltration versus preincisional caudal epidural block. J Clin Anesth 1996; 8: 634-8.
9. Kim SH, Chun DH, Chang CH, Kim TW, Kim YM, Shin YS. Effect of caudal block on sevoflurane requirement for lower limb surgery in children with cerebral palsy. Paediatr Anaesth 2011; 21: 394-8.
10. Ivani G, Mossetti V. Regional anesthesia for postoperative pain control in children: focus on continuous central and perineural infusions. Paediatr Drugs 2008; 10: 107-14.
11. Kihara S, Yaguchi Y, Inomata S, Watanabe S, Brimacombe JR, Taguchi N, Komatsuzaki T. Influence of nitrous oxide on minimum alveolar concentration of sevoflurane for laryngeal mask insertion in children. Anesthesiology 2003; 99: 1055-8.
12. Myles PS, Chan MT, Kasza J, Paech MJ, Leslie K, Peyton PJ, Sneyd JR. Severe nausea and vomiting in the evaluation of nitrous oxide in the gas mixture for anesthesia II trial. Anesthesiology 2016; 124: 1032-40.
13. Pichardo D, Luginbuehl IA, Shakur Y, Wales PW, El-Sohemy A, O'connor DL. Effect of nitrous oxide exposure during surgery on the homocysteine concentrations of children. Anesthesiology 2012; 117: 15-21.
14. Chen Y, Liu X, Cheng CH, Gin T, Leslie K, Myles P, Chan MT. Leukocyte DNA damage and wound infection after nitrous oxide administration: a randomized controlled trial. Anesthesiology 2013; 118: 1322-31.
15. Hodgson PS, Liu SS, Gras TW. Does epidural anesthesia have general anesthetic effects? A prospective, randomized, double-blind, placebo-controlled trial. Anesthesiology 1999; 91: 1687-92.
16. Hodgson PS, Liu SS. Epidural lidocaine decreases sevoflurane requirement for adequate depth of anesthesia as measured by the Bispectral Index monitor. Anesthesiology 2001; 94: 799–803.
17. Desgranges FP, Desebbe O, Pereira de Souza Neto E, Raphael D, Chassard D. Respiratory variation in aortic blood flow peak velocity to predict fluid responsiveness in mechanically ventilated children: a systematic review and meta-analysis. Paediatr Anaesth 2016; 26: 37-47.
18. Suresh S, Ecoffey C, Bosenberg A, Lonnqvist PA, de Oliveira GS Jr, de Leon Casasola O, Ivani G. The European Society of Regional Anaesthesia and Pain Therapy/American Society of Regional Anesthesia and Pain Medicine Recommendations on Local Anesthetics and Adjuvants Dosage in Pediatric Regional Anesthesia. Reg Anesth Pain Med 2018; 43: 211-6.

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Orjinal Makale

Lise son sınıf öğrencilerinin hemşirelik mesleğine yönelik tutumlarının belirlenmesi: Nevşehir ili örneği

Determination of senior high school students' attitudes towards the nursing profession: Example of Nevşehir province

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ÖZ

Amaç: Araştırma lise son sınıf öğrencilerinin hemşirelik mesleğine yönelik tutumlarını belirlemek amacıyla tanımlayıcı olarak yapılmıştır.

Gereç ve Yöntemler: Araştırmanın örneklemini 2014-2015 eğitim öğretim yılında Nevşehir İl Merkezinde devlet liselerinde lise son sınıfta okuyan 305 öğrenci oluşturmuştur. Tanıtıcı Özellikler Formu ve Hemşirelik Mesleğine Yönelik Tutum Ölçeği (HMTÖ) ile toplanmıştır.

Bulgular: Öğrencilerin HMTÖ toplam puan ortalamasının 133.63±20.81 olduğu belirlenmiştir. Kız öğrencilerin erkek öğrencilere göre, endüstri meslek lisesinde okuyanların diğerlerine göre, hemşire yakını olanların olmayanlara göre, hastane deneyimi olanların olmayanlara göre, hemşireliği tercih etmek isteyenlerin istemeyenlere göre HMTÖ toplam puanlarının daha yüksek olduğu bulunmuştur. Öğrencilerin, öğrenim gördükleri okul, hemşireliği tercih etmeyi istemeleri ile hemşirelik mesleğine yönelik tutumları arasında istatistiksel olarak anlamlı farklılık saptanmıştır ($p < 0,05$).

Sonuçlar: Çalışmada lise son sınıf öğrencilerinin hemşirelik mesleğine yönelik tutumlarının olumlu olduğu belirlenmiştir.

Anahtar kelimeler: lise öğrencisi; hemşirelik; meslek; tutum;

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ABSTRACT

Aim: This descriptive research was made in order to determine of senior high school students' attitudes towards the nursing profession.

Material and Methods: The sample of the research was 305 students who are senior high school at State schools in Nevşehir Province in 2014-2015 academic year. The data were collected with questionnaire form and Attitude Scale for Nursing Profession-ASNP.

Results: It was determined that the ASNP total score average of the students was 133.63 ± 20.81. It was found that the total score of the ASPN is higher for female, those who study in industrial vocational schools, those who are close to nurses, those who have hospital experience, and those who prefer nursing.

Conclusion: It was determined that the attitudes of senior high school students towards the nursing profession were positive in the study.

Keywords: high school students; nursing; occupation; attitude

Giriş

Bireyin mesleğini seçmesi yaşamındaki önemli aşamalardan biridir. Meslek seçimi kararı, insanın yaşamı boyunca vereceği en önemli kararlardan biridir. Meslek seçiminin bilinçli yapılması hem birey, hem meslek hem de ülke geleceği açısından büyük önem taşımaktadır. Çünkü birey verdiği kararla tüm yaşantısına şekil verecek bir süreci, yaşayacağı çevreyi ve ilişkide bulunacağı insanları da seçmiş olacaktır [1]. Kişinin mesleğinde başarılı olabilmesi fiziksel özellikleri, mesleği bilerek ve isteyerek seçmeleri ve mesleğe ruhsal ve zihinsel olarak hazır olmasıyla ilgilidir [2]. Bu nedenle kişinin mesleğe yönelik doğru karar alması yaşamında mutlu ve başarılı olabilmesinde önemli rol oynamaktadır [1].

Çoğu insan okul öncesi yıllardan itibaren gelecekte ne olacağı konusunda düşünmekte ve geleceği hakkında planlar yapmaktadır. Başlangıçta tamamen duygusal ve hayali olan bu tutum yaş ilerledikçe daha gerçekçi bir hal almaya başlamaktadır. Meslek seçimi hem kişisel hem de toplumsal önem taşımasına rağmen Türkiye'de meslek seçiminin büyük ölçüde tesadüflere bağlı olduğu bir gerçektir. Türkiye'de yapılan bir çalışmada meslek seçimine etki eden değişkenler iş bulma imkanı, yetenek, ilgi, değerler, kişilik özellikleri, kazancın iyi olması ve ailenin istemesi olarak belirtilmiştir [1].

Sağlık hizmetinin en önemli meslek gruplarından biri hemşireliktir ve hemşireler sağlık ekibinin değişmez üyeleridir. Hemşirelik bilimi son yıllarda önemli aşamalar kaydetmiş, uzun geçmişine yeni bir öz kazandırmıştır [3]. Meslek seçimi konusunda yapılan çalışmalarda hemşirelik mesleğini seçen öğrencilerin meslek seçimini etkileyen faktörler; puanının düşük, iş bulma olanaklarının, parasal getirisinin iyi ve çalışma koşullarının rahat olması, mesleğe duyulan ilgi, öğretmen, aile ve arkadaş önerisi, mesleğin toplumsal saygınlığının olması, kişinin meslekte özgür olması olarak belirtilmektedir [4-9]. Koç ve Sağlam'ın [10] çalışmasında lise öğrencilerinin %20 .2'sinin hemşirelik mesleğini tercih edecekleri ve tercih etme nedenlerini de insana yardım etme isteği, mesleğe ilgi duyma, iş bulma imkanının olması, ebeveyn ve öğretmenlerin isteği ve açıkta kalmama olarak belirlenmiştir.

Tutum, "bir kimsenin ele alınan herhangi bir nesneye, duruma veya olaya karşı olan olumlu veya olumsuz tavrı olarak tanımlanmaktadır [11]. Tutum, kendisini duygu, düşünce ve eylemlerde göstermektedir [12]. Bireyin bir mesleğe ilişkin tutumu o meslekteki başarısı ve doyumunu etkilemektedir [13]. Söz konusu meslek hemşirelik olduğunda ise, konunun önemi daha da artmaktadır. Hemşirelik mesleği doğumdan ölüme kadar canlılığın korunması ve sürdürülmesi amacına yönelik bireyi desteklemeyi amaçlayan eylemleri gerçekleştirir. Olumsuz tutumla bu mesleği tercih eden ve yapan hemşireler olumsuz tutumu mesleği gerçekleştirme eylemlerinde de gösterebilirler. Bu nedenle de olumsuz tutum hem insan yaşamına hem de mesleğe olumsuz olarak yansır. Hemşirelik mesleğinin istenilen düzeye gelebilmesi, mesleği yürütecek olan bireylerin bu mesleği bilinçli olarak seçmesi, eğitimleri süresince aldıkları bilgiyi ve geliştirdikleri becerilerini sağlık bakım ortamlarında kullanabilmeleri ile mümkün olacaktır [10].

Hemşirelik mesleğinin istenen düzeye gelebilmesi ve canlılığın korunması ve sürdürülmesi amacına yönelik bireyi desteklemeyi amaçlayan eylemlerin başarılı bir şekilde

gerçekleştirilmesi, meslek üyelerinin başarılı olabilmesi, hemşirelik mesleğini bilerek ve isteyerek seçim ile mümkündür. Bu nedenle bu çalışma lise son sınıf öğrencilerinin hemşirelik mesleğine yönelik tutumlarını belirlemek, elde edilen sonuçlar doğrultusunda öneriler geliştirmek amacıyla yapılmıştır.

Gereç ve Yöntemler

Tanımlayıcı tipte olan araştırma 2014-2015 Eğitim öğretim yılında Nevşehir İl Merkezinde Milli Eğitim Bakanlığı'na bağlı devlet liselerinde yapılmıştır. Bu liselerde belirtilen tarihlerde lise son sınıfa kayıtlı 1549 öğrenci bulunmaktadır. Araştırmanın örneklemini bu liselerin Türkçe-Matematik ve Fen (hemşirelik mesleğini tercih edebildiklerinden) bölümlerine devam eden toplam 452 öğrenci oluşturmuştur. Bu öğrencilerden 10 öğrenciye ön uygulama yapılması, 36 öğrencinin verilerin toplandığı günlerde devamsızlık yapması ve 101 öğrencinin araştırmaya katılmayı kabul etmemesi sebebiyle araştırma 305 (%67,47) öğrenci ile tamamlanmıştır. Veriler Tanıtıcı Özellikler Formu ve Hemşirelik Mesleğine Yönelik Tutum Ölçeği (HMTÖ) ile toplanmıştır. HMTÖ İpek Çoban tarafından 2010 yılında geliştirilmiş ve geçerlik ve güvenirliği yapılmıştır. İç tutarlılık için Cronbach alfa kat sayısı (∞) 0.91 ve test-tekrar test r = .90 olarak saptanmıştır. HMTÖ likert tipinde 40 soruluk ölçektir. Likert tipi ölçekteki her bir ifade 1'den 5'e puanlanmıştır. Olumlu sorular için "hiç katılmıyorum" yanıtına "1", "az katılıyorum" yanıtına "2", "orta derecede katılıyorum" yanıtına "3", "çok katılıyorum" yanıtına "4" ve "tamamen katılıyorum" yanıtına "5" puan verilmiştir. HMTÖ'nün tersten puanlanacak maddeleri ise 21., 23., 25., 26., 28., 30., 34. ve 38. maddeleridir. Ölçekten alınan puan yükseldikçe hemşirelik mesleğine yönelik olumlu tutum yükselir. Ölçekten en az 40 en fazla 200 puan alınmaktadır. Ölçekten alınan toplam puan 120'nin üzerinde ise kişilerin olumlu tutuma sahip oldukları söylenebilir [12].

Araştırmaya başlamadan önce Nevşehir İl Milli Eğitim Müdürlüğünden yazılı izin alınmıştır. Ayrıca araştırmaya katılan öğrencilere araştırmanın amacı açıklandıktan sonra, sözlü ve yazılı onamları alınmıştır.

Veri toplama araçları araştırmacı tarafından okullara gidilerek okul yöneticileri tarafından belirlenen sınıflarda öğrencilerden izin alındıktan sonra öğrenciler tarafından doldurulmuş ve araştırmacı tarafından toplanmıştır. Araştırmada veriler bilgisayar ortamında SPSS 16.0 programında değerlendirilmiştir. Verilerin değerlendirilmesinde yüzde, ortalama ve standart sapma, karşılaştırmalarda Mann Whitney U, Kruskal Wallis testleri kullanılmıştır. Çalışma için yerel etik kurul onayı alındı. Hasta onam formları imzalatıldı.

Bulgular

Öğrencilerin tanıtıcı özellikleri incelendiğinde; %44.6'sının 17 yaşında ve %52.8'inin kız, %45.2'sinin Anadolu lisesinde öğrenim gördüğü, %45.2'sinin hastane deneyimi olduğu, %56.4'ünün hemşire yakını olduğu ve %28.9'unun hemşireliği tercih edeceği belirlenmiştir (Tablo 1).

Tablo 1. Öğrencilerin Tanıtıcı Özellikleri

Özellikler	Sayı	%
Yaş		
15	6	2.0
16	23	7.5
17	136	44.6
18	130	42.3
19	10	3.6
Öğrenim görülen okul		
Fen Lisesi	16	5.2
Endüstri Meslek Lisesi	89	29.2
Anadolu Lisesi	139	45.6
Sağlık Meslek Lisesi	14	4.6
Mesleki ve Teknik Lise	47	15.4
Hastane Deneyimi		
Var	138	45.2
Yok	167	54.8
Hemşire Yakını		
Var	172	56.4
Yok	133	43.6
Hemşireliği Tercih Etmeyi İsteme		
İsteyen	88	28.9
İstemeyen	217	71.1

Bu çalışmada, öğrencilerin HMTÖ alt boyutlarından hemşirelik mesleğinin özellikleri alt boyutu puanı en fazla olan alt boyuttur (68.73±12.20), HMTÖ toplam puanının orta düzeyin üzerindedir (133.63±20.8) (Tablo 2).

Tablo 2. Öğrencilerin Hemşirelik Mesleğine Yönelik Tutumları

HMTÖ Alt Boyutları	X±SS
Hemşirelik mesleğinin özellikleri	68.73±12.20
Hemşirelik mesleğini tercih etme durumu	34.90±8.45
Hemşirelik mesleğinin genel durumu	30.00±7.47
HMTÖ toplam puan	133.63±20.81

Öğrencilerin, öğrenim gördükleri okul ile hemşirelik mesleğine yönelik tutumları arasında istatistiksel olarak anlamlı farklılık saptanmıştır ($p < 0.05$). Fen Lisesinde okuyan öğrencilerin hemşirelik mesleğine yönelik tutumları, diğer okullarda okuyanlara göre daha düşüktür. Öğrencilerin, hemşireliği tercih etmeyi istemeleri ile hemşirelik mesleğine yönelik tutumları arasında istatistiksel olarak anlamlı farklılık saptanmıştır ($p <$

0.05). Hemşireliği tercih etmeyi isteyen öğrencilerin hemşirelik mesleğine yönelik tutumları istemeyenlere göre daha yüksektir. Cinsiyet, hemşire yakını olma ve hastane deneyimi ile HMTÖ puanı arasında anlamlı ilişki bulunmamıştır($p > 0.05$) (Tablo 3).

Tablo 3. Öğrencilerin Bazı Özelliklerine Göre HMTÖ Toplam Puan Ortalamaları

Özellikler	HMTÖ toplam puan X±SS	test
Cinsiyet		
Kız	135.36±1.61	Z= -1.701
Erkek	131.71±1.75	p=0.089
Öğrenim görülen okul		
Fen Lisesi	121.00±23.21	**X^2=27.928 p=0.000**
Endüstri Meslek Lisesi	142.00±19.5	
Anadolu Lisesi	128.00±20.23	
Sağlık Meslek Lisesi	139.5±18.21	
Mesleki ve Teknik Lise	138.00±20.37	
Hemşire Yakını		
Var	136.00±20.93	Z= -0.286
Yok	134.00±20.72	p=0.775
Hastane deneyimi		
Var	134.39±20.80	Z= -1.138
Yok	131.00±20.75	p=0.255
Hemşireliği Tercih Etmeyi İsteme		
İsteyen	143.37±18.73	**Z= -5.552 p=0.000**
İstemeyen	129.62±20.33	

Tartışma

Meslek başlangıcındaki olumlu tutum, meslekle ilgili unsurları olumlu etkilemekte olup [14] meslekteki başarının en önemli belirleyicisidir [15].

Çalışmada lise son sınıf öğrencilerinin hemşirelik mesleğine yönelik tutumlarının olumlu olduğu belirlenmiştir (Tablo 3). Zencir ve Eşer'in [16] çalışmasında hemşirelik öğrencilerinin hemşirelik mesleğine yönelik tutumlarının olumlu olduğu, Eskimez ve arkadaşlarının [17] çalışmasında lise son sınıf kız öğrencilerin hemşirelik mesleği ile ilgili olumlu görüşleri olduğu ifade edilmiştir. Al-Omar'ın [18] çalışmasında Suudi Arabistan'da lise öğrencilerinin hemşirelik mesleğine yönelik tutumlarının orta düzeyde olduğu, Al Mutair ve Redwan'ın [19] çalışmasında Suudi Arabistan'da hemşirelik öğrencileri ve ailelerinin hemşirelik mesleğine karşı güçlü olumlu tutum sergiledikleri, Akoijam ve Akoijam'ın [20] çalışmasında Hindistan'da orta okul öğrencilerinin hemşirelik mesleğine karşı olumlu tutuma sahip olduğu belirtilmektedir. Lise öğrencilerinin hemşirelik mesleğine yönelik tutumlarının olumlu olması toplumda hemşirelik imajını da olumlu etkileyeceğinden bu durumdan hemşirelik mesleğinin ve meslek üyelerinin de olumlu yönde etkileneceği söylenebilir.

Çalışmada kız öğrencilerin erkek öğrencilere göre hemşirelik mesleğine yönelik tutumlarının daha olumlu olduğu saptanmıştır (Tablo 3). Türkiye'de yapılan çalışmalarda da hemşirelik mesleğini tercih edenlerin çoğunun kadın olduğu görülmektedir [21-24]. Hemşirelik mesleğini Hemşirelik Kanununda yapılan değişiklikle birlikte erkeklerin de tercih edebilmesine rağmen bu çalışmanın sonucu ülkemizde hemşirelik mesleğinin kadınlar tarafından daha çok benimsenen meslek olmaya devam ettiğini göstermektedir.

Çalışmada endüstri meslek lisesinde okuyanların hemşirelik mesleğine yönelik tutumlarının en yüksek, fen lisesinde okuyanların en düşük olduğu bulunmuştur (Tablo 3). Hemşirelik bölümünde okuyan öğrencilerle yapılan çalışmalarda hemşirelik mesleğini tercih eden öğrencilerin çoğunluğunun düz lise mezunu olduğu belirtilmektedir [22, 23, 25]. Çalışmamız sonucunda endüstri meslek lisesi öğrencilerinin hemşirelik mesleğine olumlu tutumları sevindirici olduğu kadar aldıkları mesleki eğitim doğrultusunda meslek seçimi yapmayacaklarını düşündürdüğü içinde kaygı vericidir.

Çalışmada hemşire yakını olanların olmayanlara göre hemşirelik mesleğine yönelik tutumlarının daha olumlu olduğu belirlenmiştir (Tablo 3). Çelik ve arkadaşlarının [26] çalışmasında ailesinde hemşire bulunan bireylerin hemşirelik mesleğine ilişkin olumlu görüşe sahip oldukları, Eskimez ve arkadaşlarının [17], Karakuş ve arkadaşlarının [27] ve Koç ve Sağlam'ın [10] çalışmalarında da hemşire bir yakını olan lise son sınıf öğrencilerin hemşireliği tercih etme oranlarının daha fazla olduğu belirlenmiştir. Yakın çevrede hemşire olmasının hemşirelik mesleğini tanımaya ve hemşirelik mesleğine olumlu tutum geliştirmeye neden olduğu söylenebilir.

Çalışmada hastane deneyimi olanların olmayanlara göre hemşirelik mesleğine yönelik tutumlarının daha olumlu olduğu saptanmıştır (Tablo 3). Eskimez ve arkadaşlarının [17] çalışmasında hastane deneyimi yaşayan öğrencilerin %32.2'sinin hemşireliği tercih etmeyi düşündükleri saptanmıştır. Yurtdışında yapılan çalışmalarda da hastane deneyimi yaşamanın hemşirelik mesleğinin seçiminde olumlu olduğu belirtilmektedir [28, 29]. Hastane deneyimi olan öğrencilerin hemşirelik mesleğine tutumlarının olumlu olması hastanede karşılaştıkları hemşirelerin mesleğini başkalarında olumlu izlenim yaratacak şekilde yaptıklarını göstermektedir.

Çalışmada hemşireliği tercih etmek isteyenlerin istemeyenlere göre hemşirelik mesleğine yönelik tutumlarının daha olumlu olduğu belirlenmiştir (Tablo 3). Çalışmamız sonucunda hemşirelik

mesleğine karşı olumlu tutumu olan kişilerin hemşirelik mesleğini tercih etmesinin hemşirelik mesleğine profesyonelleşme açısından olumlu katkı sağlayacağını söyleyebiliriz.

Sonuç

Bu çalışma, lise son sınıf öğrencilerin hemşirelik mesleğine yönelik tutumlarının olumlu olduğunu belirlemiştir. Hemşireliği isteyerek seçme tutumu olumlu etkilemektedir. Dolayısıyla hemşirelik mesleği olumlu tutumun arttırılması için liselerdeki rehberlik bölümleri ile hemşirelik eğitimi veren okullar, hemşirelik hizmeti veren kurumların hemşirelik hizmetleri yöneticileri ve hemşireleri ile hemşirelik derneklerinin birlikte faaliyetler yapmaları önerilebilir.

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1. Pekkaya M, Çolak N. Üniversite öğrencilerinin meslek seçimini etkileyen faktörlerin önem derecelerinin Analitik Hiyerarşi Süreci (AHP) ile belirlenmesi. International Journal of Social Science 2013; 6: 797-818.
2. Sarıkaya T, Khorsid L. Üniversite öğrencilerinin meslek seçimini etkileyen etmenlerin incelenmesi: Üniversite öğrencilerinin meslek seçimi. Türk Eğitim Bilimleri Dergisi 2009; 7: 393-423.
3. Erbil N, Yılmaz A. Hemşirelik öğrencilerinin meslek seçme kararlarını ve bakış açılarını etkileyen faktörlerin belirlenmesi. Hemşirelik Forumu 2008; 2: 46-51.
4. Altun İ. Kocaeli Sağlık Yüksekokulu öğrencilerinin kişisel değerleri ve meslek seçimlerine etki eden faktörler. I. Uluslar arası & VIII. Ulusal Hemşirelik Kongresi Kitabı (Antalya) 2000: 75- 77.
5. Dinç S, Kaya Ö, Şimşek Z. Harran üniversitesi sağlık yüksekokulu öğrencilerinin hemşirelik mesleği hakkındaki bilgi, düşünce ve beklentileri. Atatürk Üniversitesi Hemşirelik Yüksekokulu Dergisi 2007; 10: 1-9.
6. Şirin A, Öztürk R, Bezci G, Çakar G, Çoban A. Hemşirelik öğrencilerinin meslek seçimi ve mesleği uygulamaya yönelik görüşleri. Dirim Tıp Dergisi 2008; 83: 69-75.
7. Tezel A, Arslan S. Erzurum sağlık yüksekokulu 1. sınıf öğrencilerinin mesleklerini seçmeye ve mesleğe ilişkin görüşleri. Atatürk Üniversitesi Hemşirelik Yüksekokulu Dergisi 2002; 5: 39-44.
8. Tüfekçi F, Yıldız A. Öğrencilerin hemşireliği tercih etme gerekçeleri ve gelecekleri ile ilgili görüşleri. Atatürk Üniversitesi Hemşirelik Yüksekokulu Dergisi 2009; 12: 31-37.
9. Yanıkkerem E, Altınparmak S, Karadeniz G. Gençlerin meslek seçimini etkileyen faktörler ve benlik saygıları. Hemşirelik Forumu 2004; 7: 61- 62.
10. Koç Z, Sağlam Z. Lise son sınıf öğrencilerinin hemşirelik mesleğine İlişkin görüşleri ve mesleği seçme durumlarının belirlenmesi. Atatürk Üniversitesi Hemşirelik Yüksekokulu Dergisi 2009; 12: 1-11.
11. İpek C, Bayraktar Ş. Aday öğretmenlerin fen bilimleri ve sosyal bilimlere bakışları. Yüzüncü Yıl Üniversitesi Eğitim Fakültesi Dergisi 2004; 1: 35-50.
12. İpek Çoban G. Hemşirelik Mesleğine Yönelik Tutum Ölçeğinin Geliştirilmesi. Doktora Tezi, Atatürk Üniversitesi, Sağlık Bilimleri Enstitüsü, Hemşirelik Esasları ABD, Erzurum; 2010.
13. Çakır Ö. Anadolu üniversitesi açık öğretim fakültesi İngilizce öğretmenliği lisans programı (İÖLP) ve eğitim fakülteleri İngilizce öğretmenliği lisans programı öğrencilerinin mesleğe yönelik tutumları ve mesleki yeterlik algıları. İnönü Üniversitesi Eğitim Fakültesi Dergisi 2005; 9: 27-42.
14. Can Ş. Tezsiz yüksek lisans öğrencilerinin öğretmenlik mesleğine yönelik tutumları. Muğla Üniversitesi Sosyal Bilimler Enstitüsü Dergisi 2010; 24: 13-28.
15. Durmuşoğlu MC, Yanık C, Akkoyunlu B. Türk ve Azeri öğretmen adaylarının öğretmenlik mesleğine yönelik tutumları. Hacettepe Üniversitesi Eğitim Fakültesi Dergisi 2009; 36: 76-86.
16. Zencir G, Eşer İ. Hemşirelik öğrencilerinin hemşirelik mesleğine yönelik tutumları ile hemşirelik tercihi arasındaki ilişki: Türkiye Örneği. Dokuz Eylül Üniversitesi Hemşirelik Fakültesi Elektronik Dergisi 2016; 9(2). Available from http://www.deuhyoedergi.org/index.php/DEUHYOED/article/view/208. Accessed 2017 May 17
17. Eskimez A.G.Z, Öztunç G, Alparslan N. Lise son sınıfta okuyan kız öğrencilerin hemşirelik mesleğine ilişkin görüşleri. Hacettepe Üniversitesi Hemşirelik Fakültesi Dergisi 2008; 15: 58-67.
18. Al-Omar B. A. Knowledge, attitudes and intention of high school students towards the nursing profession in Riyadh city, Saudi Arabia. Saudi medical journal 2004; 25: 150-55.
19. Al Mutair A, Redwan F. Undergraduate Saudi Nursing Students Attitudes towards Nursing Profession. J Nurs Care 2016; 5: 2167-68.
20. Akoijam M.D, Akoijam S.D. Knowledge and attitude toward nursing as profession and their preference for nursing as a career among senior secondary students. International Journal of Applied Research 2015; 1: 401-403.

21. Ergün G, Güzel A. Sağlık yüksekokulu hemşirelik bölümü ilk ve son sınıf öğrencilerinin meslek seçimini etkileyen faktörlerin incelenmesi. International Journal of Human Sciences 2016; 13: 1271-84.
22. Andsoy I.I, Güngör T, Bayburtluoğlu T. Karabük üniversitesi sağlık yüksekokulu öğrencilerinin hemşireliği tercih etme nedenleri ve mesleğin geleceği ile ilgili görüşleri. Balıkesir Sağlık Bilimleri Dergisi 2012; 1: 124-30.
23. Özveren H, Gülnar E, Özden D. Hemşirelik öğrencilerinin meslek seçimini etkileyen faktörlerin belirlenmesi. Turk J Clin Lab 2017; 8: 57-64.
24. Özdelikara A, Ağaçdiken S, Aydın E. Hemşirelik Öğrencilerinin Meslek Seçimi ve Etkileyen Faktörler. ACU Sağlık Bil Derg 2016; 2: 83-88.
25. Ünal S, Gürhan N, Saral E, Özbaş A.A. Hemşirelik öğrencilerinin sosyodemografik özellikleri ve hemşirelik mesleğini seçme nedenleri. Florence Nightingale Hemşirelik Dergisi 2008; 16: 179-87.
26. Çelik A.S, Pasinlioğlu T, Kocabeyoğlu T, Çetin S. Hemşirelik mesleğinin toplumdaki imajının belirlenmesi. Florence Nightingale Hemşirelik Dergisi 2013; 21: 147-53.
27. Karakuş A, Karadağ N, Birgili F, Işıkay Ç, Çadır G, Çeker D. Lise son sınıf kız öğrencilerinin hemşirelik mesleğine bakış açıları ile mesleği tercih etme durumları. Hemşirelik Forumu Dergisi 2005; 5: 17-20.
28. Law W, Arthur D. What factors influence Hong Kong school students in their choice of a career in nursing? Int. J. Nurs. Stud. 2003; 40: 23-32.
29. Kandari FH, Lew I. Kuwaiti high school students' perceptions of nursing as a profession: implication for nursing education and practice journal of nursing education. Journal of nursing Education 2005; 44: 533-40.

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Original Article

A comparison study on the effectiveness of pager and telephone systems during emergency department consultations and length of stay of consulted emergency department patients

Acil servis konsültasyonlarında çağrı ve telefon sistemlerinin etkinlikleri ile danışılan hastaların acilde kalış sürelerinin karşılaştırmalı çalışması

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ABSTRACT

Aim: Emergency department (ED) physicians use different tools and modalities to communicate with consulted clinical divisions in all over the world. Domestic phones, pagers, consultation stations, mobile phones and smart phone applications are commonly used examples. They have a changing trend over time and technology in practice. We evaluated the effectiveness of the consultations conducted by telephone and pager systems, compared the functionality of both systems and investigated their effects on length of stay (LOS) of the patients in the ED of a tertiary teaching hospital.

Material and methods: The study was planned as prospective and descriptive. The consulted patients in ED were assigned for the study group. The domestic telephones and pagers with central operating system were used as an ED consultation tool for a two-week period, respectively and separately. LOS and consultation response time (CRT) were evaluated.

Results: Three hundred eighteen consultations were requested for a total of 228 patients. The most frequently requested consultations were from Cardiology (17.6%), General Surgery (14.2%) and Orthopaedics (13.5%). When the telephone and pager systems were compared independently from the departments, CRT was found significantly longer via telephone compared to pager (52 min vs. 18 min; p=0.56, p=0.04). The LOS was 353 min for telephone, 314 min for pager but these results were not statistically significant (p>0.05).

Conclusion: The pager system for consultation request is a time and energy reducing option for ED physicians. In addition, it shortens CRT for the patients with high urgency levels. However there is no significant difference between both methods on LOS.

Keywords: emergency; consultation; communication; pager; length of stay

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ÖZ

Amaç: Tüm dünyada Acil Servis Hekimleri konsültasyon istemlerini gerçekleştirmek için farklı araçlar ya da sistemler kullanmaktadır. Dahili telefonlar, çağrı cihazları, konsültasyon istasyonları, cep telefonları ve akıllı telefonlar sık kullanılan örneklerdir. Bu tercihleri pratikte zaman ve teknoloji ile değişen bir eğilim izlemektedir. Biz bu çalışmada konsültasyonlarda kullanılan dâhili telefonlar ile çağrı cihazlarının etkinliklerini değerlendirdik ve üçüncü basamak bir Eğitim ve Araştırma hastanesinde hastaların acil serviste bekleme süreleri (ABS) üzerine etkilerini araştırdık.

Gereç ve Yöntemler: Çalışma prospektif ve tanımlayıcı olarak planlanmıştır. AS'de konsültasyon istenen hastalar çalışma grubu olarak seçilmiştir. Dahili telefonlar ve merkezi işletim sistemli çağrı cihazları ayrı ayrı ve sırasıyla AS konsültasyon istemleri için 2 haftalık periyotlar halinde kullanılmıştır. ABS ve konsültasyon cevaplama süreleri (KCS) değerlendirilmiştir.

Bulgular: Toplam 228 hastadan 318 konsültasyon istenmiştir. En çok konsültasyon istenen bölümler Kardiyoloji (17.6%), Genel Cerrahi (14.2%) ve Ortopedi'dir (13.5%). Telefon ve çağrı cihazları bölümlerden bağımsız olarak karşılaştırıldıklarında, telefonla tespit edilen KCS değerleri çağrı cihazlarına göre belirgin uzun tespit edilmiştir (52 dk vs. 18 dk; p=0.56, p=0.04). ABS telefon için 353 dk iken çağrı cihazı için 314 dk olarak bulundu ancak bu sonuçlar istatistiksel olarak anlamlı değildi(p>0.05).

Sonuç: Çağrı cihazlar AS hekimleri için konsültasyon istemleri için zaman ve enerjiden tasarruf ettiren bir seçenektir. Ek olarak aciliyeti yüksek hastalar için KCS'yi kısaltmaktadır. Ancak AKS açısından iki yöntemle ilgili anlamlı bir fark tespit edilememiştir.

Anahtar kelimeler: acil; konsültasyon; iletişim; çağrı cihazı; yatış süresi

Introduction

Emergency departments (ED) are the units of healthcare services which should offer uninterrupted and fast care, not compromise on quality at the same time. Overcrowding in EDs is a worldwide problem [1-6]. Patient triage, radiology-laboratory examinations, consultation and treatment processes affect the length of stay (LOS) in EDs, therefore these are the enhancing factors to overcrowding problem [7].

Consultation processes are important and perpetual parts of emergency medicine practice (8). Therefore, for a holistic approach to cases, more than one field of medicine has become inevitable to work together. Consultation is the attaining procedure of patient's primary physician to a relevant speciality department via telephone or any other communication device on any matter relating to patient care [2,9,10]. Consultations requested by ED physicians may have different purposes. The most known are consultations for admission (most common), opinion only, special procedures, transfer of care and for outpatient referrals [11]. Consultations are important for requested department as much as requesting department. Because an unnecessary consultation means loss of energy, time and money for each department and for the patient. Most of the time, patients have to stay in ED until the consultation process is finished, even if the diagnosis and treatment procedures are completed [3]. Therefore, consultation difficulties and late responses by specialty departments enhance overloads in EDs in many countries by contributing to disposition delays in hospitals [3,11,12]. Inter-departmental communication-art deficiencies and the limitations of communication tools are most important consultation delay considerations. Domestic telephones, pagers, e-mail, MMS or other applications via mobile or smart phones and accessing patient information on hospital automation systems or internet are mostly used tools for consultation communication [13-16]. The aims of the study are to evaluate currently used domestic phones outcomes as consultation tool in our tertiary teaching hospital, to compare the functionality of phone and newly applied pager system and to investigate their effects on length of stay (LOS) of the patients in the ED.

Material and Method

After the approval of hospital ethics committee, a total of 8849 patients admitted to Ankara Atatürk Teaching Hospital ED between 06/06/2011 and 04/07/2011 were included into study which was designed in a prospective and descriptive structure and 2549 of them consulted during ED stay. Uncompleted consultations, consultation requested via mobile phones, coincidental consultations (seen consultant who came to ED for another patient or just crossing over in the form of "early consultation"), out-patient clinic referrals in the purpose of consultation during work-hours and the patients with missing data in the follow-up forms were excluded. Finally, 228 patients admitted to the ED included into the study with 318 consultations requested for them. Each consultation was also analyzed separately in the patients who needed more than one consultation as well. The patients were studied in two main groups based on the consultation model as "telephone" and "pager" in defined time intervals. In the first two-week period,

all the ED consultations were held with domestic phones as usual. Meanwhile, the pager system was in the off position. In the second two-week period, by activating the pager system all consultations were carried out with this method. ED physicians were asked to fill the prepared patient follow-up forms. Diagnoses, age, gender, type of admission, time of admission, judicial status, urgency of the patient, consulted departments, LOS in ED, consultation response time (CRT) and final status of the patient were recorded in the forms. During the pager system period, the data that recorded on the main computer processor were compared with the noted durations in the forms at the same time. Mismatched forms were also excluded.

The portable part of newly integrated pager system is "pager devices" which are allocated to all consultant divisions (UDEA brand, UEL-924 model). The other part of the pager system is main control display which is located in ED, has a touch screen, and where every division has its own consultation column. When ED physician decides to consult, the physician just needs to touch the relevant section area for activating the consultation process. The relevant section area colour turns into yellow from blue by activation which means the consultation is detected by the system and the signal is transmitted to the related pager devise. If on-call physician of consulted section doesn't come to ED and receives a second demand in 20 minutes, the current yellow box turns into red this time. The system alerts relevant pager device in every 1.5 minutes after 20 minutes for every unreceived consultation until the consultation demand signal is received.

The duration from actualizing the consultation demand on pager screen until the arrival of the consultant to patient side in ED is defined as CRT. The duration between the admission of the patient to the ED and the final disposition (discharge, hospitalization, operation, outpatient/inpatient referral or transfer/exitus, etc.) defined as LOS in ED.

Data analysis was performed by SPSS for Windows 18.0 package program. The categorical variables were expressed with numbers and percentages, numeric variables were summarized in mean±standard deviation (SD), median and min-max. The differences between the two groups were compared with Mann-Whitney U test and the differences between more than two groups were analyzed with the Kruskal-Wallis test. The significance level was considered as $p<0.05$. Bonferroni correction is used for poly-comparisons. Local ethics committee approved the study and informed consent was obtained from participant(s)

Results

In total, 8849 patients admitted to ED during the study interval and 2549 consultation requests were carried out (28.8%). Only 228 patients who met inclusion criteria included. Their distribution for gender (male vs. female) were [136 (59.6%) vs. 92 (40.4%)] with an average age 52.7 ± 22 (range: 01-94). A significant proportion of the study group were older than 65 years old (phone and pager for groups, respectively 40.3% vs. 42.9%), however the number of 0-19 age group was very low (9.6% vs. 4.3%). Again a large proportion of the consulted patients brought to the ED by ambulance (60.5% vs. 56.1%). There was no significant difference between phone and pager group in patients' gender, age, legal status and admission way to ED ($p>0.05$).

A total of 318 consultations were practiced in 228 patients enrolled in the study. The most requested consultation divisions were Cardiology (17.6%), General Surgery (14.2%) and Orthopaedics (13.5%), respectively. The least consulted divisions were Nephrology (0.3%), Endocrinology (0.3%), and Haematology (0.3%).

CRT was found 36±47 min in total and significantly shorter via pager comparing to telephone (52 min vs. 18 min; p=0.56, p=0.04) with average (Table 1). Also the CRT of Cardiology, Neurology and Neurosurgery departments shortened statistically in pager group; (p=0.001, p=0.001 and p=0.019). Although the arrival of all sections in pager group were shortened, it was not statistically significant for each division. Time zone analyses of CRT showed that 00:00-05:59 time zone was statistically longer (p=0.02) and this result didn't change based on consultation systems (p=0.07). The fastest respondent divisions were Internal Medicine (28.2±19.2 min)

Table 1. The mean CRT of consulted ED patients by groups and time zones.

	Telephone		Pager		Total		P
Time Zone	Number of cons.	CRT* (minutes)	Number of cons.	CRT* (minutes)	Number of cons.	CRT* (minutes)	
00:00 - 05:59 (Night)	21	82.33±80.02	19	23.57±10.90	40	54.42±64.97	0.001
06:00 – 11:59 (Morning)	34	55.44±46.35	37	15.40±7.45	71	34.57±38.04	0.000
12:00 – 17:59 (Afternoon)	55	58.98±67.00	52	19.03±20.06	107	39.57±53.69	0.000
18:00 - 23:59 (Evening)	59	33.50±45.17	41	19.14±15.23	100	27.62±36.60	0.157
Total	169	52.27±59.87	149	18.74±15.34	318	36.56±47.86	
P	0.000	0.36					

*CRT; Consultation Response Time

for phone group and Cardiology (13±9.4 min) for pager group.

It was detected that the consultation tool –whether phone or pager- didn't make significant difference on LOS of patients (353.18 vs. 314.47 min, p> 0.05, Table 2). One of the determining factors on LOS was the number of consultations required for the patient. LOS of the patients with one consultation was 273 min but it was extending to 539 min in those more than one consultation needed (p=0.000).

Table 2. The mean LOS of consulted ED patients by groups and consultation number.

LOS* (minutes)	Telephone	Pager	Total	p
	353.18±340.44	314.47±250.22	333.82±298.72	>0.05
Patients with one consultation			273.17 ± 208.18	0.000
Patients with more than one consultation			539.13 ± 298.72	

*LOS; Length of Stay

After the observation, treatment and consultation protocols completed in ED, 55.3% of the patients were discharged, 38.2% were given admission decision, 6.5% were referred to another hospital for further or special treatment. Among the whole study group, 7.5% were hospitalized to intensive care unit (ICU) and 30.7% had a ward admission. There was not a significant difference between the groups in discharge and hospitalization (p>0.05, Table 3).

Table 3. The LOS of consulted ED patients according to their final dispositions.

	Telephone			Pager			p
Final Disposition	Number	%	LOS* (min)	Number	%	LOS* (min)	
Discharge	57	50.0	378.71±350.76	69	60.5	338.52±251.17	0.64
Hospitalization(ward)	44	38.5	314.13±276.05	26	22.8	255.38±171.18	0.41
Hospitalization (ICU)	6	5.2	249.50±362.55	11	9.6	228.18±363.07	0.96
Exitus	0	0.0		1	0.8	330.00	
Transfer to another hospital	4	3.5	757.00±650.47	4	3.5	333.50±125.31	0.34
Voluntarily abandonment	3	2.6	109.66±47.12	3	2.6	559.33±382.673	0.10
Total	114	100	353.18±340.44	114	100	314.472±250.22	

*LOS; Length of Stay

When the delay causes were investigated for the patients who had a unexpected longer LOS, it was seen that the majority of delays occurred in telephone group and the main reason was inability to reach to the on-call physician by the domestic line (18 of 49 patients). In the general evaluation for both consultation systems; waiting for an empty bed, long duration of ordered treatments in ED, insufficient ED staff and waiting for the relatives of the patient were the major causes of delay.

Discussion

The studies about ED consultations were initiated in the mid 90's [1,2,7,10,16,20-22]. In recent years there are precious studies showing the influences of consultation process on patient burden of EDs and patient care [23-24]. In this study, we aimed to compare the effectiveness of the mostly used consultation tools (domestic telephone and pager) for ED consultations in our country on LOS and CRT.

In our ED, 28.8% of the all patients presenting to ED require at least one consultation. The rate of consultations for ED patients ranges from 20% to 60% according to the characteristics of the studies [11]. In the literature, gender is not a variable [16] but age is an important determinative for consultation rate, for example the geriatric patient populations have a higher consultation rate [8].

The guidelines prepared by professional emergency organizations indicate that a reasonable consultation response duration is between 30-45 min for an ED based consultation demand but it's also emphasized that main determinant is the patient's clinical exigency[19]. The fastest mean CRT among all specialities was Internal Medicine (28.2 min) in telephone group and Cardiology (13 min) in pager group. CRT was significantly shortened in Cardiology, Neurology and Neurosurgery via pager. These three main divisions are the disciplines investigate the pathologies leading causes of adult death in the world, have "time=brain" and "time=heart" paradigms and practice urgent treatments and invasive procedures simultaneously with diagnoses.

The average LOS of an ED patient is 3.2 hour (192 min) according to 2007 CDC (Center for Disease Control) Survey in United States [17]. In a study conducted in California [18], LOS calculated 56 minutes, and Oktay et al [19] reported 3.3 hours (198 min). Average LOS was calculated 333 min in our study. But the main difference between our results and these studies probably may generate from focusing on just consulted ED patients only in the study also excluding out patient referrals and simultaneous early consultations. Cho et al [3] constructed a computerized

consultation management system to improve consultation process, compared it with previously used consultation system (mobile phone) and evaluated the results on LOS similarly with our study. They found significantly decreased ED LOS (311 min). But what we found is LOS was not altered by our newly implemented pager system. We detected some altering factors on LOS separately from consultation system (weekday admission, ambulance arrival and more than one consultation). Our results showed much longer LOS than expected compared with most of the studies. But it should be considered that only consulted patients were included. When the literature on ED consultations is perused, it can be notified there are a few studies including the number of consultations. Cho et all identified 77.6% of the patients needed at least one consultation and the number of consulted departments was associated with increased ED LOS. Single consultation need for a patient is calculated as 92% in a Canada based study [8]. And we calculated the single consultation rate as 77.6% similarly. Unexpected longer LOS was associated with insufficient bed capacity and uncompleted consultation processes mainly, as in the literature [3,5,6,10,20].

There are some advantages and disadvantages for both mentioned systems in our study. Among the delay reasons on domestic telephone system; broken telephones, hold position of the line accidently, multiple alternative number existence, not having a proper and up-to-date telephone number list on ED can be counted. In addition due to other responsibilities of the consultant, the physician's physical distance to the stationary phone is an important disadvantage. To be able to give the consultant detailed information about the patient is an incontrovertible advantage of the phone despite the difficulties in reaching and time spent. Pager system facilitates reaching the consultant with its portable structure and saves time for ED physicians, also the warning feature with frequent intervals provides the consultant's turn faster. However there are disadvantages like battery failure, forgotten on somewhere or failure on giving information about the patient.

Need for hospitalization, admission decision, physical challenges for admission preadmission processes increase the burden of EDs. According to the consultation purpose, almost all of the studies indicate the most common reason for consultation is for hospitalization of the patient [11]. The admission rate was reported 87% in the study Cortazzone et al. [25], 54% in the study of Woods et al [8]and 64-68% in the study Curry and Wang [26]. The admission rate in our study was 38.2%. According to our results, the admission rate is lower than expected compared to the examples in the literature. This difference can be due to the exclusion of a large group of patients with incomplete forms and simultaneous consultations.

Conclusion

Every delaying step in emergency care should be investigated thoroughly for more functional emergency departments. We focused on consultation system tools for this purpose. The usage of pager system for consultation request is a time and energy reducing method for ED physicians. In addition, it shortens CRT for the patients with high urgency levels. However there is no significant difference between both methods on LOS. Also more further consultation system analyses and comparisons are needed.

Declaration of conflict of interest

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References

1. Rosen P. Emergency department disposition and knowledge of other specialties. J Emerg Med 1986; 4: 325-26.
2. Tintinalli JE, McCall K. Importance of emergency physicians as referral sources for academic medical centers. Ann Emerg Med 1994; 23: 65-69.
3. Cho SJ, Jeong J. Decreased emergency department length of stay by application of a computerized consultation management system. Academic Emergency Medicine 2011; 18: 398–402.
4. Li G, Lau JT, McCarthy ML et al. Emergency department utilization in the United States and Ontario, Canada. AcadEmerg Med 2007; 14: 582–84.
5. Olshaker JS, Rathlev NK. Emergency department overcrowding and ambulance diversion: The impact and potential solutions of extended boarding of admitted patients in the emergency department. J Emerg Med 2006; 30: 351–56.
6. Richardson S, Ardagh M, Hider P. New Zealand health professionals do not agree about what defines appropriate attendance at an emergency department. N Z Med J 2006; 119: 1933.
7. Barber Perez P, Gonzalez Lopez, Valcarcel B. Stimulation of a Hospital Emergency Department and Its Potential Use in Management. GacSanit 1994; 8: 239–47.
8. Woods R, Lee R. Consultation outcomes in the emergency department: exploring rates and complexity. CJEM 2008; 10: 25-31.
9. Kessler C, Kutka BM, Badillo C. Consultation in the Emergency Department: A Qualitative Analysis and Review. J Emerg Med 2011; 42: 704-11
10. Holliman JC. The Art Of Dealing With Consultants: The Journal Of Emergency Medicine 1993; 11: 633-40.
11. Lee RS, Woods R, Bullard M. Consultations in the emergency department: a systematic review of the literature. Emerg Med J 2008; 25: 4–9.

12. Brenner BE, Holmes TM, Simpsin DDT et al. Reducing specialty consultation times in the emergency department [abstract]. Acad Emerg Med 2004; 11:463.
13. Williams S, Crouch R. Emergency department patient classification systems: A systematic review. AccidEmergNurs 2006 Jul; 14: 160-70.
14. Williams S, Crouch R. Patient dependency in the emergency department (ED): Reliability and validity of the Jones Dependency Tool (JDT). Accident and Emergency Nursing 2006; 14: 219-29.
15. http://www.saglik.gov.tr/TR/belge/1-13438/saglik-istatistikleri-yilligi-2010.html
16. Young GP, Wagner MB, Kellerman AL et al. Ambulatory visits to hospital emergency departments. JAMA 1996; 276: 460–65.
17. http://www.cdc.gov/nchs/data/nhsr/nhsr026.pdf
18. Lambe S, Washington DL, Fink A et al. Waiting time in California's emergency departmants. Ann. Emerg. Med 2003; 44: 35–43.
19. Hexter DA. Working with consultants. ACEP Foresight 2002; 5
20. Vincent TS. The art of consultation. Res Staff Phys 1987; 33: 116-20.
21. Bender AS. Commandments for consultants. Res Staff Phys 1986; 32:122-23.
22. Gutterman JJ, Franaszek JB, Murdy D et al. The 1980 patient urgency study: Further analysis of the data. Ann Emergy Med 1985; 12: 1191–98.
23. Kellar DK, Chaturvedi SK, Malhotra SA. A study of emergency psychiatric referrals in a teaching hospital. India J Psychiatry 1982; 24: 366-69.
24. Yoon P, Steiner I, Reinhardt G. Analysis of factors influencing length of stay in the emergency department. Can J Emerg. Med 2003; 5: 155-61
25. Cortazzo JM, Guertler AT, Rice MM. Consultation and referral patterns from a teaching hospital emergency department. Am J Emerg Med 1993; 11: 456-59
26. Curry DG, Wang DM. Variations of consultation practice in urban emergency physicians (abstract). Can J Emerg. Med 2006; 8: 182-83

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Original Article

Wilson's disease in children: Analysis of 41 cases

Çocuklarda Wilson hastalığı: 41 olgunun analizi

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ABSTRACT

Aim: This study aimed to present clinical and laboratory features of 41 children with Wilson's disease.

Material and Methods: The medical records of all of the patients who had got a diagnosis of Wilson's disease between 2001 June and 2005 March in Ankara Dr. Sami Ulus Training& Research Hospital, Turkey. Demographic, clinical and biochemical information was obtained from the patients' records. Findings were retrospectively analyzed by the SPSS Windows 16.0 (SPSS Inc. IL, USA) statistical software.

Results: A total of 41 patients had got the diagnosis of Wilson's disease: 24 boys and 17 girls, between in the range of 3-14 years old. The mean age of patients was 9.05±2.84 years. Kayser-Fleischer rings were observed in 24 patients. Urinary copper excretion in 24-hours urine was high in 39 of 40 patients. Serum ceruloplasmin levels were found low in 35 of 40 patients. Thirteen of patients were diagnosed after the family screening. Pathologic brain MR findings were detected in 4 of 8 patients without neurological system complaints or physical examination findings.

Conclusion: Especially in societies that consanguineous marriages are so common, Wilson's disease should be considered in differential diagnosis of chronic liver diseases, prolonged hypertransaminasemia, and degenerative brain disorders of unknown origin. In our study, it has been shown that Wilson's disease diagnosis and follow-up preserved the value of classical diagnostic methods and it has been shown that neuroimaging may be useful for early detection of neurological involvement even if neurological findings do not occur.

Keywords: wilson's disease; children; chronic liver diseases; copper metabolism; neurological involvement;

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ÖZ

Amaç: Bu çalışmada Wilson hastalığı olan 41 çocuğun klinik ve laboratuvar özelliklerinin sunulması amaçlanmıştır.

Gereç ve Yöntemler: Ankara Dr. Sami Ulus Eğitim ve Araştırma Hastanesi'nde 2001 Haziran - 2005 Mart tarihleri arasında Wilson hastalığı tanısı konulan tüm hastaların tıbbi kayıtları geriye dönük olarak incelendi. Hastaların kayıtlarından demografik, klinik ve biyokimyasal bilgiler alındı. Bulgular SPSS Windows 16.0 (SPSS Inc. IL, USA) istatistik yazılımı ile analiz edildi.

Bulgular: Toplam 41 hasta Wilson hastalığı tanısı almıştı: 3-14 yaş aralığında 24 erkek ve 17 kız idi. Hastaların yaş ortalaması 9.05 ± 2.84 yıldı. 24 hastada Kayser-Fleischer halkaları gözlendi. 24 saatlik idrarda idrar bakır atılımı 40 hastanın 39'unda yüksekti. Serum seruloplazmin düzeyleri 40 hastanın 35'inde düşük bulundu. Hastaların on üçü aile taramasından sonra tanı aldı. Nörolojik sistem şikayeti veya fizik muayene bulguları olmayan 8 hastanın 4'ünde patolojik beyin MR bulguları saptandı.

Sonuç: Özellikle akraba evliliklerinin çok yaygın olduğu toplumlarda, kronik karaciğer hastalıklarının ayırıcı tanısında, uzamış hipertransamineminin ve nedeni bilinmeyen dejeneratif beyin bozukluklarının ayırıcı tanısında Wilson hastalığı da düşünülmelidir.

Bizim çalışmamızda Wilson hastalığı tanısı ve izleminin klasik tanı yöntemlerinin değerini koruduğu ve nörolojik bulgular ortaya çıkmasa bile nörolojik tutulumun erken saptanmasında nörogörüntülemenin yararlı olabileceği gösterilmiştir.

Anahtar kelimeler: Wilson hastalığı; çocuklar; kronik karaciğer hastalıkları; bakır metabolizması; nörolojik tutulum

Introduction

Wilson's disease (WD) is a disorder of copper metabolism, resulting from the autosomal recessive occurrence of the ATP7B mutation in the short arm of chromosome 13. It is a rare congenital disorder of metabolism, with a frequency of 1/30,000 in live births[1,2]. Decreased biliary copper excretion and reduced combining of copper into ceruloplasmin, leading to excessive copper accumulation in many organs, predominantly to the liver, brain, and cornea. The clinical manifestations of WD are widely variable due to more than 500 disease-causing mutations[3]. It often presents with hepatic manifestations in early childhood, neurological manifestations add after the age of 20 years[4]. Due to lack of such descriptive tests, the diagnosis should be established on the combination of clinical features, laboratory findings, and the results of mutation analysis. In adults, the presence of typical clinical and laboratory findings, such as Kayser-Fleischer (K-F) rings and low serum ceruloplasmin levels can make easily to establish the diagnosis. However, in children typical clinical features are rarely seen before the age of 5 years and making the diagnosis of the disease more difficult than in adults[5,6]. In this study, clinical and laboratory features of 41 children with Wilson's disease were presented.

Material and Methods

This study was conducted in Ankara Dr. Sami Ulus Training & Research Hospital, a tertiary care institution in Turkey. The medical records of all of the patients who had got a diagnosis of WD between 2001 June and 2005 March in the pediatric gastroenterology division were reviewed. Demographic, clinical and biochemical information was obtained from the patients' records. The diagnosis of WD has been established in the presence of the specific clinical features of the disease and abnormal copper metabolism tests. Slit lamp examination for the presence of K-F rings, measurement of serum ceruloplasmin levels, and determination of 24-hour urinary copper excretion before and after penicillamine administration were performed in the evaluation of the all patients. Serum ceruloplasmin level was measured by a nephelometric assay. Standard methods were used for liver function tests and other routine laboratory parameters. A percutaneous liver biopsy was performed in most patients after coagulation abnormalities had been corrected. The liver copper content was determined in selected cases. After the diagnosis was confirmed, siblings and first-degree relatives were screened for WD. The genetic analysis was not performed in patients and their families due to the lack of it in our center in the period which the study was conducted. Statistical analysis was performed by the SPSS Windows 16.0 (SPSS Inc. IL, USA) statistical software; the Fisher exact test was used for comparison of categorical variables and the Student t-test for continuous variables. $P<0.05$ was considered statistically significant.

This study was approved by the institutional review board of the related institution. Local ethics committee approved the study and informed consent was obtained from participant(s)

Results

Epidemiology

A total of 41 patients had got the diagnosis of WD: 24 (58.5%) boys and 17 (41.5%) girls, between in the range of 3-14 years

old. The mean age of patients during the first examination was 9.05±2.84 years. The majority of our patients were between the ages of 7-10 years. Mean age (±SD) at diagnosis was 9.05±2.84 years (range 3 years-14 years). 28 patients (68.2%) were 10 years old age or older. In 32 (78%) of the patients, there was consanguinity between the parents. In the history of patients, six families (14.7 %) had WD and 23 families (56.1%) had chronic liver diseases. Thirteen patients (31.7%) were diagnosed in family screening, and 4 of these pateints (30.7%) were diagnosed in presymptomatic period (Table 1).

Table 1. Baseline demographic characteristics and history of WD patients

Age (M±SD)		9.05±2.84
Gender	Female (n)	17 (41.5%)
	Male (n)	24 (58.5%)
Diagnosis with family screening (n)		13 (31.7%)
Asymptomatic (n)		4 (9.7%)
Family history of WD (n)		6 (14.7)
Family history of undiagnosed chronic liver disease (n)		23 (56.1%)
Consanguity between parents (n)		32 (78%)

Clinical Characteristics

Thirty-seven (90.2%) patients were symptomatic. The presentations of the patients are shown in Table 2 Four patients (9.8%), with a positive family screening, were asymptomatic. Hepatomegaly was the most common clinical finding in 58.5% of patients, followed by splenomegaly in 43.9%. K-F rings were present in 24 of 41 patients (58.5%). Other most common clinical findings are shown in Table 2. In laboratory studies, the most common finding was high transaminase levels. 30 patients presented with WD hepatic involvement; 19 (63.3%) patients with least two-fold elevated AST levels, compared to ALT level, 3 of them had ALT levels was at least twice as high compared to AST levels, 8 of them hadn't significant difference between AST and ALT levels Urinary copper excretion in 24-hours urine was high in 39 of 40 patients (97.5%). 21 of 40 patients had anemia (51.2%) and 4 of them (2.4%) was coombs negative hemolytic anemia.

Serum ceruloplasmin levels were found low in 35 (87.5%) of 40 patients. One patient had no a registry of the serum ceruloplasmin level. Most of the patients (n= 30, 73.2%) were presented as the hepatic form of WD. The major laboratory parameters of the patients are shown in Table 2.

Table2. Presenting symptoms, signs and particular laboratory findings of patients

Presenting symptoms & signs	Frequency n (%)
Abdominal distantion	19(46.3)
Abdominal pain	18(43.9)
Jaundice	15(36.6)
Headache	8(19.5)
Recurrent Epistaxis	7(17)
Gastrointestinal bleeding	4(9.8)
Speech disturbance	2(4.9)
Artralgia	3(7.3)
Signs	
Hepatomegaly	24(58.5)
Splenomegaly	18(43.9)
Ascites	14(34.1)
Edema	11(26.8)
Particular laboratory findings	
Increased 24-hour urinary copper excretion*	39(97.5)
Low serum ceruloplasmin level*	35(87.5)
Elevated AST	31(75.6)
Elevated ALT	28(68.3)
Prolonged protrombin time	27(65.9)
Prolonged partial thromboplastin time	25(61.0)
Hypouricemia	25(61.0)
Hypoalbuminemia	24(58.5)
Anemia	21(51.2)
Hypergammaglobulinemia	18(43.9)
Hyperbilirubinemia	17(41.5)
Hyopphosphatemia	15(36.6)

*24-hour urinary copper excretion and serum ceruloplasmin levels were measured in 40 patients.
10 patients (25%) had high levels of urinary copper after D-penicillamine challenge test.

Two of 5 patients below 5 years old were asymptomatic and remains were presented as the hepatic form of WD. 21 of 23 patients who were in 6-10 years old were presented as hepatic form, 1 of them was presented as the neurologic form, and 1 was asymptomatic.

Six of 13 patients older than 10 years were diagnosed as the hepatic form of WD, 5 of them were combined form, 1 of them was neurologic form, and 1 of them was asymptomatic. The youngest patient who had neurological symptoms was 9 years old. Clinical features according to age are shown in Table 3.

Table 3. Clinical features according to age of patients

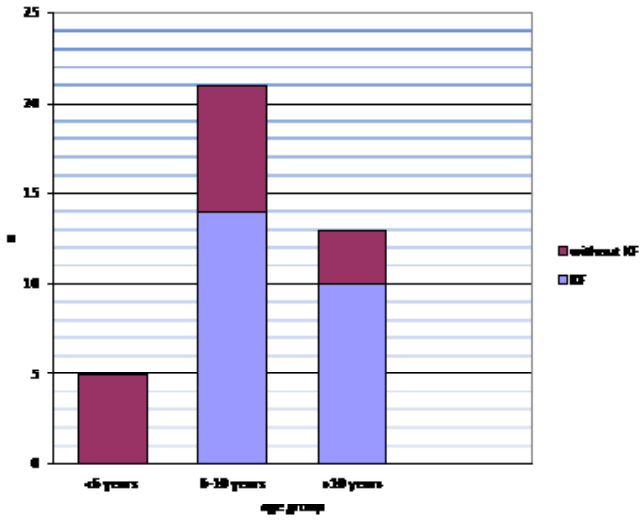
Age (years)	Hepatic form n (%)	Neurologic form n (%)	Combined form n (%)	Asymptomatic form n (%)	n (%) Total
5≤	3 (7.4%)	-	-	2 (4.9%)	5 (12.2%)
6-10	21 (51.2%)	1 (2.45%)	-	1 (2.45%)	23 (56.1%)
≥11	6 (14.6%)	1 (2.45%)	5 (12.2%)	1 (2.45%)	13 (31.7%)
n (%) Total	30 (73.2%)	2 (4.9%)	5 (12.2%)	4 (9.8%)	41 (100%)

K-F rings existed in all 7 (100%) of patients with the neurological and combined form, 17/30 of (56.6%) those with the hepatic form. The youngest patient who had K-F rings on eye examination was 7 years old. The frequency of appearance of the K-F rings according to the clinical forms and distribution age of the patients are shown in Table 4 and Figure 1 respectively.

Table 4. Kayser-Fleischer rings frequency according to the clinical forms

Clinical form	Patients number	Patients with KF number (%)
Neurologic	2	2(100)
Combined	5	5 (100)
Hepatic	30	17 (56.6)
Asymptomatic	4	0 (0)

Figure 1. K-F rings according to age group of the patients.



Thirteen of patients (31.7%) were diagnosed after the family screening. Four of them (30.7%) were asymptomatic, three of them had K-F rings on eye examination.

24-hour urinary copper excretion was measured in 40 patients. 29 patients (72.5%) had high levels of urinary copper excretion, in first evaluation. 10 patients (25%) had high levels of urinary copper after D-penicillamine challenge test and one patient (2.5%) was normal. Respectively, urinary copper excretions were as; in seven patients above 1000 mg/24h, in 16 patients between 501-1000 mg/24h, in 11 patients between 201-500 mg/24h and in 5 patients between 100-200 mg/24h. A patient whose 24-hour urinary copper excretion couldn't be measured was transferred to another institution for emergency liver transplantation.

The liver copper content was measured in 18 patients. While 14 patients' copper contents were above 250 µg/g dry weight (77.8%), 4 patients' were between 120-250 µgr/gr.

Abdominal ultrasonography (USG) was performed in 39 patients. 34 of them (87.2%) had at least one pathological finding. The most common sonographic findings were hepatomegaly and splenomegaly (Table 5). Portal venous Doppler USG was performed in 19 patients. Six of them (31.5%) had portal hypertension.

Table 5. Abdominal ultrasound findings

Ultrasound findings	Patient number	Frequency (%)
Hepatomegaly	28	71.8
Splenomegaly	25	64.1
Ascites	17	43.6
Increased renal parenchymal echogenicity	15	38.5
Gallstone	2	5.1
Cholecystitis	2	5.1

Brain magnetic resonance imaging (MRI) was performed in 14 patients. Eight patients hadn't neurological symptom or any physical examination finding and these patients above 11 years old. Pathologic brain MRI findings were detected in 4 (50%) of 8 patients without neurological system complaints or physical examination findings. Six patients who performed brain MRI had headache, dysarthria, dystonia and confusion.

All patients with neurological symptoms had pathological brain MRI findings. The pathological MRI findings were cerebral atrophy and paramagnetic matter deposition in the basal ganglia.

Percutaneous liver biopsy was performed in 21 patients, of whom 14 patients with the hepatic form, 4 patients with were asymptomatic, 2 patients with combined form, and 1 patient with the neurological symptoms existed. In patients with the hepatic form, a liver biopsy performed and liver cirrhosis was found in 7 patients (50%), in 6 patients (42.8%) chronic active hepatitis, and in 1 patient (7.2%) had only inflammatory cell infiltration. In two patients with combined form of WD, also had liver cirrhosis. In one patient, who had been affected only neurologically, had chronic active hepatitis on biopsy evaluation. Three of 4 patients who are asymptomatic had only inflammatory cell infiltration and hepatocellular degeneration, only 1 of them had chronic active hepatitis. Of the 10 patients who underwent upper gastrointestinal endoscopy, 3 normal, 2 gastritis, and 5 esophageal varices.

Extrahepatic manifestations apart from neurological disease of patients are shown in Table 6.

Table 6. Extrahepatic involvements apart from neurological disease of patients

	n (%)
Hematuria	6(14.6)
Proteinuria	5(12.1)
Coombs-negative hemolytic anemia	4(1)
Joint pain	3(0.7)
Cholecystitis	2(0.5)
Gallbladder stones	2(0.5)
Membranoproliferative glomerulonephritis	1(0.2)

Treatment and Outcome

Penicillamine and zinc were administered as the initial treatment. One patient received trientine as the initial treatment, because his sibling had a history of nephropathy caused by penicillamine treatment. Penicillamine was discontinued because of an allergic rash in one patient and of penicillamine-induced dermopathy in the first week of treatment in another.

Four patients had never got chelation treatment in their history. One presented with fulminant hepatic failure and transported for emergency transplantation. Other 3 patients who have not taken chelation treatment were asymptomatic patients who were diagnosed by sibling screening and they only received zinc for treatment. Other than 4 patients who never had treatment and 3 patients who had trientine treatment, all remaining patients (n=34) received penicillamine and/or zinc treatment.

Two of 37 patients who had started to chelation treatment, discontinuied treatment right after the treatment started. Eight of them got worse clinically and transported to another center for liver transplantation. There were no side effects in patients who had trientine treatment. In patients who received penicillamine; 1 patient had neutropenia, 1 patient had nephropathy, 1 patient had dermopathy, 1 patient had an allergic rash, and 1 patient had hypocomplementemia.

Discussion

Early diagnosis and treatment of WD are very important in those with the chronic liver disease. Patients who are diagnosed earlier not only can survive healthy if the treatment is started early, but also treatment can prevent serious organ damage and even after cirrhosis is present, treatment can lead to improvement of the disease [1, 4, 6]. Therefore, it is necessary to understand the disease fully, screening should be done in suspected cases, and relatives of diagnosed patients should be screened for the disease.

Early diagnosis requires suspicion, in patients who are with unexplained liver, neurological, psychiatric disorders, acute hemolysis or Fanconi syndrome. In our study, proportions of patients who are younger than 5 years old are determined relatively high (17%). It's thought that the reason for it is patients who are diagnosed by sibling screening. In 78% of our patients, there was consanguinity between parents. Of patients' 31.7% were diagnosed after the family screening. All these findings show the importance of sibling screening.

In WD, average diagnosis age changes due to clinical form of the disease. The hepatic form is more common in pediatric age group [2, 3, 5, 7]. In our study, average diagnosis age is determined as 9.05±2.84 years. This finding is consistent with the fact that majority of our patients have the hepatic form of the disease. In pediatric age group, first complaints are mostly related to hepatic involvement and the most common ones are abdominal distention, abdominal pain, and jaundice [2, 4, 5, 8, 9]. Congruently, our study showed first application complaints were abdominal distention, abdominal pain, and jaundice, by order frequency.

Wilson patients can apply to physician's office with neuropsychiatric complaints like speech disturbances, a decline in school success, dystonia, tremor and behavioral disturbances; although it's seen relatively less in childhood [5, 10, 11]. In our patients with neurological involvement, most common complaints were speech disturbances and dystonia.

In our study group, all four patients who are followed up with fulminant hepatic failure had jaundice and loss of consciousness, they had low serum ceruloplasmin levels, high 24-hour urinary copper excretion levels, higher AST levels than ALT levels and despite significant hyperbilirubinemia, serum ALP levels were normal [5, 12, 13].

Involvement of neurological system is mostly in ganglion basale but there can also be copper accumulation in pons, thalamus, mesencephalon, and cerebellum. In WD, the damage is limited to motor system and the sensory system is almost always preserved. Neurological findings include tremors ataxia, dysarthria, stiffness, oropharyngeal dysfunction such as dysphonia. Dysarthria and tremor are the most common neurological manifestations of WD and they will appear in the early stages [5, 7, 14, 15]. In this study, among limited number of neurologically affected patients (n=7, 17%), common findings were dysarthria, dystonia and behaviour disturbances.

In WD, besides hepatic and neurological findings, rarely, atypical findings related to other organ involvements can be the first physical findings. Other organ involvement signs are more often in patients older than 10 years old and 25% of patients can be affected in two or more different organ systems [1, 2, 8]. Glomerulonephritis, hemolytic anemia, osteoarthritis, arrhythmia, endocrine disorders and hyperpigmentation can be detected due to multisystemic involvement [5, 6, 8, 14]. There is no patient who is presented with other organ system symptoms, without liver and/or neurological involvement in our study group. Extrahepatic involvements apart from neurological disease of patients are shown in Table 6.

Similar to previous clinical studies [4, 9, 14, 16-18] in the pediatric age group, the majority of patients were hepatic form in our study. Nevertheless, in our study, neurological form of the disease has seen less than reported in the literature. It is thought that the reason of this, is most of our patients (68%) are younger than 10 years old. It is very well known that neurological form is less common in patients younger than 10 years old [4, 5, 19, 20].

Kayser-Fleischer ring occurs with copper accumulation in Descemet's membrane and it is characterized by green-brown color. Its presence is not pathognomonic because it can also be detected in chronic active hepatitis, primer biliary cirrhosis and intrahepatic cholestatic cirrhosis[1, 2, 14]. In the hepatic form of WD, it is detected in 50% of the patients and it's detected in almost every patient with neurological involvement [6, 8, 10]. In our study, similarly with literature [14, 16, 17] 56% of patients with hepatic involvement had K-F rings and it's detected in every patient with neurological involvement. K-F rings are more commonly detected with older age and it's unusual for patients younger than 6 years old. In our study group, the youngest patient who had K-F rings was 7 years old.

At the asymptomatic stage of the disease, the only sign of WD can be elevated liver enzymes. Therefore, in the differential diagnosis of asymptomatic transaminasemia, WD should be considered even if there aren't any classical findings of the disease [10, 21]. Serum aminotransferase levels characteristically mildly/moderately high. Generally, elevation in AST levels is more significant than the elevation in ALT levels but this finding is not sufficiently invariable to be diagnostic [5, 21-23]. Similarly in our study, the most common biochemical indicator of liver involvement is transaminase elevation. In the majority of patients (63%) AST levels were as twice as high compared to ALT levels.

In WD diagnosis, serum ceruloplasmin level is one of the first workups to be chosen. Co-occurrence of K-F rings existence and low serum ceruloplasmin levels is considered sufficient to establish the diagnosis of WD [4, 6, 8, 19]. Furthermore, solo serum ceruloplasmin levels can be detected as low in other diseases that affect liver functions besides WD, like malabsorption, malnutrition, severe liver failure, protein-losing enteropathy, in cases of hypoproteinemia like nephrotic syndrome, severe liver deficiency, Menkes disease, and hereditary aceruloplasminemia. Ceruloplasmin levels can also be high in active inflammatory and malignant conditions as acute phase reactant [5, 8, 18, 19]. Therefore, serum ceruloplasmin level shouldn't be used as only definitive diagnostic criteria and it should be supported by other diagnostic evaluation tests.

Two of 5 patients who had normal ceruloplasmin levels were siblings and they were diagnosed with sibling screening that is done because of another sibling who has WD. Three patients had parental consanguinity. In WD, even if serum ceruloplasmin levels are normal, especially if there is significant family history, patients should be investigated with other diagnostic methods. Approximately one-third of our patients had been diagnosed with family screening.

In WD, high levels of 24-hour urinary copper excretion are almost always present and its diagnostic value is significantly high. It can be incorrectly negative in presymptomatic stage of disease; however it can be incorrectly positive in patients who receive copper chelation treatment, primary biliary cirrhosis, chronic active hepatitis, autoimmune hepatitis, fulminant hepatitis, cholestatic cirrhosis, and nephrotic syndrome. Therefore, high urinary copper excretion level is not specific for WD. Previous studies have shown that urinary copper excretion may be less than 100 µg at the presentation in 16% to 23 % of patients [6]. In our study, all patients except one had high levels of 24-hour urinary copper excretion. 10 of them (25%) had basal 24-hour urinary copper excretion lower than 100 µg and penicillamine challenge resulted in an increase of copper excretion. The diagnostic performance of urinary copper excretion can be improved after penicillamine challenge and this technique is considered useful. The patient who had normal 24-hour urinary copper excretion was a presymptomatic patient who is diagnosed with sibling screening.

Measurement of quantitative copper amounts in liver tissue is considered as the best biochemical test for diagnosis [5, 8]. Normal liver copper concentration is below 50 µg/g dry liver weight. In patients and presymptomatic cases whose age older than 3 years old it's above 200-250 µg/g dry weight. In carriers, it can be measured as high as 150-200 µg/g but it does not exceed 250µg/g [5].

In present study, liver tissue could be measured copper dry weight of 18 patients. In 14 of theese higher than 250 µg/g, in four 120-250 µg/g dry weight was detected. All of the patients who have the dry liver copper weight lower than 250 µg/g had high levels of 24-hour urinary copper excretion, three of them had low serum ceruloplasmine levels, three of them had K-F rings, three of them had a family history of WD and all of them had parental consanguinity confirming the diagnosis.

Main histopathological liver findings in WD are steatosis, acute hepatitis, chronic active hepatitis, cirrhosis and fulminant hepatic necrosis. It is not helpful in in all cases, because histopathological findings of liver have a broad spectrum from hepatosteatosis to cirrhosis. The most common liver histopathological findings were cirrhosis (50%) and chronic active hepatitis (42.8%) followingly in our study.

In WD early diagnosis and treatment is lifesaving. Therefore, siblings of patients who are older than 3 years old should be screened [5, 8]. One third of our patients in our study group are diagnosed by sibling screening.

WD has a potential of causing progressive liver damage. Therefore, patients should be monitored for possible portal hypertension, with portal venous Doppler USG. Patients who have portal hypertension should be examined with upper gastrointestinal

system endoscopy for esophageal varices. Possible complications can be prevented by these evaluations [24]. In our study group, one-third of patients who were performed portal venous Doppler USG were diagnosed with portal hypertension. Half of the patients who were performed upper gastrointestinal system endoscopy were diagnosed with esophageal varices.

Main cranial imagining findings in WD are; dilatation of ventricles, cortical atrophy, atrophies of brainstem, pathological changes in ganglion basale and atrophy of posterior fossa. Abnormal imagine findings can be identified in patients with asymptomatic patients and only hepatic involvement. Correlation of these findings with clinical signs is not clear and their diagnostic value is poor [2, 7, 8, 25]. In our study, patients who were performed brain MRI, all patients with neurological involvement and 50% of patients without neurological involvement have pathological findings such as cerebral atrophy and symmetric paramagnetic matter accumulation in ganglion basale.

The goal of treatment in WD is dropping the amount of stored copper in tissues and prevention of reaccumulation. Low copper diet and zinc, chelation with ''D-penicillamine" or trientine is the classical recommended treatment [14, 26]. In asymptomatic patients who diagnosed early, zinc administration alone is sufficient [5, 14]. Although there are more side effects of chelation treatment, 'D-penicillamine" still is the first choice for standart treatment, because it is very well known and used for many years, so it is an easily accessible agent. Trientine is the alternative medicine for pregnant patients or patients who experienced serious side effects with "D-penicillamine" use [8, 27]. In present study, patients primarily received standard treatment. One of patients who received "D-penicillamine" treatment initially, experienced an allergic reaction and another one has dermopathy. Hence their medicine changed with trientine. Another patient has begun trientine treatment at first, cause of his sibling had a nephropathy history after "D-penicillamine" treatment. Although "D-penicillamine is the first choice in treatment, the hypersensitivity story of the patient should be considered.

Our study had several limitations. First, study design was retrospectively. Sample number was low and study reflects single centre results. The genetic analysis was not performed in patients and their families due to the lack of it in our center in the period which the study was conducted. Data collection from conventional archive files was difficult for reaching reliable information. There might be missing data about laboratory and radiologic investigatements.

Conclusion

Especially in societies that consanguineous marriages are so common, WD should be considered in differential diagnosis of chronic liver diseases, prolonged hypertransaminasemia, and degenerative brain disorders of unknown origin. This report presents the clinical manifestations and laboratory findings of WD in children and underlines the importance of early diagnosis in positive clinical progress.

In our study, it has been shown that WD diagnosis and follow-up preserved the value of classical diagnostic methods and it has been shown that neuroimaging may be useful for early detection of neurological involvement even if neurological findings do not occur. This issue should be evaluated with larger patient series in multicentre prospective studies.

Declaration of conflict of interest

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References

1. John LG TJ. Wilson disease in 1998 genetic, diagnostic and therapeutic aspects. Journal of Hepatology 1998; 28: 28-36.
2. Ala A, Walker AP, Ashkan K, Dooley JS, Schilsky ML. Wilson's disease. Lancet 2007; 369: 397-408.
3. Simsek Papur O, Asik Akman S, Terzioglu O. Clinical and genetic analysis of pediatric patients with Wilson disease. Turk J Gastroenterol 2015; 26: 397-403.
4. Merle U, Schaefer M, Ferenci P, Stremmel W. Clinical presentation, diagnosis and long-term outcome of Wilson's disease: a cohort study. Gut 2007; 56: 115-20.
5. Roberts EA, Schilsky ML, American Association for Study of Liver D. Diagnosis and treatment of Wilson disease: an update. Hepatology 2008; 47: 2089-111.
6. Roberts EA, Schilsky ML, Division of G, Nutrition HfSCTOC. A practice guideline on Wilson disease. Hepatology 2003; 37: 1475-92.
7. Kozic D SM, Petrovic B, Dragasevic N, Semnic R and Kostic VS. MR imaging of the brain in patients with hepatic form of Wilson's disease. Eur J Neurol 2003; 10: 587-92.
8. European Association for Study of L. EASL Clinical Practice Guidelines: Wilson's disease. J Hepatol 2012; 56: 671-85.
9. Arıkan Ç. ea. Wilson's Disease in Childhood: Evaluation of 46 Cases in Respect to Clinical, Laboratory and Histopathological Features Along With Treatment Results. . Ege Pediatri Bülteni 2007; 14: 157-65.
10. Jones EA, Weissenborn K. Neurology and the liver. J Neurol Neurosurg Psychiatry 1997; 63: 279-93.
11. Gow PJ, Smallwood RA, Angus PW, Smith AL, Wall AJ, Sewell RB. Diagnosis of Wilson's disease: an experience over three decades. Gut 2000; 46: 415-19.

12. Kenngott S, Bilzer M. Inverse correlation of serum bilirubin and alkaline phosphatase in fulminant Wilson's disease. J Hepatol 1998; 29: 683.
13. Berman DH, Leventhal RI, Gavaler JS, Cadoff EM, Van Thiel DH. Clinical differentiation of fulminant Wilsonian hepatitis from other causes of hepatic failure. Gastroenterology 1991; 100: 1129-34.
14. Liu J, Luan J, Zhou X, Cui Y, Han J. Epidemiology, diagnosis, and treatment of Wilson's disease. Intractable Rare Dis Res 2017; 6: 249-55.
15. Burke JF, Dayalu P, Nan B, Askari F, Brewer GJ, Lorincz MT. Prognostic significance of neurologic examination findings in Wilson disease. Parkinsonism Relat Disord 2011; 17: 551-56.
16. Pooya AAA, Eslami NS, Haghighat M. Wilson disease in Southern Iran. Turkish Journal of Gastroenterology 2005; 16: 71-74.
17. Yuce A, Kocak N, Demir H et al. Evaluation of diagnostic parameters of Wilson's disease in childhood. Indian journal of gastroenterology : official journal of the Indian Society of Gastroenterology 2003; 22: 4-6.
18. Manolaki N, Nikolopoulou G, Daikos GL et al. Wilson disease in children: analysis of 57 cases. J Pediatr Gastroenterol Nutr 2009; 48: 72-77.
19. Bandmann O, Weiss KH, Kaler SG. Wilson's disease and other neurological copper disorders. Lancet Neurol. 2015;14(1):103-13.
20. Ranjan A, Kalita J, Kumar S, Bhoi SK, Misra UK. A study of MRI changes in Wilson disease and its correlation with clinical features and outcome. Clin Neurol Neurosurg 2015; 138: 31-36.
21. El-Youssef M. Wilson disease. Mayo Clin Proc 2003; 78: 1126-36.
22. Wilson DC, Phillips MJ, Cox DW, Roberts EA. Severe hepatic Wilson's disease in preschool-aged children. J Pediatr 2000; 137: 719-22.
23. Emre S, Atillasoy EO, Ozdemir S, Schilsky M, Rathna Varma CVR, Thung SN, et al. Orthotopic Liver Transplantation for Wilson???S Disease. Transplantation 2001; 72: 1232-36.
24. D'Antiga L. Medical management of esophageal varices and portal hypertension in children. Semin Pediatr Surg 2012; 21: 211-18.
25. Alanen A, Komu M, Penttinen M, Leino R. Magnetic resonance imaging and proton MR spectroscopy in Wilson's disease. Br J Radiol 1999; 72: 749-56.
26. Durand F, Bernuau J, Giostra E et al. Wilson's disease with severe hepatic insufficiency: beneficial effects of early administration of D-penicillamine. Gut 2001; 48: 849-52.
27. Brewer GJ, Askari FK, Lorincz MT et al. Diagnosis and Treatment of Wilson's Disease With an Update on Anticopper Treatment for Other Diseases. Biomedical Research on Trace Elements 2004; 15: 211-21.

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Original Article

Amiodarone versus direct current cardioversion in treatment of atrial fibrillation after cardiac surgery

Kalp cerrahisi sonrası gelişen atriyal fibrilasyon tedavisinde amiodarone ve doğru akım kardiyoversiyonun karşılaştırılması

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ABSTRACT

Aim: Postoperative atrial fibrillation is common after cardiac surgery and is associated with higher rates of complications and mortality. Despite the importance of postoperative atrial fibrillation, the most effective management strategy for this common surgical complication remains uncertain. The aim of this study was to evaluate the effectiveness of amiodarone and early direct current cardioversion to restore sinus rhythm in new onset postoperative atrial fibrillation.

Material and Methods: This was a prospective, open-labeled randomized- controlled trial. A total of 50 patients who had new onset postoperative atrial fibrillation longer than 30 minutes were enrolled in the study; 26 patients were randomized to control group and 24 to amiodarone group. Patients in whom sinus rhythm did not return within 24 hours, then external electrical direct current cardioversion was performed for both groups. The primary endpoint of the study was a restoration of sinus rhythm at the 24th hour. Secondary endpoints needed for direct current cardioversion, success rate, sinus rhythm at discharge, sinus rhythm at 30th days and crossover rates.

Results: There was a significantly higher number of patients with sinus rhythm at the 24th hour in the amiodarone group than the control group (79.2% vs. 46.2%, p=0.022). Need for direct current cardioversion (p=0.022) and crossover ratio (p=0.021) were significantly higher in control group than amiodarone group. Direct current cardioversion success rate, normal sinus rhythm at discharge and 1st month did not differ significantly between groups.

Conclusion: Amiodarone therapy seems effective in restoring sinus rhythm within 24 hours and decreases the need for direct current cardioversion.

Keywords: antiarrhythmic agents; atrial fibrillation; cardiovascular surgery; post-CABG atrial fibrillation

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ÖZ

Amaç: Atriyal fibrilasyon kalp cerrahisinden sonra sık görülmektedir. Postoperatif atriyal fibrilasyon komplikasyonların ve mortalitenin artmasına neden olmaktadır. Ancak tedavisi hususunda fikir birliği yoktur. Bu çalışmanın amacı postoperatif dönemde yeni başlayan atriyal fibrilasyonu olan hastalarda amiodaron kullanımı ile erken dönemde doğru akım elektriksel kardiyoversiyonun sinüs ritmininin sağlanması üzerine olan etkilerini karşılaştırmaktır.

Gereç ve Yöntemler: Çalışma prospektif, randomize, açık kontrollü olarak tasarlanmıştır. Çalışmaya kalp cerrahisi sonrası 30 dakikadan uzun yeni başlangıçlı atriyal fibrilasyonu olan toplam 50 hasta alındı; 26 hasta kontrol grubuna; 24 hasta amiodaron grubuna randomize edildi. Her iki grupta da 24 saat içinde sinüs ritminin sağlanamadığı hastalarda doğru akım elektriksel kardiyoversiyon uygulandı. Çalışmanın birincil son noktası 24. saatte sinüs ritminin sağlanmasıydı. Çalışmanın ikincil son noktaları ise doğru akım elektriksel kardiyoversiyon oranı, başarı oranı, taburculukta sinüs ritminin varlığı, 30. günde sinüs ritminin varlığı ve grup değiştirme oranıydı.

Bulgular: Amiodaron grubunda 24. saatte sinüs ritminde olan hasta sayısı kontrol grubuna göre anlamlı olarak daha fazla saptandı (%79,2'ye karşı %46,2, p = 0.022). Doğru akım kardiyoversiyon oranı (p = 0,022) ve grup değiştirme oranı (p = 0,005) kontrol grubunda anlamlı derecede yüksekti. Taburculukta ve birinci ayda sinüs ritmi varlığı ve doğru akım kardiyoversiyon başarı oranları açısından gruplar arasında anlamlı fark saptanmadı.

Sonuç: Amiodaron tedavisi 24 saat içinde sinüs ritmininin sağlanmasında etkin görünmekte ve doğru akım kardiyoversiyon ihtiyacını azaltmaktadır.

Anahtar kelimeler: amiodaron; atriyal fibrilasyon; kalp cerrahisi; doğru akım kardiyoversiyon

Introduction

Postoperative atrial fibrillation (POAF) is the most common complication and rhythm disturbance occurring after cardiac surgery [1]. Its incidence ranges from 28-33% in contemporary series [2]. POAF is associated with an increase in the risk of operative death, renal insufficiency, stroke and prolonged hospitalization [3,4]. It is generally a self-terminating arrhythmia and despite the importance of POAF, the most effective management strategy remains still uncertain. Previously, many strategies, such as beta-blockers, intravenous magnesium, sotalol, amiodarone, and atrial pacing have been used to prevent POAF [5-7]. A medium-sized recent study randomized patients with POAF to either rhythm control with amiodarone or to rate control and the authors did not find a difference in hospital admissions during a 60-day follow-up [8]. Current guidelines recommend direct current cardioversion (DCCV) or antiarrhythmic drugs for the restoration of sinus rhythm (SR) in POAF with hemodynamic instability. Rhythm control therapy is recommended to improve AF-related symptoms in hemodynamically stable patients. Amiodarone or vernakalant are effective antiarrhythmic drugs in converting POAF to sinus rhythm [1]. Amiodarone is the most accessible antiarrhythmic drug but has several side effects limiting its use.

Material and Methods

The aim of our study was to evaluate the effectiveness of amiodarone and early DCCV postoperatively to restore SR in patients with new-onset AF after cardiac surgery. Local ethics committee approved the study and informed consent was obtained from participant(s)

Patient Population and Study Protocol

This study was a prospective, open-labeled randomized controlled trial. Patients with coronary artery disease who had new-onset AF longer than 30 minutes after cardiac surgery were considered for enrollment. Random generated numbers table was used for randomization. Exclusion criteria were: permanent AF, known paroxysmal AF, emergent cardiac surgery, hypotension (blood pressure lower than 90 mm Hg), and use of amiodarone in the prior 2 months. The study was conducted in compliance with the Declaration of Helsinki. The research protocol was approved by the local ethics committee of Baskent University. Informed consent was obtained from all patients.

A total of 822 patients who underwent cardiac surgery were prospectively evaluated and patients with known AF (135 patients) were excluded. Postoperative AF longer than 30 minutes developed in 102 patients: 16 patients were excluded because of treatment with amiodarone in the prior 2 months, 10 were excluded because of contraindications to amiodarone, 18 were excluded because of hemodynamic instability and 8 were excluded because patient or surgeon did not accept to attend to the study. Thus, a total of 50 patients (mean age, 68 ± 8 years; 33 men) fulfilling the inclusion criteria were included to the study; 26 patients were randomized to control group and 24 to the amiodarone group. Rhythm monitoring was done by 24-hour telemetry monitoring and confirmed with 12-lead electrocardiography during hospital follow up. All patients were questioned for AF at the 30th day, 12-lead electrocardiography (ECG) and a 48 hours Holter monitoring were performed.

The amiodarone group received 300 mg of amiodarone bolus intravenously (iv) in 30 minutes and an iv infusion of 50 mg/hours over a 24-hour period afterward. If SR returned within 24 hours, then iv infusion was discontinued (Figure 1). If SR did not return

within 24 hours, then DCCV was performed. After iv amiodarone infusion, oral amiodarone was maintained at 400 mg twice daily for 5 days and 200 mg twice daily for the following 25 days.

The therapy for the control group was determined according to physician preferences and beta-blockers, calcium channel blockers and/or digoxin were used to slow heart rate, with a goal of achieving a resting heart rate of less than 100 beats per minute. (Figure 1). If SR did not return within 24 hours, then DCCV was performed. In the control group, if SR did not return after DCCV patients were switched to the amiodarone group if the surgeon thought that such treatment was necessary to alleviate symptoms or improve hemodynamic status.

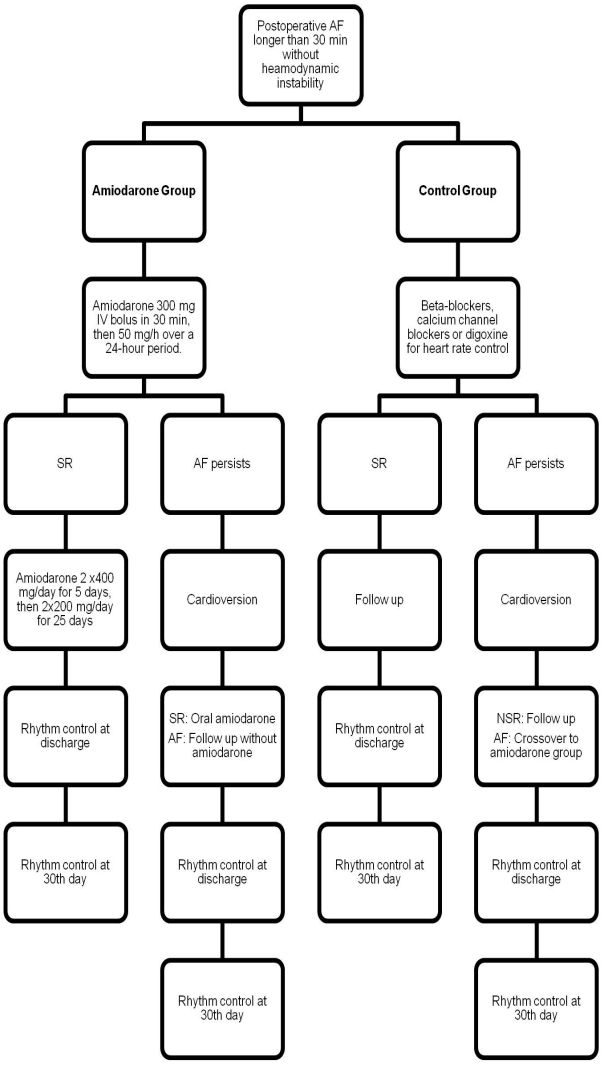

Figure 1: Study protocol

All patients received anticoagulant therapy in the hospital with heparin, but at the time of discharge, anticoagulant therapy was continued according to the surgeon's preferences.

Primary endpoints of the study were a restoration of SR at the 24th hour and needs for DCCV ratio. Secondary endpoints of the study were DCCV success ratio, SR at discharge, SR at 30th days and crossover ratio.

Statistical Analysis

MINITAB 15.0 statistical software was used for the sample size calculations and power analysis. We determined the sample sizes for the statistical tests by power/sample size formulas. The power analyses of the tests were conducted to determine the number of participants needed to detect the critical value with an adequate level of statistical power. Alpha levels for the analyses were set at 0.05. To achieve the power of 0.80 sample size of 25 in per groups were adequate.

The statistical package SPSS (Statistical Package for the Social Sciences, version 17.0, SSPS Inc, Chicago, Ill, USA) was used for statistical analyses. Intention to treat analysis was used to evaluate primary and secondary endpoints. Continuous variables are expressed as means ± standard deviation (median). All continuous variables were checked with Shapiro-Wilks normality test to show their distributions. Continuous variables with normal distributions such as age, left ventricle diameters, duration of intubations, levels of low-density lipoprotein (LDL) cholesterol and potassium were compared using the Student's t-test. Continuous variables with abnormal distributions such as body mass index, mean left ventricular ejection fraction, by-pass pump time, aorta cross-clamp time, length of hospital stay, postoperative AF onset time, number of grafts, left atrial diameter, right atrial diameter, levels of fasting blood glucose, hemoglobin, creatinine and sodium were compared using the Mann-Whitney U test. For categorical variables, the chi-square test was used. Values for p less than 0.05 were considered statistically significant.

Results

Postoperative AF developed in 102 patients (14.8% of patients without known AF); 50 of these patients underwent randomization. The mean age was 67.9±8.1 years, and 66% were male. Baseline clinical, laboratory and echocardiographic characteristics of both groups were similar (Table 1). Cardiac surgery operation properties were similar in the two groups and most of the patients underwent coronary artery bypass graft surgery (Table 2). The average time to onset of POAF was similar between groups (59.1±38.9 to 58.9±31.8 hours). Statistics about the primary and secondary endpoints are demonstrated in Table 3. There was a significantly higher number of patients with SR at the 24th hour in the amiodarone group than the control group (19 patients 79.2% vs. 12 patients 46.2%, p=0.022). Need for DCCV was significantly higher in control group than amiodarone group (53.8% vs. 20.8%, p=0.022). The DCCV success rate was slightly higher in the amiodarone group than the control group but this difference did not reach statistical significance. DCCV was performed to 11 patients in the control group and SR returned in 6 patients. DCCV was performed to 2 patients in the amiodarone group and SR returned in both patients (54.5% vs. 100%, p=0.487). DCCV was not performed in 3 patients in the control group and 3 patients in the amiodarone group because the patients or surgeon refused the therapy.

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Table 1. Demographic and clinical characteristics of patients

	Control group n = 26	Amiodarone group n = 24	p value
Age, year	68.6±8.2 (67)	67.4±8.5 (69)	0.601
Body mass index, kg/m2	27.9±3.6 (27.4)	27.1±4.3 26.0)	0.332
Male, n (%)	16 (61.5)	17 (70.8)	0.559
Clinic presentations of patients previous CABG			
SAP, n (%)	7 (26.9)	10 (41.7)	0.373
USAP/NSTEMI, n (%)	15 (57.7)	10 (41.7)	0.396
Atypical angina, n (%)	1 (3.8)	1 (4.2)	1.000
Others, n (%)	3 (11.5)	3 (12.5)	1.000
Hypertension, n (%)	25 (96.2)	22 (91.7)	0.602
Diabetes mellitus, n (%)	13 (50)	10 (41.7)	0.584
Smoking, n (%)	15 (57.7)	15 (62.5)	0.779
Dyslipidemia, n (%)	19 (73.1)	17 (70.8)	1.000
History of previous MI, n (%)	13 (50)	7 (29.2)	0.159
COPD, n (%)	2 (7.7)	3 (12.5)	0.661
History of PAF, n (%)	0	2 (8.3)	0.225
History of previous PCI, n (%)	4 (15.4)	4 (16.7)	1.000
History of previous CABG, n (%)	2 (7.7)	3 (12.5)	0.661
Left ventricular ejection fraction, %	45.2±10.8 (43.5)	49.8±9.0 (51)	0.139
Left ventricular systolic dysfunction, n (%)	19 (73.1)	13 (54.2)	0.239
Left atrial diameter, cm	4.1±0.7 (3.9)	4.1±0.7 (4.1)	0.724
All mitral regurgitation, n (%)	18 (69.2)	17 (77.3)	0.746
Severe mitral regurgitation, n (%)	1 (3.8)	1 (4.2)	1.000
Right atrial diameter, cm	3.6±0.3 (3.6)	3.7±0.7 (3.6)	0.915
Left ventricular diameter, cm	4.8±0.7 (4.7)	5.0±0.6 (4.9)	0.349
Fasting blood glucose (mg/dL)	119±38 (111)	110±25 (105)	0.433
Creatinine (mg/dL)	1.0±0.4 (0.9)	0.9±0.2 (0.9)	0.203
LDL cholesterol (mg/dL)	117±30 (124)	114±39 (105)	0.777
Haemoglobin (g/dL)	12.3±2.0 (11.9)	12.4±1.8 (11.9)	0.778

CABG: Coronary artery by-pass graft surgery, SAP: Stable angina pectoris, USAP/NSTEMI: Unstable angina pectoris/Non ST elevation myocardial infarction, MI: Myocardial infarction, COPD: Chronic obstructive pulmonary disease, PAF: Paroxysmal atrial fibrillation, PCI: Percutaneous coronary intervention, LDL: Low-Density Lipoprotein.

Table 2. Surgical and postoperative atrial fibrillation data

	Control group n = 26	Amiodarone group n = 24	p value
Perioperative beta-blocker, n (%)	20 (76.9)	18 (75)	1.000
Perioperative ACEI or ARB, n (%)	21 (80.8)	15 (62.5	0.211
Perioperative statin, n (%)	12 (46.2)	13 (54.2)	0.778
Operation type			
Isolated CABG, n (%)	24 (92.3)	19 (79.2)	0.239
CABG plus valve surgery, n (%)	2 (7.7)	5 (20.8)	0.239
Number of grafts/patient	3.2±1.2 (3)	2.9±1.4 (3)	0.477
Bypass pump time, min	89±32 (75)	85±41 (77)	0.621
Aorta cross-clamp time, min	43±26 (39)	56±37 (45)	0.354
Continuous Monitor follow up duration, hour	121±90 (98)	104±37 (96)	0.938
Length of hospital stay, day	10.3±5.4 (7.5)	8.7±2.8 (8.5)	0.739
Intubations length, hour	16.9±8.1 (15)	13.9±6.7 (12.5)	0.167
Onset time of atrial fibrillation, hour	59.1±38.9 (47)	58.9±31.8 (48)	0.983
AF mean ventricular rate, beat/min	121±21 (125)	138±21 (134)	0.004

ACEI: Angiotensin-converting enzyme inhibitors, ARB: Angiotensin receptor blockers, CABG: Coronary artery bypass graft surgery

Table 3. Primary and secondary endpoints of study and complications

	Control group n = 26	Amiodarone group n = 24	p value
Primary endpoints			
Sinus rhythm at 24th hour, n (%)	12 (46.2)	19 (79.2)	0.022
Need for DCCV, n (%)	14 (53.8)	5 (20.8)	0.022
Secondary endpoints			
DCCV performed, n (%)	11 (42.3)	2 (8.3)	0.009
DCCV success rate, n (%)	6/11 (54.5)	2/2 (100)	0.487
DCCV not performed, n (%)	3 (11.5)	3 (12.5)	1.0
Sinus rhythm at discharge, n (%)	23 (88.5)	24 (100)	0.236
Sinus rhythm at 30th day, n (%)	20 (83.3)	21 (95.5)	0.349
Crossover, n (%)	10 (38.5)	5 (20.8)	0.021
Complications			
Patients with any postoperative complications, n (%)	10 (38.5)	6 (26.1)	0.382
Death, n (%)	2 (7.7)	0	0.491
Any infection, n (%)	4 (15.4)	4 (17.4)	1.000
Renal impairment (creatinine > 2.0 mg/dL), n (%)	3 (11.5)	0	0.237
Myocardial infarction, n (%)	1 (3.8)	0	1.000
Stroke, n (%)	2 (7.7)	3 (12.5)	0.655
Respiratory failure, n (%)	3 (11.5)	1 (4.3)	0.612
Atrio-ventricular block, n (%)	1 (3.8)	0	1.000
Hypotension, n (%)	1 (3.8)	3 (12.5)	0.612

DCCV: Direct current cardioversion

Crossover ratio was significantly higher in control group (10 patients 38.5% vs. 5 patients 20.8%, p=0.021). Reasons for the crossover in the control group were unsuccessful DCCV (4 patients), patients or surgeon preference to refuse DCCV at the 24th hour (3 patients) and repetitive AF attacks after the restoration of SR (3 patients). Reasons for the crossover in amiodarone group were symptomatic bradycardia (2 patients) and severe QT prolongation (3 patients). In hospital follow up SR was achieved in all patients in the control group who crossed over to amiodarone group. Sinus rhythm incidences at discharge and 30th days were similar between groups (Table 3).

Complication rates were similar between groups (Table 3). Two patients (7.7%) died during the study period in the control group and no patients died in the amiodarone group. One of these patients died after a severe stroke and the other patient died after respiratory failure and sepsis. There were 2 (7.7%) ischemic strokes in the control group and 3 (12.5%) ischemic strokes in amiodarone group. All patients with stroke were on SR when stroke developed and three of them were on oral anticoagulant therapy. Thyroid function abnormalities were detected in 2 patients and referred to an endocrinologist.

Discussion

In this study, we showed that amiodarone therapy significantly increases SR rate at the 24th hour and decreases the DCCV requirement and crossover ratio.

Postoperative AF developed in 14.8% of our patients. Although POAF incidence changes between series our result confirm that it is still a common complication after cardiac surgery. Gillinov AM et al. showed that average time to the onset of POAF was 2.4 days among their patients [8]. The average time to the onset of POAF in our patients was similar between groups (59.1±38.9 to 58.9±31.8 hours, p=0.91) and consistent with the literature.

Postoperative AF is usually accepted as a transient situation and spontaneous conversion to SR thought to be high [9,10]. The spontaneous conversion rate in our study was lower than previous studies. This may be related to relatively small sample size, but strongly supports that POAF is not always a transient condition in contrast to suppose. Most of our POAF cases (more than 50% percent) did not return to SR without anti-arrhythmic therapy at the 24th hour.

A study comparing rhythm versus rate control in POAF showed that a total of 89.9% of patients in the rate control group and 93.5% of those in rhythm control group had a stable, sustained heart rhythm without AF at discharge (P = 0.14). And from discharge to 60 days, the percentages fell to 84.2% in the rate-control group and 86.9% in the rhythm-control group (P = 0.41) [8]. Similar to

these findings our results showed that SR rates at discharge and 30th day were similar between amiodarone and control groups. This result may be related to high DCCV rate and amiodarone usage after the 24th hour in the control group. A high number of patients had to use amiodarone and needed DCCV therapy after the 24th hour in the control group. At the end of the study, most of the patients (33 of 50 patients, 66%) received amiodarone and amiodarone therapy was effective in restoring SR even started after the 24th hour of AF in the control group.

The risk factors of POAF are advanced age, previous history of AF, male gender, left ventricular systolic dysfunction, left atrial enlargement, valvular heart surgery, chronic obstructive pulmonary disease, chronic renal failure, diabetes mellitus, rheumatic heart disease and obesity [9]. Previously, beta-blockers, amiodarone, bi-atrial pacing, statins, magnesium and steroids were shown to be effective in the prevention of POAF [5-7,9]. And many drugs such as digoxin, propafenone, sotalol, dofetilide, ibutilide, procainamide, flecainide, diltiazem, esmolol and amiodarone were tested to treat POAF [10]. In one study, ibutilide was more effective than placebo for treatment of POAF [11]. But there is very little evidence to support any of these drugs over another. Current guidelines suggest only amiodarone or vernakalant and DCCV restore sinus rhythm in patients with POAF [1]. But the level of evidence is C for these recommendations because of the lack of prospective studies. Stronger recommendations are partly based on prevention trials and extrapolation from Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial which evaluated nonsurgical patients. We aimed to clarify the scientific gap in this subject but we could not reach a high number of patients as discussed under study limitations subheading.

Amiodarone, a class III antiarrhythmic drug, has been used extensively in the treatment of AF in the short and long-term. Intravenous high-dose amiodarone safely facilitates the conversion of recent onset paroxysmal AF to NSR [12]. A meta-analysis demonstrated that 18 trials (3295 patients), with a variety of dosing strategies, have evaluated amiodarone for the prevention of postoperative AF and amiodarone reduced AF from an average incidence of 33.2% in the control group to 19.8% (OR 0.48, 95% CI 0.40–0.57) and amiodarone was associated with an increased risk of bradycardia (OR 1.66, 95% CI 1.73–2.47) [7]. Symptomatic bradycardia (2 patients) and severe QT prolongation (3 patients) were the main side effects seen among our patients treated with amiodarone. Previously, some studies evaluated amiodarone for the treatment of new-onset AF after cardiac surgery but none had a placebo group or evaluated amiodarone and DCCV together [13-18]. In these studies amiodarone treatment regimens were generally similar, administering 5 mg/kg intravenously over 5 to 30 min, followed by a maintenance dose of 15-40 mg/h. We used a similar dose compatible with literature. These studies demonstrated that the rate of conversion to SR at the 24th hour was similar with amiodarone, digoxin, propafenone and ibutilide [13-17]. In contrast to these studies, we showed that amiodarone significantly increases the rate of conversion to SR at the 24th hour. One study demonstrated that quinidine might be superior to amiodarone but more complications occurred with quinidine [18].

Conventional treatment strategies are similar to other AF patients in patients with POAF including prevention of thromboembolic events, control of the ventricular rate, and restoring/maintaining sinus rhythm. In a retrospective study, Samuels et al. showed that amiodarone and early DCCV were more effective than non-amiodarone therapies in restoring SR for patients with AF after elective cardiac surgery and complication rates were similar between groups [19]. Similar to Samuel et al.'s findings complication rates were similar between groups in our study. There were 2 (7.7%) ischemic strokes in the control group and 3 (12.5%) ischemic strokes in the amiodarone group. Three patients were on oral anticoagulant therapy when stroke developed. Although this study was not designed to compare anticoagulation strategies, this result may be related to inadequate use (or inadequate doses) of anticoagulants and shows the importance of adequate anticoagulation in POAF. Crossover rates may seem high (38.5% in control group vs. 20.8% in amiodarone group) but crossover rates were 15 to 38% in AFFIRM trial which evaluated stable nonsurgical patients who were not acutely ill as our patients [20].

Study Limitations

This was a single center study. The sample size is relatively small, and the study is openly labeled. But a trial with the power to detect differences in these endpoints has to enroll thousands of patients. During 1 month follow up, stroke was observed in 5 (10%) patients and one of these patients died. A quality-of-life questionnaire would have provided effects of treatment. But not included because of the short duration of the study and the effects of surgery would overshadow the effects of POAF and treatment. All patients were questioned for AF at the 30th day a 12-lead ECG and 48 hours Holter monitoring was performed but a continuous home monitoring system was not used. This might have led to an underestimation of the true incidence of AF. A total of 6 patients (3 patients in the control group, 3

patients in the amiodarone group) did not complete the full course of study because of the patients or surgeons preferences.

Conclusion

Our study is the first randomized, prospective, controlled study conducted to evaluate the effect of amiodarone and early DCCV on POAF. We showed that POAF is not a transient situation and spontaneous conversion to SR is seen less frequently than expected and most of the patients need amiodarone or DCCV. Amiodarone therapy seems effective in restoring SR in the first 24 hours. Amiodarone decreased the DCCV requirement and it was effective in restoration of SR even used after 24 hours.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

References

1. Kirchhof P, Benussi S, Kotecha D et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J 2016; 7: 2893-962.
2. Koletsis EN, Prokakis C, Crockett JR et al. Prognostic factors of atrial fibrillation following elective coronary artery bypass grafting: the impact of quantified intraoperative myocardial ischemia. J Cardiothorac Surg 2011; 6: 127.
3. Mathew JP, Fontes ML, Tudor IC et al. A multicenter risk index for atrial fibrillation after cardiac surgery. JAMA 2004; 291: 1720-29.
4. Villareal RP, Hariharan R, Liu BC et al. Postoperative atrial fibrillation and mortality after coronary artery bypass surgery. J Am Coll Cardiol 2004; 43: 742-48.
5. Aerra V, Kuduvalli M, Moloto AN et al. Does prophylactic sotalol and magnesium decrease the incidence of atrial fibrillation following coronary artery bypass surgery: a propensity-matched analysis. J Cardiothorac Surg 2006; 1: 6.
6. Gecmen C, Güler GB, Erdoğan E et al. SYNTAX score predicts postoperative atrial fibrillation in patients undergoing on-pump isolated coronary artery bypass grafting surgery. Anatol J Cardiol 2016; 16: 655-61.
7. Mithani S, Akbar MS, Johnson DJ et al. Dose dependent effect of statins on postoperative atrial fibrillation after cardiac surgery among patients treated with beta blockers. J Cardiothorac Surg 2009; 4: 61.
8. Gillinov AM, Bagiella E, Moskowitz AJ et al. Rate Control versus Rhythm Control for Atrial Fibrillation after Cardiac Surgery. N Engl J Med 2016; 374: 1911-21.
9. Aydın U, Yılmaz M, Duzyol C et al. Efficiency of postoperative statin treatment for preventing new-onset postoperative atrial fibrillation in patients undergoing isolated coronary artery bypass grafting: A prospective randomized study. Anatol J Cardiol 2015; 15: 491-95.
10. Dunning J, Khasati N, Prendergast B. What is the optimal medical treatment for stable cardiac surgical patients who go into atrial fibrillation after their operation? Interact Cardiovasc Thorac Surg. 2004; 3: 46-51.
11. VanderLugt JT, Mattioni T, Denker S et al. Efficacy and safety of ibutilide fumarate for the conversion of atrial arrhythmias after cardiac surgery. Circulation 1999; 100: 369-75.
12. Cotter G, Blatt A, Kaluski E et al. Conversion of recent onset paroxysmal atrial fibrillation to normal sinus rhythm: the effect of no treatment and high-dose amiodarone. A randomized, placebo-controlled study. Eur Heart J 1999; 20: 1833-42.
13. Kaireviciute D, Aidietis A, Lip GY. Atrial fibrillation following cardiac surgery: clinical features and preventative strategies. Eur Heart J 2009; 30: 410-25.
14. Cameron MJ, Tran DTT, Abboud J, Newton EK, Rashidian H, Dupuis JY. Prospective external validation of three preoperative risk scores for prediction of new onset atrial fibrillation after cardiac surgery. Anesth Analg 2018; 126: 33–38.
15. Di Biasi P, Scrofani R, Paje A, Cappiello E, Mangini A, Santoli C. Intravenous amiodarone vs propafenone for atrial fibrillation and flutter after cardiac operation. Eur J Cardiothorac Surg 1995; 9: 587-91.
16. Bernard EO, Schmid ER, Schmidlin D, Scharf C, Candinas R, Germann R. Ibutilide versus amiodarone in atrial fibrillation: a double-blinded, randomized study. Crit Care Med 2003; 31: 1031-34.
17. Larbuisson R, Venneman I, Stiels B. The efficacy and safety of intravenous propafenone versus intravenous amiodarone in the conversion of atrial fibrillation or flutter after cardiac surgery. J Cardiothorac Vasc Anesth. 1996; 10: 229-34.
18. Greenberg JW, Lancaster TS, Schuessler RB, Melby SJ. Postoperative atrial fibrillation following cardiac surgery: a persistent complication. Eur J Cardiothorac Surg 2017; 52: 665-72.
19. Samuels LE, Holmes EC, Samuels FL. Selective use of amiodarone and early cardioversion for postoperative atrial fibrillation. Ann Thorac Surg 2005; 79: 113-16.
20. The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. N Engl J Med 2002; 347: 1825-33.

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Original Article

Analysis of myocardial texture in patients with isolated left ventricular noncompaction

İzole sol ventrikül noncompaction olan hastalarda miyokard dokusunun analizi

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ABSTRACT

Aim: Videodensitometric myocardial texture analysis (VMTA) has been widely used to investigate left ventricular (LV) dysfunction in various cardiac disorders. Patients with isolated left ventricular noncompaction (IVNC) experience an undulating decline in LV function. The aim of this study was to assess the value of VMTA for evaluating deterioration of LV function in this patient group.

Material and Methods: Twenty-two patients with IVNC (10 asymptomatic [preserved LV function], 12 symptomatic [LV dysfunction]) and 12 healthy controls were evaluated. Videodensitometry was used to record background-corrected mean gray levels (BC-MGL) for 2 regions of the mid-basal LV wall (the interventricular septum [IVS] and the posterior wall [PW]) at end-systole and end-diastole. The cyclic variation (CV) index for each region was calculated according to the formula, CV index % = ([BC-MGLend-diastole – BC-MGLend-systole] ÷ BC-MGLend-diastole) × 100.

Results: The mean IVS-CV index in the symptomatic IVNC group (12.3 ± 4.9%) was significantly lower than the corresponding findings in the asymptomatic IVNC group (32.3 ± 14.8%, $p < 0.05$) and control group (36.6 ± 12.1%, $p < 0.001$). The mean PW-CV index in the symptomatic group (15.1 ± 5.5%) was also significantly lower than the corresponding values in the asymptomatic (27.0 ± 10.4%, $p < 0.05$) and control groups (28.8 ± 10.9%, $p < 0.001$).

Conclusion: VMTA is a practical, useful adjunct to conventional echocardiography for assessing LV myocardium in patients with IVNC. Detection of reduced CV index values might predict the early stages of LV deterioration in this group.

Keywords: videodensitometric myocardial texture analysis; isolated left ventricular noncompaction; cardiomyopathy; heart failure; non-invasive cardiac imaging

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ÖZ

Amaç: Videodensitometrik miyokardiyal doku analizi (VMTA), çeşitli kardiyak hastalıklarda sol ventrikül (LV) disfonksiyonunu araştırmak için yaygın olarak kullanılmıştır. İzole sol ventrikül noncompaction (IVNC) olan hastalar LV fonksiyonunda dalgalı bir düşüş yaşarlar. Bu çalışmanın amacı, bu hasta grubunda LV fonksiyonunun bozulmasını değerlendirmek için VMTA değerini değerlendirmektir.

Gereç ve Yöntemler: IVNC'li 25 hasta (10 asemptomatik [korunmuş LV fonksiyonu], 12 semptomatik [LV disfonksiyon]) ve 12 sağlıklı kontrol olacak şekilde değerlendirildi. Sistol sonunda ve diyastolde orta bazal LV duvarının 2 bölgesi (interventriküler septum [IVS] ve arka duvar [PW]) için arka plan düzeltmeli ortalama gri seviyelerini (BC-MGL) kaydetmek için videodensitometri kullanıldı. Her bölge için siklik varyasyon (CV) indeksi, formül CV'ye göre hesaplandı, CV indeksi, %= ([[BC-MGLend-diastol - BC-MGL end-sistol]] ÷ BC- MGLend-diastol) × 100.

Bulgular: Semptomatik IVNC grubundaki ortalama IVS-CV indeksi (% 12.3 ± 4.9), asemptomatik IVNC grubundaki (% 32.3 ± 14.8; p <0.05) ve kontrol grubundaki (% 36.6 ± 12.1) karşılık gelen bulgulardan anlamlı olarak düşüktü (p <0.001). Semptomatik gruptaki ortalama PW-CV indeksi (% 15.1 ± 5.5), asemptomatik (27.0 ± 10.4; p <0.05) ve kontrol gruplarındaki (28.8 ± 10.9; p <0.001) karşılık gelen değerlerden anlamlı olarak düşüktü.

Sonuç: VMTA, IVNC'li hastalarda LV miyokardiyumu değerlendirmek için konvansiyonel ekokardiyografiye pratik ve faydalı bir yardımcıdır. Azaltılmış CV indeks değerlerinin tespiti, bu grupta LV bozulmasının erken aşamalarını öngörebilir.

Anahtar kelimeler: videodensitometrik miyokardiyal doku analizi; izole sol ventrikül noncompaction kardiyomiyopati; kalp yetmezliği; non-invaziv kalp görüntüleme

Introduction

Isolated left ventricular noncompaction (IVNC) is a congenital form of cardiomyopathy that has not yet been classified by the World Health Organization [1]. In early life, the myocardium of the left ventricle (LV) undergoes a distinct form of morphogenesis characterized by changes in the trabecular patterning on the endocardial surface [2]. During normal morphogenesis, the myocardium becomes condensed and large recesses in the trabecular meshwork flatten out or completely disappear [2]. If this process is arrested, the result is ventricular noncompaction [3-5]. Initial studies suggested that noncompaction was associated with grave prognosis due to heart failure, embolic events and malignant arrhythmias [4-8]. However, subsequent research has demonstrated that the prognosis is not as grim as originally thought [7-9]. Thus, practical, non-invasive cardiac imaging techniques are important for monitoring the status and deterioration of the LV in patients with noncompaction.

Noncompaction is generally an abnormality of the LV apex and adjacent portions of the LV wall; it is unusual for the basal segments of the ventricle to be affected [4-7,9]. The role of conventional echocardiography for assessing or predicting ventricular deterioration in patients with early-phase IVNC remains controversial.

Videodensitometric myocardial texture analysis (VMTA) has been used to document the cyclic variation (CV) of myocardial acoustic properties in various cardiac disorders, including those of ischemic and non-ischemic origin [10-12]. In this study, we used this technique to assess the acoustic properties of LV myocardium in the setting of IVNC. Specifically, the videodensitometric findings for the LV aspect of the interventricular septum (IVS) and the posterior wall of the LV (PW) were evaluated in subgroups of patients with IVNC, and findings were compared to those in healthy subjects.

Material and Methods

Study Population

Between February 2013 and March 2016, 22 consecutive patients with IVNC (11 men and 11 women; mean age, 38 ± 14 years) who met the inclusion criteria for this study (details below) were enrolled in the study. We also investigated 12 healthy hospital-staff volunteers (6 men and 6 women; mean age, 39 ± 14 years) as controls. None of the controls had cardiovascular symptoms or evidence of any systemic disease, as assessed by physical examination, chest radiography, electrocardiography (ECG) and echocardiography.

The diagnostic criteria for IVNC were as follows: (1) absence of coexisting cardiac anomalies, (2) presence of excessive numbers of large trabeculae, (3) multiple deep intertrabecular

recesses filled with blood from the ventricular cavity, as demonstrated by color Doppler imaging, and (4) ratio of the thickness of the noncompacted endocardial layer to that of the compacted epicardial layer (NC/C ratio) ≥ 2 (6-9) (Fig 1). The exclusion criteria were rhythm other than sinus, bundle branch block, any pre-excitation syndrome, cardiogenic shock, significant valvular regurgitation or valvular stenosis, any systemic disease (diabetes, hypertension, goiter and others), neuromuscular disease at time of presentation, involvement of the right ventricle, clinical and ECG evidence of ischemic heart disease, stroke in the 2 months prior to the study, history of cardiotoxic agent use (chemotherapeutics or long-term alcohol consumption), hypertrabeculation on the side that the ROI would be positioned for VMTA.

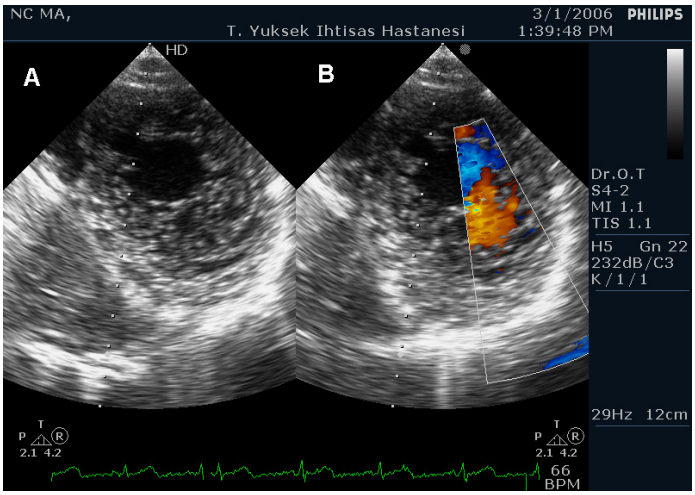

Fig. 1. Modified apical view of the left ventricular apex in a patient with isolated left ventricular noncompaction. Two-dimensional echocardiography reveals the 2 layers of myocardium (compacted and noncompacted), excessive numbers of large trabeculae (Panel A), and multiple deep intertrabecular recesses filled with blood from the ventricular cavity as shown on color Doppler (Panel B).

For analysis, the 22 patients with IVNC were divided into 2 groups: an asymptomatic group (n = 10; 5 men and 5 women; mean age, 39 ± 11 years) and a symptomatic group (n=12; 6 men and 6 women; mean age, 36 ± 12 years). The 10 asymptomatic patients showed no clinical signs of heart failure (8 cases diagnosed during family screening, 2 diagnosed incidentally during echocardiography for other reasons). The 12 symptomatic individuals were in clinical heart failure and each had been hospitalized at least once for decompensated heart failure. These 12 patients were all taking appropriate medical therapy, such as diuretics, β-blockers, digitalis, anticoagulants and angiotensin-converting enzyme inhibitors. Patients who were on medications that affect LV performance (β-blockers or digoxin) were taken off these drugs for at least 5 days before the echocardiographic examination was done.

All subjects were informed about the study and each gave written consent to participate.

Transthoracic Echocardiography

Conventional M-mode, 2-dimensional and color Doppler images were obtained for all subjects using a commercially available echocardiography unit (Philips Ultrasound EnVisor C HD, Andover, MA, USA) with a 2- to 4-MHz phased-array multifrequency transducer. Subjects were all examined in left lateral decubitus position while breathing calmly. Imaging was done through parasternal and apical windows. LV end-diastolic diameter (LVEDD), LV end-systolic diameter (LVESD), thickness of the IVS during diastole, thickness of the PW during diastole, and maximal left atrial diameter (LAD) were measured from M-mode tracings according to the recommendations of the American Society of Echocardiography.

For each patient with IVNC, the number of regions/segments exhibiting noncompaction, the specific locations of these, and the NC/C ratio were recorded. As noted, the NC/C ratio was calculated based on the thicknesses of the 2 layers of myocardium (compacted and noncompacted). These measurements were taken at the site of the most prominent trabecular meshwork in end-systole, as this allowed best visualization of the layers [6]. Sites of noncompaction were recorded by dividing the LV wall into 16 regions/segments: the inferior wall, lateral wall, anterior wall, and septum on the short-axis apical view; the anterior septum, posterior septum, and the posterior, inferior, lateral and anterior LV walls on the short-axis mid-ventricular view and the short-axis basal view.

LV systolic function was assessed based on ejection fraction (EF) and fractional shortening (FS). LV EF was calculated from apical views using the biplane area length method [9]. FS was calculated from M-mode tracings of the parasternal long axis using the equation, FS (%) = ([LVEDD – LVESD] ÷ LVEDD) × 100.

All examinations were conducted by the same observer (O.T.). For each parameter, the mean value calculated from 3 consecutive heartbeats was recorded.

Videodensitometric Analysis of Myocardial Texture

The same gain settings and compensation profiles were used for all participants to achieve approximately uniform brightness of the IVS and PW throughout all the echocardiography exams. Harmonic imaging was not used, and the gray-scale

transfer function was adjusted to be linear at a depth of 16 to 18 cm. Dynamic range, emission power, focal plane, filters, and overall gain were adjusted to fixed settings in all the exams so as to minimize noise on the image. To avoid bias in data analysis, the manual adjustment for depth gain compensation (linear curve) was kept at zero. Care was taken to ensure that the angle of incidence of the ultrasound beam was kept perpendicular to the mid-basal segments of the IVS and PW when the parasternal long axis of the LV was scanned.

For each subject, the optimal ECG-guided end-diastolic and end-systolic 2-dimensional echocardiographic images of 3 consecutive beats in the cine loop were transferred directly from the screen to the digital archive of the echocardiography system. This was done using an image format of 24-bit intensity range and resolution of 800 × 564 pixels. End-diastole was defined as the point in the cardiac cycle marked by the start of the R wave on ECG. End-systole was defined as the time of minimal LV chamber size, marked by the peak of the T wave on ECG. The digitized images were transferred from the echocardiography unit to a personal computer for VMTA.

The same observer (O.T.) analyzed all cases. Using dedicated software (NIH-ImageJ-1.35s, National Institutes of Health, USA), the images were converted to a format of 8-bit intensity range and 800 × 564 resolution, with each pixel featuring 256 gray levels (0 = black, 255 = white). The same software allows the examiner to generate a histogram that depicts echocardiographic gray-level distribution across each image. A histogram was generated for each ROI by plotting gray-level distribution on the abscissa and frequency on the ordinate (Fig. 2). For images captured in the parasternal long axis view, a trackball-controlled cursor was used to outline and highlight the ROI on each image (all ROIs identical in each set of images). Effort was made to position each ROI at the same location on the IVS and on the PW in each case (i.e., near the tips of the mitral valve leaflets in end-systolic and end-diastolic frames) [11-13]. Only normal myocardial segments were analyzed (i.e., segments without the abnormal trabeculae that characterize noncompaction), and endocardial and epicardial specular echoes were excluded to avoid areas of "echo drop-out" and obvious artifacts. For each ROI in each wall region (IVS and PW), the background signal was subtracted from the mean gray level (MGL) to obtain background-corrected MGL (BC-MGL). The CV index of the gray-level amplitude for each ROI was calculated according to the formula, CV Index (%) =([BC-MGLend-diastole – BC-MGLend-systole] ÷ BC-MGLend-diastole) × 100. To assess the variability of these measures, 3 consecutive cycles were analyzed.

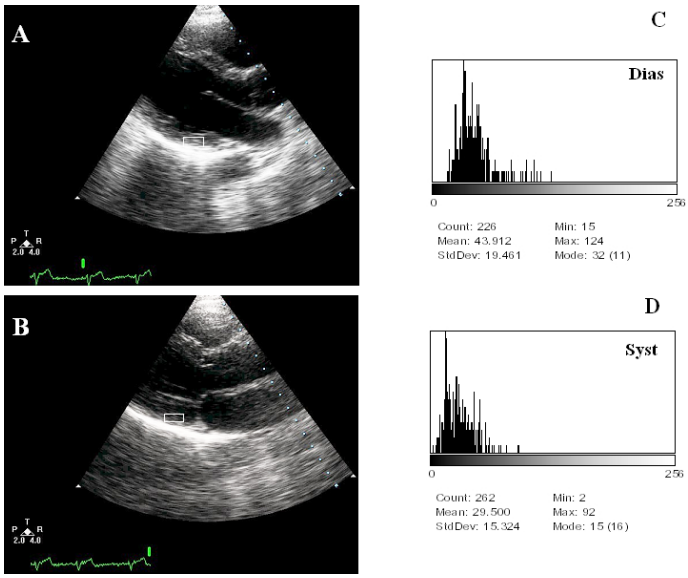

Fig. 2. Digitized images from a healthy subject show the position of the region of interest on the posterior wall of the left ventricle in end-diastole (Panel A) and end-systole (Panel B) (cycle phases determined from electrocardiography). A histogram was generated (the gray-level distribution on abscissa, frequency on the ordinate) for each region of interest at end-diastole (Panel C) and end-systole (Panel D).

Local ethics committee approved the study and informed consent was obtained from participant(s)

Statistical Analysis

Descriptive data for the continuous variables are presented as mean ± 1 standard deviation. The Mann-Whitney U test, Wilcoxon rank-sum test, and chi-square test were used as appropriate. Spearman's correlation coefficient was used for correlation analysis. A p value < 0.05 was considered statistically significant.

Results

Clinical and Echocardiographic Findings

Table 1 summarizes the results for the clinical and transthoracic echocardiography variables in the 3 groups (asymptomatic IVNC, symptomatic IVNC, healthy controls). There were no significant differences among the groups with respect to mean age, sex distribution, mean blood pressure or mean heart rate findings. The symptomatic IVNC group had significantly larger mean LAD, LVEDD and LVESD than the asymptomatic IVNC and control groups, and registered significantly lower mean FS and mean EF than the asymptomatic IVNC and control groups.

Findings Related to Myocardial Texture

The VMTA results are shown in Table 2. There were no significant differences among the 3 groups with respect to mean diastolic BC-MGL for the IVS. The mean diastolic BC-MGL

for the PW in the symptomatic IVNC group was significantly higher than the corresponding value in the control group ($p < 0.01$), but was not significantly different from that in the asymptomatic IVNC group. The symptomatic IVNC group also had significantly higher mean systolic BC-MGL for the IVS and mean systolic BC-MGL for the PW than the control group ($p < 0.01$, for IVS; $p < 0.01$, for PW). There were no significant differences between the asymptomatic IVNC group and the control group with respect to these means.

Table 1. Group Results for the Clinical and Transthoracic Echocardiography Variables

	Healthy Controls	Symptomatic IVNC Group	Asymptomatic IVNC Group
	n = 12	n = 12	n = 10
Clinical Characteristics			
Age (yrs)	39 ± 14	36 ± 12	39 ± 11
Sex (male/female)	6/6	6/6	5/5
NYHA Functional Class	NA	2.8 ± 0.5	NA
Heart Rate (bpm)	72 ± 10	74 ± 11	71 ± 12
Systolic BP (mmHg)	118 ± 14	116 ± 15	120 ± 11
Diastolic BP (mmHg)	79 ± 12	80 ± 5	78 ± 11
Medication Use n (%)			
ACE Inhibitor	NA	12 (100%)	NA
β-blocker	NA	6 (50%)	1(10%)
Digoxin	NA	7 (58%)	NA
Diuretic	NA	9 (75%)	NA
Anticoagulant	NA	1 (8%)	NA
Echocardiographic Data			
IVS (mm)	9.0 ± 0.9	9.0 ± 1.0	9.0 ± 1.1
PW (mm)	9.0 ± 0.8	9.0 ± 1.1	10.0 ± 1.0
LVEDD (mm)	47 ± 7	59 ± 8 *	49 ± 6
LVESD (mm)	30 ± 4	47 ± 3 *	31 ± 5
LAD (mm)	32 ± 4	43 ± 2 *	31 ± 3
FS (%)	36 ± 3	20 ± 3 *	36 ± 5
EF (%)	67 ± 8	37 ± 5 *	67 ± 4
NC/C Ratio	NA	3.1 ± 0.5	3.2 ± 0.7
No. of Segments showing Noncompaction	NA	6.1 ± 2.1	5.8 ± 3

IVNC, isolated left ventricular noncompaction; NYHA, New York Heart Association; NA, not applicable; ACE, angiotensin-converting enzyme; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; FS, left ventricular fractional shortening; EF, left ventricular ejection fraction; IVS, thickness of the left ventricular aspect of the interventricular septum during diastole; PW, thickness of the posterior wall of the left ventricle during diastole; NC/C, noncompaction to compaction. Values are expressed as mean ± standard deviation. * $p < 0.01$ vs. control group and asymptomatic IVNC group.

Table 2. Group Results for the Videodensitometric Myocardial Texture Analysis

	Healthy Controls	Symptomatic IVNC Group	Asymptomatic IVNC Group
IVS			
Diastolic BC-MGL	68.4 ± 21.2	61.6 ± 20.4	68.1 ± 28.2
Systolic BC-MGL	37.1 ± 12.1	53.8 ± 17.2*	39.3 ± 19.5
CV Index (%)	36.6 ± 12.1	12.3 ± 4.9†‡	32.3 ± 14.8
PW			
Diastolic BC-MGL	79.7 ± 22.1	113.1 ± 27.9*	92.3 ± 26.1
Systolic BC-MGL	56.3 ± 13.1	94.5 ± 24.2*	62.0 ± 18.8
CV Index (%)	28.8 ± 10.9	15.1 ± 5.5†‡	27.0 ± 10.4

IVNC isolated left ventricular noncompaction; IVS left ventricular aspect of the interventricular septum; BC-MGL background-corrected mean gray level; CV Index (%) cyclic variation index; PW, posterior wall of the left ventricle. Values are expressed as mean ± standard deviation. * $p < 0.01$ vs. control group; † $p < 0.001$ vs. control group; ‡ $p < 0.05$ vs. asymptomatic IVNC group.

The control group and asymptomatic IVNC group had statistically similar mean CV index values for the IVS and the PW, respectively. However, the mean CV index for the IVS in the symptomatic IVNC group was significantly lower than the corresponding values in the control group ($p < 0.01$) and the asymptomatic IVNC group ($p < 0.05$) (Fig. 3). The mean CV index for the PW in the symptomatic IVNC group was also significantly lower than the corresponding values in the other groups (controls $p < 0.001$; asymptomatic IVNC group $p < 0.05$) (Fig. 4).

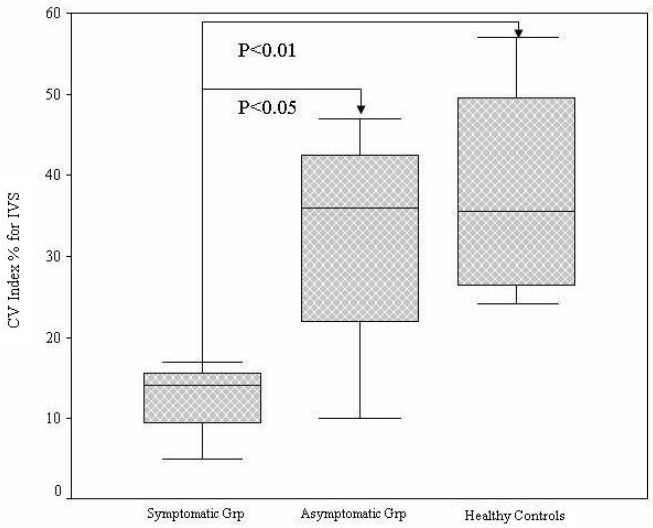

Fig. 3. The mean cyclic variation index values for the region of interest in the left ventricular aspect of the interventricular septum in all 3 groups (symptomatic IVNC, asymptomatic IVNC, healthy controls). See the text for results of statistical comparison among the groups. CV Index %, cyclic variation index; IVS, left ventricular aspect of the interventricular septum; Grp, group.

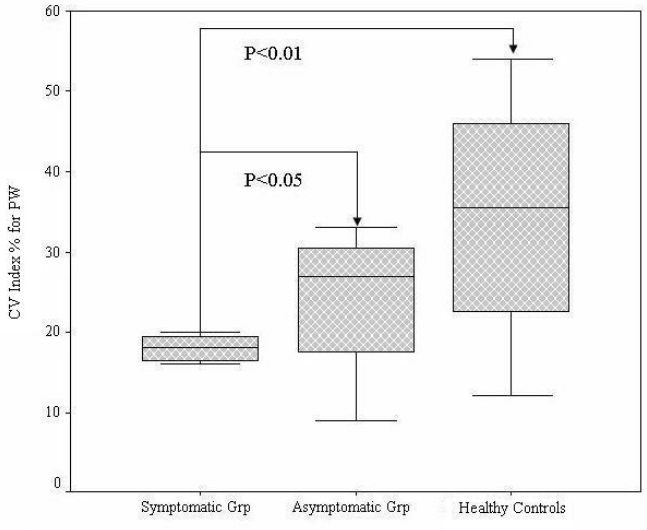

Fig. 4. The mean cyclic variation index values for region of interest in the posterior wall of the left ventricle in all 3 groups (symptomatic IVNC, asymptomatic IVNC, healthy controls). See the text for results of statistical comparison among the groups. CV Index %, cyclic variation index; PW, posterior wall of the left ventricle; Grp, group.

Separate analysis of the patient subgroup data (symptomatic IVNC, asymptomatic IVNC) revealed no significant correlations between the texture analysis parameters and any of the echocardiographic variables investigated (LVEDD, LVESD, LAD, FS, EF, IVS and PW thickness during diastole, NC/C ratio, number of segments with noncompaction).

Discussion

Regions of myocardium with the typical signs of noncompaction can exhibit a variety of different histopathologic features. These include ischemic lesions, interstitial fibrosis, endomyocardial thickening, inflammatory reaction, subendocardial fibrosis, fibroelastosis, myocyte hypertrophy, myocardial fibrosis, myocardial disorganization, myocardial degeneration, and myocardial scarring [4-6, 15-16]. However, in most patients with IVNC, the basal segments of the LV do not exhibit the abnormal trabeculae that are typical of noncompaction. This portion of the ventricle appears normal on gross inspection, and it is not known whether such histopathology also exists in this region. The fact that the basal wall appears normal does not rule out underlying abnormality in these compacted regions.

Analyzing myocardial texture with echocardiography provides practical information about the condition of the heart muscle. This technique is a useful adjunct to conventional echocardiographic methods that are used to assess myocardium [10-12, 17]. Currently, there are 2 methods for assessing myocardial texture ultrasonographically: 1) integrated backscatter, which examines the acoustic intensity of the native echocardiographic signal, and 2) VMTA, which quantifies data from echocardiographic images and yields an MGL value for each ROI [14]. Integrated backscatter has been used both experimentally [18] and clinically [19] to quantify collagen and fibrosis in myocardium. As noted, VMTA has been used to investigate ischemic and non-ischemic myocardial disease, and to assess clinical prognosis in various cardiac disorders [11-12]. Research performed with the videodensitometry method has shown that, in patients with idiopathic dilated cardiomyopathy (DCMP) and ischemic myocardial disorders, the CV index values for the IVS and PW are lower than normal [12]. The same studies revealed that reduced CV index values are strongly correlated with poor prognosis. Our investigation with VMTA also revealed significantly lower CV index values for the IVS and the PW in patients with symptomatic IVNC (clinical LV dysfunction)

compared to patients with asymptomatic IVNC and healthy controls (Fig. 3-4). The prognosis for symptomatic IVNC is known to be poor [6]. Therefore, our findings suggest that CV index values for the IVS and the PW in patients with IVNC are independent indicators of prognosis.

Previous studies have shown that VMTA can identify changes in the myocardium before conventional echocardiography demonstrates any abnormality [19]. Videodensitometry can also confirm echocardiographic markers of myocardial pathology that are detected with conventional methods (for example, abnormal LV mass index, LV volume, LVEDD, LVESD and others) [19]. Excess parathyroid hormone is thought to be a major uremic toxin for myocardium that promotes activation of myocardial fibroblasts and causes cardiac fibrosis.. Rossi et al. [20] also observed a relationship between altered myocardium as noted on videodensitometry and elevated serum aldosterone in patients with primary hyperaldosteronism. In this disorder, the excess aldosterone leads to cardiac fibrosis and subsequent cardiac dysfunction. However, neither of these studies documented any correlations between CV index values for the IVS or the PW and myocardial performance parameters on conventional echocardiography. Analysis of the data from our patients with IVNC showed that none of the VMTA parameters was significantly correlated with conventional echocardiography parameters of LV myocardial function (FS and EF) or echocardiography findings related to noncompaction (NC/C ratio, number of segments exhibiting noncompaction). Our results suggest that, in the setting of IVNC, videodensitometry findings can identify changes in the myocardium before conventional echocardiography demonstrates any abnormality.

VMTA is a reliable, noninvasive way to evaluate myocardial ischemia. Marini et al. [11] used this technique to investigate 34 patients who exhibited resting dyssynergia in the IVS and/or the inferior portion of the PW. Viable regions of the myocardium were identified as those that exhibited improved wall motion after revascularization. The authors observed that, prior to revascularization, videodensitometry revealed higher CV index values in these viable areas than in necrotic regions. In our study, the mean CV index values for the IVS and the PW in the symptomatic IVNC group were both significantly lower than the corresponding values in healthy individuals (the controls). However, we also observed a trend towards decreased CV index values for these sites in the asymptomatic IVNC group, patients who may be in a transitional phase that will progress to grave LV deterioration (Table 2). The findings in both our IVNC subgroups support the theory that microcirculatory ischemic dysfunction plays a role in IVNC.

Although IVNC is a distinct form of congenital cardiomyopathy, patients who exhibit LV dysfunction due to IVNC can be misdiagnosed as having DCMP. As noted, there are a number of imaging features of the LV myocardium that typify IVNC: prominent trabeculae, deep intertrabecular recesses, compacted/noncompacted layers, and recesses filled with blood from the LV cavity. In the normal heart, the base is the thickest region of the LV wall; the muscle tissue becomes remarkably thin towards the apex, and the apical portion of the wall features only small trabeculae [14]. In contrast, in the setting of IVNC the apex is thicker and has larger trabeculae, and only a few patients with this condition have trabeculae at the base of the LV [2-7]. During the course of DCMP, the LV becomes dilated as the walls become progressively thinner, and the ventricle takes on a spherical shape. In cases of IVNC, LV wall thickness does not change and the chamber does not dilate in proportion to the degree of spherical remodeling that occurs [9]. This is unlike all other cardiac conditions that feature marked systolic LV dysfunction [9]. To the best of our knowledge, the present study is the first to have applied VMTA in patients with IVNC. We found that some of the findings were similar to those reported for DCMP. Dagdeviren et al. [23]. identified a relationship between contractile reserve during dobutamine stress and CV index values for the IVS and PW in DCMP. A different report by Dagdeviren et al. [12] confirmed that lower CV index values for these wall regions predict prognosis in the setting of DCMP. The CV index values for our patients with low LV EF (the symptomatic IVNC group) were similar to those that have been documented for patients with DCMP. In contrast, the mean CV index values for the asymptomatic IVNC group were considerably higher.

Although IVNC is still considered a rare cardiac disorder, it has been detected more frequently in recent years owing to improvements in cardiac imaging. Aras et al. [24] showed that age at initial presentation, ratio of NC/C, and number of affected segments seem to be major determinants of LV systolic dysfunction. As noted, IVNC is not always fatal; some patients exhibit an "undulating phenotype" with recovery of LV function for periods of time before further deterioration occurs [7]. The mechanism of distinct undulating LV dysfunction that occurs in IVNC, the cause of the LV deterioration, and the prognosis for this disorder are still in question. Pignatelli et al. [7] reported that patients with IVNC exhibit serial alterations in LV function; there

may be varying periods of recovery of systolic ventricular function before further deterioration. In line with this, a previous report by our group documented the case of a 78-year-old patient with asymptomatic IVNC who showed preserved systolic LV function [8]. Due to the nature of the disorder, patients with IVNC require continuous monitoring of LV function. For this purpose, VMTA might be a useful adjunct to conventional echocardiography in the early stages of the disease[25].

Study Limitations

Very few patients who are referred to our echocardiography laboratory have IVNC, and this restricted the number of patients in our study. For ethical reasons, we did not obtain cardiac biopsies from our subjects with IVNC. We interpreted the videodensitometry data based on findings in previous, well-designed investigations of other patient groups. Configurational changes due to translation, rotation and twisting of the heart during the cardiac cycle can lead to misinterpretation of videodensitometry data. We tried to minimize such problems in multiple ways. As previous investigators have done, we positioned the 2 ROIs for our study at mid-basal locations on the IVS and PW, respectively. These segments were distant from regions of abnormal trabeculation (noncompacted areas), thus we avoided the echo drop-out that would have occurred in regions of noncompaction. In addition, the orientation of the ultrasound beam was such that it was almost perpendicular to the myocardial fibers in the IVS and the PW. This meant that problems with anisotropy were also avoided as much as possible. Another limitation we recognized is that we have not used two dimensional (2D) speckle tracking echocardiography (STE) which is a promising new imaging modality, similar to tissue Doppler imaging (TDI), it permits offline calculation of myocardial velocities and deformation parameters such as strain and strain rate (SR) and it has an important role in the diagnosis and follow-up in IVCN [50]. Finally, all of our subjects were adults, and results for this population cannot be extrapolated to IVNC in childhood.

Conclusion

In conclusion, VMTA is a practical, noninvasive way to assess LV myocardium in the setting of IVNC. This technique adds important information to that obtained with conventional echocardiography. VMTA may be useful for monitoring LV status and LV deterioration in patients with IVNC.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

References

1. Richardson P, McKenna W, Bristow M et al. Report of the 1995 World Health Organization/International Society and Federation of Cardiology Task Force on the definition and classification of cardiomyopathies. Circulation 1996; 93: 841–42.
2. Sedmera D, Pexieder T, Vuillemin M, Thompson RP, Anderson RH. Developmental patterning of the myocardium. Anat Rec 2000; 258: 319-37.
3. Jenni R, Goebel N, Tartini R, Schneider J, Arbenz U, Oelz O. Persisting myocardial sinusoids of both ventricles as an isolated anomaly: echocardiographic, angiographic, and pathologic anatomical findings. Cardiovasc Intervent Radiol 1986; 9: 127-31.
4. Chin TK, Perloff JK, Williams RG, Jue K, Mohrmann R. Isolated noncompaction of left ventricular myocardium: a study of eight cases. Circulation 1990; 82: 507-13.
5. Oechslin EN, Attenhofer Jost CH, Rojas JR, Kaufmann PA, Jenni R. Long-term follow-up of 34 adults with isolated left ventricular noncompaction: a distinct cardiomyopathy with poor prognosis. J Am Coll Cardiol 2000; 36: 493-500.
6. Jenni R, Oechslin E, Schneider J, Attenhofer Jost C, Kaufmann PA. Attenhofer Jost C, Kaufmann PA. Echocardiographic and pathoanatomical characteristics of isolated left ventricular non-compaction: a step towards classification as a distinct cardiomyopathy. Heart 2001; 86: 666-71.
7. Pignatelli RH, McMahon CJ, Dreyer WJ et al. Clinical characterization of left ventricular noncompaction in children: a relatively common form of cardiomyopathy. Circulation. 2003; 108: 2672-28.
8. Aras D, Tufekcioglu O, Topaloglu S et al. Preserved systolic function with isolated left ventricular noncompaction in an elderly patient. Eur J Echocardiogr 2006; 7: 71-74.
9. Sengupta PP, Mohan JC, Mehta V et al. Comparison of echocardiographic features of noncompaction of the left ventricle in adults versus idiopathic dilated cardiomyopathy in adults. Am J Cardiol 2004; 94: 389-91.
10. Picano E, Faletra F, Marini C et al. Increased echodensity of transiently asynergic myocardium in humans: a novel echocardiographic sign of myocardial ischemia. J Am Coll Cardiol 1993; 21: 199-207.
11. Marini C, Picano E, Varga A, Marzullo P, Pingitore A, Paterni M. Cyclic variation in myocardial gray level as a marker of viability in man. A videodensitometric study. Eur Heart J 1996; 17: 472-79.
12. Di Bello V, Pedrinelli R, Giorgi D et al. Ultrasonic videodensitometric analysis of two different models of left ventricular hypertrophy. Athlete's heart and hypertension. Hypertension 1997; 29: 937-44.

13. Di Bello V, Pedrinelli R, Giorgi D et al.Ultrasonic myocardial texture versus Doppler analysis in hypertensive heart: a preliminary study. Hypertension 1999; 33: 66-73.
14. Zoni A, Regolisti G, Aschieri D, Borghetti A. Myocardial ultrasonic tissue characterization in patients with different types of left ventricular hypertrophy: a videodensitometric approach. J Am Soc Echocardiogr 1997; 10: 74-82.
15. Dagdeviren B, Akdemir O, Eren M et al. Prognostic implication of myocardial texture analysis in idiopathic dilated cardiomyopathy. Eur J Heart Fail 2002; 4: 41-48.
16. Jenni R, Vieli A, Hess O, Anliker M, Krayenbuehl HP. Estimation of left ventricular volume from apical orthogonal 2-D echocardiograms. Eur Heart J 1981; 2: 217 - 25.
17. Lasserre R, Gosse P, Mansour S. Myocardial Tissue Characterization in Echocardiography with Videodensitometry: Evaluation of a New Semi-automatic Software Applied on a Population of Hypertensive Patients. Eur J Echocardiogr 2003; 4: 292-99.
18. Stamou SC, Lefrak EA, Athari FC, Burton NA, Massimiano PS. Heart transplantation in a patient with isolated noncompaction of the left ventricular myocardium. Ann Thorac Surg 2004; 77: 1806-8.
19. Burke A, Mont E, Kutys R, Virmani R. Left ventricular noncompaction: a pathological study of 14 cases. Hum Pathol 2005; 36: 403-11.
20. Skorton DJ, Melton HE Jr, Pandian NG et al. Detection of acute myocardial infarction in closed-chest dogs by analysis of regional two-dimensional echocardiographic gray-level distributions. Circ Res 1983; 52: 36-44.
21. Hoyt RM, Skorton DJ, Collins SM, Melton HE Jr. Ultrasonic backscatter and collagen in normal ventricular myocardium. Circulation 1984; 69: 775-82.
22. Bello VD, Giorgi D, Viacava P et al. Severe aortic stenosis and myocardial function diagnostic and prognostic usefulness of ultrasonic integrated backscatter analysis. Circulation 2004; 110: 849-55.
23. Rossi Gp, Di Bello V, Ganzaroli C et al. Excess aldosterone is associated with alterations of myocardial texture in primary aldosteronism. Hypertension 2002; 40: 23-27.
24. Williams RI, Masani ND, Buchalter MB, Fraser AG. Abnormal myocardial strain rate in noncompaction of the left ventricle. J Am Soc Echocardiogr 2003; 16:293-96.
25. Greenbaum RA, Ho SY, Gibson DG, Becker AE, Anderson RH. Left ventricular fibre arthitecture in man. Br Heart J 1981; 45: 248-63.
26. Dagdeviren B, Akdemir O, Bolca O, Eren M, Gürlertop Y, Tezel T. Myocardial texture analysis in idiopathic dilated cardiomyopathy: prediction of contractile reserve on dobutamine echocardiography. J Am Soc Echocardiogr 2002; 15: 36-42.
27. Aras D, Tufekcioglu O, Ergun K et al. Clinical features of isolated ventricular noncompaction in adults long-term clinical course, echocardiographic properties, and predictors of left ventricular failure J Card Fail 2006; 12: 726-33.
28. Bennett CE, Freudenberger R. The Current Approach to Diagnosis and Management of Left Ventricular Noncompaction Cardiomyopathy: Review of the Literature. Cardiol Res Pract 2016; 2016: 5172308

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Original Article

Cardiovascular effects of thiopental-sevoflurane compared with thiopental-isoflurane in angora goats undergoing ovariectomy

Ankara keçilerinde ovariektomi operasyonlarında tiopental-sevofluran ile tiopental-isofluran'ın kardiyovasküler sistem üzerine etkilerinin karşılaştırılması

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ABSTRACT

Aim: The purpose of this study was to evaluate the effects of inhalation anaesthetics on cardiovascular functions in 16 healthy female Angora goats undergoing ovariectomy.

Material and Methods: Anaesthesia was induced with thiopental sodium then maintained with isoflurane or sevoflurane in oxygen. Cardiovascular parameters were measured before and at 0, 15th, 30th, 60th and 90th minutes after induction of anaesthesia. Recovery variables including time to extubation, first lift of the head, thoracic recumbency and standing up were also recorded.

Results: The mean induction dose of thiopental was 18.23 ± 3.87 mg / kg. There were no significant differences between groups for heart rate (HR), respiration rate (RR), noninvasive blood pressure and body temperature measured prior to and under anaesthesia. All animals recovered uneventfully in both groups.

Conclusion: There were no statistical differences between groups for their cardiovascular parameters and recovery times although the results of this study showed a rapid recovery time in each parameter for sevoflurane anaesthesia. On the basis of the results, sevoflurane and isoflurane are suitable inhalation anaesthetics in goats.

Keywords: anaesthesia; sevoflurane, isoflurane; angora goat; cardiovascular

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ÖZ

Amaç: Bu çalışmada 16 adet sağlıklı Ankara keçisinin ovarektomi operasyonlarında kullanılan inhalasyon anesteziklerinin kardiyovasküler sistem üzerine etkilerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Anestezinin indüksiyonu tiopental sodyum ile yapılmış ve devamında izofluran ve sevofluran inhalasyon anestezikleri kullanılmıştır. Kardiyovasküler değerler indüksiyondan önce ve indüksiyon sonrası 0. 15. 30. 60 ve 90. dakikalarda kayıt edilmiştir. Ekstubasyon ve kafayı ilk kaldırma zamanı, sternal pozisyona gelme ve ayağa kalkma zamanları uyanma kriterlerini oluşturmuştur.

Bulgular: Tiopental sodyumun ortalama indüksiyon dozu 18.23±3.87 mg/kg olarak belirlenmiştir. Gruplar arasında, anestezi sırasında ve anesteziden önce nabız sayısı, solunum sayısı, noninvaziv tansiyon değerleri ve vücut ısısında farklılık gözlenmemiştir. Tüm hayvanların anesteziden uyanmaları sorunsuz bir şekilde gerçekleşmiştir.

Sonuç: Çalışmanın sonucunda kullanılan anesteziklerin uyanma zamanları ve kardiyovasküler değerler üzerine etkileri arasında istatistiksel olarak farklılık olmadığı tespit edilmiştir. Sevofluran anestezisinde tüm uyanma kriterlerinin daha hızlı şekillendiği görülmüştür. Sonuç olarak her iki anestezik maddeninde keçilerin inhalasyon anestezisinde kullanımının uygun olduğu kanısına varılmıştır.

Anahtar kelimeler: anestezi; sevofluran; isofluran; ankara keçisi kardiyovasküler,

Introduction

Ovariectomy provides many advantages for livestock animals, such as easier handling, prevents pregnancy and also reduce problems related to the estrous cycle. Another purpose of ovariectomy in livestock animals include enhancement of weight gain performance (faster weight gain) and improvement of the carcass quality [1-2]. Sevoflurane and isoflurane are most commonly used inhalant agents for anaesthesia in small ruminants. Sevoflorane is a non-flammable agent that provides rapid induction and recovery from anaesthesia and easy control of the depth of anaesthesia. It has a lower blood/gas partition coefficient and rapid recovery time compared to isoflurane. The cardiovascular effects of these agents are similar. Both agents cause a dose dependent myocardial depression and decrease in arterial blood pressure. At higher doses they affect cardiac output [3-6]. In spontaneously ventilating goats, the heart rate was measured higher during anaesthesia than preanaesthesia [4].

The aim of this study was to determine the effects of thiopental-sevoflurane and thiopental-isoflurane anaesthesia on the cardiovascular system and recovery time in spontaneously ventilating Angora goats undergoing ovariectomy.

Material and Methods

Animals

This research was approved by the Animal Research Local Ethics Committee of Kirikkale University. Sixteen healthy female Angora goats were used in the study. The age of the goats varied between 3 - 6 years and the weight between 39.4 - 49 kg. The goats were randomly allocated into two groups; sevoflurane (n=8) and isoflurane group (n = 8). The animals were considered healthy on the basis of physical examination, complete blood count and serum biochemical analyses. All goats were fed ad libitum with ruminant concentrate and hay. Food was withheld for 18 hours prior to anaesthesia, but water was unrestricted until the time of operation.

Anaesthesia

An intravenous catheter was placed in the auricular vein for induction of anaesthesia and fluid administration. Another catheter was inserted in the auricular artery for measurement of blood pressure (Petaş, KMA 800, Turkey). Anaesthesia was induced with 10 mg/kg initial dose of thiopental sodium (Pental®Sodyum 1g, I.E. Ulagay, Turkey). Additional doses were required to provide adequate depth of anaesthesia. Tracheal intubation was performed after the jaw tone was reduced and there was no lingual response to traction. Anaesthesia was maintained with either isoflurane (Isoflurane-usp®, Adeka, Turkey) (1.5 - 3%) or sevoflurane (Sevorane®, Abbott, UK) (2.5 - 4%) concentration as 100% oxygen at 3 L/min in spontaneously ventilating goats. An orogastric tube was introduced for prevention of tympany. Meloxicam (0.5 mg/kg) (Maxicam, Sanovel, Turkey) was administered intravenously to provide perioperative analgesia. The heart rate (HR), respiratory rate (RR), end-tidal CO2 (EtCO2), and oesophageal temperature were recorded (Petaş, KMA 800, Turkey). All of these parameters

were measured prior to anaesthesia, at induction and 15, 30, 60 and 90 minutes thereafter. All goats kept in dorsal recumbency for the duration of operation and connected to a semi-closed circle rebreathing system (TMS Maxi 2000, Turkey). The fresh gas flow was 3 l/min. Lactated ringer solution (Ringesol, Vilsan, Turkey) was administered at a dose of 10 ml/kg/hr intravenously throughout the anaesthesia. Ovariectomy was performed following a median laparotomy. Recovery times were recorded after surgery. Local ethics committee approved the study and informed consent was obtained from participant(s)

Statistical Analysis

Statistical analyses were performed with commercial software (SPSS Inc., Chicago, IL,USA). Data were reported as median±IQR. Changes in HR, RR, mean arterial blood pressure (MABP), systolic arterial blood pressure (SABP), diastolic arterial blood pressure (DABP) and body temperature and the difference in recovery times between groups were evaluated with analyses of variance (ANOVA). Friedman test was used to compare values within each groups and differences between groups was determined by the Mann-Whitney U test after the test of normality. P value < 0.01 was considered as significant.

Results

The mean dose of thiopental sodium, which was required for intubation, was 18.23 ± 3.87 mg/kg (mean ± SD) in all groups. After administration of thiopental sodium, intubation was performed easily. In one case of the sevoflurane group apnoea occurred after induction that lasted more than 30 seconds. In this case, the intermittent positive pressure ventilation initiated manually and the spontaneous breathing restarted within two minutes. There were no other complications.

There were no significant differences between groups for HR, RR, MABP, SABP, DABP and body temperature measured prior to and under anaesthesia (Table 1).

Table 1. Maintenance data comparing isoflurane and sevoflurane in Angora goats (minutes).

Anaestheticagent	Parameter	Baseline	After Thiopental	5 min	15 min	30 min	60 min	90 min
	HR*	74.00±10	97.50±9	96.00±20	87.50±25	87.50±19	94.00±14	93.00±12
	MABP*	99.00±18	105.00±25	77.00±42	69.00±32	71.50±38	75.00±36	76.50±37
Isoflurane	DABP*	79.00±13	86.00±15	63.50±30	57.00±32	60.50±28	66.50±29	67.00±25
	SABP*	124.00±17	116.00±17	93.50±36	84.00±39	86.00±37	88.50±33	91.00±26
	RR	24.00±3	18.00±4	21.00±7	24.50±15	27.00±17	32.00±16	27.50±15
	Temp*	39.30±0.7	39.20±0.7	39.00±1.0	38.95±0.5	38.70±0.3	38.35±0.4	38.10±0.0
	HR*	75.50±18	97.50±36	95.50±30	88.00±17	85.50±9	91.50±26	89.50±31
	MABP*	100.00±31	81.50±27	63.50±20	76.00±13	71.00±11	72.00±18	69.50±16
Sevoflurane	DABP	75.00±26	69.50±24	50.00±24	64.50±20	63.00±9	59.00±25	62.00±20
	SABP	120.00±38	96.50±33	81.00±17	94.00±19	85.00±26	89.00±25	88.50±15
	RR	24.50±3	16.50±9	18.50±10	29.00±9	30.00±14	29.00±14	26.00±28
	Temp*	39.05±1.3	38.90±1.4	38.50±1.0	38.65±1.3	38.65±1.0	38.45±1.0	39.00±1.0

*Significant change with time within the same group (p<0.01).

All animals recovered uneventfully in both groups. Three goats regurgitated a small amount of gastric content in the isoflurane group during the postoperative period. The recovery time was shorter in sevoflurane than isoflurane group, but these differences were not statistically significant (Table 2).

Table 2. Event variables for goats recovering from isoflurane and sevoflurane anaesthesia (minutes).

Parameter (min.)	Isoflurane	Sevoflurane
Extubation	17.50±9	14.50±4
First lift of the head	25.00±32	22.00±8
Thoracic recumbency	44.00±31	39.50±42
Standing up	60.00±20	54.50±43

Discussion

Administration of any sedative agent is not recommended before induction of anaesthesia in sheep and goats because of regurgitation risks and late recovery time. An anaesthetic agent with short duration of action is recommended to provide calm and rapid induction instead of a sedative drug [7,8]. It was reported that thiopental provides short duration of action time (10 - 20 min.) in goats [9]. In this study, thiopental provides an adequate depth of anaesthesia for intubation, and there were no negative effect during the post-operative recovery.

Prassinos et al. (2005) reported that intubation was accomplished easily 1 minute after thiopental injection. In the present study, thiopental provided a rapid induction and easy intubation.

Thiopental has a wide range of administration dose (7 - 20 mg/kg) without premedication in goats. The initial dose of thiopental was 5 - 7 mg/kg to avoid the side effects. The initial dose applied during 30 seconds to evaluate the effects of the administered dose on the central nervous system [8]. Hikasa et al. (2002) recommended that 14.3 mg/kg thiopental is safe for goats. In a similar study, 8 mg/kg dose of thiopental was caused apnea in two of seven goats [7]. Branson (2007) reported that 8 - 15 mg/kg dose of thiopental sodium provided a sufficient depth of anesthesia for induction in small ruminants. In the present study, we recorded that less than 10 mg/kg of thiopental was not enough for intubation in Angora goats. We found that 18.23 ± 3.27 mg/kg mean dose of thiopental provided sufficient depth of anesthesia to achieve intubation in Angora goats.

Arterial hypoxia was reported after administration of thiopental in small ruminants, and its intensity varies depending on the individual characteristics [7]. In the study reported here, a hundred percent oxygen was given through the endotracheal tube during the study period. Capnography values were in reference limits (≤ 35 mmHg) throughout anaesthesia period except in a goat (≥ 55 mmHg) in which occurred apnea after thiopental injection and resolved within 3 minutes following mechanical ventilation.

Regurgitation is an important complication before tracheal intubation in small ruminants [6,10]. In a study, four of seven goats regurgitated after thiopental anaesthesia [7]. Basis on the result of our study, we suggest that 18.23 mg/kg mean dose of intravenous thiopental administration depresses both swallowing and laryngeal reflex and provides sufficient depth of anaesthesia for tracheal intubation. After administration of thiopental, the incidence of regurgitation in this study was lower compared to a previous study by Prassinos et al. (2005). The low regurgitation rate might have occurred due to the fact that the dose thiopental administered in this study was 2 – 3 times higher compared to that study by Prassinos et al. (2005). The high dose of thiopental administration depressed both laryngeal and swallowing reflex and intubation was easy without any complication and delaying. In our study, regurgitation occurred in three goats during the postoperative period. Active regurgitation in the postoperative period could have been related to surgery or postoperative pain.

It has been reported that thiopental increases the heart rate in goats and dogs [7,11]. In the present study, the heart rate increased after administration of thiopental and remained high throughout anaesthesia.

Isoflurane and sevoflurane increase the heart rate in dogs, goats [3,4,12,13], whereas the heart rate remains unchanged in horses and calves [14,15]. Contrary to dog and goat, the rate generally decreases in cat, sheep and lambs [6,16,18]. In the present study, the heart rate increased after both administration of thiopental and inhalation anesthesia. This condition related with baroreceptor reflex.

MABP, SABP and DABP are increased in dogs and decreased in goats [5,11]. In the present study, it was found that DABP increased slightly while SABP and MABP values were decreased. It could be suggested that SABP and MABP decreased because of the high dosage of thiopental.

Isoflurane and sevoflurane cause a dose dependent decrease in blood pressure, cardiac output and systemic vascular resistance in goats, dog, horse and sheep [3-5,19]. SABP, DABP and MABP values are decreased in dog, horse, goat [12-14]. SABP and DABP values increased under isoflurane and sevoflurane anaesthesia in sheep, but these changes were insignificant between isoflurane and sevoflurane groups [6]. As suggested by Mohamadnia et al. (2008), the reason of this rise in values was associated with painful orthopaedic surgery. In the present study, after the administration of inhalation agents, SABP, DABP and MABP values decreased as early as beginning of the anaesthesia and these values increased within 15 minutes and began to decrease toward to the end of the study. Such a change could be related to the type and severity of surgical manipulations in the ovaries. The DABP values were found nearly to levels of preoperative anaesthetic until end of the operation.

Sevoflurane and isoflurane can cause a dose dependent decrease in RR in dogs, horses, sheep and goats [12-14,19]. In the present study, RR decreased after induction with thiopental but neither isoflurane nor sevoflurane caused significant effects in RR.

In previous studies, the time to standing was shorter for sevoflurane than isoflurane anaesthesia in horse, sheep, calf, lamb, goat and dog [3,4,13,20-22]. It was reported that sheep were extubated in 6.37 and 7.66 minutes when anaesthetized with isoflorane and sevoflurane, respectively [6]. In the present study, extubation time was longer than that study. The reason of rapid recovery time could be associated with painful effects of orthopaedic surgery in the study of Mohamadnia et al. (2008). Recovery times were shorter in sevoflurane group than isoflurane group. It is concluded that sevoflurane could be considered as the first choice drug because of its short recovery time.

In conclusion, 18.23 mg/kg mean dose of thiopental administration is safe for induction of anaesthesia in goats. Sevoflurane and isoflurane are both suitable anaesthetics for the maintenance of general anaesthesia in Angora goats undergoing ovariectomy. The results of the study showed that there are no significant differences between sevoflurane and isoflurane for cardiovascular parameters. The recovery time from anaesthesia with sevoflurane is shorter than isoflurane although the difference is not statistically significant. Sevoflurane could be considered having advantageous to isoflurane because of the rapid recovery times.

References

1. Bleul U, Hollenstein K, Kahn W. Laparascopic ovariectomy in standing cows. Ani Reprod Sci 2005; 90: 193-200.
2. Barros FFPC, Teixeira PPM, Silva MAM et. al. Single-port laparoscopic ovariectomy using a pre-tied loop ligature in Santa Ines ewes. Cienc Rural 2015; 45: 2033-38.
3. Mutoh T, Nishimura R, Kim HY, Matsunaga S, Sasaki N. Cardiopulmonary effects of sevoflurane, compared with halothane, enflurane and isoflurane in dogs. Am J Vet Res 1997; 58: 885-90.
4. Hikasa Y, Hokushin S, Takase K, Ogasawara S. Cardiopulmonary, hematological, serum biochemical and behavioral effects of sevoflurane compared with isoflurane or halothane in spontaneously ventilating goats. Small Rum Res 2002; 43: 167-78.
5. Steffey EP, Mama KR, Brosnan JR. Inhalation anesthetics. In: Grim KA. Lamont LA. Tranquilli WJ. Greene SA. Robertson SA (eds). Lumb and Lones' Veterinary anesthesia and analgesia. 5th ed. USA: Blackwell Publishing; 2007: 297-332.
6. Mohamadnia AR, Hughes G, Clarke KW. Maintenance of anaesthesia in sheep with isoflurane, desflurane or sevoflurane. Vet Rec 2008; 163: 210-15.
7. Prassinos NN, Galatos AD, Raptopoulos D. A comparison of propofol, thiopental or ketamine as induction agents in goats. Vet Anaesth Analg 2005; 32: 289-96.
8. Hall LW, Clarke KW, Trim CM. Anesthesia of sheep, goats and other herbivores. In: Veterinary anaesthesia. 10th ed. China: W. B. Saunders 2001: 341-65.
9. Branson KR. Injectable and alternative anesthetic techniques. In: Tranquilli WJ. Thurmon JC. Grim KA (eds). Lumb and Lones' Veterinary anesthesia and analgesia. 4th ed. USA: Blackwell Publishing 2007: 273-99.
10. Riebold TW. Ruminants. In: Grim KA. Lamont LA. Tranquilli WJ. Greene SA. Robertson SA (eds). Lumb and Lones' Veterinary anesthesia and analgesia. 5th ed. USA: Blackwell Publishing 2007: 912-28.
11. Enouri SS, Kerr CL, McDonell WN, Dyson DH. Cardiopulmonary effects of anesthetic induction with thiopental, propofol, or a combination of ketamine hydrocloride and diazepam in dogs sedated with a combination of medetomidine and hydromorphone. Am J Vet Res 2008; 69: 586-95.
12. Johnson RA, Striler E, Sawyer DC, Brunson DB. Comparison of isoflurane with sevoflurane for anesthesia induction and recovery in adult dogs. Am J Vet Res 1998; 59: 478-81.
13. Kumandaş A, Elma E. Comparison of sevoflurane and isoflurane effects on cardiovascular and respiratory system during spontaneous ventilation in Angora goats. Turkish J Vet An Sci 2015; 39: 501-506.
14. Grosenbaugh DA, Muir WW. Cardiorespiratory effects of sevoflurane, isoflurane and halothane anesthesia in horses. Am J Vet Res 1998; 59: 101-106.
15. Offinger J, Meyer H, Fischer J, Kastner SBR, Piechotta M, Rehage J. Comparision of isoflurane inhalation anaesthesia, injection anaesthesia and high volume caudal epidural anaesthesia for umbilical surgery in calves; metabolic, endocrine and cardiopulmonary effects. Vet Anaesth Analg 2012; 39: 123-36.
16. Brett CM, Teitel DF, Heymann MA, Rudolph AM. The cardiovascular effects of isoflurane in lambs. Anesthesiology 1987; 67: 60-65.
17. Hikasa Y, Ohe N, Takase K, Ogasawara S. Cardiopulmonary effects of sevoflurane in cats: comparison with isoflurane, halothane and enflurane. Res Vet Sci 1997; 63: 205-10.
18. Gençcelep M, Atasoy N, Taş A. The effects of inhalation anesthetics (halothane and isoflurane) on certain clinical and haematological parameters of sheep. Small Rum Res 2004; 53: 157-60.
19. Hikasa Y, Okuyama K, Kakuta T, Takase K, Ogasawara S. Anesthetic potency and cardiopulmonary effects of sevoflurane in goats: comparison with İsoflurane and Halothane. Can J Vet Res 1998; 62: 299-306.
20. Matthews NS, Hartsfield SM, Mercer D, Beleau MH, Mackenthun A. Recovery from sevoflurane anesthesia in horses: comparison to isoflurane and effect of postmedication with xylazine. Vet Surg 1998; 27: 480-85.
21. Vettorato E, Schöffmann G, Burke JG, Gibson AJN, Clutton ER. Clinical effects of isoflurane and sevoflurane in lambs. Vet Anaesth Analg 2012; 39: 495-502.
22. Sellers G, Lin HC, Chamorro MF, Walz PH. Comparison of isoflurane and sevoflurane anesthesia in holstein calves for placement of portal and jugular vein cannulas. Am J An Vet Sci 2013; 8: 1-7.

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Original Article

Ankle brachial index measurement in first-line health care: A simple and inexpensive but very valuable method

Birinci basamak sağlık hizmetinde ayak bileği brakial indeks ölçümü: Basit, ucuz ama çok değerli bir yöntem

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ABSTRACT

Aim: Peripheral arterial disease (PAD) affects more than 30 million people in the World. Ankle Brachial Index (ABI) is a simple method to detect PAD. Patients are referred to vascular surgery department with prediagnosis of PAD, but many of them are mis-diagnosed. The aim of this study was to determine the importance of ABI in first-line health care.

Material and Methods: From December 2017 – November 2018; 108 patients were referred from first-line health care units to our department. Patients were analyzed retrospectively regarding risk factors, ABI and real diagnosis.

Results: 24 patients (22,22%) were diagnosed PAD. Mean ABI in PAD and non-PAD patients was 0.545±0.193 and 0.996±0.093, respectively.

Conclusion: The use of ABI measurement in first-line health care could avoid the mis-diagnosis of PAD and related loss of time and additional costs.

Key words: ankle brachial index; first-line health care; peripheral arterial disease

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ÖZ

Amaç: Periferik arter hastalığı (PAH) dünyada 30 milyondan fazla insanı etkileyen bir hastalıktır. Ayak Bileği Brakiyal İndeksi (ABI), PAH'ı saptamak için basit bir yöntemdir. Hastalar PAH öntanısı ile vasküler cerrahi bölümüne yönlendirilir, ancak çoğunda teşhis doğrulanamamaktadır. Bu çalışmanın amacı, birinci basamak sağlık hizmetlerinde ABI ölçümünün önemini belirlemektir.

Gereç ve Yöntemler: Aralık 2017 – Kasım 2018 tarihlerinde 108 hasta birinci basamak sağlık biriminden bölümümüze yönlendirildi. Tüm hastalar risk faktörleri, ABI ve gerçek tanı ile ilgili olarak retrospektif analiz edildi.

Bulgular: 24 hastada (% 22,22) PAH tanısı doğrulanmıştır. PAH ve PAH olmayan hastalardaki ortalama ABI sırasıyla 0,545±0,193 ve 0,996±0,093 idi.

Sonuç: Birinci basamak sağlık hizmetlerinde ABI ölçümünün kullanılması, PAH'ın yanlış teşhisini ve bununla ilgili zaman kaybını ve ek maliyetleri önleyecektir.

Anahtar kelimeler: ayak bileği brakial indeksi; birinci basamak sağlık hizmeti; periferik arter hastalığı

Introduction

Peripheral arterial disease (PAD) is a disease manifested by constriction or obstruction of the arteries from the abdominal aorta to the distal arteries as a result of progressive atherosclerosis. Peripheral artery disease is an important health problem with increasing incidence. It is estimated that over 30 million people in the world are affected by PAD.

PAD may be asymptomatic or may be seen with atypical symptoms, so there may be skips or delays in the diagnosis, and therefore it is generally estimated to be less than real prevalence [1]. The prevalence of peripheral arterial disease increases with age. The prolongation of life expectancy also led to an increase in prevalence of PAD compared to previous years [1].

Clinical manifestations of peripheral arterial disease are caused by significant obstruction of

vessels. At first, pain in the legs occures when walking (claudicatio intermittens), but later on at rest. Systolic blood pressure ankle-brachial index (ABI) is primarily used in the clinical diagnosis of peripheral arterial disease. The ankle-brachial index is a non-invasive screening method for the general population and shows 95% sensitivity and 99% specificity in PAD's diagnosed by angiography. The ankle-brachial index is considered normal between 1.0 and 1.3. The presence of ABI ≤0.9 is diagnostic for PAD [1]. Highly calcified arteries in diabetes and kidney disease can cause abnormally high ABI values [1]. Low ABI is an important predictor for cardiovascular morbidity and mortality. Table-1 demostrates ABI interpretations. Risk factors for peripheral arterial disease are male gender, advanced age, smoking habit, hyperlipidemia, hypertension, diabetes mellitus and metabolic syndrome [2,3].

Table-1: ABI Interpretation

ABI	
0.9 – 1.3	Normal
<0.9	ischemia
<0.6	Severe ischemia
>1.3	Severe medial calcification

Early diagnosis of PAD is important because of several risky consequences. Asymptomatic patients can be detected by ABI measurement, which is a non-invasive method, and undesirable results can be prevented. Furthermore, it is necessary to know the risk factors of PAD and take precautions for those who can be modified.

ABI is simple and inexpensive and an increase of ABI measurement in first-line healthcare providers would prevent accumulation of patients in vascular surgery clinics, especially of those who are not PAD patients. Based on this idea, the following study was planned.

Material and Methods

Patients with leg pain and prediagnosed as PAD referred to our clinic in the last year (December 2017-November 2018) were evaluated retrospectively. Patients were evaluated in terms of age, gender, history of cardiovascular disease, hypertension, hyperlipidemia, diabetes mellitus, previous cerebrovascular accident, obesity, smoking habit and sedentary life habit. Patients whose ABI value was taken and confirmed by Doppler ultrasonography were included in the study.

Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg or using antihypertensive medication. Patients with total cholesterol-low density lipoprotein ratio over 5 and / or cholesterol-lowering drugs were considered to have hyperlipidemia. The obesity criterion was accepted as a BMI > 26 kg/m2. Local ethics committee approved the study and informed consent was obtained from participant(s)

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Ankle Brachial Index Measurement

Brachial artery (BA) systolic pressure was measured with a sphygmomanometer from both upper extremities in the supine position. In both lower extremities, systolic pressure measurements were taken from both the dorsalis pedis artery (DPA) and posterior tibial artery (PTA) with a 8 MHz vascular portable Doppler device. ABI value was determined with this formula:

$$\text{ABİ} = \frac{\text{Higher value of DPA and PTA systolic pressures}}{\text{Higher value of BA systolic pressure}}$$

Results

108 patients were included in the study. The mean age of these patients was 61.7 ± 9.9 and 94 patients (87.03%) were male. Diagnosis of the patients was confirmed by ABI measurement and Doppler ultrasonography. Accordingly, 24 of 108 patients were diagnosed as peripheral arterial disease (PAD) (22,22%). Eight of these patients underwent surgical or interventional treatment, while the other patients were followed up with medical treatment. The data were examined in two groups, PAD patients and non-PAD patients (non-PAD). Mean age of PAD group was 63.6 ± 7.6 (56-76 years), the mean age was 61.1 ± 10.4 years in the non-PAD group (32-82 years) (p> 0.05) and the male patient ratio was 83.3% in the PAD group and 88.1% in the non-PAD group. Only one patient had a history of stroke (non-PAD group). The rate of patients with a history of cardiovascular disease was significantly higher in the PAD group (33.3% versus 4.7%). The presence of hypertension, diabetes mellitus, smoking habits and sedentary lifestyle were higher in the PAD group, whereas the rate of obesity and hyperlipidemia was higher in the non-PAD group. In the PAD group, the ABI value was 0.545 ± 0.193, and was 0.996 ± 0.093 in the non-PAD group, the difference was statistically significant (p <0.001). The data are demostrated in Table-2.

Tablo 2: Patient Results

	PAD	non-PAD	p
Number	24 (22,22%)	84 (77,78%)	>0.005
ABI	0.545 ± 0.198	0.995 ± 0.093	<0.001
Male (n)	20 (%83.3)	74 (%88.1)	>0.05
Age	63.58 ± 7.81	61.17 ± 10.44	>0.05
Previous cardiovascular disease	4 (%33.3)	2 (%4.7)	<0.05
Hypertension	11 (%91.6)	3 (%7.1)	<0.05
Hyperlipidemia	2 (%16.6)	23 (%54.8)	<0.05
Diabetes mellitus	9 (%75)	15 (%35.7)	<0.05
Stroke	0 (%0)	1 (%2.4)	>0.05
Obesity	1 (%8.3)	8 (%19.0)	<0.05
Smoking habbit	9 (%75)	(25 (%59.5)	<0.05
Sedantery life style	11 (%91.6)	20 (%47.6)	<0.05

Statistical analysis

Statistical analysis was performed using the Windows-based SPSS (Statistical Package for the Social Sciences) 23 statistical package program. For the variables indicated by measurement mean ± standard deviation (X ± SD); for the variables specified by counting the percentage (%) value is calculated. In this study, independent groups which were not distributed normally were evaluated with Mann-Whitney U Test.

Discussion

Most of cardiovascular events have been reported in individuals without any previous clinical signs [4]. In order to prevent these events, it is important to follow people with risk factors to diagnose them early. For this purpose, risk factors such as smoking, HT, total and HDL cholesterol levels and diabetes as well as predictors such as C-reactive protein (CRP) are recommended to be examnined [5]. 72% of PAD patients had coronary artery disease [6]. The measurement of ankle brachial index has also been reported as a method of providing useful information in predicting the risk of cardiovascular disease [5,7]. When peripheral arterial disease is asymptomatic, it can be detected by controlling the lower extremity pulses during physical examination and by ABI measurement. When the ankle-brachial index is <0.9, it is abnormal and indicates PAD [2].

The high ankle-brachial index (> 1.3) was reported to have a role in the diagnosis of peripheral arterial disease because of its sensitivity and specificity and it should be evaluated as PAD [8]. In a study of 1762 patients who presented with vascular disease symptoms, ABI measurements were performed, 64.6% had low, 27% had normal, and 8.4% had high (≥1.3) ABI values. It was observed that the distribution did not show any features in terms of gender, and as the age increased, the prevalence of low ABI values increased. The prevalence of high ABI was not related to age. In the same study, it was emphasized that 62.2% of patients with high ABI had PAD, and the clinical significance of this condition was not clear since those with high ABI values were excluded from the PAD studies [8]. Poredos and Jug [9] reported that 952 patients in the high-risk group of cardiovascular diseases had symptomatic atherosclerosis in 821 (86.2%) and at least two risk factors were present in asymptomatic patients. In the same study, PAD was observed in 42% of patients with coronary artery disease (CAD) and there was no significant difference in risk profile in CAD and PAD groups.

In the United States, at age 40 and above the prevalence of

PAD (ABI <0.9) was 5% and 8.7% for borderline PAD (ABI 0.90-0.99) [9]. The prevalence of PAD at age 60 and above was found to be 12.2% [10]. The prevalence for low-normal ABI values (1.00-1.09) and normal ABI values (1.10-1.29) was reported to be 27.8% and 54.8%, respectively [11]. The prevalence of peripheral arterial disease and borderline PAD increased with age. In the same study, smoking, hypertension, diabetes and obesity were higher in the ABI group. These findings are consistent with the results of this publication except obesity. Obesity was found to be low in the PAD group. In a study that examined 33,629 patients with peripheral arterial disease, it was found that diabetes was associated with 29% and increased all-cause mortality [12]. In this study, the rate of diabetes was significantly higher in the PAD group.

Smoking habit, diabetes, hypertension and hyperlipidemia were positively associated with PAD in people over 40 years of age representing the general population in the United States [13]. In Spain, the prevalence of PAD detected by ABI in the age of 40 and over was found to be 9.7% in women and 11.4% in men [14]. Smoking, hypertension, hypercholesterolemia and diabetes were positively correlated with PAD. More than 91% of patients with peripheral artery disease have at least one of the risk factors for cardiovascular disease [14].

In this study, male gender, history of cardiovascular disease, hypertension, diabetes, smoking habit and sedentary lifestyle seem to be directly related to the presence of PAD. However, hyperlipidemia and obesity were not associated with PAD. The aim of this study was not to determine the risk factors for PAD. To identify risk factors, the number of patients included in the study should be higher. However, the aim of the study was not to determine the risk factors but to evaluate the patients who applied to the family physician or the first-line health providers. All patients were admitted with the complaint of leg pain and were referred to the vascular surgery clinic with a prediagnosis of PAD. PAD was confirmed in 22,22% and 77,78% not, which were suggested to apply to a non-vascular clinic. Since peripheral arterial disease can be asymptomatic or may be seen with atypical symptoms, it may be difficult to diagnose and delays in diagnosis could happen [1], and it may be difficult to establish a correct initial diagnosis for first-line health providers. Antza C. et al. emphasized the importanec of early diagnosis for PAD [15]. Ankle-brachial index measurement is a simple and inexpensive diagnostic method. The spread of this diagnostic method seems to be very useful in making a correct diagnosis. According to a study by Pearson et al., the time required for ABI measurement was 3-11 minutes, on average 5 minutes [16]. The diagnosis of PAD would be confirmed and delay in diagnosis would be prevented, as well as accumulation of non-PAD patients in vascular clinics.

Conclusion

The use of ABI measurement in first-line health care could avoid the mis-diagnosis of PAD and related loss of time and additional costs.

Declaration of conflict of interest

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References

1. Welten GM, Schouten O, Chonchol M, Hoeks SE, Bax JJ, Van Domburg RT, Poldermans D. Prognosis of patients with peripheral arterial disease. J Cardiovasc Surg (Torino). 2009; 50: 109-21.
2. Shammas NW. Epidemiology, classification, and modifiable risk factors of peripheral arterial disease. Vasc Health Risk Manag. 2007; 3: 229-34.
3. Nastasi DR, Smith JR, Moxon JV, Trollope A, Golledge J. Prescription of Pharmacotherapy and the Incidence of Stroke in Patients With Symptoms of Peripheral Artery Disease. Stroke. 2018; 49: 2953-60
4. Gardner AW, Afaq A. Management of lower extremity peripheral arterial disease. J Cardiopulm Rehabil Prev 2008; 28: 349-57.
5. Fowkes FG, Murray GD, Butcher I et al. Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a meta-analysis. JAMA. 2008; 300: 197-208.
6. Królczyk J, Piotrowicz K, Chudek J. Clinical examination of peripheral arterial disease and ankle-brachial index in a nationwide cohort of older subjects: practical implications. Aging Clin Exp Res Dec 2018.
7. Ramos R, Quesada M, Solanas P. Prevalence of symptomatic and asymptomatic peripheral arterial disease and the value of the ankle-brachial index to stratify cardiovascular risk. Eur J Vasc Endovasc Surg 2009; 38: 305-11.
8. Suominen V, Rantanen T, Venermo M, Saarinen J, Salenius J. Prevalence and risk factors of PAD among patients with elevated ABI. Eur J Vasc Endovasc Surg 2008; 35: 709-14.
9. Poredos P, Jug B. The prevalence of peripheral arterial disease in high risk subjects and coronary or cerebrovascular patients. Angiology 2007; 58: 309-15.

10. Ostchega Y, Paulose-Ram R, Dillon CF, Gu Q, Hughes JP. Prevalence of peripheral arterial disease and risk factors in persons aged 60 and older: data from the National Health and Nutrition Examination Survey 1999-2004. J Am Geriatr Soc 2007; 55: 583-89.
11. Menke A, Muntner P, Wildman RP, Dreisbach AW, Raggi P. Relation of borderline peripheral arterial disease to cardiovascular disease risk. Am J Cardiol 2006; 98: 1226-30.
12. Kamalesh M, Shen J. Diabetes and peripheral arterial disease in men: trends in prevalence, mortality, and effect of concomitant coronary disease. Clin Cardiol. 2009; 32: 442-46.
13. Selvin E, Erlinger TP. Prevalence of and risk factors for peripheral arterial disease in the United States: results from the National Health and Nutrition Examination Survey, 1999-2000. Circulation 2004; 110: 738-43.
14. Carbayo JA, Divisón JA, Escribano J. Using ankle-brachial index to detect peripheral arterial disease: prevalence and associated risk factors in a random population sample. Nutr Metab Cardiovasc Dis. 2007; 17: 41-49.
15. Cunha PG, Boutouyrie P, Nilsson PM, Laurent S. Early Vascular Ageing (EVA): Definitions and Clinical Applicability. Curr Hypertens Rev. 2017; 13: 8-15
16. Pearson T, Kukulka G, Rahman ZU. Ankle Brachial Index measurement in primary care setting; How long does it Take? South Med J 2009; 11: 1106-10

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Orjinal Makale

Kronik ürtikerli hastalarda troid otoimmünitesi ve artmış nötrofil lenfosit oranı

Thyroid autoimmunity and increased neutrophil lymphocyte ratio in patients with chronic urticaria

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ÖZ

Amaç: Kronik ürtikerin (KÜ) etyopatogenezi henüz net değildir. Ancak otoimmünitenin ve inflamasyonun rol oynadığı yapılan çalışmalarda gösterilmiştir. Bu çalışmamızda KÜ'li hastalarda tiroid otoimmünitesinin saptanması, hastalık şiddetiyle ilişkisinin araştırılması ve inflamatuar belirteçler olan nötrofil lenfosit oranı (NLO), eosinofil lenfosit oranı (ELO) ve monosit lenfosit oranlarının (MLO) kontrol grup ile karşılaştırılması amaçlanmıştır.

Gereç ve Yöntemler: Erişkin allerji-immünoloji polikliniğinde KÜ nedeniyle takip edilen hastaların kayıtları geriye dönük olarak incelendi. Çalışmaya 100 KÜ'li hasta ve kontrol grubu olarak 100 sağlıklı birey alındı. KÜ'li hastaların demografik verileri, yedi günlük ürtikeryal aktivite skorları (UAS 7), kullandığı ilaçlar, laboratuar verilerinden anti-tiroglobülin (anti-Tg) ve anti-tiroid peroksidaz (anti-Tpo), antinükleer antikor (ANA) sonuçları ve kan sayımı parametreleri kayıt edildi. Kontrol grubu olarak yaş ve cinsiyet uyumlu sağlıklı bireylerin kan sayımı parametreleri kayıt edildi.

Bulgular: KÜ hastalarda anti-Tpo % 19 hastada pozitif iken, anti-Tg % 8, ANA % 17 hastada pozitif idi. KÜ hastalar UAS 7'ye göre hafif, orta ve şiddetli olarak, gruplara ayrılarak değerlendirildiğinde, gruplar arası anti-Tpo, anti-Tg ve ANA sonuçları açısından fark saptanmadı (p>0,05). KÜ hastalar ve kontrol grupları arasında NLO, MLO ve ELO kıyaslandığında, NLO ve MLO istatistiksel olarak anlamlı yüksek tespit edilirken (p=0,028, p=0,001, sırasıyla) ELO açısından istatistiksel olarak anlamlı fark yoktu (p=0,094). KÜ'li hastalarda NLO, MLO ve ELO değerleri anti-Tpo, anti-Tg ve ANA pozitif ve negatif olan gruplar arasında kıyaslandığında anlamlı fark saptanmadı (p>0,05).

Sonuç: KÜ'de otoimmünitenin ve inflamasyonun önemi yapılan çalışmalarda gösterilmişti. Ek olarak bu çalışmada hastalık aktivitesi ile tiroid otoimmünitesi arasında ilişki saptanmazken inflamatuar bir belirteç olan NLO'ya ek olarak MLO da yüksek olarak tespit edildi.

Anahtar kelimeler: Kronik ürtiker; tiroid otoimmünitesi; nötrofil lenfosit oranı; monosit lenfosit oranı, eosinofil lenfosit oranı; ürtikerde otoimmünite

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ABSTRACT

Aim: The etiopathogenesis of chronic urticaria (CU) is not clear yet. However, it has been shown that autoimmunity and inflammation play important roles in most of the studies. In this study, we aimed to determine the prevalence of thyroid autoimmunity in patients with CU and to investigate the relationship between the severity of the disease and thyroid autoimmunity. and also we aimed to compare the neutrophil lymphocyte ratio (NLR), eosinophil lymphocyte ratio (ELR) and monocyte lymphocyte ratio (MLR) which are inflammatory markers between the CU group and the control group.

Material and Methods: Medical records of CU patients who were followed in adult allergy-immunology policlinic were retrospectively analyzed. A total of 100 patients with CU and 100 healthy subjects were included in the study. Patients' demographic datas, seven-day urticarial activity scores (UAS 7), drugs that were used, anti-thyroglobulin (anti-Tg) and anti-thyroid peroxidase (anti-Tpo), anti-nuclear antibody (ANA) and blood count parameters as laboratory data were recorded. As control group blood count parameters of healthy individuals that age and gender-matched were recorded.

Results: Anti-Tpo was positive in 19%, anti-Tpo was positive in 8% and ANA was positive in 17% of the patients with CU. When we divided patients with CU according to UAS 7 into three groups as mild, moderate and severe, there were no significant difference between the groups as anti-Tpo, anti-Tg and ANA results ($p>0.05$). When we compare NLR, MLR and ELR parameters between the patients and healthy group,we found that NLR and MLR parameters were statistically significant higher in patients groups ($P=0.028$, $p=0.001$, respectively) but there was no difference between the groups as ELR parameter ($p=0,094$). When we classified patients with CU as anti-Tpo, anti-Tg and ANA positive and negative, there were no significant differences between the groups as NLR, MLR and ELR results ($p>0.05$).

Conclusion: The importance of autoimmunity and inflammation in CU has been shown in studies. In addition, in this study the relationship between the disease activity of urticaria and the thyroid autoimmunity was not determined but the NLR and MLR parameters were found higher in CU as inflammatory markers.

Keywords: Chronic urticaria; thyroid autoimmunity; neutrophil lymphocyte ratio; monocyte-lymphocyte ratio; eosinophil lymphocyte ratio; autoimmunity in urticaria

Giriş

Ürtiker tüm toplumlarda sık görülen ve aniden ortaya çıkıp 1-24 sa içinde kendiliğinden kaybolan kaşıntılı ve farklı boyutlarda ödemli plaklar ile karakterize bir deri hastalığıdır. Cilt lezyonlarının 6 haftadan uzun sürdüğünde kronik ürtiker (KÜ) olarak tanımlanmaktadır [1]. Genel popülasyonda prevelansının %0,5 den %5' e kadar değiştiği bildirilmekte olup, önemli bir sağlık sorunudur [2].

KÜ etiyolojisinde sorumlu tutulan birçok neden vardır. Başlıca spontan ve uyarılabilir ürtiker olarak iki ana gruba ayrılmaktadır [1].Uyarılabilir ürtikerde neden çoğunlukla bellidir. Spontan ürtiker etiyolojisinde ise ilaçlar, gıdalar, gıda katkı maddeleri, enfeksiyonlar ve parazitik enfestasyonlar, allerjenler, otoimmünite, maligniteler ve diğer dermatolojik hastalıklar, psikolojik faktörler yer alsa da çoğu hastada etyoloji saptanamamaktadır [3,4]. Nötrofil lenfosit oranı (NLO), platelet lenfosit oranı gibi inflamatuar göstergelerin hastalık aktivitesi ve prognozla ilişkisi bir çok dermatolojik hastalıklarda gösterilmiştir [5,6].

Bu çalışmada KÜ'li hastalarda tiroid otoimmünitesi sıklığının saptanması, tiroid otoimmünitesinin hastalık şiddetiyle ilişkisinin araştırılması ve inflamatuar belirteçler olan NLO, eosinofil lenfosit (ELO) ve monosit lenfosit oranlarının (MLO) kontrol grup ile karşılaştırılması amaçlanmıştır.

Gereç ve Yöntemler

Hasta seçimi

Dr. Ersin Arslan Eğitim ve Araştırma Hastanesi erişkin Allerji-İmmünoloji polikliniğinde, 2018 yılında KÜ nedeniyle takip edilen 100 erişkin hasta çalışmaya dahil edildi. Bu hastaların tanısı EAACI/GA2LEN/EDF/WAO ürtiker klavuzuna göre, kaşıntılı ve ödemli papül/plaklarla veya anjioödem ile ya da her ikisinin birden gelişimiyle kendini gösteren lezyonların hastalarda altı haftadan daha uzun süreli görülmesi ile konuldu [1]. Fiziksel ürtikeri olanlar çalışma dışı bırakıldı. Hastalara ait demografik, klinik ve laboratuar verileri otomasyon sistemine kayıtlı hasta dosyalarından geriye dönük olarak taranarak elde edildi. Aktif enfeksiyonu olanlar ve tiroid uyarıcı hormonu normal sınırlarda olmayanlar çalışma dışı bırakıldı. Hastaların dosyalarından cinsiyet, yaş, hastalık süresi, kullandığı ilaçlar, ek hastalıkları olup olmadığı, yedi günlük ürtikeryal aktivite skorları (UAS 7) kayıt edildi. Laboratuar verisi

olarak serum anti-tiroglobülin (anti-Tg) ve anti-tiroid peroksidaz (anti-Tpo), antinükleer antikor (ANA) sonuçları ve kan sayımı parametrelerinden nötrofil, eosinofil, lenfosit, monosit değerleri kayıt edildi. Hastalık şiddetinin değerlendirilmesinde Türkiye Ürtiker Tanı ve Tedavi Klavuzunda belirtildiği şekilde hasta tarafından günlük olarak kabarıklık sayısını (0-3 puan) ve kaşıntı şiddetinin (0-3 puan) belirtilmesine dayanan bir skorlama olan UAS'ın yedi gün süresince hesaplanması sonucu bulunan UAS 7 kullanıldı. UAS 7 skoruna göre (minimum 0-maksimum 42) ≤6 iyi kontrollü, 7-15 arası olması hafif, 16-27 arası olması orta ve 28-42 olması ise şiddetli ürtiker olarak değerlendirildi. Kontrol grubu olarak hasta grubu ile yaş ve cinsiyet olarak uyumlu 100 sağlıklı kişinin kan sayımı sonuçları kayıt edildi. Çalışma için yerel etik kurul onayı alındı. Hasta onam formları imzalatıldı.

İstatistiksel Analiz

Araştırma verilerinin istatistiksel analizlerinde tanımlayıcı istatistikler kısmında kategorik değişkenler sayı, yüzde verilerek, sürekli değişkenler ise ortalama ± standart sapma ve ortanca (minimum-maksimum) ile sunulmuştur. Sürekli değişkenlerin normal dağılıma uygunluğu görsel (histogram ve olasılık grafikleri) ve analitik yöntemler (Kolmogorov-Smirnov/Shapiro-Wilk testleri) kullanılarak değerlendirilmiştir. Yapılan normallik analizleri sonucu sürekli değişkenlere ait verilerin normal dağılmadığı saptanmıştır. Normal dağılıma uymayan bu verilerin, iki grup arasındaki karşılaştırma analizleri için Mann-Whitney U testi, 3 grup arasındaki karşılaştırma analizleri için Kruskal Wallis testi kullanılmıştır. Bazı sürekli değişkenler arasındaki ilişki Sperman korelasyon testi ile değerlendirilmiştir. Bağımsız gruplar arasında kategorik değişkenler için yapılan karşılaştırma analizinde Pearson ki-kare testi kullanılmıştır. Bu çalışmada istatistik anlamlılık seviyesi p<0,05 olarak kabul edilmiştir.

Bulgular

Çalışmaya alınan 100 KÜ'li hastanın %69 u kadın olup yaş ortalaması 38,2+/-13,7 idi. İlk başvuru anında hastaların % 45'inin hastalık şiddeti hafif, % 41 hastanın orta, % 14 hastanınki şiddetli idi. KÜ hastalarda anti-Tpo % 19 hastada pozitif iken, anti-Tg % 8, ANA %17 hastada pozitif idi. Hastalar semptomlarına göre hafif, orta ve şiddetli olarak 3 gruba ayrılarak anti-Tpo, anti-Tg ve ANA pozitifliği açısından değerlendirildi. İstatistiksel olarak anlamlı fark saptanmadı. (Tablo 1). Spearman korelasyon testi ile de değerlendirme yapıldı ancak hastalık şiddeti ile anti-Tpo ve anti-Tg arasında istatistiksel olarak anlamlı bir ilişki saptanmadı (r=0,195; p=0,052 ve r=0,178; p=0,076).

Tablo 1. Kronik ürtikerli hastalarda, hastalık şiddetine göre anti-Tpo, anti-Tg ve ANA parametrelerinin değerlendirilmesi

Parametreler	Hafif ürtiker n=45 (%45,0)	Orta ürtiker n=41 (%41,0)	Şiddetli ürtiker n=14 (%14,0)	P değeri
Anti-Tpo, n (%)*				
Negatif	38 (84,4)	33 (80,5)	10 (71,4)	0,552[1]
Pozitif	7 (15,6)	8 (19,5)	4 (28,6)	
Anti-Tg, n (%)				
Negatif	41 (91,1)	37 (90,2)	14 (100)	AUD
Pozitif	4 (8,9)	4 (9,8)	0	
ANA, n (%)				
Negatif	36 (80,0)	35 (85,4)	12 (85,7)	0,770[1]
Pozitif	9 (20,0)	6 (14,6)	2 (14,3)	

*Sütun yüzdesi, 1Pearson Ki-kare testi, AUD; veriler analize uygun değil

KÜ'li hastalarla kontrol grubu arasında ELO, MLO, NLO değerleri karşılaştırıldı. İki grup arasında NLO ve MLO değerleri arasında anlamlı fark saptanırken (p=0,028, p=0,001, sırasıyla), ELO açısından istatistiksel olarak anlamlı fark yoktu (p=0,094) (Tablo 2). Hastalık şiddeti ile ELO, MLO ve NLO değerleri arasında da istatistiksel anlamlı ilişki saptanmamıştır (Spearman korelasyon testi r=0,069;p=0,497, r=0,099;p=0,327 ve r=0,122;p=0,225, sırasıyla).

Tablo 2. Kronik ürtiker ve kontrol grubunda eosinofil / lenfosit, monosit / lenfosit, nötrofil / lenfosit parametleri

Parametreler	Kronik Ürtiker n=100 (%50,0)	Kontrol n=100 (%50,0)	P değeri
Cinsiyet, n (%)			
Kadın	69 (69,0)	71 (71,0)	0,7581
Erkek	31 (31,0)	29 (29,0)	
Yaş (yıl)			
Ortalama±ss	38,24±13,71	39,44±12,81	0,3722
Ortanca(min-mak)	35,5 (18,0-74,0)	37,5 (19,0-76,0)	
Eosinofil/Lenfosit			
Ortalama±ss	0,07±0,07	0,06±0,05	0,0942
Ortanca(min-mak)	0,05 (0-0,37)	0,06 (0-21,0)	
Monosit/Lenfosit			
Ortalama±ss	0,27±0,13	0,18±0,07	0,0012
Ortanca(min-mak)	0,23 (0,09-1,14)	0,17 (0,06-0,51)	
Nötrofil/Lenfosit			
Ortalama±ss	2,29±1,24	1,88±0,69	0,0282
Ortanca(min-mak)	1,96 (0,72-9,51)	1,75 (0,75-3,68)	

[1]Pearson Ki-kare testi, [2]Mann Whitney U testi

KÜ'li grupta ELO, MLO, NLO değerleri hastalık şiddetine, anti-Tpo, anti-Tg ve ANA sonuçlarına göre değerlendirildi. Ancak gruplar arasında istatistiksel olarak anlamlı fark saptanmadı (p>0,05) (Tablo 3).

Tablo 3. Kronik Ürtiker hastalarının gruplar arasında ELO, MLO ve NLO oranlarının değerlendirilmesi

	Parametreler	Ortalama±ss	Ortanca(min-mak)	P
Eozinofil/Lenfosit Oranı	Hastalık Şiddeti Hafif (n=45) Orta (n=41) Şiddetli (n=14)	 0,07±0,06 0,09±0,05 0,07±0,05	 0,05(0-0,30) 0,05(0,01-0,37) 0,06(0,01-0,16)	0,6491
	Anti-Tpo Negatif (n=81) Pozitif(n=19)	 0,07±0,07 0,07±0,07	 0,05(0-0,37) 0,04(0,01-0,26)	0,3272
	Anti-Tg Negatif (n=92) Pozitif(n=8)	0,07±0,06 0,12±0,12	0,05(0-0,37) 0,06(0,01-0,30)	0,5092
	ANA Negatif (n=83) Pozitif(n=17)	 0,08±0,06 0,06±0,08	 0,06(0-0,30) 0,04(0,01-0,37)	0,0552
Monosit/Lenfosit Oranı	Hastalık Şiddeti Hafif (n=45) Orta (n=41) Şiddetli (n=14)	 0,26±0,10 0,25±0,10 0,34±0,24	 0,23(0,16-0,56) 0,22(0,09-0,66) 0,30(0,16-1,14)	0,3321
	Anti-Tpo Negatif (n=81) Pozitif(n=19)	 0,25±0,09 0,33±0,24	 0,23(0,11-0,56) 0,27(0,09-1,14)	0,3192
	Anti-Tg Negatif (n=92) Pozitif(n=8)	 0,27±0,13 0,31±0,15	 0,23(0,09-1,14) 0,26(0,19-0,66)	0,3092
	ANA Negatif (n=83) Pozitif(n=17)	 0,26±0,13 0,30±0,13	 0,23(0,09-1,14) 0,25(0,17-0,56)	0,2752
Nötrofil/Lenfosit Oranı	Hastalık Şiddeti Hafif (n=45) Orta (n=41) Şiddetli (n=14)	 2,33±1,47 2,09±0,83 2,77±1,34	 1,81(0,93-9,51) 1,85(0,72-4,19) 2,34(1,30-5,95)	0,1811
	Anti-Tpo Negatif (n=81) Pozitif(n=19)	 2,20±1,18 2,69±1,41	 1,81(0,72-9,51) 2,08(1,30-5,95)	0,1532
	Anti-Tg Negatif (n=92) Pozitif(n=8)	 2,33±1,27 1,85±0,55	 1,99(0,72-9,51) 1,56(1,38-3,00)	0,3542
	ANA Negatif (n=83) Pozitif(n=17)	 2,27±1,30 2,44±0,88	 1,95(0,72-9,51) 2,80(1,23-3,78)	0,1972

1Kruskal Wallis testi, 2Mann Whitney U testi

Tartışma

KÜ etyopatogenezi henüz net olmamakla birlikte, hastalığın değerlendirilmesinde klavuzlara göre UAS ile şiddetinin değerlendirilmesi önerilmekte iken ek olarak etyolojiye yönelik tam kan sayımı, CRP, eritrosit sedimantasyon hızı bakılması, hastanın öyküsüne göre diğer ayrıntılı tetkiklerin yapılması gerektiği belirtilmiştir [3]. Bizim hasta grubumuzda da etyolojiyi saptamaya yönelik yapılan tetkiklerde otoantikorlardan anti-Tpo % 19 hastada pozitif iken, anti-Tg % 8, ANA %17, toplamda 100 hastanın 37'sinde bu belirteçlerden en az biri pozitif olarak tespit edildi. Ancak hastalık şiddeti ile ilişkisi tespit edilemedi. Yapılan bir çok çalışmada ürtikerin otoimmün ilişkisi ortaya konulmuştur [7] ve bu hastalık gruplarından en sık olarak da tiroid hastalıklarının eşlik ettiği bildirilmiştir.

Literatüre baktığımızda Akarsu ve arkadaşları KÜ'li 146 hastanın %9,6 sında anti-tiroid peroksidaz, %4,8'inde anti-tiroglobulini pozitif bulmuşlardır [8]. Angulo ve ark. 343 KÜ'li hasta ve 282 sağlıklı gönüllüleri karşılaştırdıkları çalışmalarında KÜ'li hastalarda anti-Tpo %20.4, anti-Tg %15,2 olarak saptamışlar ve kontrol grubu ile kıyasladıklarında anlamlı ölçüde yükseklik tespit etmişler ($p<0.001$) [9]. Cebeci ve ark. yaptıkları çalışmalarında otoimmün tiroidi KÜ hastalarında %44,2 oranında bulmuşlardır [10]. Haliloviç ve ark KÜ li hastalarda anti-Tg'i % 23, anti-TPO % 30 hastada pozitif tespit etmişken, kontrol grubunda 2 kişide (%2,86) pozitif tiroid otoimmünitesi saptamışlar ve iki grubu kıyaslayınca istatistiksel olarak anlamlı ölçüde KÜ'li grupta yükseklik tespit etmişlerdir [11]. Ancak farklı olarak Ülker ve ark. yaptıkları çalışmada 77 KÜ'li hasta ve kontrol grubunda anti-TPO ve anti-TG düzeyleri karşılaştırmışlar ancak her iki grup arasında anlamlı farklılık saptamamışlardır [12].

Bu çalışmada KÜ'li hastalarla kontrol grubu ELO, MLO, NLO değerleri karşılaştırıldığında iki grup arasında NLO ve MLO değerleri arasında anlamlı fark saptanırken ELO açısından istatistiksel olarak anlamlı fark saptanmadı. Ek olarak KÜ'li grupta ELO, MLO, NLO değerleri hastalık şiddetine, anti-Tpo, anti-Tg ve ANA sonuçlarına göre değerlendirildi. Ancak gruplar arasında istatistiksel olarak anlamlı fark saptanmadı. Saraç ve ark. ürtikerde yapmış oldukları çalışmalarında NLO değerini akut ürtiker, kronik ürtiker ve kontrol grupları arasında kıyaslamışlar ve anlamlı fark bulmuşlar ($p<0,001$) ancak KÜ de hastalık süresi 90 gün altı ve üstü olan hasta gruplarını karşılaştırınca anlamlı fark bulmamışlardır [13]. Karabay ve arkadaşları NLO ve CRP düzeylerini KÜ hastalarında sağlıklı kontrollere göre anlamlı olarak daha yüksek saptamışlar ($p<0,001$) ancak hastalık şiddeti ile bu değerler arasında bu çalışmada olduğu gibi bir ilişki saptamamışlardır [14].

Sonuç

KÜ'in etyopatogenezi tam aydınlatılamamış olsa da, otoimmünitenin de rol oynadığı ve inflamasyonun da mevcut olduğu bir hastalık olduğu bilinmektedir. Bu çalışmada da literatür ile uyumlu sonuçlar bulunmuştur. Ancak KÜ de hastalık şiddetini etkileyen faktörler üzerine ve inflamatuar

bir belirteç olduğu kanıtlanmış olan NLO değerinin KÜ'de yeri üzerine daha fazla sayıda çalışmaya ihtiyaç vardır.

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Kaynaklar

1. Zuberbier T, Aberer W, Asero R et al. The EAACI/GA2LEN/EDF/WAO guide¬line for the definition, classification, diagnosis and management of urti¬caria. Allergy 2018; 73: 1393-414.
2. Bernstein JA, Lang DM, Khan DA et al. The diagnosis and management of acute and chronic urticaria: 2014 update. J Allergy Clin Immunol 2014; 133: 1270-77.
3. Kocatürk Göncü E, Aktan Ş, Atakan N et al. Türkiye Ürtiker Tanı ve Tedavi Kılavuzu-2016. Turkderm – Arch Turk Dermatol Venerology 2016; 50: 82-98.
4. Tat TS. Higher Levels of Depression and Anxiety in Patients with Chronic Urticaria. Med Sci Monit 2019; 25: 115-20.
5. Ozturk C, Balta S, Balta I et al. Neutrophil–lymphocyte ratio and carotid-intima media thickness in patients with Behcet disease without cardiovascular involvement. Angiology 2014; 66: 291-96.
6. Ma J, Kuzman J, Ray A et al. Neutrophil-to-lymphocyte Ratio (NLR) as a predictor for recurrence in patients with stage III melanoma. Sci Rep 2018; 8: 4044.
7. Antia C, Baquerizo K, Korman A, Bernstein JA, Alikhan A. Urticaria: A comprehensive review: Epidemiology, diagnosis, andwork-up. J Am Acad Dermatol 2018; 79: 599-614.
8. Akarsu S, Ilknur T, Özbagçıvan Ö, Fetil E. Kronik spontan ürtiker ve ürtikeryal vaskülitli olgulardaki eşlik eden durumlar: Retrospektif bir çalışmanın sonuçları. Türkderm 2015; 49: 18-24.
9. Díaz-Angulo S, López-Hoyos M, MuñozCacho P, Fernández M, López-Escobar M, Rodríguez F, González-López MA. Prevalence of thyroid autoimmunity in spanish patients with chronic idiopathic urticaria: a case-controlstudy involving 343 subjects. J Eur Acad Dermatol Venereol 2016; 30: 692-93.
10. Cebeci F, Tanrikut A, Topcu E et al. Association between chronic urticaria And thyroid autoimmunity. Eur J Dermatol 2006; 16: 402-5.
11. Kasumagic-Halilovic E, Beslic N, Ovcina-Kurtovic N. Thyroid Autoimmunity in Patients with Chronic Urticaria. Med Arch 2017; 71: 29-31.
12. Gül Ü, Çakmak S, Gönül M, Soylu S, Kılıç A. Kronik ürtikerde tiroid fonksiyon testleri ve tiroid otoantikorları istenmeli mi? Asthma Allergy Immunol 2009; 7: 39-43.
13. Saraç G, Mantar İ, Sener S, Cenk H, Kapicioglu Y. Assessment of change in neutrophil-lymphocyte ratio, platelet-lymphocyteratio in patients with acute and chronic urticaria.J Tugut Ozal Med Cent 2018; 25: 719-22.
14. Karabay EA, Çerman AA, Altunay İK. Serum C-reactive protein, neutrophil-lymphocyte ratio and uric acid levels in chronic spontaneous urticaria. Turkiye Klin J Dermatology 2016; 26: 125-31.

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Original Article

Long-term follow-up of non-diabetic obese children and adolescents treated with metformin

Metformin ile tedavi edilen non-diyabetik obez çocuk ve adolesanların uzun sureli izlemi

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ABSTRACT

Aim: Childhood obesity is an important public health problem with increasing prevalence. Type 2 diabetes mellitus(T2DM) is strongly associated with obesity and metabolic syndrome. Adressing obesity and insulin resistance by drug treatment represents a rational strategy for the prevention of T2DM. The aim of our study was to evaluate the one year metformin treatment'slong-term effectiveness in children and adolescent.

Material and Methods: Patients who were diagnosed with obesity (VKİ>+2 SDS) and found to have insulin resistance (total insulin at OGTT >300 mIU/ml and homa-IR >3.4)and other obesity co-morbidities, aged between 10-18 years, treated with metformin in addition to lifestyle change for a year and with regular follow-up for a minimum of 2 years after metformin treatmentin our clinic were included inthe study.

Results: A total of 12 cases including 8 girls with a mean age of 13.2±2.1 years and mean follow-up duration of 3.9±1 years were included in the study. While the body mass index (BMI) of the cases at presentation was 31.2±5.6 kg/m2 and BMI-SDS was 2.7±0.7, the BMI-SDS value after one year of metformin treatment was found to have regressed to 1.9±1 (p:0.04), and the BMI-SDS value two years after the interruption of metformin treatment had increased to 2.1±1.04 but was not as high as the period before metformin treatment (p:0.033).

Conclusion: One-year metformin treatment improved the BMI SDS and homa-IR values of the obese children and this improvement decreased but continued in the second year after the discontinuation of the treatment.

Keywords: obesity; insulin resistance; childhood

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ÖZ

Amaç: Çocukluk döneminde obezite artan sıklıkla izlenen önemli bir halk sağlığı problemidir. Tip 2 Diyabetes mellitus (T2DM) obezite ve metabolik sendrom ile güçlü ilişki içindedir. Tip 2 DM 'nin önlenmesi için obezite ve insulin direncini hedef alan ilaç tedavileri rasyonel bir strateji olarak görülmektedir. Çalışmamızın amacı bir yıl süre ile metformin tedavisi alan çocuk ve adolesanlarda bu tedavinin uzun dönem etkinliğini değerlendirmektir.

Gereç ve Yöntemler: Kliniğimizde obezite (VKI>+ 2SDS) tanısı alan ve insulin direnci olan (OGTT'de total insulin düzeyi >300 mIU/ml ve homa IR >3,4) ve diğer obezite ilişkili komorbiditeleri bulunan, yaşları 10-18 arası değişen, yaşam tarzı değişikliği ile birlikte bir yıl süre ile metformin tedavisi alan ve ardından en az iki yıl süre ile takip edilen hastalar dahil edildi.

Bulgular: Çalışmaya 8' i kız , ortalama yaşı 13,2±2,1 yıl olan ve ortalama izlem süresi 3,9±1 yıl olan toplam 12 dahil edildi. Başlangıçta olguların vücut kitle indeksi (VKİ) 31,2±5,6 kg/m2 ve VKİ-SDS'i 2,7±0,7 iken bir yıllık metformin tedavisi ile VKİ-SDS'inin 1,9±1 (p:0,04) ' e gerilediği, iki yıl süre ile metformin tedavisi kesilen olguların VKİ-SDS' inin 2,1±1,04 (p:0,033)' e yükseldiği ancak metformin tedavisi öncesi kadar yüksek olmadığı görüldü.

Sonuç: Bir yıllık metformin tedavisinin obez çocuk ve adolesanlarda VKİ-SDS ve Homa-IR değerlerinde düzelme sağladığı, bu düzelmenin tedavi kesiminden sonraki ikinci yılda da azalmakla birlikte devam ettiği saptandı.

Anahtar kelimeler: obezite; insülin direnci; çocukluk dönemi

Introduction

Obesity is currently the leading topic of discussion related to child health due to its increasing prevalence and the low treatment success rate [1]. More than 20% of the children living in the USA, Europe, Australia and East Mediterranean are overweight or obese [2]. An increase was found in almost all countries in a study evaluating the changes in obesity prevalence worldwide between 1980 and 2005 in school-age children from 25 countries and pre-school age children from 42 countries [3].

A significant increase in insulin resistance was observed in children and adolescents simultaneous with the increase in obesity incidence in childhood. A relationship is known to be present between insulin resistance and obesity and the obesity-related metabolic and cardiovascular problems. Therefore, the treatment of children and adolescents with insulin resistance in the early stages is important. Patients who are not treated progress to type 2 diabetes mellitus (T2DM), and atherosclerosis develops at an early stage [2].

Lifestyle change is the treatment strategy to be used first in the treatment of obesity and obesity-related complications[4]. Data obtained from a large number of studies show that changes made in the lifestyle enables weight loss, increases insulin sensitivity and decreases the risk of T2DM development. However, results of lifestyle changes can be disappointing in the long term and the obesity and T2DM incidences continue to increase [5]. Pharmacologic agents that will prevent T2DM by preventing obesity and insulin resistance in obese children and adolescents are therefore required. Park et al published a meta-analysis evaluating the efficiency of metformin treatment in obese children without a T2DM diagnosis in 2009. They concluded that metformin treatment reduced the body mass index (BMI) and decreased the homeostasis model assessment of insulin resistance (homa-IR) score [6]. Other studies evaluating the effect of metformin have been published after this study [7-15]. However, the effectiveness and safety of metformin in obese children with a normal glucose metabolism is still contradictory. There is also no study reporting long-term follow-up after treatment.

The aim of our study was to evaluate the effectiveness of long-term metformin treatment in children and adolescent patients who were treated with metformin for a year in addition to lifestyle changes.

Material and Methods

Patients who were diagnosed with obesity at Clinics of Pediatric Endocrinology, Health Sciences University, Dr Sami Ulus Obstetrics and Gynecology, Children's Health and Disease, Health Implementation and Research Center were screened retrospectively. The diagnosis of obesity was made with a body weight over +2 SD of the body weight for age and gender. Patients who had undergone an oral glucose tolerance test (OGTT) and found to have insulin resistance (total insulin at OGTT>300 mIU/ml and homa-IR>3.4). In this patients,obesity

related problems such as abnormal liver function test and/or fatty liver, hypertension, dyslipidemia, metabolic syndrome (according to WHO criteria) were present. Patients whose aged between 10 and 18 years, and treated with 2*425 mg (total 850 mg/day)metformin bd in addition to lifestyle change for a year were included in the study. The study group consisted of 12 cases without a T2DM diagnosis or additional medical problems, who had no previous history of drug use for insulin resistance or drug use that could cause obesity, and with regular follow-up for a minimum of two years after metformin treatment of one year. Fasting glucose and fasting insulin level were used to measure the homa-IR value of the cases during the follow-up. Anthropometric measurements, fasting blood sugar, insulin values, hba1c, homa-IR, results and the changes in these parameters during follow-up were recorded. Local ethics committee approved the study and informed consent was obtained from participant(s)

Results

A total of 12 cases including 8 girls with a mean age of 13.2±2.1 years and mean follow-up duration of 3.9±1 years were included in the study. While the body mass index (BMI) of the cases at presentation was 31.2±5.6 kg/m2 and BMI-SDS was 2.7±0.7, the BMI-SDS value after one year of metformin treatment was found to have regressed to 1.9±1 (p:0.04), and the BMI-SDS value two years after the interruption of metformin treatment had increased to 2.1±1.04 but was not as high as the period before metformin treatment (p:0.033). The mean homa-IR value measured at the beginning was 4.8±1.66 and was found to have regressed to 2.5±1.5at the end of the 1st year (p:0.008). Although it increased to 3.5±1.6 2 years after the interruption of metformin treatment, it was still lower than the homa-IR value before metformin treatment was started (p:0.021). Table 1 presents the anthropometric measurements, fasting blood sugar, insulin, hba1c, homa-IR at the first year of the treatment, and one year and two years after the discontinuation of metformin.

Only one case had symptoms related to the gastrointestinal system during metformin treatment but these symptoms regressed rapidly. No serious side effects that could cause drug discontinuation were observed.

Table 1. Anthropometric measurements, fasting blood sugar, insulin, Hba1C, homa-IR results and evaluated with these parameters of the cases before metformin, at the first year of metformin treatment, and one and two years after the discontinuation of metformin

	Pre-metformin	Metformin treatment 1st Year	1st year after the discontinuation of metformin	2nd year after the discontinuation of metformin
BMI	31.2±5.6	28.4±5.8	28.3±6.1	30.4±6.4
BMI-SDS	2.7±0.7	1.9±1	1.98±1.05	2.1±1.04
Fasting glucose (mg/dl)	87.5±0.8	85.3±8.8	85.6±5.4	85.3±4.3
Fasting insulin (µIU/ml)	21.9±6.8	11.5±6.9	14.1±3.6	16.7±7.7
Homa-IR	4.7±1.7	2.5±1.5	3±0.8	3.5±1.6
Hba1C (%)	5.3±0.35	5.1±0.26	5±0.37	5.1±0.25

Discussion

Obesity in childhood and the adolescent period constitutes an increased risk for many metabolic complications such as insulin resistance, impaired glucose tolerance and T2DM. Insulin resistance develops on the basis of these disorders and is the most common metabolic change related to obesity [15]. Insulin leads to a biological response that is lower than expected in insulin resistance. There is especially a decrease in the ability of insulin to stimulate glucose use by muscle and fat tissue and suppress the production and secretion of hepatic glucose [16]. Type 2 diabetes mellitus is known to develop at the final stage in adults as a result of the progressive impairment in insulin resistance and secretion. The situation in children and adolescents is not clear. However, a study has indicated the need to start treatment in children at an early stage in order to prevent the development of diabetes as a result of insulin resistance and beta cell dysfunction [17].

Lifestyle change is known to provide weight loss and increase insulin sensitivity and therefore decrease T2DM development [5]. However, the effectiveness of life style change is known to depend on the content of the program and to be subjective with limited long-term success [12]. Metformin efficiency is evaluated as an important treatment alternative in obese, non-diabetic cases due to its effectiveness, reliability, and metabolic and cardiologic benefits [5]. Success has been reported regarding weight loss after 6-12 months of metformin treatment in most of the relevant studies [7-10,12-14]. There are also studies that report an improvement in fasting glucose and insulin resistance [Homa-IR and the quantitative insulin sensitivity check index (QUICKI)[7-9,11]. These studies indicate

in general that metformin is anti-obesity agent with moderate effectiveness [5,7-14]. Our clinical observation is that lifestyle change with metformin treatment is more successful than lifestyle change alone. One of the reasons may be that the children disregard the diet when recommended by itself but taking it more seriously when recommended together with a drug. Another factor may be the easy adaptation of the patients to the changes regarding nutrition because of the gastrointestinal side effects of metformin treatment.

Studies on the effectiveness of metformin treatment in childhood and the adolescent period have evaluated relatively short-term metformin treatment. A reduction in BMI-SDS and homa-IR was seen with 12 months of metformin treatment in our study. Long-term follow-up results after metformin treatment are not available in childhood and the adolescent age group. Data regarding results of the cases that were followed-up only for one year after metformin treatment were reported by Wilson et al. The positive effects on weight obtained with metformin treatment were reported to disappear after the end of one year[12]. We were able to obtain two-year follow-up results of the cases after metformin treatment in our study and the positive effects were reported to continue although decreased.

The most common side effects in metformin treatment are gastrointestinal problems such as abdominal pain and diarrhea. However, these symptoms usually resolve spontaneously within a short time. Lactic acidosis is the most serious side effect. It has been reported rarely in adult studies but there is no case reported in childhood and the adolescent period [2].Gastrointestinal symptoms occurred in one of the cases in our study but did not require metformin treatment to be interrupted and the symptoms regressed in a short time. No other side effect related to lactic acidosis or metformin use was observed in any of our cases.

One of the important limitations of our study is its retrospective design and the inability to homogenize the lifestyle changes that were recommended. Another limitation is the limited number of cases that could be included in the study. Another cause of potential difficulties in the comparison of the results from previous studies with our results is the different doses of metformin used. However, there is no relationship between the metformin dose and the BMI decrease [5]. We used a minimum metformin dose of 425 mg bd for effectiveness in our study.

Conclusion

We determined in our study that one-year metformin treatment improved the BMI SDS and homa-IR values of the obese children and this improvement decreased but continued in the second year after the discontinuation of the treatment. A severe side effect of metformin was not observed in any case. We conclude that metformin treatment has a positive effect on BMI and insulin resistance in obese children and adolescents and its effects on metabolic syndrome needs to be evaluated with larger case studies.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

References

1. McDonagh MS, Selph S, Ozpınar A, Foley C. Systematic reviewof the benefits and risks ofmetforminin treating obesity in children aged 18 years and younger. JAMA Pediatr 2014; 168: 178-84
2. Ho M, Garnet SP, Baur LA. Childhood Obesity and Insulin Resistance: How should It be Managed?.Curr Treat Cardio Med 2014; 16: 351
3. Wang Y, Lobstein T. Worldwide trends in childhood overweight and obesity. IntJ PediatrObes, 2006; 1: 11-25
4. van der Aa MP, Elst MA, van Mil EG, Knibbe CA, van der Vorst MM. METFORMIN: an efficacy, safety and pharmacokinetic study on the short-term and long-term use in obese children and adolescents - study protocol of a randomized controlled study. Trials 2014; 15: 207
5. Brufani C, Crino A, Fintini D, Patera IP, Cappa M, Manco M. Systematic Review of Metformin Use in Obese Nondiabetic Children and Adolescents. Horm Res Paediatr 2013; 80: 78-80
6. Park MH, Kinra S, Ward KI,White B, VinerRM. Metformin for obesity in children and adolescents: a systematicreview. Diabetes Care 2009; 32: 1743-45
7. Freemark M, Bursey D. The effects of metformin on body mass index and glucose tolerance in obese adolescents with fasting hyperinsulinemia and a family history of type 2 diabetes. Pediatrics 2001; 107: 55
8. Srinivasan S, Ambler GR, Baur LA, Garnett SP, Tepsa M, Yap F, Ward GM, Cowell CT. Randomized, controlled trial of metformin for obesity and insulin resistance in children and adolescents: improvement in body composition and fasting insulin. J ClinEndocrinolMetab 2006; 91: 2074–80
9. Atabek ME, Pirgon O. Use of metformin in obese adolescents with hyperinsulinemia: a 6-month, randomized, double-blind, placebo-controlled clinical trial. J Pediatr Endocrinol Metab 2008; 21: 339–48

10. Clarson CL, Mahmud FH, Baker JE, Clark HE, McKay WM, Schauteet VD, Hill DJ. Metformin in combination with structured lifestyle intervention improved body mass index in obese adolescents, but did not improve insulin resistance. Endocrine 2009; 36: 141–46
11. Wiegand S, l'Allemand D, Hübel H, Krude H, Bürmann M, Martus P, Grüters A, Holl RW. Metformin and placebo therapy both improve weight management and fasting insulin in obese insulin resistant adolescents: a prospective, placebo-controlled, randomized study. Eur J Endocrinol 2010; 163: 585–92
12. Wilson D.M, Abrams SH, Aye T, Lee PDK, Lenders C, Lusting RH, OsganianSV, Feldman HA. Metformin extended release treatment of adolescent obesity. Arch PediatrAdolescMed 2010; 164: 116-23
13. Rynders C, Weltman A, Delgiorno C, Balagopal P, Damaso L, Killen K, Mauras N. Lifestyle intervention improves fitness independent of metformin in obese adolescents. Med Sci Sports Exerc 2012; 44: 786–92
14. Mauras N, DelGiorno C, Hossain J, Bird K, Killen K, Merinbaum D, Weltman A, Damaso L, Balagopal P. Metformin use in children with obesity and normal glucose toleranceeffects on cardiovascular markers and intrahepatic fat. J PediatrEndocrinolMetab 2012; 25: 33–40
15. Weiss R, Kaufman FR. Metabolic complications of childhood obesity: identifying and mitigating the risk. DiabetesCare 2008; 31: 310-16
16. MatthaeiS, Stumvoll M, Kellerer M, Haring HU. Pathophysiology and pharmacological treatment of insulin resistance. Endocr Rev 2000; 21: 585-618
17. Cali AM, Man CD, Cobelli C, Dziura J, Seyal A, Shaw M, Allen K, Chen S, Caprio S. Primary defects in ß-cell function further exacerbated by worsening of insulin resistance mark the development of impaired glucose tolerance in obese adolescents. Diabetes Care 2009; 32: 456-61

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Original Article

The prognostic role of fragmented QRS complex in acute myocarditis

Akut miyokarditte fragmante QRS kompleksinin prognostik rolü

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ABSTRACT

Aim: Although a fulminant course of the myocarditis is difficult to predict, it may lead to acute heart failure and death. Previous studies have demonstrated that reduced left ventricular systolic function and prolonged QRS duration can predict the fulminant course. This study aimed to identify whether fragmented QRS complex (fQRS) could also be predictive of fulminant disease in this population.

Material and Methods: We retrospectively included 156 patients diagnosed with acute myocarditis. They were divided into the fulminant group (n = 18) and the non-fulminant group (n = 138). Multivariate logistic regression analysis was used to identify the independent factors predictive of fulminant disease.

Results: Fragmented QRS developed in 11 (61%) in the fulminant group and only 10 patients (7%) in the non-fulminant group (p <0.001). Patients with fulminant myocarditis had a higher mortality rate than those with non-fulminant disease (44.6% vs. 0%, p < 0.001). Multivariate analysis revealed that the presence of fQRS (p=0.019), longer Tpe/qt ratio (p=0.022) and clinical heart failure (<0.001) were significant predictors associated with a fulminant course of myocarditis.

Conclusion: The presence of fQRS complex, as a simple and feasible electrocardiographic marker, seems to be a novel predictor fulminant myocarditis. This simpleparameter may be used in identifying patients at high risk for fulminancy and so early mechanical support could provide improved patient outcomes.

Keywords: acute nyocarditis; fragmented QRS; Tp-e/QT ratio; heart failure.

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ÖZ

Amaç: Miyokarditin fulminan seyrini tahmin etmek zor olsa da, akut kalp yetmezliği ve ölüme neden olabilir. Önceki çalışmalar, sol ventrikül sistolik fonksiyonunun azaldığını ve uzamış QRS süresinin fulminan seyrini öngörebileceğini göstermiştir. Bu çalışma, fragmante QRS kompleksinin (fQRS) de bu popülasyondaki fulminan hastalığın öngörüsü olup olmadığını belirlemeyi amaçlamıştır.

Gereç ve Yöntemler: Akut miyokardit tanısı almış 156 hastayı retrospektif olarak dahil ettik. Hastalar fulminan (n = 18) ve fulminan olmayan gruba (n = 138) ayrıldı. Fulminan hastalığı öngören bağımsız faktörleri tanımlamak için çok değişkenli lojistik regresyon analizi kullanılmıştır.

Bulgular: Fragmante QRS fulminan grupta 11 (% 61), fulminan olmayan grupta sadece 10 hasta (% 7) gelişti (p <0.001). Fulminan miyokardit hastaları fulminan olmayan hastalardan daha yüksek mortalite oranına sahipti (% 44.6 vs.% 0, p <0.001). Çok değişkenli analiz, fQRS (p = 0.019), daha uzun Tp-e / QT oranının (p = 0.022) ve klinik kalp yetmezliğinin (<0.001) varlığında, fulminan bir miyokardit seyri ile ilişkili önemli belirleyiciler olduğunu ortaya koydu.

Sonuç: Basit ve uygulanabilir bir elektrokardiyografik belirteç olarak fQRS kompleksinin varlığı, fulminan miyokarditin yeni bir belirleyicisi olarak görünmektedir. Bu basit parametre, uygunluk riski yüksek olan hastaları belirlemek için kullanılabilir ve bu nedenle erken mekanik destek daha iyi hasta sonuçları sağlayabilir.

Anahtar kelimeler: akut miyokardit; fragmante QRS; Tp-e / QT oranı; kalp yetersizliği

Introdcution

Myocarditis is the inflammation of heart muscle. The pathogenesis of myocarditis is the the injury of heart muscle after the activation of immune system by a cause. Generally myocarditis occurs as a response of immune system to external antigens such as viruses, bacterias, toxins, parasites etc. or autoimmune response to self antigens[1]. The incidence of myocarditis vary between studies because of the difference between diagnostic criterias. The incidence of overall population is supposed to be between 8-10/100.000. It can be thought that the incidence could be higher because of undiagnosed subclinical cases and deaths ocuured before diagnose. Fabre A. et al found the incidence of myocarditis 8.6% in an autopsy study of young adults who suffered sudden death [2]. Nugent AW et al. showed that 10-40% of idiopathic dilate cardiomyopathies between children were because of myocarditis[3]. In the study of Towbin JA et al. about children with dilated cardiomyopathy 46% of cases could be attributed to prior myocarditis [4]. 15% of patients with pericarditis also have myocarditis. The incidence of myocarditis is increasing by the time with use of newer moleculer techniques. In the biopsies of patient with clinical myocarditis but without immune cells or myocite necrosis which is a must for diagnoses of myocarditis according to Dallas criteria cardiotropic viral agents and upregulation of immune markers suggesting that a postviral immun response is the ethiologic cause of myocarditis [5, 6].

A catastrophic form of myocarditis is fulminant myocarditis. 10% of myocarditis patients develop fulminant myocarditis. Patient with fulminant myocarditis usually have global hypofunction of heart with increased wall thickness (because of myocardial edema). Hypotension and hemodynamic instability is common and vasopressor agents and mechanical support are often required. Depending on clinical presentation and etiological cause prognosis of myocarditis may vary in a big range. In one study 11 year fallow up of patients with fulminan myocarditis transplant free survival rate was found as 93% [7]. Shigeru kato et al. and many other investigators showed that C-reactive protein, creatine kinase concentration, decreased ejection fraction and interventriculer conduction disturbances at admission are predictors of fulminant myocarditis [8, 9].

Fragmented QRS complex (fQRS) on a routine 12-lead electrocardiogram, as a marker of depolarization abnormality, represents the conduction delay in myocardial activation because of myocardial scarring and suggested to be a novel indicator of mortality and malignant arrhythmic events in various cardiovascular diseases[10-12]. However, there are scarce data on the prognostic role of fQRS in cardiac arrhythmias and mortality in myocarditis. Therefore, we aimed to evaluate the prognostic role of fQRS in development of fulminant myocarditis.

Material and Methods

Study population

Between 2009 and 2017, 172 patients with a diagnosis of acute myocarditis at a tertiary medical center in Turkey were enrolled in a retrospective medical records review; patients under the age of 15 years were excluded. A diagnosis of acute myocarditis was based on the clinical features of

acute heart failure following recent flu-like symptoms, or according to the Dallas criteria. Of these 172 patients, two patient was excluded due to incomplete data, 5 were excluded due to discharge against medical advice, and 9 were excluded because coronary angiography revealed significant obstructive coronary artery disease (Figure 1). Therefore, 156 patients with acute viral myocarditis were evaluated. These 156 patients were divided into the fulminant group (n=18) and the non-fulminant group (n=138). The definition of a fulminant course of acute myocarditis was the presence of severe hemodynamic compromise requiring inotropic agents or ventricular assist devices, such as an intra-aortic balloon pump (IABP), left ventricular assist device, or extracorporeal membrane oxygenation (ECMO).

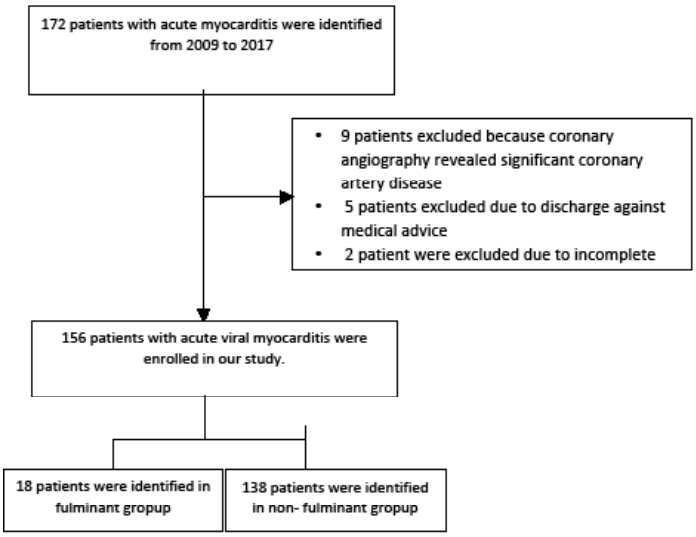

Figure 1. Study cohort

Patient characteristics

Demographic, ECG, and echocardiographic data of all patients were collected from clinical follow-up visits, patients' files, and the electronic database. Informed consent was taken from each patient before enrollment. The study was in compliance with the principles outlined in the Declaration of Helsinki and approved by institutional ethics committee.

Electrocardiography

The 12-lead electrocardiogram (ECG) was recorded at a paper speed of 50 mm/sec (Hewlett Packard, Page-writer, USA) in the supine position. ECGs were performed while the patient at rest and at 8:00-10:00 AM in the morning. All of the ECGs were scanned and transferred to a personal computer to decrease the error measurements, and then used for x400% magnification by Adobe Photoshop software. fQRS was defined as the presence of various RSR' patterns with different morphologies of QRS complexes with or without the Q wave. Various RSR' patterns included an additional R wave (R'), notching of the R wave or the S wave, or the presence of >1 R' (fragmentation) without a typical bundle branch block in 2 contiguous leads corresponding to a major lead set for major coronary artery territory (Figure 2). Any QRS morphology with a QRS duration >120 ms, including bundle branch block or intraventricular conduction delay, was excluded. ECG measurements of QT and Tp-e intervals were performed by two cardiologists who were blinded to the patient data. Subjects with U waves on their ECGs were excluded from the study. A mean value of three readings was calculated for each lead. The QT interval was measured from the beginning of the QRS complex to the end of the T wave and corrected for heart rate using the Bazett formula: $cQT = QT\sqrt{}$ (R-R interval). The Tp-e interval was defined as the interval from the peak of T wave to the end of T wave. Measurements of the Tp-e interval were performed from precordial leads. The Tp-e/QT ratio was calculated from these measurements. Interobserver and intraobserver coefficients of variation were 2.1% and 2.9%, respectively.

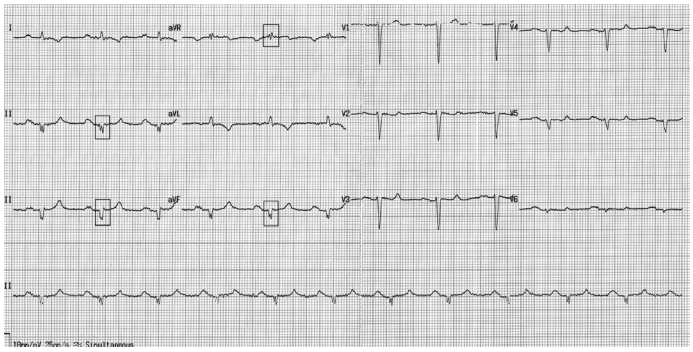

Figure 2. Examples of fQRSs in our patients with fulminat myocarditis.

Echocardiography

All patients underwent standard trans-thoracic echocardiography at the time of presentation. Various parameters, including the left ventricular ejection fraction (LVEF), left atrium (LA) diameter, left ventricular endsystolic dimensions (LVEDs), thicknesses of the left ventricular post wall (LVPW), and the maximal interventricular septum (IVS), were calculated by using linear measurements.

Laboratory Assessments

Peripheral venous blood samples were drawn from the antecubital vein after 12-hour of fasting in the morning. Blood samples were taken into standardized tubes containing dipotassium ethylenedinitro tetraacetic acid (EDTA) for complete blood count (CBC). Coulter Counter LH Series (Beckman coulter Inc, Hialeah, Florida) was used for CBC. Plasma levels of triglyceride, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C),glucose, creatinine were evaluated using an automated chemistry analyzer (Abbott Aeroset, USA) using commercially available kits (Abbott, USA). Local ethics committee approved the study and informed consent was obtained from participant(s)

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Statistical Analysis

In all statistical analysis SPSS 21.0 Statistical Package Program for Windows (SPSS Inc., Chicago, IL, USA) was used. In order to test normality of distribution Kolmogorov-Smirnov test was used. Quantitative variables with a normal distribution were specified as the mean ± standard deviation. Categorical variables were shown as number and percentage values. Differences between groups were evaluated by using Student's t-test. Categorical variables were compared with Chi-square test. A univariate logistic regression analysis of the various clinical variables was performed to determine the predictors of a fulminant course in patients with acute myocarditis. The variables selected in the multivariate logistic analysis were those with a p-value < 0.05 in the univariate models. A two-sided p-value < 0.05 was considered statistically significant.

Results

The study population was categorized into 2 groups as according to the presence of fulminancy (n=18) or not (n=138). Baseline clinical characteristics and electrocardiographic findings of the study population were shown in Table 1. There was no significant difference between groups regarding gender, white blood cell count, CRP, creatinin, troponin and glucose levels (P > 0.05). It was demonstrated that Tp-e interval, QT interval and QRS duration are also similar between groups (P>0.05). The mean PR interval (140 ms vs. 160 ms, p<0.001), the mean QTc interval (426 ms vs. 481 ms p<0.001), Tp-e/QT ratio (0.20 vs. 0.24, p=0.010) were both significantly longer in the fulminant group than those in the non-fulminant group. Fragmented QRS developed in 11 (61%) in the fulminant group and only 10 patients (7%) in the non-fulminant group (p <0.001). We found trends toward higher heart rates [70 (65-85)vs. 79 (63-86) beats per min; p = 0.12] in the fulminant group. With respect to echocardiographic findings, the LVEF was significantly lower in the fulminant group than in the non-fulminant group [62 (55-67) vs 25(23-30);p<0.001]. Pericardial effusion [30(21%) vs 11 (61%); p<0.001] and cardiac tamponade [8 (5%) vs5 (27%); p=0.002] were seen more frequent in the fulminant group than non-fulminant group. Other parameters, such as left atrial dimensions and left ventricular systolic and diastolic dimensions, showed no statistical differences between the 2 groups.

Table 1. Demographical, laboratory, electrocardiographic, echocardiographic and clinical characteristics of study and control subjects

	Non-fulminant group (N = 138)	Fulminant group (N = 18)	p-value
Age (years)	28 ± (16.01)	34 ± (14.85)	0.144
Female Gender, n(%)	20 (14)	3 (16)	0.807
White Blood Cell(x103/µL)	8.8 (6.5-10.0)	8.8 (8.0-9.6)	0.267
CRP(mg/dL)	5.0 (2.0-12)	4.0 (1.4-9.0)	0.170
Creatinin (IU/L)	0.80 (0.60-0.90)	0.79 (0.90-2.08)	0.158
Glucose(mg/dL)	97 (88-100)	102 (96-106)	0.056
Troponin-I (ng/L)	0.46 (0.08-2.56)	0.49 (0.06-2.58)	0.601
HR (per minute)	70 (65-85)	79 (63-86)	0.12
QRS (ms)	92 (78-98)	101 (80-110)	0.647
PR (ms	140 (130-160)	160 (158-170)	<0.001
QT (ms)	390 (370-402)	381 (352-401)	0.198
QTc (ms)	426 (401-447)	481 (448-503)	<0.001
Tp-e interval, ms	81 (76-84)	82 (74-101)	0.469
Tp-e/QT ratio	0.20 (0.18-0.22)	0.24 (0.20-0.26)	0.010
Tp-e/QTc ratio	0.18 (0.19-0.21)	0.17 (0.15-0.20)	0.045
Fragmante qrs n(%)	10 (7)	11 (61)	<0.001
IVS (mm)	0.8 (0.8-1.0)	0.9 (0.8-1.35)	0.267
LVPW (mm)	0.9 (0.7-1.0)	1.0 (0.8-1.5)	0.355
LA dimension (mm)	3.2 ± 0.7	3.5 ± 0.9	0.061
LVEDs (mm)	2.7 (2.4-3.5)	2.9 (1.7-3.2)	0.689
LVEDd (mm)	4.6 (4.0-5.0)	4.9 (4.5-6.5)	0.090
LVEF (%)	62 (55-67)	25 (23-30)	<0.001
Pericardial effusion n(%)	30 (21)	11 (61)	<0.001
Cardiac tamponade n(%)	8 (5)	5 (27)	0.002
Clinical heart failure n(%)	1 (0.7)	17 (94)	<0.001
ECMO- LVAD n(%)	0 (0)	16 (88)	<0.001
1 month mortality n(%)	0 (0)	8 (44.5)	<0.001

Data are given as mean ± SD or %. CRP, C-reactive protein; ECMO, Extracorporeal Membrane Oxygenation; HR, heart rate; IVS, intraventricular septum; LA, left atrium; LVEDd, end-diastolic left ventricular diameter; LVEDs, end-systolic left ventricular diameter; LVEF, left ventricular ejection fraction; LVPW, left ventricular posterior wall; LVAD, Left Ventricular Assist Device

Clinical outcome

Among patients with fulminant myocarditis, 16 (88%) patients underwent IABP, ECMO or LVAD. Clinical heart failure were seen 17(94%) patients in fulminan group but only seen 1(0.7%) patients in non-fulminant group. Eight patients in the fulminant group died of the disease, compared with none in the non-fulminant group. These 8 patients died of cardiogenic shock, with multiple organ failure. The overall mortality was 44.5 % and was significantly higher in the fulminant group than in the non-fulminant group ($p < 0.001$).

Predictors of fulminant myocarditis

In the univariate logistic regression analysis, Tp-e/QT ratio ($p<0.001$), fragmanted QRS ($p<0.001$), cardiac tamponade ($p=0.004$), LVEF ($p=0.035$), clinical heart failure ($p<0.001$) predicted the incidence of fulminant myocarditis (Table 2). The multivariate logistic regression model demonstrated that presence of fragmented qrs ($p = 0.019$), higher Tp-e/QT ratio ($p = 0.022$) and presence of clinical heart failure ($p<0.001$) remained as independent predictors of fulminant myocarditis (Table 2).

Table 2. Univariate and multivariate logistic regression analysis showing the predictors for fulminancy.

	Univariable		Multivariable	
Variables	**OR (95 % CI)**	**p-value**	**OR (95 % CI)**	**p-value**
Age	1.071 (1.032-1.113)	**<0.001**	1.044 (0.995-1.106)	0.144
Heart Rate	1.059 (0.914-1.195)	**0.108**	-	-
Tp-e/QT ratio	1.062 (1.034-1.091)	**<0.001**	1.024 (1.017-1.071)	**0.022**
Fragmanted QRS	20.114 (6.398-63.239)	**<0.001**	6.825 (1.370-13.071)	**0.019**
Cardiac Tamponade	6.250 (1.783-21.911)	**0.004**	5.337 (0.711-40.072)	0.104
LVEF, (%)	1.150 ((1.034-1.191)	**0.035**	1.013 (0.896-1.123)	0.234
Clinical Heart Failure	2329 (139-38966)	**<0.001**	999 (35-28013)	**<0.001**

Data are given as mean ± SD or %. CI, confidence interval; LVEF, left ventricular ejection fraction; OR, odds ratio.

Discussion

This study assessed the potential of fQRS on surface ECG to play a role in development of fulminant myocarditis. According to multivariate logistic regression analysis presence of fQRS, Tp-e/QT ratio and clinical heart failure were found to be related with fulminant course of myocarditis.

Mortality rates of fulminant myocarditis varies according to different studies. In a most recent trial by Ammirati et al. which including 187 patients with a diagnosis of acute myocarditis, the composite of mortality and heart transplantation was 25.5% at fulminant group and 0% at non-fulminant group ($p < 0.0001$), respectively [13]. In an earlier study by Mccarthy et al. fulminant myocarditis was an independent predictor of survival after adjustments were made for age, histopathological findings, and hemodynamic variables[7]. Because of this high mortality rates and worse prognosis with fulminant myocarditis early recognition of patients at the risk of progression to fulminant forms is essential. Acute myocarditis evolving into fulminant f n on echocardiogram, ST-T segment abnormalities ECG, high release of troponins, hypotension, and frequent arrhythmia[14].

Several studies have investigated the potential risk factors for fulminant myocarditis. Some studies focused on serum inflammatory marker levels such as high C-reactive protein and interleukins, some studies demonstrated extensive myocardial injury with measurement of serum creatine kinase MB isoenzyme to predict develeopment of fulminant course of myocarditis[8, 9, 15]. Apart from serum biomarkers, changes in electrocardiographic and electroechocardiographic findings have also been investigated. Intraventricular conduction disturbances and QRS complex widths > 120 ms at admission have been reported in patients with fulminant myocarditis; these QRS complex widths were longer than those in the non-fulminant group[8]. Similarly in a more recent trial by Hung et al. demonstrated that wider QRS durations (133.22 ± 45.85 ms vs. 92.81 ± 15.56 ms, $p = 0.030$) and longer QTc intervals (482.78 ± 69.76 ms vs. 412.00 ± 33.31 ms, $p = 0.016$) were significant predictors associated with a fulminant course of myocarditis[16]. Parallel to these studies in our study we found that longer QTc interval and Tp-e/QT ratio in patients with fulminant myocarditis compared to non-fulminant ones.

Fragmented QRS complex (fQRS), which was defined by the presence of changes in QRS morphology including an additional R wave, a notching of the R wave or S wave, or the presence of >1 additional R wave in 2 contiguous leads is a novel electrocardiographic parameter to define high risk patients in various circumstances[17]. It has been related to a number of cardiac diseases including Brugada syndrome, ventricular aneurysm, dilated cardiomyopathy, essential hypertension, coronary artery disease, tetralogy of Fallot, takotsubo cardiomyopathy, cardiac AL amyloidosis, heart failure and acute aortic dissection[18-21]. It is now clearly demonstrated that fQRS is associated with moycardial fibrosis and systemic inflammation. Acute myocarditis, which is an

inflammation of myocardium may cause fragmentation of QRS with a high probability. Also we found a significantly more number of patients with fQRS in fulminant group compared to non-fulminant group (61% vs 7%, p<0.001).

Study Limitations

There were several potential limitations to our study. First, the diagnosis of acute myocarditis was made based upon a clinical diagnosis, and not all patients received routine endomyocardial biopsy to confirm the diagnosis. This study is the limitednumber of patients that may have affected thestatistical power of the study.Nevertheless, the reason was due to the low prevalence of fulminant myocarditis. This study involved a retrospectivecase-control study and the patients werenot followed for future arrhythmic episodes thatthe relation between ventricular arrhythmias withTp-e/QTc ratio and fQRS. Long-term follow-up and large-scale prospective studies are needed to investigate the relationship between the value of fragmanted QRS and Tp-e/QT ratio and fulminant myocarditis.

Conclusion

Patients with fulminant myocarditishad higher in-hospital mortality rates than non-fulminant

patients. Early and aggressive mechanical circulatorysupport might decrease the associated mortality rate. Several clinical and electrocardiographic factors are related to fulminant course in acute myocarditis setting. In our study presence of clinical heart failure, fragmanted QRS and Tp-e/QT ratio were found to be related with fulminant myocarditis.

Declaration of conflict of interest

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References

1. Cooper LT, Jr. Myocarditis. N Engl J Med 2009; 360: 1526-38.
2. Fabre A, Sheppard MN. Sudden adult death syndrome and other non-ischaemic causes of sudden cardiac death. Heart 2006; 92: 316-20.
3. Nugent AW, Daubeney PE, Chondros P et al. The epidemiology of childhood cardiomyopathy in Australia. N Engl J Med 2003; 348: 1639-46.
4. Towbin JA, Lowe AM, Colan SD et al. Incidence, causes, and outcomes of dilated cardiomyopathy in children. JAMA 2006; 296: 1867-76.
5. Tschope C, Bock CT, Kasner M et al. High prevalence of cardiac parvovirus B19 infection in patients with isolated left ventricular diastolic dysfunction. Circulation 2005; 111: 879-86.
6. Kuhl U, Pauschinger M, Noutsias M et al. High prevalence of viral genomes and multiple viral infections in the myocardium of adults with "idiopathic" left ventricular dysfunction. Circulation 2005; 111: 887-93.
7. McCarthy RE, 3rd, Boehmer JP, Hruban RH et al. Long-term outcome of fulminant myocarditis as compared with acute (nonfulminant) myocarditis. N Engl J Med 2000; 342: 690-95.
8. Kato S, Morimoto S, Hiramitsu S et al. Risk factors for patients developing a fulminant course with acute myocarditis. Circ J 2004; 68: 734-39.
9. Lee CH, Tsai WC, Hsu CH, Liu PY, Lin LJ, Chen JH. Predictive factors of a fulminant course in acute myocarditis. Int J Cardiol 2006; 109: 142-45.
10. Das MK, Suradi H, Maskoun W et al. Fragmented wide QRS on a 12-lead ECG: a sign of myocardial scar and poor prognosis. Circ Arrhythm Electrophysiol 2008; 1: 258-68.
11. Das MK, Saha C, El Masry H et al. Fragmented QRS on a 12-lead ECG: a predictor of mortality and cardiac events in patients with coronary artery disease. Heart Rhythm 2007; 4: 1385-92.
12. Das MK, Maskoun W, Shen C et al. Fragmented QRS on twelve-lead electrocardiogram predicts arrhythmic events in patients with ischemic and nonischemic cardiomyopathy. Heart Rhythm 2010; 7: 74-80.
13. Ammirati E, Cipriani M, Lilliu M et al. Survival and Left Ventricular Function Changes in Fulminant Versus Nonfulminant Acute Myocarditis. Circulation 2017; 136: 529-45.
14. Veronese G, Ammirati E, Cipriani M, Frigerio M. Fulminant myocarditis: Characteristics, treatment, and outcomes. Anatol J Cardiol 2018; 19: 279-86.
15. Nishii M, Inomata T, Takehana H et al. Serum levels of interleukin-10 on admission as a prognostic predictor of human fulminant myocarditis. J Am Coll Cardiol 2004; 44: 1292-97.
16. Hung Y, Lin WH, Lin CS et al. The Prognostic Role of QTc Interval in Acute Myocarditis. Acta Cardiol Sin 2016; 32: 223-30.
17. Gong B, Li Z. Total Mortality, Major Adverse Cardiac Events, and Echocardiographic-Derived Cardiac Parameters with Fragmented QRS Complex. Ann Noninvasive Electrocardiol 2016; 21: 404-12.
18. Morita H, Kusano KF, Miura D et al. Fragmented QRS as a marker of conduction abnormality and a predictor of prognosis of Brugada syndrome. Circulation 2008; 118: 1697-704.
19. Zhang B, Zhen Y, Shen D, Zhang G. Significance of fragmented QRS complexes for identifying left ventricular hypertrophy in patients with hypertension. Ann Noninvasive Electrocardiol 2015; 20: 175-80.
20. Yilmaz H, Gungor B, Kemaloglu T et al. The presence of fragmented QRS on 12-lead ECG in patients with coronary slow flow. Kardiol Pol 2014; 72: 14-19.
21. Shimizu M, Nishizaki M, Yamawake N et al. J wave and fragmented QRS formation during the hyperacute phase in Takotsubo cardiomyopathy. Circ J 2014; 78: 943-49.

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Original Article

The usefulness of monocyte to high density lipoprotein cholesterol ratio in prediction for coronary artery ectasia

Monosit/yüksek yoğunluklu lipoprotein oranının koroner arter ektaziyi öngörmedeki yararı

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ABSTRACT

Aim: Monocyte count to high density lipoprotein cholesterol ratio (MHR) has been shown to be a useful inflammatory marker in patients with coronary artery disease. Hence, the aim of the study was to evaluate whether there is an association between coronary artery ectasia (CAE) and MHR.

Material and methods: In this retrospective case-control study, a total of 5500 patients who underwent an elective coronary angiography between July 2013 and July 2016 were retrospectively screened. Of these patients, 150 (2.7%) patients were found to have an isolated CAE. The control group was consisted of 150 normal coronary artery patients who matched with this group in terms of age, gender, and body mass index.

Results: The median value of MHR was found to be a statistically higher in patients with CAE ($p<0.05$). In multivariable analyses, MHR (OR: 1.71, 95% CI: 1.219-2.484, $p=0.002$) was found to be an independent predictor of CAE.

Conclusion: We observed that MHR levels were higher in CAE patients when compared to healthy subjects. Our findings may indicate a common pathophysiological mechanism between CAE and coronary artery disease.

Keywords: MHR; inflammation; coronary artery ectasy

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ÖZ

Amaç: Monosit sayısının yüksek yoğunluklu lipoprotein kolesterole oranı (MYYLKO) koroner arter hastalığı olan hastalarda yararlı bir enflamasyon belirteci olduğu gösterilmiştir. Bu nedenle, çalışmamızdaki amacımız MYYLKO'nın koroner arter ektazi (KAE) arasında ilişki olup olmadığını araştırmaktı.

Gereç ve yöntemler: Geriye dönük vaka-kontrol çalışmasında, Temmuz 2013 ve Temmuz 2016 tarihleri arasında elektif koroner anjiyografi olan toplam 5500 hasta tarandı. Bu hastalardan, 150 (2,7%) hastada KAE bulundu. Kontrol grubu yaş, cinsiyet ve vücut kitle indeksi açısından eşleşen 150 normal koroner arter hastalarından oluştu.

Bulgular: MYYLKO'nın ortanca değeri istatistiksel olarak KAE hastalarında daha yüksek bulundu ($p<0.05$).Çoklu değişken analizde, MYYLKO (Odds oranı:1.71, 95%Güven Aralığı:1.219-2.484, $p=0.002$) KAE'nin bağımsız öngörücüsü olarak saptandı.

Sonuç: MYYLKO'nın KAE'li hastalarda sağlıklı kişilere göre daha yüksek olduğunu gözlemledik. Bu bulgularımız KAE ile koroner arter hastalığının ortak bir patofizyolojik mekanizmayı işaret edebilir.

Anahtar kelimeler: MYYLKO; enflamasyon; koroner arter ektazi

Introduction

Coronary artery ectasia (CAE) is described as 1.5 or more times greater dilatation of the normal coronary artery [1]. The involvement of the coronary artery in CAE may be diffuse or focal [1]. In addition, CAE might be found in patient with an obstructive coronary artery disease. Several previous studies reported that the incidence of CAE during elective coronary angiography may range from 0.3 to 4.9% [2-4]. The main underlying mechanism that is responsible for ectasia formation has not been clearly described yet; however, previous studies reported that CAE may be an another form of atherosclerosis. Also, it has been found that the inflammation within the CAE vessel is more potent compared to the normal vessel [5, 6].

In recent years, there has been an increasing interest in describing a simple inflammatory marker in order to facilitate early recognition of patients who may have an increasing risk for future cardiovascular disease. In a recent study, monocyte count to HDL-C ratio (MHR) has been shown as a novel marker of inflammation to predict coronary artery disease severity and future major cardiovascular adverse events in patients with acute coronary syndrome [7]. As the inflammation plays a significant role for the development of CAE, we hypothesized that there may be a relation between MHR and CAE. Hence, in the present study, we aimed to evaluate the potential utility of MHR in predicting CAE.

Material and methods

Study population

In this retrospective case-control study, a total of 5500 patients who underwent an elective coronary angiography between July 2013 and July 2016 in our tertiary heart center due to a presume diagnosis of coronary artery disease were screened. The patients who had an acute coronary syndrome, acute or chronic infection, had use of any glucocorticoid treatment within in three months, had a hematologic and auto-immune disease, undergoing chronic peritoneal dialysis or hemodialysis treatment were excluded from the study. In addition, the patients who had a diagnosis of previous myocardial infarction and patients with liver and gallbladder diseases were excluded from the study. After evaluation regarding with exclusion criteria, 150 (2.7%) patients were found to have an isolated CAE. Also, CAE patients who had non-obstructive coronary artery disease were also excluded from the study. The control group was consisted of 150 angiographically normal coronary artery patients who matched with this group in terms of age, gender, and body mass index. Baseline demographic characteristics and related clinical information were retrieved from the hospital's electronic database. Our local ethics committee approved the study protocol in accordance with the principle of the Declaration of Helsinki. An informed consent was waived because this study had a retrospective design.

Laboratory analysis

In the present study, a complete blood count and biochemical profile was obtained after an overnight fasting in all subjects. The tubes with EDTA were used for automatic blood count. The blood counts were measured using a Sysmex XT-1800i Hematology Analyzer device (Sysmex Corporation, Kobe, Japan). MHR was calculated as the ratio of the number of monocyte to HDL-C and the neutrophil to lymphocyte ratio (NLR) was calculated as the ratio of the number of neutrophil to lymphocytes, both of which obtained from the same blood samples. In our laboratory, the reference value for monocyte count was 2% to 10% of total white blood cells. The C-reactive protein (CRP) level was measured using an automatic biochemical analyzer (Roche Diagonistics Cobas 8000 c502).

Coronary angiography

In the current study, the patients who accepted as having typical angina or with a suspected or positive finding in one of the non-invasive methods that is performed for detection of coronary ischemia underwent an elective coronary angiography. Coronary angiography was performed via femoral or radial artery according to Judkins's technique. All coronary angiograms were recorded into DICOM digital media with a rate of 25 frames/msc. All coronary angiograms were evaluated by two experienced interventional cardiologists who were blinded to patient's clinical data.

Definitions

The CAE was defined as proposed in a previous study [8]. Hypertension was defined as a systolic blood pressure of 140 mmHg or higher, diastolic blood pressure of 90 mm or higher or using an antihypertensive medicine [9]. The presence of diabetes mellitus was accepted as fasting blood glucose of ≥126 mg/dL or higher or currently using an antidiabetic treatment or being on a diet [10]. Local ethics committee approved the study and informed consent was obtained from participant(s)

Statistical analysis

The data was expressed as percentage (%) and median (range: minimum-maximum) values, where appropriate. The Fisher's exact test and Pearson chi-square analysis performed for categorical variables. Fitness to normal distribution was analyzed with the Kolmogorov-Simirnov test. Mann-Whitney-U test was used for comparing quantitative variables with abnormal distribution. The independent risk factors for CAE were analyzed using a multivariate logistic regression analyses with variables that showed statistically significant associations with CAE in the univariate analyses. Statistical analysis was made using the computer software Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, version 21.0. released 2012, IBM Corp., Armonk, New York, USA). A p-value < 0.05 was considered statistically significant.

Results

In the present study, 150 CAE patients and 150 age-sex-body mass index-matched control subjects constituted the study population. Baseline demographic characteristics and laboratory findings of all patients are shown in Table 1. The frequency of hypertension, diabetes mellitus, and smoking did not reach a statistical significance between the groups (p>0.05 for each). In terms of laboratory findings, there were significant differences between two groups for white blood cell count, monocyte count, lymphocyte count, and creatinine levels (p<0.05 for each). The median value of NLR and MHR were found to be a statistically higher in patients with CAE (p<0.05 for each).

Table 1 Demographic characteristics and laboratory findings of control and study groups

	Control group	CAE presence group	P value
Age, years	55 (40-78)	56 (42-79)	0.124
Gender (female), (%)	80 (53.3)	89 (59.3)	0.295
BMI, kg/m2	25.0 (23.0-27.5)	25.8 (22.0-28.0)	0.252
Hypertension, (%)	80 (53.3)	86 (57.3)	0.486
Diabetes mellitus, (%)	60.7 (91)	58.0 (87)	0.638
Smoking, (%)	62 (41.3)	49 (32.7)	0.120
White blood cell count, 109/µL	7500 (4400-12400)	8400 (4500-10700)	0.004*
Hemoglobin, g/L	140 (108-160)	140 (100-163)	0.631
Monocyte count, 109/µL	400 (0.0-920)	600 (0.0-1500)	<0.001*
Lymphocyte count, 109/µL	1400 (1000-3500)	1300 (700-2500)	0.005*
Neutrophil count, 109/µL	4950 (2160-8680)	5040 (2600-3960)	0.200
Platelet count, 109/µL	288500 (145000-652000)	287000 (198000-652000)	0.997
RDW, %	15.2 (12.2-21.2)	15.3 (12.2-21.2)	0.055
MPV, fL	9.6 (7.9-13.5)	9.6 (7.8-13.5)	0.536
AST, U/L	15 (1-35)	15 (1-35)	0.457
ALT, U/L	15 (2-35)	15 (1-35)	0.400
Creatinine, mg/dL	0.8 (0.5-1.2)	0.9 (0.5-1.5)	0.032*
Total cholesterol, mg/dL	188 (164-226)	195 (165-230)	0.078
LDL cholesterol, mg/dL	125 (20-178)	130 (75-180)	0.363
HDL cholesterol, mg/dL	39 (32-59)	39 (34-55)	0.978
C-reactive protein, mg/L	10 (5-50)	9 (1-50)	0.466
NLR	2.9 (1.8-5.0)	3.5 (2.0-6.4)	0.004*
MHR	9 (1-14)	14 (1-32)	<0.001*

*p<0.05, Continuous variables are presented with median, nominal variables are presented with frequency.
Abbreviations: CAE: coronary artery ectasia, BMI: body mass index, RDW: red cell distribution width, MPV: mean platelet volume, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDL: low density lipoprotein, HDL: high density lipoprotein, MHR: monocyte high density lipoprotein ratio, NLR: neutrophil lymphocyte ratio.

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In univariate analysis, age, white blood cell, NLR, MHR, monocyte and lymphocyte count were found to be related with CAE (Table 2). In order to identify the independent predictors of CAE, multivariate logistic regression analyses with a stepwise backward model was performed using variables that showed marginal association with CAE in the univariate analyses. In multivariate analyses, only MHR (OR: 1.71, 95% CI: 1.219-2.484, p=0.002) was found to be an independent predictor of CAE. A box plot was drawn to show the difference between the MHR and NLR values of control subjects and CAE patients (Figure 1-2).

Table 2 Univariate and multivariate logistic regression analysis giving information about the independent risk factors for CAE

	Univariate analysis			Multivariate analysis		
	95% CI		P value	95% CI		P value
	Lower	Upper		Lower	Upper	
Age	1.000	1.059	0.048	0.983	1.052	0.324
Gender	0.808	2.017	0.295	-	-	-
BMI	0.932	1.316	0.246	-	-	-
Hypertension	0.539	1.341	0.486	-	-	-
Diabetes mellitus	0.704	1.771	0.638	-	-	-
Smoking	0.907	2.326	0.121	-	-	-
White blood cell count	1.029	1.445	0.022	0.727	1.609	0.698
NLR	1.259	1.993	<0.001	0.604	1.919	0.803
MHR	8.693	2.946	<0.001	1.219	2.484	0.002*
Creatinine	0.679	1.418	0.918	-	-	-
Hemoglobin	0.958	1.170	0.263	-	-	-
C-reactive protein	0.764	1.203	0.716	-	-	-
Monocyte count	1.954	8.848	<0.001	0.001	1.640	0.086
Lymphocyte count	0.269	0.823	0.008	0.106	2.371	0.383
Neutrophil count	0.924	1.423	0.215	-	-	-
Platelet count	0.996	1.004	0.991	-	-	-
RDW	0.969	1.239	0.147	-	-	-
MPV	0.979	1.042	0.548	-		
AST	0.955	1.023	0.500	-	-	-
ALT	0.980	1.056	0.371	-	-	-
Total cholesterol	1.000	1.023	0.046	0.999	1.026	0.077
HDL cholesterol	0.949	1.037	0.725	-	-	-
LDL cholesterol	0.987	1.005	0.354	-	-	-

*p<0.05, All clinically relevant parameters were included in the model.
Abbreviations: CAE: coronary artery ectasia, BMI: body mass index, RDW: red cell distribution width, MPV: mean platelet volume, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDL: low density lipoprotein, HDL: high density lipoprotein, MHR: monocyte high density lipoprotein ratio, NLR: neutrophil lymphocyte ratio.

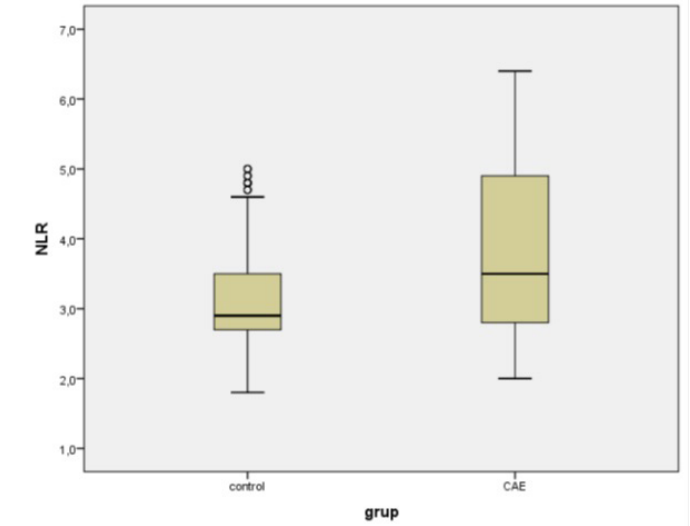

Figure 1: A box plot showing the difference between NLR values of control subjects and CAE patients
Abbreviations: NLR: neutrophil to lymphocyte ratio, MHR: monocyte count to high density lipoprotein cholesterol ratio, CAE: coronary artery ectasia.

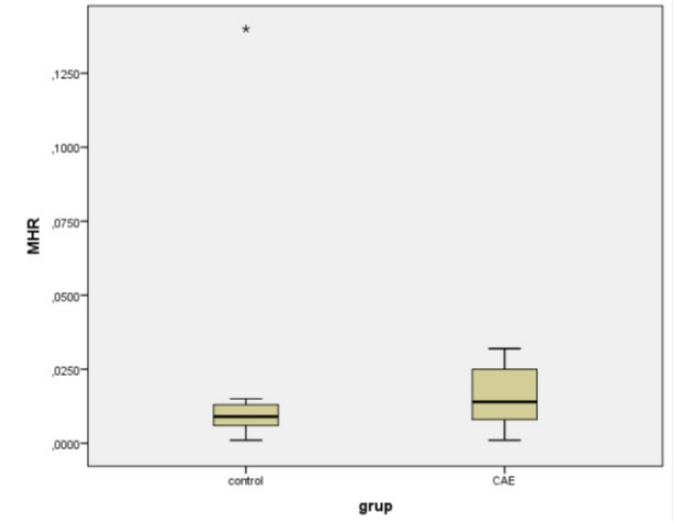

Figure 2: A box plot showing the difference between MHR values of control subjects and CAE patients
Abbreviations: NLR: neutrophil to lymphocyte ratio, MHR: monocyte count to high density lipoprotein cholesterol ratio, CAE: coronary artery ectasia.

Discussion

In the present study, we observed that an elevated MHR may be an independent predictor of CAE. As a simple and easily obtained hematologic parameter from complete blood count, MHR may be used in predicting risk of CAE.

Previously, the inflammatory markers such as CRP, interleukin-6, and vascular adhesion molecules were investigated in patients with CEA [11]. A recent study done by Li and colleagues has shown that interleukin-6 and CRP were significantly higher in patients with CAE when compared to patients with normal coronary arteries [12]. In contrast to this reported previous study, in our study, there was no a significant difference of CRP levels between the groups. This finding may be due to patient-related selection or the size of study sample. Furthermore, plasma soluble intercellular adhesion molecule (ICAM)-1, vascular cell adhesion molecule (VCAM)-1, and E-selectin levels were found to be higher in patients with CAE than in patients with normal coronary arteries [13]. The NLR, which is also a marker of inflammation, has been investigated in patients with CAE. In a recent published study which constituted of 85 CAE patients, a possible association between NLR and the presence of CAE was examined [14]. The authors found that an increased NLR is an independent predictor of the presence of CAE. Similarly, in our study, we observed a notable increase of median NLR in CAE patients. However, the NLR did not reach a statistical significance in multivariate analysis in our study.

Monocytes secrete several cytokines which may affect platelets and endothelial cells resulting in the stimulation of the proinflammatory and prothrombotic pathways in the human body [15]. During atherosclerosis process, monocytes migrate into subendothelial area and differentiate into macrophages, in which there release some metalloproteinases such as elastase and collagenase [16]. Several previously published studies demonstrated that the differentiation of monocytes into macrophages is the first step in the beginning of atherosclerosis [15, 17]. In contrast to monocyte inflammatory effects, HDL-C has an anti-inflammatory, anti-oxidant as well as anti-platelet effect via several pathways in the human body [16]. These anti-inflammatory and anti-oxidant pathways may include a contribution to the cholesterol outflow from macrophages, inhibition of endothelial adhesion protein expression, and encouraging reverse transport of oxidized molecules [15-17]. Moreover, HDL-C may decrease the inflammation via inhibiting the activation of monocyte and interrupting the differentiation of monocytes to macrophages [18]. Consequently, we thought that a combination of HDL-C and monocyte counts in a single parameter, namely MHR, may better represent the inflammatory process in the human body.

The importance of MHR in cardiovascular disease has been investigated in a few studies. Canpolat et al. investigated the pre-procedural MHR for the prediction of atrial fibrillation recurrence after cryoballoon-based catheter ablation [19]. This study finding demonstrated that an increased MHR was related with an increased recurrence of atrial fibrillation after cryoballoon-based catheter ablation. In addition, it has been shown that MHR may be used to predict coronary artery disease severity [7]. Moreover, in a recent study which consisted of patients with CAE, obstructive coronary artery disease, and normal coronary artery, Kundi et al. reported that high MHR is an independent predictor of CAE and obstructive coronary artery disease [20]. In our study, we also found similar results. However, CAE patients that had non-obstructive coronary artery disease, which was not obvious in the aforementioned study, were not enrolled in our study.

Our results provided evidence that the inflammatory process caused by high MHR levels may cause a microvascular dysfunction in CAE patients. The MHR is a simple and inexpensive marker of inflammation and, it can be calculated easily from complete blood count parameters. An elevated MHR, which is a newly introduced inflammatory marker, may have a predictive value for the prediction of CAE in daily clinical practice.

Study Limitations

This study had some limitations. First, our study had a retrospective design. Second, we were not able to evaluate the plaque burden because patients without evidence of luminal narrowing by angiography may also have plaque burden in the wall of the coronary vessels. Third, by using a spot laboratory value rather than values at a time interval may be another limitation because the development of CAE is a chronic condition. Finally, we did not evaluate other well-known inflammatory markers such as fibrinogen in the study.

Conclusion

We observed that MHR levels were higher in CAE patients when compared to healthy subjects. Our findings may indicate a common pathophysiological mechanism between CAE and coronary artery disease. Finally, our findings warrant further studies to describe a clear role of this marker.

Declaration of conflict of interest

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References

1. Swaye PS, Fisher LD, Litwin P et al. Aneurysmal coronary artery disease. Circulation 1983; 67: 134-38.
2. Befeler B, Aranda MJ, Embi A, Mullin FL, El-Sherif N, Lazzara R. Coronary artery aneurysms: study of the etiology, clinical course and effect on left ventricular function and prognosis. Am J Med 1977; 62: 597-607.
3. Oliveros RA, Falsetti HL, Carroll RJ, Heinle RA, Ryan GF. Atherosclerotic coronary artery aneurysm. Report of five cases and review of literature. Arch Intern Med 1974; 134: 1072-76.
4. Kruger D, Stierle U, Herrmann G, Simon R, Sheikhzadeh A. Exercise-induced myocardial ischemia in isolated coronary artery ectasias and aneurysms ("dilated coronopathy"). J Am Coll Cardiol 1999; 34: 1461-70.
5. Alford WC Jr, Stoney WS, Burrus GR, Frist RA, Thomas CS Jr. Recognition and operative management of patients with arteriosclerotic coronary artery aneurysms. Ann Thorac Surg 1976; 22: 317-21.
6. Ancuta P, Wang J, Gabuzda D. CD16+ monocytes produce IL-6, CCL2, and matrix metalloproteinase-9 upon interaction with CX3CL1-expressing endothelial cells. J Leukoc Biol 2006; 80: 1156-64.
7. Cetin MS, Ozcan Cetin EH, Kalender E et al. Monocyte to HDL Cholesterol Ratio Predicts Coronary Artery Disease Severity and Future Major Cardiovascular Adverse Events in Acute Coronary Syndrome. Hear Lung Circ. 2016; 25: 1077-86.
8. Markis JE, Joffe CD, Cohn PF, Feen DJ, Herman MV, Gorlin R. Clinical significance of coronary arterial ectasia. Am J Cardiol. 1976; 37: 217-22.
9. Mancia G, Fagard R, Narkiewicz K et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J 2013; 34: 2159-19.
10. Mancia G, De Backer G, Dominiczak A et al. 2007 guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens. 2007; 25: 1105-87.
11. Sadr-Ameli M, Sharifi M. The natural history of ectatic coronary artery disease. Iranian Heart J 2001; 2: 12-16.
12. Li JJ, Nie SP, Qian XW, Zeng HS, Zhang CY. Chronic inflammatory status in patients with coronary artery ectasia. Cytokine 2009; 46: 61-64.
13. Turhan H, Erbay AR, Yasar AS et al. Plasma soluble adhesion molecules; intercellular adhesion molecule-1, vascular cell adhesion molecule-1 and E-selectin levels in patients with isolated coronary artery ectasia. Coron Artery Dis 2005; 16: 45-50.
14. Işık T, Ayhan E, Uyarel H, Tanboğa IH, Kurt M, Uluganyan M, Ergelen M, Eksik A. Association of neutrophil to lymphocyte ratio with presence of isolated coronary artery ectasia. Turk Kardiyol Dern Ars 2013; 41: 123-30.
15. Takahashi K, Takeya M, Sakashita N. Multifunctional roles of macrophages in the development and progression of atherosclerosis in humans and experimental animals. Med Electron Microsc 2002; 35: 179-203.
16. Hessler JR, Robertson AL, Chisolm GM. LDL-induced cytotoxicity and its inhibition by HDL in human vascular smooth muscle and endothelial cells in culture. Atherosclerosis 1979; 32: 213-29.
17. Gratchev A, Sobenin I, Orekhov A, Kzhyshkowska J. Monocytes as a diagnostic marker of cardiovascular diseases. Immunobiology 2012; 217: 476-82.
18. Murphy AJ, Woollard KJ, Hoang A et al. High-density lipoprotein reduces the human monocyte inflammatory response. Arterioscler Thromb Vasc Biol 2008; 28: 2071-77.
19. Canpolat U, Aytemir K, Yorgun H et al. The role of preprocedural monocyte-to-high-density lipoprotein ratio in prediction of atrial fibrillation recurrence after cryoballoon-based catheter ablation. Europace 2015; 17: 1807-15.
20. Kundi H, Gok M, Kiziltunc E, Cetin M, Cicekcioglu H, Cetin ZG, Karayigit O, Ornek E. Relation Between Monocyte to High-Density Lipoprotein Cholesterol Ratio With Presence and Severity of Isolated Coronary Artery Ectasia. Am J Cardiol. 2015; 116: 1685-89.

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Original Article

Treatment for venous aneurysm: A salvage technique of AVF with an early cannulation prosthetic graft

Venöz anevrizma tedavisi: Erken kanüle edilebilen prostetik grefti ile AVF kurtarma tekniği

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ABSTRACT

Aim: A Venous aneurysm (VA) is one of the complications of arteriovenous fistulas (AVF) and may lead to rupture and potentially fatal bleeding. VA formation in AVF is mostly seen in the upper arm.

Material and Methods: Between January 2018 and December 2018, a total of 12 VA patients underwent surgery to end-to-end anastomosis using a vascular graft.

Results: Eight of the patients (66%) were males, and the mean age was 43.1 years (range 25-69 years). All of the fistulas were in the upper arm; two were basilic transpositions, and 10 were brachiocephalic AVF. Mean VA diameter was 4,7 cm (range 3-7 cm). All patients cannulated successfully within 24-48 hours from the newly placed AV access.

Conclusions: The procedure we described in this series is a successful and effective method for the treatment of VA in AFV. Postoperatively, most of the patients discharged early, and the VA site could be used for HD in 24-48 hours.

Keywords: early cannulation; vascular graft; arteriovenous fistula; venous aneurysm

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ÖZ

Amaç: Venöz anevrizma (VA), rüptür ve ölümcül kanamalara da sebep olabilen arteriyovenöz fistüllerin sık görülen komplikasyonudur. AVF' de venöz anevrizma çoğu üst ekstremite de görülür.

Gereç ve Yöntemler: Ocak 2018 ile Aralık 2018 tarihleri arasında toplam 12 venöz anevrizma hastasına vasküler greft kullanılarak end-to-end anastomoz yapılmıştır.

Bulgular: Hastaların 8 (%66) tanesi erkekti. Ortalama yaş 43.1 yaşdı.(25-69 yaş aralığı). Tüm fistüller üst ekstremite yer alıyordu, 2 tanesi bazilik ven transpozisyonu ve 10 tanesi brakiyosefalik arteriyovenöz fistüldü. Venöz anevrizma ortalama çapı 4.7cm (3-7cm aralığı) tespit edildi. Tüm hastalarda kullanılan vasküler greft ilk 24-48 saat içinde başarılı bir şekilde AV giriş için kullanıldı.

Tartışma: Bu seride anlattığımız prosedür, AVF' de sık görülen venöz anevrizma komplikasyonunun çözümü için başarılı ve etkin bir yöntemdir. Postoperatif dönemde hastaların erken taburcu edilebilmesi ve VA bölgesindeki greftin 24-48 saat içinde hemodiyaliz için kullanılabilir olması işlemin avantajı olarak görülmüştür.

Anahtar kelimeler: erken kanülasyon; vasküler greft; arteriyovenöz fistül; venöz anevrizma

Introduction

Arteriovenous fistula (AVF) is now widely accepted as the vascular access in patients undergoing HD (Hemodialysis) due to its low complication and high patency rate. Although superior to grafts and catheters, venous aneursym (VA), one of the significant difficulties of AVF, can cause rupture and even fatal bleeding. VA formation in AVF is mostly seen in the upper arm [1].

The most often cause of VA formation is repeated punctures at the vascular access sites. This repeated injury results in weakening of the vascular wall and consequently a VA formation [2]. The other mechanism that causes VA formation is proximal stenosis raising the pressure in the AVF. Expansion and rupture of the VA are the main complications, and this expansion can lead to skin atrophy and ulceration that may result in infection and rupture of the aneurysmatic vein. VA can also severely reduce the patient's quality of life. Ligation is the best treatment option for VA of the AVF and creation of a new access site. Salvage is possible by resection of the VA followed by end-to-end anastomosis, thus in such patients bypass needed [3]. Experience has shown that bypass using a prosthetic material is reliable [4] and early cannulation from the new access site is successful.

Material and Methods

Twelve patients included in the study who underwent VA resection between January 2018 and December 2018 at Ankara Numune and Research Hospital. Data were retrieved from our hospital medical record system.

All 12 patients underwent a preoperative colour Doppler ultrasound examination to determine aneurysm diameter, detect intraluminal thrombus, identify stenosis, measure flow through the AVF, and assess the central outflow. Sedation and local anaesthesia used for the procedure (Figure 1). No heparin given during surgery and antibiotics were not used. A longitudinal incision was performed on the VA (Figure 2). VA was completely skeletonised using this incision (Figure 3). Vascular clamps used to control the proximal and distal portion of the AVF. Then the VA was circumferentially dissected, and a large amount of organised thrombus material was removed, and the aneurysm sac was resected. End-to-end anastomosis performed between the proximal and distal portion of the AVF with 6 mm of Acuseal ® Vascular Graft (Gore Ltd, Flagstaff, AZ) (Figure 4). This vascular graft is a multi-layer vascular graft which includes an elastomer membrane between the inner and outer layers of expanded polytetrafluoroethylene (ePTFE). The lumen of the Acuseal vascular graft incorporates the CBAS Heparin Surface which imparts thromboresistant properties to the vascular graft. After placing the vascular graft the excess skin over the AVF resected and hemostasis achieved. HD was successfully performed on patients with interpositional Acuseal vascular graft the following day. These patients did not require preoperative placement of a tunnelled HD catheter. Local ethics committee approved the study and informed consent was obtained from participant(s)

Figure 1. Preoperative massive aneurysmal arteriovenous fistula (AVF).

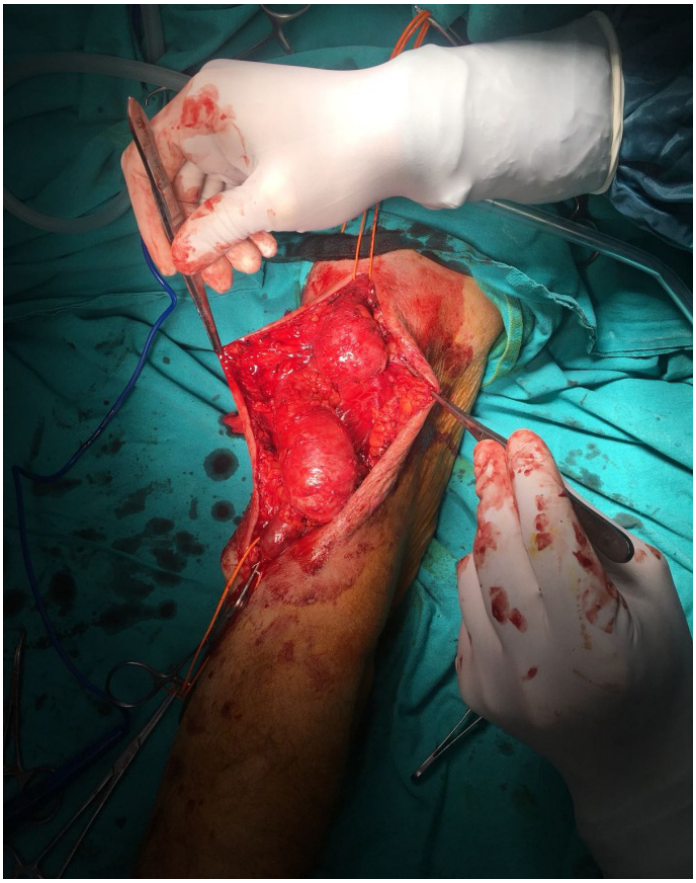

Figure 2. Intraoperative venous aneurysm.

Figure 3. Circumferential dissection of a venous aneurysm (VA).

Figure 4. End-to-end anastomosis was performed between the proximal and distal portion of the AVF with 6 mm of Acuseal vascular graft.

Results

A total of 12 patients underwent this procedure within one year. Eight of the patients (66%) were males, and mean age was 43.1 years (range 25-69 years). In 6 patients (%50) the indication for operation was skin necrosis and erosion with imminent danger of bleeding, stenosis related to an aneurysm in two (16%) and difficulty with needle cannulation in four (33%).

All patients discharged on day two. The average operative duration was 65 minutes, and there was only one complication after surgery which was wound bleeding and stopped with adrenaline packing.

All of the fistulas were in the upper arm; two were basilic transpositions, and 10 were brachiocephalic AVF' s. Mean VA diameter was 4.7 cm (range 3-7 cm). All patients were able to enter HD within 24-48 hours — no postoperative complications seen such as infection, hematoma, lymphatic leak, or skin flap necrosis. There was no 30-day mortality. In two of the patient, there were swelling on the forearm, but the flow of AVF was normal two months after the surgery. Colour Doppler ultrasound revealed a stenosis segment of the axillary vein in one patient and the patient treated with percutaneous transluminal angioplasty. No vascular complications were seen during the follow-up period and all patients with functional AVF.

Discussion

VA, may disrupt the function of AVF, may limit vascular access sites for HD and can result in rupture and massive bleeding. Unfortunately, most of our patients have been cannulated for dialysis from the VA segments. This is because of the dialysis staff awareness or carelessness or insufficient vascular access sites along the AVF, or both. [5]. The incidence of rupture after vascular access is 0.8% to 5.2% [6,7]. The primary goal of VA treatment is to remove the VA segment with the weakened vascular wall and to preserve the AVF functionality. It is known that the aneursym continues to expand from this weak vessel wall segments and increases the risk of rupture during HD cannulation. Also in time, makes it difficult to find a proper and safe cannulation site. In tortuous and aneurysmal AVF, thrombus formation is typical and can affect the flow during HD.

Several techniques for treatment like the surgical or endovascular treatment of VA have been described in the literature. In the surgical procedure, VA resection or ligation can be performed and after a new AVF can be created [8]. One of the salvage techniques is aneurysmorrhaphy and external porous polyethene terephthalate (PET) prosthesis. This method also could prevent possible new aneursyms at access site [9,10]. Ligation or resection of the VA and creation of a new AVF in another location is undesirable for patients because until the newly created avf becomes available for cannulation the patients will require a temporary vascular access catheter insertion. Catheters also have their problems and complications, and it is uncomfortable for the patients.

Other surgical options include vascular grafting after ligation and resection. Although the patency rate of the prosthetic graft we use is satisfactory, its superiority over PTFE grafts in the long term is not clear. It is reported that the Acuseal grafts have shown almost the same patency comparable to conventional PTFE grafts used for AVF. These grafts low bleeding rates and contains elastomeric middle membrane between the inner and outer layers of PTFE [11]. Covalently bonded heparin coated luminal surface provides the maintenance of bioactivity and gives thromboresistant properties to the graft [12]. The most significant advantages compared to other standard grafts are that the patients can be cannulated for HD almost immediately after surgery, and patients do not need central venous catheterisation. Finally, this surgical approach should be considered for treatment of VA and rescue of AVF.

The procedure that we have described in this series is a novel and highly successful approach to the problem of diffuse VA change in AVF for dialysis. Postoperatively, most of the patients were discharged early, and the VA site could be used for HD.

Declaration of conflict of interest

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References:

1. Salahi H, Fazelzadeh A, Mehdizadeh A, Razmkon A, Malek-Hosseini SA. Complications of arteriovenous fistula in dialysis patients. Transplant Proc 2006; 38: 1261-64.
2. Jürg Schmidli et al. Vascular Access: 2018 Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS). Eur J Vasc Endovasc Surg 2018; 55: 757-818
3. Management of aneurysms: Vascular Access Society guidelines, http://www.vascularaccesssociety.com; October 30, 2009.
4. Huber TS, Carter JW, Carter RL, Seeger JM. Patency of autogenous and polytetrafluoroethylene upper extremity arteriovenous HD accesses a systematic review. J Vasc Surg 2003; 38: 1005-11.

5. Gilmore J. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for 2006 Updates: HD adequacy, peritoneal dialysis adequacy, and vascular access. Am J Kidney Dis 2006; 48: 1-322.
6. Haimov M, Baez A, Neff M, Slifkin R. Complications of arteriovenous fistulas for HD. Arch Surg 1975; 110: 708-12.
7. Zibari GB, Rohr MS, Landreneau MD et al. Complications from permanent HD vascular access. Surgery 1988; 104: 681-86.
8. Woo K, Cook PR, Garg J, Hye RJ, Canty TG. Midterm results of a novel technique to salvage autogenous dialysis access in aneurysmal arteriovenous fistulas. J Vasc Surg 2010; 51: 921-25.
9. Dedow E, Kaduk M. The Biocompound Shunt as a method of treatment of a.v. fistula aneurysm-a critical assessment. Zentralbl Chir 2006; 131: 42-44.
10. Balaz P, Rokosny S, Klein D, Adamec M. Aneurysmorrhaphy is an easy technique for arteriovenous fistula salvage. J Vasc Access 2008; 9: 81-84.
11. Maytham GG, Sran HK, Chemla ES. The use of the early cannulation prosthetic graft (Acuseal™) for angioaccess for HD. J Vasc Access 2015; 16: 467-61.
12. Chiang N, Hulme KR, Haggart PC, Vasudevan T. Comparison of FLIXENE™ and standard PTFE arteriovenous graft for early HD. J Vasc Access 2014; 15: 116-22.

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Orijinal Makale

Trombositoz saptanan çocuklarda klinik ve hematolojik profilin değerlendirilmesi

Evaluation of clinic and hematological profile of children with thrombocytosis

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ÖZ

Amaç: Trombositoz çocuklarda beklenmeyen bir bulgu olarak karşımıza çıkmakta ve daha çok reaktif trombositoz görülmektedir.Bu çalışmanın amacı çocuklarda trombositozun; sıklığını, nedenlerini, düzelme süresini, trombosit parametreleri ve enfeksiyon belirteçleri ile korelasyonunu belirlemektir.

Gereç ve Yöntemler: Ekim 2016 ile Mayıs 2018 tarihleri arasında Dr. Sami Ulus Kadın Doğum ve Çocuk Sağlığı ve Hastalıkları Eğitim ve Araştırma Hastanesinde 6 ay 18 yaş arası trombositoz saptanan çocukların dahil edildiği tanımlayıcı bir çalışmadır.

Bulgular: Toplam 107564 hastanın %10,8 (n=11643)'inde trombositoz saptandı. Bu hastaların %64,5'i 6ay-2 yaş arası çocuklardan oluşuyordu. Ciddi trombositozun 141(%1,2) hastada geliştiği görüldü.En sık ciddi trombositoz nedenleri sırası ile 80 hastada (%56,8) enfeksiyonlar, 21 hastada anemi (%14,9), 14 (%9,9) hastada ise otoimmun hastalıklar idi. Ciddi trombositozların ortalama düzelme süresi 40,2±34 gün (3-210) olarak hesaplandı. Hastaların hiçbirinde tromboembolik komplikasyon görülmedi. Trombosit sayısı ile ortalama trombosit hacmi arasında istatistiksel olarak anlamlı negatif korelasyon olduğu görüldü ($p<0,05$, $r=-0,214$). Trombosit dağılım genişliği düzeyi ile trombosit sayısı arasında korelasyon görülmedi ($p=0,95$). CRP düzeyi ile trombosit sayısı arasında istatistiksel olarak anlamlı korelasyon saptanmadı ($p=0,15$). Trombosit sayısı ile sedimantasyon hızı arasında ise istatistiksel olarak anlamlı korelasyon bulundu ($p<0,05$, $r=0,233$).

Sonuç: Çalışmamızda reaktif trombositozun sık rastlanılan bir bulgu olduğunu ve bu büyük örneklemde primer trombositozun hiç görülmediğini, sekonder trombositozda altta yatan birçok farklı nedenin olabileceğini saptadık. Dolayısı ile trombositozun ayırıcı tanısı ve yaklaşımı pediatri uzmanı tarafından yapılmalıdır ve hematoloji bölümü konsültasyonu nadiren gerekmektedir. Özellikle ciddi trombositozlarda gösterebildiğimiz enfeksiyon veya anemi yoksa kronik inflamatuar hastalıkların altta yatan neden olabileceği unutulmamalıdır.

Anahtar Kelimeler: trombositoz; primer etyoloji; sekonder etyoloji

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ABSTRACT

Aim: Thrombocytosis is come across as an unexpected finding in children and usually appears as reactive thrombocytosis. The objective of this study is to determine the incidence rate of thrombocytosis in children, the etiologic factors, duration until normalization of thrombocytosis and the correlation between thrombocytosis and thrombocyte parameters and other variables.

Material and Methods: The study included the children between 6 months and 18 years of age who were admitted to Dr. Sami Ulus Maternity and Children's Health and Diseases Training and Research Hospital and were diagnosed as thrombocytosis.

Results: The incidence of thrombocytosis was found to be 10.8% among 107564 pediatric patients throughout two years period. Sixty four point five percent of these patients were the children between ages of 6 months and 2 years. Severe thrombocytosis developed in 141(1.2%) patients. The most common acute thrombocytosis causes were, infection in 80 patients (56.8%), anemia in 21 patients (14.9%), autoimmune diseases in 14 patients (9.9%) respectively. The average normalization of acute thrombocytosis was 40.2±34 days (3-210). No thromboembolic events were observed. There was a significant negative correlation between the platelet number and the MPV ($p<0.05$, $r=-0.214$). No correlation was found between platelet numbers and PDW levels ($p=0.95$). Statistically significant correlation was found between the number of platelet and the sedimentation rate ($p<0.05$, $r=0,233$) while no correlation was found between CRP level and thrombocyte number ($p=0.15$).

Conclusions: The study showed that reactive thrombocytosis is a common finding which implies varying underlying reasons. In our sample of patients primary thrombocytosis was never observed. For this reason the differential diagnosis and treatment of thrombocytosis can be evaluated by basic pediatric approach and hematology consultation is rarely needed. Especially in acute thrombocytosis if there is no observable infection or anemia the underlying causes can be the chronic inflammatory diseases.

Key words: thrombocytosis; primary etiology; secondary etiology

Giriş

Sağlıklı çocuklarda normal trombosit sayısı 150000-450000/µL olarak kabul edilmektedir. Trombosit sayısının +2standart deviasyon skorunun (SDS)üzerine çıkması trombositoz olarak değerlendirilir.Trombositoz; trombosit sayısı 450000-700000 /µL arasında ise hafif, 700000-900000 /µL arası orta, >900000/µL ciddi olarak tanımlanmaktadır. Aynı zamanda trombositoz saptanan hastaları nedene göre primer ve sekonder olarak da sınıflandırmak mümkündür[1]. Primer(esansiyel) trombositoz, hematopoetik hücrelerin kontrolsüz çoğalmasına bağlı oluşan miyeloproliferatif bir bozukluktur. Sekonder trombositoz ise enfeksiyon, inflamasyon, demir eksikliği anemisi, malignensi gibi altta yatan birçok nedene bağlı olarak görülmektedir. Primer-sekonder ayrımını yapmak bazen güç olabilir. Klinikte trombositoz beklenmeyen ancak sık bir bulgu olarak karşımıza çıkmaktadır. Trombositozun nedenini saptamak için bazen ayrıntılı incelemelere gerek duyulmaktadır. Bu çalışmanın amacı çocuklarda trombositozun; sıklığını, nedenlerini, düzelme süresini, trombosit parametreleri ve enfeksiyon belirteçleri ile korelasyonunu belirlemek ve trombositoz için farkındalık oluşturmaktır.

Gereç ve Yöntemler

Bu çalışma Ekim 2016 ile Mayıs 2018 tarihleri arasında Dr. Sami Ulus Kadın Doğum ve Çocuk Sağlığı ve Hastalıkları Eğitim ve Araştırma Hastanesinderetrospektif olarak yapıldı. Yaşı altı ay ve üstü olup hastanemize çeşitli nedenlerle başvuran ve tam kan sayımı yapılan çocuklardan trombositoz (trombosit sayısı>450x103/µL) saptananlar çalışmaya dahiledildi. Çocukların yaşları, cinsiyetleri, hemoglobin (Hb), ortalama eritrosit hacmi (MCV), eritrosit dağılım genişliği (RDW), beyaz küre sayısı (WBC), ortalama trombosit hacmi (MPV)[6,8-9,7fL], trombosit dağılım genişliği (PDW) [%44-56], C-reaktif protein (CRP)[0-4 mg/L], sedimantasyon [0-20 mm/saat] değerleri kaydedildi. Ağır trombositoz saptanan hastaların hastaneye başvuru şikâyetleri, kullanmakta olduğu ilaçlar, splenektomi hikayesi ve trombositozun ne kadar sürede düzeldiği kaydedildi. Trombositoz sınıflaması aşağıdaki gibi yapıldı.

1) Hafif trombositoz (450x103/µL-700 x103/µL)
2) Orta trombositoz (700 x103/µL-900 x103/µL)
3) Ciddi trombositoz (900 x103/µL ve üstü)

Trombositoz etiyolojisi klinik ve laboratuvar veriler hasta dosyaları incelenerek elde belirlendi.

Çalışma için lokal etik kuruldanonay alındı. Çalışma Helsinki İlkeler Deklerasyonuna uyularak gerçekleştirilmiştir.

Veriler SPSS 15 paket programı kullanılarak analiz edildi. Tanımlayıcı istatistikler; sürekli değişkenler için ± standart sapma, kategorik değişkenler için ise sayı ve yüzde olarak ifade edildi. İstatistik hesaplamalarda anlamlılık (önemlilik) düzeyi %5 olarak alındı. Ortalamaların ve yüzdelerin gruplar arası karşılaştırılmasında ANOVA testi kullanıldı.Korelasyon analizlerinde pearson korelasyon (r) katsayısı kullanıldı. Çalışma için yerel etik kurul onayı alındı. Hasta onam formları imzalatıldı.

Bulgular

Ekim 2016 ile Mayıs 2018 tarihleri arasında Dr. Sami Ulus Kadın Doğum ve Çocuk Sağlığı ve Hastalıkları Eğitim ve Araştırma Hastanesinde 6 ay-18 yaş arası çocuklarda bakılan toplam hemogram sayısı 152179 idi. Hemogram bakılan toplam hasta sayısı ise 107564 olarak bulundu. Hemogram bakılan hastaların %10,8 (n:11643)'inde trombositoz saptandı. Trombositoz saptanan hastaların %56,7'sini erkekleroluşturuyordu, yaş ortalaması 36,9±44,2 (6-216 ay) idi. Çalışmaya dahil edilen çocukların %64,5 (n=7512)'i 6ay-2 yaş arasında, %19,3(2246)'ü 2-5 yaş arası çocuklar oluşturuyordu. Hastaların %92,4'ünü (n=10765) hafif trombositozlu olgular, %6,3 (n=737)'ünü orta derecede trombositozu olanlar, %1,2 (n=141)'sini ise ağır trombositozu olan hastalar oluşturuyordu (Tablo1).

Tablo1: Trombositoz saptanan hastaların yaşa ve trombositoz derecesine göre dağılımı

Trombositoz	6ay-2 yaş	2-5 yaş	5 yaş<	Toplam
Hafif Trombositoz	6948	2061	1756	10765 (%92,5)
Orta Trombositoz	473	158	106	737 (%63,3)
Ağır Trombositoz	91	27	23	141 (%12,2)
Toplam	7512 (%64.5)	2246 (%19,3)	1885 (%16,2)	11643 (%100)

Ağır trombositoz nedenlerine bakıldığında sırası ile 80 hastada (%56,8) enfeksiyonlar, 21 hastada anemi (%14,9), 14 (%9,9) hastada ise otoimmun (kronik inflamatuar) hastalıklar olarak saptandı (Tablo 2). Sekiz (%5,7) hastada ise herhangi bir neden bulunamadı. En sık enfeksiyöz hastalıklar alt solunum yolu enfeksiyonları (%55,3), akut gastroenteritler(%15,8) ve idrar yolu enfeksiyonları (%11,8) idi. Trombositoza neden olan otoimmun hastalıklar sırası ile 8 hastada Kawasaki Hastalığı, 4 hastada Henoch Schönlein Purpurası, 1 hastada inflamatuar bağırsak hastalığı (İBH), 1 hastada ise akut romatizmal ateş idi. Sekiz hastada malignite saptandı; bunların 6'sında enfeksiyona bağlı trombositoz, 2'sinde ise ilaca (filgrastim, deksametazon) bağlı trombositoz geliştiği görüldü.İki hastada perfore appandisite bağlı trombositoz görüldü. 1 hastada anemi ile birlikte raşitizim vardı. Anemi saptanan 32 hastanın 28'inde demir eksikliği anemisi saptanırken diğer 4 hastada sırası ile herediter sferositoz(splenektomi ile birlikte (n=2)), talasemi intermedia (n=1), otoimmun hemolitik anemi (n=1)olduğu belirlendi. Çalışmamızda primer trombositoz görülmedi. Hiçbir hastada trombotik komplikasyon görülmedi.

Tablo 2: Ciddi Trombositoz Nedenleri

	Sayı=141	Yüzde:100
II) PrimerTrombositoz	0	%0
II)Reaktif Trombositozis	141	%100
Enfeksiyon	80	%56,8
Anemi	21	%14,9
Anemi+ Enfeksiyon	11	% 7,8
Kawasaki	8	%5,7
HenochSchönleinPurpurası (HSP)	4	%2,8
Konjenital Kalp Hastalığı	2	% 1,4
İlaca bağlı	2	%1,4
Perfore appandisit	2	% 1,4
İnflamatuar bağırsak hastalığı	1	% 0,7
Akut Romatizmal Ateş	1	% 0,7
İdiopatik	9	% 6,4

Hastaların başvuru şikayetlerigözden geçirildiğinde %48,2 (n=63)'sinin ateş şikayeti ile %33,3 (n=47)'nün solunum sistemi semptomları, %12,1 (n=17)'ningastrointestinal semptomlar ile %1,4 (n=2)'ünün ise hiçbir şikayet yokken başvurduğu tespit edildi. Şikayeti olmayan bu iki hastada demir eksikliği anemisi saptandı.

Ciddi trombositozların ortalama düzelme süresi 40,2±34 gün(3-210 gün) olarak hesaplandı. Ciddi trombositozların %64,5'i (n=91) hastanede yatan hastalardan oluşuyordu. Hastanede yatışı sırasında trombositoz saptanan hastaların hepsine intravenöz hidrasyon başlandığı tespit edildi.Dokuz hastaya aspirin başlandı;bunların 8 tanesi Kawasaki Hastalığı tanısı almıştı, 1 tanesi ise ARA nedeni ile takipli idi.

Tüm gruplarda trombosit parametrelerine bakıldığında MPV ortalama değeri hafif trombositoz grubunda 7,56fL, orta derece trombositoz saptanan grupta 7,41fL, ciddi trombositoz olan grupta ise 7,35fL bulundu. Trombosit sayısı ile MPV arasında istatistiksel olarak anlamlı negatif korelasyon olduğu görüldü($p<0,05$, $r=-0,214$). Gruplar arası ortalama PDW düzeyleri arasında istatistiksel olarak anlamlı fark saptanmadı ($p=0,35$). PDW düzeyi ile trombosit sayısı arasında korelasyon da görülmedi ($p=0,95$). CRP düzeyi ile trombositoz sayısı arasında korelasyon saptanmazken ($p=0,15$), trombosit sayısı ile sedimantasyon arasında ise istatistiksel olarak anlamlı korelasyon bulundu ($p<0,05$, $r=0,233$) (Tablo 3).

Tablo 3: Trombositozşiddetiiletrombositindeksleriveakutfazreaktanlarıortalamalarınınkorelasyonu

	Hafif Trombositoz	OrtaTrombositoz	CiddiTrombositoz	r değeri (p değeri)
Ortalama MPV (fL)	7,56±0,81	7,41±0,79	7,35±0,78	-0,214 (<0,05)
Ortalama PDW (%)	39,5±0,68	41,3±0,72	37,6±0,71	-0,051 (0,95)
OrtalamaCRP (mg/L)	48,4±10,9	42,5±11,3	49,4±11,6	0,562 (0,15)
Ortalama Sedimantasyon hızı (mm/saat)	18,6±5,6	28,3±3,2	64,7±5,9	0,233 (<0,05)

Tartışma

Trombositoz çocuklarda sık rastlanan ancak yeterince araştırılmamışbir bulgudur. Bunun nedeni nadiren semptoma yol açması ve çoğunlukla akut faz reaksiyonu olarak görülmesidir[2]. Üçüncübasamak çocuk hastanesinde retrospektif olarak yaptığımız bu çalışmada trombositoz insidansı%10,8 olarak bulundu.Literatürde çocuklarda sekondertrombositozsıklığıileilgiliyapılmışçalışmalarda%6-15 arası değişen sonuçlar verilmiştir. Ancak bu çalışma yatan hastalarda yapılmıştır[3]. Çalışmamızda trombositozların sadece % 12,2'sinde ciddi trombositoz saptanırken etiyolojide % 56,8 oranında enfeksiyonlar ilk sırada yer almaktaydı. Enfeksiyon hastalıklarını anemi ve otoimmun hastalıklar takip etti.Erişkin çalışmalarında primer trombositoza çok daha sık rastlanırken çocuklarda daha çok ikincil nedenlere bağlı reaktif trombositoz görülmektedir.Reaktif trombositozda mekanizma altta yatan nedene göre değişkenlik göstermektedir. Megakaryosit proliferasyonu, trombosit salınımının artması ve/veya trombosit sekestrasyonunun veya döngüsünün azalması patofizyolojide rol oynamaktadır. Primer trombositoz megakaryosit öncüllerinin spontan olarak üretimindeki ve trombopoetine (Tpo) duyarlılıklarındaki artışa bağlı gelişmektedir. Sekonde rtrombositoz ise akut faz cevabı olarak hepatik Tpo sentezindeki artışa bağlı olarak megakaryosit öncüllerini uyarılması ile gelişmektedir[4]. Literatürde esansiyel trombositoz insidansı 100000'de 0,6-2,5 olarak bildirilmiştir[5]. Onbir bin altıyüz kırk üç (11643) trombositoz saptanan hastanın tarandığı çalışmamızda esansiyel trombositoz görülmedi. Sekonder trombositoza 2 yaş altında daha sık rastlanılmaktadır[6]. Benzer olarak çalışmamızda da trombositozların %64,5'i 2 yaş altındaki çocuklarda görüldü.

Çalışmalarda çocuklarda sekonder trombositozların en sık nedeni olarak enfeksiyonlar bildirilmiş olup bizim çalışmamızda da aynı sonuca ulaşılmıştır. Solunum yolu enfeksiyonlarında trombositoza sık rastlanırken literatürde gastrointestinal ve üriner sistem enfeksiyonları da dikkat çekicidir [7].

Trombosit sayısı, inflamatuar bağırsak hastalığı, Kawasaki gibi kronik inflamasyonla giden hastalıklarda yükselmektedir. Çalışmamızda da ciddi trombositoz olan grupta, 8 hastada Kawasaki, 1 hastada inflamatuar bağırsak hastalığı, 1 hastada ise akut romatizmal ateş tanısı olduğu görüldü. Kronik inflamatuar hastalıklarda, inflamatuar mediatörlerin salınımına bağlı olarak kemik iliğinde trombosit yapımı uyarılmakta ve trombosit ömrü uzamaktadır[8]. Kronik inflamatuar hastalıklardan Kawasaki Hastalığı çocukluk çağının göreceli olarak daha sık rastlanan vaskülitidir. Özellikle infantlarda klinik bulguların daha silik olması nedeni ile tanı koymada zorluk yaşanmaktadır. Lise ve arkadaşlarının yaptıkları çalışmada ciddi trombositoz saptanan hastalarda Kawasaki Hastalığı olma ihtimalinin 17 kat arttığı tespit edilmiştir[9]. Kawasaki Hastalığı'nın çocuklarda görülme sıklığı yüzbinde 8,9 olarak bildirilmektedir[10]. Bizim çalışmamızda ciddi trombositozu olan grupta Kawasaki hastalığı sıklığı %5,7 olarak bulundu.Benzer şekilde kronik inflamatuar bir hastalık olan İBH'da yapılan çalışmalar trombositozun hastalık aktivitesi ve demir eksikliği anemisi ile belirgin korelasyonu olduğunu göstermiştir. Hastaların takibinde trombosit sayısının artışının diğer akut faz reaktanlarına göre daha anlamlı olduğu görülmüştür[8,11]. Çalışmamızda ciddi trombositoz saptanan hastalardan dördünde Henoch Schönlein Purpurası (HSP) olduğu belirlendi. Yine hastalığın ciddiyeti ile orantılı şekilde HSP tanısı alan hastalarının yaklaşık %60-70'inde trombositoz saptanmaktadır bu da trombopoetinden ziyade IL-6 ilişkili kronik inflamasyona bağlanmıştır[12]. Kronik inflamasyon göstergesi olan sedimantasyon değerinin çalışmamızda trombosit sayısı ile anlamlı korelasyon gösterdiğini saptadık. Ancak trombosit sayısı ile CRP arasında istatistiksel olarak anlamlı korelasyon saptanmadı. Griesshammer ve arkadaşlarının yaptıkları çalışmada sedimantasyonun sekonder trombositozu olan olgularda primer trombositozlara göre anlamlı olarak daha yüksek olduğu gösterilmiştir[13].

Çalışmamızda 2 hastada ilaca bağlı trombositoz görüldü. Vakalardan bir tanesi Burkitt lenfoma nedeniyle deksametazon tedavisi alırken,diğeri ise non-hodgkin lenfoma kemoterapi tedavisi sonrası filgrastim(granulocyte colony stimulating factor-GCSF) tedavisinin 2. gününde trombositoz geliştirmişti. Literatürde GCSF'e bağlı ciddi trombositoz çok nadir bildirilmiştir ve megakaryosit yüzeyinde eksprese edilen GCSF reseptörüne bağlı olarak geliştiği düşünülmektedir[14]. Kortikosteroidlerin ise dalakta depolanmış trombositlerin dolaşıma salınmasına yol açarak geçici trombositoz yaptığı bilinmektedir[4].

Demir eksikliği anemisi klinik tecrübe ve literatürde yapılmış çalışmalar eritropoetik ve trombotik büyüme faktörleri arasındaki ilişki sonucu trombosit üretimindeki artışa bağlı olarak artmaktadır. Bir başka mekanizmada ise demir eksikliğinde trombositlerdeki tübülin sentezinin azalmasına bağlı kompanzatuar trombosit yapımının arttığı düşünülmektedir[15]. Çalışmamızda enfeksiyondan sonra en sık görülen trombositoz nedeni demir eksikliği anemisi olarak bulundu. Bir hasta da talasemi intermedia nedeniyle takipli idi. Benzer çalışmalarda da anemi trombositoza sık neden olan bir durum olarak tespit edilmiştir[16].. İki hasta ise herediter sferositoz nedeniyle splenektomi olmuştu ve splenektomi sonrası bu hastalarda trombositoz gelişmişti. Splenektomi sonrası görülen reaktif trombositoz sıklığı %75-82 olarak bildirilmektedir ve 280 vakalık erişkinlerde yapılmış bir çalışmada trombositoz yapan nedenler içinde splenektomi%19oranında bildirilmiştir. Çocuklarda ise daha nadirdir.Trombosit regülasyonunda önemli rol oynayan dalağın alınması ile 1-3 hafta içerisinde trombositoz gelişmektedir. Trombosit sayısının normale dönmesi haftalar veya aylar içinde olmakta nadiren de yıllarca sürebilmektedir[17].

Trombositozda tedaviyi belirlemede en önemli soru trombositozun primer mi sekonder mi olduğudur. Reaktif trombositozdat rombosit sayısının düşürülmesine veya antitrombosit tedavisinin verilmesine gerek yoktur. Anormal trombosit sayısı kendi başına hastayı hemostatik ve vasküler olaylar için riske sokmaz. Sekonder trombositozda altta yatan hastalığın tedavisini yapmak yeterlidir.Trombosit sayısını azaltmaya çalışmak gibi bir amacımız olmamalıdır. Hidrasyon, aspirin ve diğer ajanlar sekonder trombositozda önerilmez. Çocuklarda tedavi sadece esansiyel trombositozlarda ve tromboembolik komplikasyonlarda kullanılmalıdır. Ayrıca esansiyel trombositozda bile erişkinlere göre çocuklardaki tedavide daha konservatif yaklaşım önerilmektedir[18,19]. Çalışmamızda Kawasaki Hastalığı ve ARA nedeniyle takipli toplam 9 hastaya doğru endikasyonla aspirin tedavisi verildiği görüldü. Ciddi trombositozu olan hastaların ise %64,5'ine literatürde önerilmediği halde intravenöz hidrasyon yapıldığı tespit edildi. Ciddi trombositozun düzelme süresini ortalama 40,2±34 gün olarak bulduk, literatürde ise düzelme süresi ile ilgili nadir çalışmaya rastladık ve düzelme zamanı ile ilgili farklı sonuçlara rastladık. Rowa ve arkadaşlarının 36 tane sekonder trombositoz saptanan hastada yaptıkları çalışmada sadece 21 hasta takibe alınabildiği ve bu hastaların hepsinin trombosit sayısının üçüncü ayın sonunda düzeldiği ve ortanca düzelme süresinin ise 4 hafta olduğu belirtilmiştir. Chan ve arkadaşları ise trombositozun ikinci günden sonra düzelmeye başladığını bildirmiştir[20,21].Trombositozun düzelme süresi ile ilgili bu farklılığın nedeni trombosit ömrü, inflamasyonun geçiş süresi ve altta yatan hastalığın iyileşme zamanından kaynaklı olabilir.

Bu çalışmada artan trombosit sayısı ile MPV değeri arasında negatif istatistiksel olarak anlamlı korelasyon saptanırken PDW değeri ile trombositoz ciddiyeti arasında anlamlı korelasyon görülmedi. Literatürdeki benzer çalışmalarda da aralarında negatif korelasyon olduğu gösterilmiştir[22]. Çünkü MPV değerinin düşük olması trombosit fonksiyonu ve aktivasyonu için bir gösterge olarak bilinmektedir[23].

Sonuç

Çalışmamızda reaktif trombositozun sık rastlanılan bir bulgu olduğunu ve bu büyük örneklemde primer trombositozun hiç görülmediğini, sekonder trombositozdaaltta yatan birçok farklı nedenin olabileceğini saptadık. Trombositozun ayırıcı tanısı ve yaklaşımı pediatri uzmanı tarafından yapılmalıdır. Çalışmamızın da trombositoz konusunda farkındalık oluşturacağını düşünüyoruz. Özellikle ciddi trombositozlarda gösterebildiğimiz enfeksiyon veya anemi yoksa kronik inflamatuar hastalıkların altta yatan neden olabileceği unutulmamalıdır.

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Kaynaklar

1. Chiarello P, Magnolia M, Rubino M, Liguori S, Miniero R. Thrombocytosis in children. Minerva pediatrica 2011; 63: 507-13.
2. Harrison CN, Bareford D, Butt N et al. Guideline for investigation and management of adults and children presenting with a thrombocytosis. British journal of haematology 2010; 149: 352-75.
3. Dame C, Sutor AH. Primary and secondary thrombocytosis in childhood. British journal of haematology 2005; 129: 165-77.

4. Kucine N, Chastain KM, Mahler MB, Bussel JB. Primary thrombocytosis in children. Haematologica 2014; 99: 620-28.
5. Aladily TN, Mohammad RS, Al-Khader A, Awidi AS. Essential Thrombocythemia in a Two-year-old Child, Responsive to Hydroxyurea but Not Aspirin. Oman medical journal 2017; 32: 243.
6. Indolfi G, Catania P, Bartolini E et al. Incidence and clinical significance of reactive thrombocytosis in children aged 1 to 24 months, hospitalized for community-acquired infections. Platelets 2008; 19: 409-14.
7. Zheng S-Y, Xiao Q-Y, Xie X-H et al. Association between secondary thrombocytosis and viral respiratory tract infections in children. Scientific reports 2016; 6: 22964.
8. Matowicka-Karna J. Markers of inflammation, activation of blood platelets and coagulation disorders in inflammatory bowel diseases. Postepy higieny i medycyny doswiadczalnej (Online) 2016; 70: 305-12.
9. Nigrovic LE, Nigrovic PA, Harper MB, Chiang VW. Extreme thrombocytosis predicts Kawasaki disease in infants. Clinical pediatrics 2006; 45: 446-52.
10. Özdemir H, Çiftçi E, Tapısız A et al. Clinical and epidemiological characteristics of children with Kawasaki disease in Turkey. Journal of tropical pediatrics 2009; 56: 260-62.
11. Voudoukis E, Karmiris K, Koutroubakis IE. Multipotent role of platelets in inflammatory bowel diseases: a clinical approach. World Journal of Gastroenterology: WJG 2014; 20: 3180.
12. Lin C, Yang Y, Lee C, Huang C, Wang L, Chiang B. Thrombopoietin and interleukin-6 levels in Henoch-Schonlein purpura. Journal of Microbiology Immunology and Infection 2006; 39: 476.
13. Griesshammer M, Bangerter M, Sauer T, Wennauer R, Bergmann L, Heimpel H. Aetiology and clinical significance of thrombocytosis: analysis of 732 patients with an elevated platelet count. Journal of internal medicine 1999; 245: 295-300.
14. Dihingia S, Deka K, Bhuyan D, Mondal SK. Life-threatening thrombocytosis following GCSF treatment in a case of clozapine-induced agranulocytosis. General hospital psychiatry 2012; 34: 320.
15. Yung KC, Zhang ZW, Yu WJ et al. Preliminary investigation about the expression of tubulin in platelets from patients with iron deficiency anemia and thrombocytosis. Hematology 2018; 23: 549-57.
16. Subramaniam N, Mundkur S, Kini P, Bhaskaranand N, Aroor S. Clinicohematological study of thrombocytosis in children. ISRN hematology 2014; 2014: 389257.
17. Khan PN, Nair RJ, Olivares J, Tingle LE, Li Z. Postsplenectomy reactive thrombocytosis. Baylor University Medical Center Proceedings; 2009: Taylor & Francis.
18. Kiro K, Ganjoo P, Saigal D, Hansda U. Incidental thrombocytosis: Should it concern the anesthesiologist? Journal of anaesthesiology, clinical pharmacology 2014; 30: 281.
19. Mantadakis E, Tsalkidis A, Chatzimichael A. Thrombocytosis in childhood. Indian pediatrics 2008; 45: 669.
20. Vora A, Lilleyman J. Secondary thrombocytosis. Archives of disease in childhood 1993; 68: 88-90.
21. Chan KW, Kaikov Y, Wadsworth LD. Thrombocytosis in childhood: a survey of 94 patients. Pediatrics 1989; 84: 1064-67.
22. Sarangi R, Pradhan S, Dhanawat A, Patanayak R, Benia G. Thrombocytosis in children: Clinico-hematological profile from a single centre in Eastern India. Journal of laboratory physicians 2018; 10: 34.
23. Gokcek E, Kaydu A. Investigation of mean platelet volume and platelet count in the blood of patients with lumbago and sciatica. Anesthesia, essays and researches 2018; 12: 855.

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Orijinal Makale

Wolf Parkinson White sendromu (WPW) ablasyonu yapılan hastaların özellikleri: Tek merkez vaka serisi

Characteristics of patients with Wolf Parkinson's White syndrome (WPW) ablation: Single center case series

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ÖZ

Amaç: Aksesuar yol varlığı ile oluşan atriyoventriküler reentran taşikardiler (AVRT) paroksismal supraventriküler taşikardilerin yaklaşık dörtte birini oluşturur. Bizim retrospektif çalışmamızın amacı katater ablasyon işlemi yapılan yüksek volümlü bir merkezde, AVRT ablasyon yapılan hastaların demografik özellikleri, etiyolojik faktörler ve komplikasyon oranları hakkında bilgi vermektir.

Gereç ve Yöntemler: Hastanemizin kardiyoloji kliniğinde Ocak 2014 ve Ocak 2018 yılları arasında SVT ablasyonu uygulanan 1107 hasta tarandı ve katater ablasyon yapılmış 232 WPW 'li hasta çalışmaya dahil edildi. Bu hastalar demografik özellikleri, etiyolojik faktörleri, aksesuar yol lokalizasyonları, işlem başarısı ve komplikasyon gelişimi açısından değerlendirilmiştir.

Bulgular: Hastaların yaş ortalaması 38 ±16,1 olup ve kadın cinsiyet oranı %37.1 dir. En sık görülen lokalizasyonun sol aksesuar kaynaklı yolak olduğu görüldü (%53,1). Tüm lokalizasyonlar için akut dönemde işlem başarısı %93,1 saptandı. Tüm hastalarda karşılaşılan komplikasyon oranı % 3,3 iken, en sık karşılaşılan komplikasyon girişim yeri hematomu olarak karşımıza çıkmıştır(% 2,1).

Tartışma: Tüm yaş gruplarını etkileyebilen ve yaşam kalitesini oldukça kötüleştirebilen bir hastalık grubu supraventriküler taşikardiler (SVT) dir. Bu grubun ikinci sıklıkta görülen üyesi AVRT'nin bilinen küratif tedavisi radyofrekans katater (RF) ablasyondur. Ablasyon tedavisi yapan hekim sayısı ve işlemin yapıldığı merkez sayısı giderek artış göstermektedir. Özellikle gelişebilecek komplikasyonlar açısından dikkat çekmek amaçlı AVRT ablasyon tecrübelerimiz bu çalışma ile sunulmuştur.

Anahtar kelimeler: atriyoventriküler; aksesuar yol, komplikasyon

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ABSTRACT

Aim: Atrioventricular reentrant tachycardia (AVRT) formed by the presence of accessory pathway accounts for about one quarter of paroxysmal supraventricular tachycardias. In our retrospective study, demographic characteristics, etiological factors and complication rates of patients undergoing AVRT ablation were reported in a high-volume center where catheter ablation was performed.

Material and Methods: In our cardiology clinic, between January 2014 and January 2018, 1107 patients who underwent SVT ablation were screened and 232 WPW patients with catheter ablation were included in the study. These patients were evaluated in terms of their demographic characteristics, etiological factors, accessory path localizations, operation success and complication development.

Results: The mean age of the patients was 38 ± 16.1 and the female gender percentage was 37.1. The most common localization was found to be left accessory origin (53.1%). While the complication rate was 3.3% in all patients, the most common complication was seen as a site of hematoma (2.1%).

Discussion: Supraventricular tachycardia (SVT) is a group of diseases that can affect all age groups and can impair the quality of life. The second most common of this group is AVRT. Catheter ablation, is the known curative treatment of it. The number of physicians performing ablation treatment and the number of centers in which the procedure is performed increase. Our experience with AVRT ablation was reported with this study.

Keywords: atrioventricular; accessory pathway, complication

Giriş

Atriyoventriküler reentran taşikardi (AVRT); anatomik olarak normal ileti sistemi ve aksesuar ileti yolun farklı ileti süresi ve refrakter özellik göstermesi nedeniyle prematür ekstrasistol veya ventriküler ekstra sistol ile oluşabilen makroreentran taşikardilerdendir [1]. Paroksismal supraventriküler taşikardilerin yaklaşık dörtte birini oluşturur. Artan yaşla birlikte azalma eğiliminde olup erkeklerde biraz daha fazla görülme eğimindedir [2]. Aksesuar yollar atriyoventriküler nodal ileti yolundan farklı özellikler gösterirler. Aksesuar yolun her iki anterograd ve retrograd iletisi sık olmakla birlikte sadece retrograd iletisi olan ve en nadir sadece anterograd iletisi olmak üzere farklılıklar gösterir[3]. Yüzeyel asemptomatik EKG de belirgin delta dalgaları olup supraventriküler taşikardi ataklarıyla seyretmesine Wolf-Parkinson-White sendromu (WPW) denir.

Akseuar ileti özelliğine göre AVRT taşikardiler ortodromik ve antidromik olmak üzere ikiye ayrılırlar. AVRT'lerin %95'i ortodromik özellik gösterirler [1]. AVRT'lerin kronik dönem tedavisinde ablasyon işlemi önerilmektedir[4, 5]. Ablasyon işleminde komplikasyon oranı yaklaşık %2,8 civarındadır[6]. Ancak deneyimli merkezlerde bu oranlar daha da düşük görülmektedir. Bu çalışmanın amacı yaklaşık 5 yıllık dönemde RF ablasyon yaptığımız AVRT hastalarının karakteristik özelliklerini, başarı ve komplikasyon oranlarını bildirmektir.

Gereç ve Yöntemler

Çalışmamızda; Ocak 2014 ve Ocak 2018 yılları içinde kardiyoloji kliniğimizde SVT ablasyonu uygulanan 1107 hasta tarandı ve RFA yapılmış 232 WPW 'li hasta dahil edildi. (Resim 1) Tüm hastalardan çalışmaya dahil edilebilmeleri imzalı onay formları alındı, çalışma için hastanemiz etik kurulundan onay alındı. Framingham koroner arter risk sınıflamasına göre orta ve yüksek saptanan hastalara ek olarak femoral arter yolu ile koroner anjiyografi yapıldı. Hastaların diyabetik, hipertansif, hiperlipidemik olup olmadığı kaydedildi. Antekübital venden alınmış rutin kan örneğinden çalışılan sonuçlar kayıt edildi. Rutin ekokardiyografik değerlendirmede (Vivid-7, GE Wingmed sound Horten, Norway); sol atriyum çapı (LAD), sol ventrikül sistolik ve diastolik çapları, sol ventrikül duvar kalınlıkları ve ejeksiyon fraksiyonu hesaplandı. Aksesuar yol lokasyonlarına göre işlem başarısı ile ilgili klinik sonuçlar ve girişimsel değişkenler kayıt altına alındı. Çalışma için yerel etik kurul onayı alındı. Hasta onam formları imzalatıldı.

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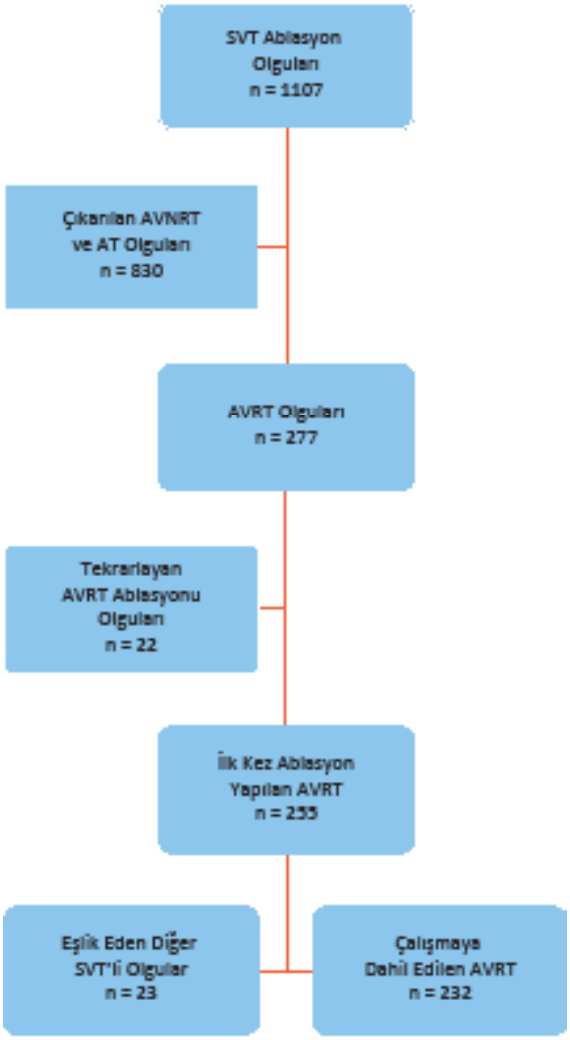
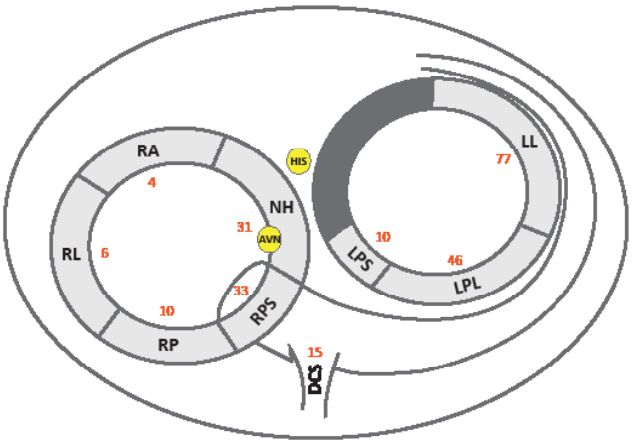


Figür 1 AVRT Ablasyon çalışması akış şeması.

Elektrofizyolojik çalışma

Bütün hastaların katater ablasyon tedavisi öncesi bilgilendirilmiş onamları alındı. Hastaların kullandıkları antiaritmik ilaç tedavisi en az beş yarı ömür öncesinden kesildi. Tüm prosedürler lokal anestezi altında yapıldı. Elektrofizyolojik çalışma ve ablasyon tedavisi femoral bölgeden kateterler yerleştirilerek EP Tracer cihazı (Medtronic, Inc., USA) ile yapıldı. Dört kutuplu tanısal kateter (6F, 110 cm, Marinr® SC Series, Medtro nic, Minneapolis, MN, USA) yüksek lateral sağ atriyuma yerleştirildi. Ek olarak on kutuplu tanısal katater (6F , 110 cm, Inquiry™ ,St. Jude Medical , St. Paul, Minnesota, USA) koroner sinüse femoral ven yada sağ internal juguler ven yolu ile yerleştirildi. Ayrıca dört kutuplu RFA kateteri (7F, 110 cm, RF Mariner® MC, Medtronic, USA) his kaydının alındığı sağ ventrikül bölgesine yerleştirildi. İlk olarak; Atriyum-His (A-H) ve His -Ventrikül (H-V) süreleri, Wenckebach noktası, atriyum, ventrikül, AV nod ve aksesuar yol efektif refrakter periyotları ölçüldü ve kayıt altına alındı. Aksesuar yolun lokalizasyonu, koroner sinüs kateterinin rehberliği ya da ablasyon katateri ile tespit edildi. Preeksitasyonu belirgin olmayan hastalarda atriyal pacing ile preeksitasyon görünür hale getirildi. Gizli aksesuar yolu olan hastalarda AVRT'yi indüklemek için programlı veya burst atriyal ya da ventriküler pacing protokolleri uygulandı. Taşikardinin indüklenmediği durumlarda isoproterenol (2–6 mcg/kg/min) ya da atropin (0.6–1.0 mg) ile sinüs ritmi en az yüzde 20 arttırıldıktan sonra uyarılar tekrarlanarak AVRT indüklendi. Taşikardi indüklendikten sonra AVRT tanısı yaygın olarak kabul edilen kriterlere göre yapıldı [7] (Resim 2).



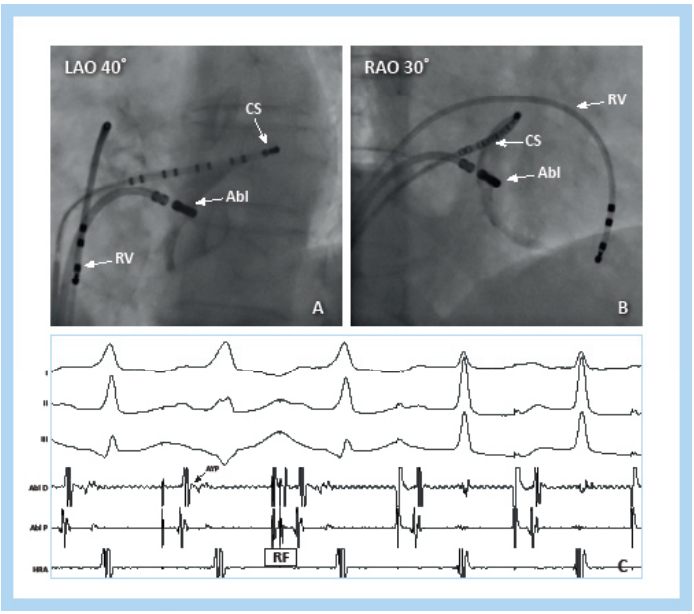
Figür 2 Aksesuar yol ablasyon lokalizasyon dağılımı.

Radyofrekans ablasyon

Temel elektrofizyolojik çalışmanın tamamlanmasından sonra, WPW ablasyonu RFA kateteri (7F, 110 cm, RF Mariner® MC, Medtronic, USA) ile floroskopik anatomik belirteçler ve karakteristik intrakardiyak elektrokardiyogram kılavuzluğunda gerçekleştirildi. Atriyoventriküler (AV) bileşkede bulunan aksesuar yollar, manifest aksesuar yollarda sinüs ritmi sırasındaki AV füzyon ile gizli WPW sendromlarda ise ventrikül pacing yada ortadromik AVRT sırasında VA füzyonu gösteren elektrogramlar kullanılarak tespit edildi.

Sol taraflı aksesuar yolların ablasyonu transaortik retrograd ya da transseptal ponksiyon yolu ile gerşekleştirildi. (Resim 2) RFA ısı kontrol modda (50°- 60°C and 30–50 W) uygulandı. Midseptal ve anteroseptal yerleşimli nodo-hisian aksesuar yollar ise RF enerji ile 40ºC ile başlanıp AV blok ya da nodal ritim gelişmediği taktirde enerji basamaklı olarak arttırılıp işlem tamamlandı. Eğer AV blok riski oluşuyor ise RFA 'dan daha güvenli olan kryoenerji kullanıldı[8]. Derin koroner sinüs kaynaklı aksesuar yol ablasyonunda ise irrigasyonlu RF ablasyon katateri (FlexAbility®, DF curve, St. Jude Medical) kullanıldı. (Resim 3) RFA güç kontrol modda (25–35 W) gerçekleştirildi. Özellikle sağ taraflı WPW ablasyonunda RFA kateter stabilitesinin yetersiz olması durumunda uzun bir kılıf (Agilis® NxT Steerable Introducer, St. Jude Medical, St. Paul, MN, ABD) kullanıldı. RF prosedürün

bitiş noktası, yüzeyel EKG'de delta dalgasının kaybolması, aksesuar iletinin antegrad ve retrograd kaybolması ve taşikardi indüklenmemesi olarak kabul edildi. Tüm hastalardan işlem sonrası elektrokardiyogramlar alınıp ekokardiyografi ile perikardiyal efüzyon varlığı değerlendirildi. Taburculuk sonrası 1. ayda poliklinik kontrolüne çağrılıp 6 aylık aralıklarla telefonla aranıp nüks ve komplikasyon açısından takip edildi.



Figür 3 Derin koroner sinüs ven kaynaklı aksesuar yol ablasyonu.

İstatistiksel Analiz

İstatiksel çalışma SPSS 17 (SPSS Inc., Chicago, IL, United States) paket bilgisayar programı kullanılarak yapıldı. Normal dağılım gösteren değişkenler ortalama ± standart sapma, normal dağılım göstermeyen değişkenler ise medyan (interquartile range: IQR) olarak ifade edildi. Kategorik değişkenler ise sıklık ve yüzde (%) olarak verildi. Normal dağılan sayısal değişkenlerin iki farklı grupta karşılaştırılmasında Student's t testi kullanılırken, normal dağılmayan sayısal değişkenler için Mann Whitney U testi kullanıldı. Nominal verilerin karşılaştırılması için ki-kare ya da Fisher's exact testleri kullanıldı. Çalışmamızda üç grup arasındaki farkın belirlenmesine yönelik Bonferroni çoklu karşılaştırma testi kullanıldı. p değeri <0.05 anlamlı olarak kabul edildi.

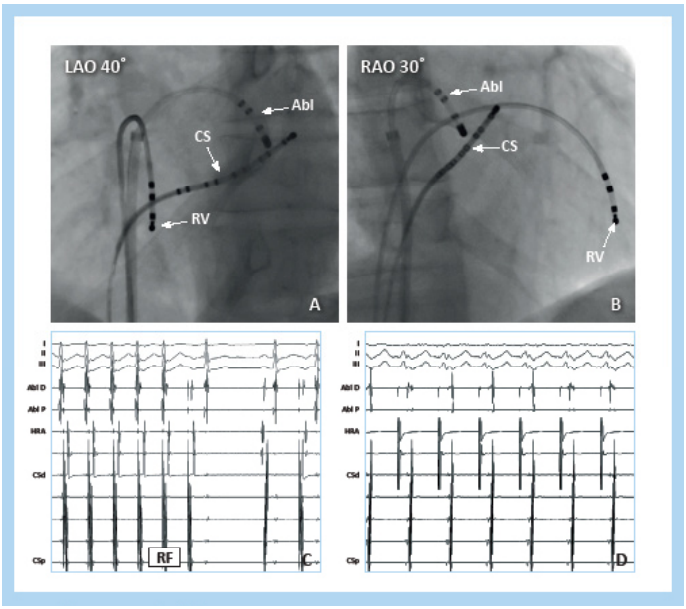
Bulgular

Çalışmada yaş ortalaması 38 ±16,1 yıl olarak saptanmıştır. Kadın cinsiyet oranı ise % 37,1 olarak görüldü. Aksesuar yolların %59,9'nun manifest aksesuar yolak olduğu tespit edildi. Manifest aksesuar yola sahip hastaların asemptomatik olma oranı %32,4 olup, çalışmaya dahil edilen tüm aksesuar yol ablasyonu uygulanan hastalarda bu oran %19,4 saptanmıştır. Çalışma grubunun demografik özellikleri, laboratuar bulguları ve ekokardiyografik ölçümleri Tablo 1'de sunulmuştur. Çalışmaya alınan hastalara koroner anjiyografi yapılma oranı %18,9 olarak saptandı. Uyarılan AVRT'lerin %8.6 'sı sağ aksesuar, %38,3'ü septal aksesuar ve %53,1'i sol aksesuar kaynaklı olduğu görüldü. (Resim 4) Hastaların % 9,1 'inde en sık atriyoventriküler nodal reentran taşikardi olmak üzere ikinci bir atriyal aritmi tespit edildi. İşlem süresi 79 ± 16 dakika, floroskopi süresi 28 ± 7,7 dakika ve toplam ablasyon süresi 368 ± 47 saniye olarak ölçülmüştür.

Tablo-1. Hastaların demografik, laboratuvar ve ekokardiyografik özellikleri

	Tüm Hastalar n=232
Yaş	38 ± 16.1
Kadın Cinsiyet, n (%)	86 (37.1)
Sigara, n (%)	30 (12.9)
Hipertansiyon, n (%)	17 (0.3)
Hiperlipidemi, n (%)	14 (6)
Diyabetes Mellitus, n (%)	10 (4.3)
LVEF (%)	57.9 ± 5.1
Septal kalınlık,mm	0.78 ± 0.18
Posterior duvar kalınlık, mm	0.81 ± 0.2
Sol ventrikül diastolic çap , mm	45 ± 3.7
Sol ventrikül sistolic çap , mm	29 ± 3.7
Sol atrial çap , mm	30 ± 2.8
LDL, mg/dL	109 ± 46
HDL, mg/dL	41 ± 11
Trigliserid, mg/dL	161 ± 60
Glukoz, mg/dL	92 ± 16
Kreatinine, mg/dL	0.8 ± 0.88
Sodyum, mg/dl	139 ± 2.9
Potasyum,mg/dl	4.2 ± 1.1
Hemoglobin, g/dL	13.1 ± 1.2
WBC, x109/L	7.1 ± 1.8
Tiroid Stimulan Hormon, mU/L	1.35 ± 1.0

LVEF: Sol ventriküler ejeksiyon fraksiyonu ; LDL: Düşük yoğunluklu lipoprotein ; HDL: Yüksek yoğunluklu lipoprotein ; WBC: beyaz kan hücresi



Figür 4 Sol lateral yerleşimli gizli aksesuar yol ablasyonu.

Akut dönemde işlem başarısı %93,1 iken uzun dönem işlem başarısı literatüre benzer şekilde %89,2 olarak karşımıza çıkmıştır. Tüm hastalarda karşılaşılan komplikasyon oranı % 3,3 iken, en sık karşılaşılan komplikasyon girişim yeri hematomu olarak saptandı (%2,1). AV tam blok ise literatüre benzer şekilde %0.8 olarak saptanmıştır. Hasta gruplarının prosedür özellikleri ve komplikasyon sıklıkları Tablo 2'de sunulmuştur.

Tablo-2 Prosedür özellikleri ve komplikasyonlar

	Tüm Hastalar n=232
Aksesuar yolak dağılımı, n (%) Sağ anterior Sağ lateral Sağ posterior Sağ paraseptal Nodo-hisian Derin koroner sinus Sol paraseptal Sol posterolateral Sol lateral	4 (1.7) 6 (2.6) 10 (4.3) 33 (14.2) 31 (13.3) 15 (6.4) 10 (4.3) 46 (19.8) 77((33.2)
Eşlik eden diğer ritim bozuklukları, n=255 (%) AVNRT Fokal atriyal taşikardi Atriyal fibrilasyon/flutter	10 (3.9) 5 (1.9) 8 (3.1)
Koroner anjio girişimi, n (%)	44 (18.9)
Akut işlem başarısı, n (%)	213 (93.1)
Uzun dönem işlem başarısı, n (%)	207 (89.2)
İşlem Süresi, dakika	79 ± 16
Ablasyon Süresi, saniye	368 ± 47
Floroskopi Süresi, dakika	28 ± 7.7
Ölüm, n (%)	0 (0)
Girişim yeri hematomu, n (%)	5 (2.1)
AV Tam blok, n (%)	2 (0.8)
Tamponad, n (%)	1 (0.04)

AVNRT, Atriyoventriküler nodal reentran taşikardi ;

Aksesuar yol lokasyonlarına göre işlem başarısı ile ilgili klinik sonuçlar ve girişimsel değişkenler karşılaştırıldığında; sağ, septal ve sol kaynaklı aksesuar yol ablasyonunda akut işlem başarısı ve rekürrens oranlarında fark saptanmadı. (sırasıyla; 18 (90%) & 81(91%) & 114 (%92,6) p=0,71 / 1 (5%) & 2 (2,2%) & 3 (2,4%) p= 0,24) Floroskopi süresi ve işlem süresi sol kaynaklı aksesuar yol ablasyonunda daha düşük saptanmıştır. (sırasıyla; 31,8 ± 10,7 & 27,7 ± 11,7 & 20,6±7,9 p< 0,05 / 79 ± 16,4 & 72 ± 15,9 & 56 ± 12,7 p< 0,05) Total ablasyon süresi ise sağ kaynaklı aksesuar yol ablasyonunda daha yüksek saptanmıştır. (sırasıyla; 407 ± 63 & 271 ± 38 & 305±41 p< 0,05) İşlem başarısı ile ilgili klinik sonuçlar ve girişimsel değişkenler Tablo 3'de sunulmuştur.

Tablo3. Aksesuar yol lokasyonlarına göre İşlem başarısı ile ilgili klinik sonuçlar ve girişimsel değişkenler

Değişkenler	Sağ aksesuar (n=20)	Septal aksesuar (n=89)	Sol aksesuar (n=123)	P değeri
Yaş (yıl)	37,8 ± 15,8	39,2 ± 17,1	38,2 ± 16,3	0,79
Cinsiyet (kadın)	35,9 %	39,9 %	37,2 %	0,88
Hipertansiyon	7,4 %	7,1 %	7,3%	0,80
Diyabetes Mellitus	4 %	4,2%	4,4%	0,91
Akut işlem başarısı	18 (90%)	81 (91%)	114 (%92,6)	0,71
Rekürrens	1 (5%)	2 (2,2%)	3 (2,4%)	0,24
İşlem Süresi (dakika)	79 ± 16,4 a	72 ± 15,9 a	56 ± 12,7 b	<0,05
Florosokopi Süresi (dakika)	31,8 ± 10,7 a	27,7 ± 11,7 a	20,6±7,9 b	<0,05
Total ablasyon Süresi (saniye)	407 ± 63 b	271 ± 38 a	305±41 a	<0,05
Total komplikasyon oranı	5 %	2,7 %	2,9	0,58

P <0,05 istatistiksel olarak anlamlı kabul edildi . a,b,c aynı harfler, Bonferroni çoklu karşılaştırma testlerine dayanan gruplar arasında anlamlı bir fark olmadığını gösteriyor.

Tartışma

Aksesuar yol ablasyonu uygulanan hastalarımızın akut ve uzun dönem başarısı sırasıyla %93,1 - %89,2 saptanmış olup, başarılı ablasyon lokalizasyonlarına göre sınıflandırıldıklarında %8.6 'sı sağ serbest duvar kaynaklı, %38,3'ü septal /derin koroner sinüs ve %53,1'i sol aksesuar kaynaklı olduğu saptandı. Bu oran Arruda MS ve ark. yaptığı çalışmayla kıyaslandığında, benzer yaş, cinsiyet ve lokalizasyon dağılım oranlarına sahip olduğu görülmektedir[9]. Başarı oranlarına bakıldığında, Calkins H ark. yaptığı vaka serisinde akut ablasyon başarısı %93, nüks oranı ise %8 saptanmış olup, çalışmamızda nüks oranı %3,9 ile daha düşük tespit edilmiştir[10]. Vaka serimizde, komplikasyon oranlarına bakıldığında, tüm komplikasyon oranı % 2,9 olup, kalıcı kalp pili gerektiren AV blok (%0,4), kan transfüzyonu yada cerrahi işlem gerektiren girişim yeri hematomu (%0,8), tamponad (%0,4) gibi majör komplikasyonların oranı % 1,6 olarak saptanmıştır ancak ölüm izlenmemiştir. Bu sonuçlar Spector P. ve ark. atriyal flutter ve supraventriküler taşikardi ablasyonu yapılan hastalardan oluşan vaka serisiyle kıyaslandığında benzer oranlarda olduğu görülmektedir [11].

Çalışmaya alınan hastalarda, işlem süresi 79 ± 16 dakika,

floroskopi süresi 28 ± 7,7 dakika ve toplam ablasyon süresi 368 ± 47 saniye ölçülmüştür. Önceki çalışmalar, eğitimli operatörler tarafından uygulanan CARTO (Biosense, Diamond Bar, CA, ABD) ve EnSite NavX (St. Jude Medical, Saint Paul, MN, ABD) gibi yaygın kullanılan bilgisayar tabanlı iç boyutlu elektroanatomik haritalama sistemleri(3D-EAM) ile konvansiyonel RFCA yöntemleri karşılaştırıldığında radyasyona maruzuyeti azaltabileceğini göstermiştir[12,13]. Jorge R. ve ark. yaptıkları çalışmanın subgrup analizinde, çalışmaya alınan ve yaklaşık dörtte biri WPW 'li olan 522 SVT ablasyonu yapılan olgular değerlendirilmiş. 3D-EAM ve konvansiyonel RFCA yapılan olgular karşılaştırıldığında, her iki grup arasında benzer akut başarı ve komplikasyon oranları tespit edilmiştir. İşlem, floroskopi ve ablasyon süreleri karşılaştırıldığında konvansiyonel RFCA yapılan grupta daha kısa saptandığı görülmüştür. 3D- EAM sistemlerinin özellikle tecrübenin az olduğu merkezlerde kullanılması, floroskopi süresini önemli ölçüde azaltmadığı ve geleneksel haritalama ile karşılaştırıldığında akut sonuçları iyileştirmediği vurgulanmıştır. Çalışmamıza dahil edilen hastaların tamamı konvansiyonel haritalama kullanılarak yapılmış olup, Jorge R. ve ark. yapmış olduğu bu çalışma ile kıyaslandığında, işlem süresi daha kısa olduğu ve floroskopi süresi ise 3D- EAM ile yapılan ablasyon grupları ile eşit olduğu görülmektedir. (Sırasıyla 272.9 & 79 dakika / 28 & 27.3 dakika)[14]. Bu bulgular; kateter manipülasyonu sırasında floroskopi kullanımını azaltarak güvenliği artırmasına izin veren; intrakardiyak ultrason, destek kataterlerinin 3D-EAM kullanımındaki tecrübelerin geliştirilmesinin gerekli olduğu fikrini desteklemektedir.

Vaka serimizde, aksesuar yolların %59,9'nun manifest aksesuar yolak olduğu tespit edildi ve manifest aksesuar yola sahip hastaların asemptomatik olma oranı %32,4 olduğu saptandı. Preeksitasyonu olup senkop veya çarpıntı gibi semptomlar eşlik eden semptomatik WPW sendromlu hastalarda, yaşam boyu % 4'e yakın ani kalp ölümü (AKÖ) riski vardır. Bu nedenle, bu semptomatik hastaların, özellikle elektrofizyolojik (EP) bir çalışma ile risk sınıflandırması ve aksesuar yolunun kateter ablasyonu önerilmektedir[15]. Bununla birlikte, elektrokardiyografik preeksitasyon saptanan hastalar, asemptomatik olduklarında, aritmik olayların sıklığı ve AKÖ riski açık değildir. Bununla birlikte elektrokardiyografide preeksitasyon saptanan hastaların ilk semptomu AKÖ olabilir[16]. Pappone ve ark. 209 WPW'li hastanın asemptomatik olan 129'unu (%62) ortalama 38 ay takip ettikleri çalışmada; 33'ünde(% 16) aritmik olay yaşadıklarını gözlemlemiş, bu 33 hastanın 25'inde SVT, 8'inde atriyal fibrilasyon (AF), 3'ünde ventriküler fibrilasyon (VF) (iki hastada AF sonrası VF'ye dönüşme, birinde ise ölüm) geliştiği belgelenmiştir[17]. 2014 yılında Pappone ve ark. asemptomatik olan ve ablasyon uygulanmayan 550 hastanın ortalama 22 aylık takiplerinde, hastaların tamamını çocuk ve adelosanlardan oluşan 13'ünde (% 2) VF geliştiğini belirtmiştir [18]." 2015 Amerikan Kardiyoloji Koleji (ACC) / Amerikan Kalp Cemiyeti (AHA) / Kalp Ritm Derneği (HRS) Supraventriküler Taşikardili Yetişkin Hasta Yönetimi Klavuzunda"; Elektrofizyolojik çalışma'nın (EFÇ), preeksitasyonu olan asemptomatik hastalarda, aritmik olaylar için risk sınıflandırması yapmak için uygun bir yöntem olduğu vurgulanmıştır[15]. Semptomların yokluğunda, klinik öncelik, artmış aritmik olay riski taşıyan aksesuar yolakları belirlemek için yapılan EFÇ'de; a) İndüklenmiş AF sırasında en kısa R-R aralığının < 250 msn olması b) Birden fazla aksesuar yol varlığı c) Sürekli AVRT'nin indüklenmesi d) Aksesuar yolun refrakter periodunun <240 msn olması maddelerinin bir yada daha fazlasının olması malign aritmi gelişimi ile korelasyon gösterdiği saptanmıştır[17-19]. Vaka serimize dahil olan asemptomatik preeksitasyonlu hastalara, tüm bu verilere ve kılavuz bilgilerine dayanarak ablasyon tedavisi uygulandı. Ancak EFÇ'de malign aritmi açısından yüksek risk kriterleri saptanmayan hastalara, ablasyon tedavisinin olası riskleri dikkate alınarak, olası kar-zarar hesabı yapılıp tedavi planlaması yapılabilinir.

Sonuç

SVT grubun ikinci sıklıkta görülen üyesi olan AVRT'nin bilinen küratif tedavisi radyofrekans katater ablasyondur. 232 hastayı kapsayan tek merkez olgu serimizde, geçmiş kohort analizlerine kıyasla benzer akut ve uzun dönem başarı oranları görülmektedir. Komplikasyon sıklığı açısından bakıldığında aksesuar yol ablasyonu sonrası gelişen kalıcı AV blok oranları benzerlik göstermektedir. Ek olarak asemptomatik preeksitasyon saptanan hastalar, AKÖ açısından, elektrofizyolojik çalışma yapılarak değerlendirilmelidir.

Maddi Destek ve Çıkar İlişkisi

Çalışmayı maddi olarak destekleyen kişi/kuruluş yoktur ve yazarların çıkara dayalı bir ilişkisi yoktur.

Kaynaklar

1. Katritsis D.G, G Boriani, FG Cosio et al. European Heart Rhythm Association (EHRA) consensus document on the management of supraventricular arrhythmias, endorsed by Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS), and Sociedad Latinoamericana de Estimulación Cardiaca y Electrofisiologia (SOLAECE). EP Europace 2017; 19: 465-511

2. Porter, M.J, JB Morton, R Denman et al. Influence of age and gender on the mechanism of supraventricular tachycardia. Heart Rhythm 2004; 1: 393-96.
3. Issa Z, M.J , Zipes DP , Issa Z et al. Atrioventricular reentrant tachycardia. In: Issa ZF,Miller JM, Zipes DP (eds). Clinical Arrhythmology and Electrophysiology: A Companion to Braunwald's Heart Disease.ElsevierW.B. Saunders, Philadelphia; 2012: p411-67.
4. Pappone C, G Vicedomini, F Manguso et al. WPW syndrome in the era of catheter ablation: insights from a registry study of 2169 patients. Circulation 2014; 130: 811-19
5. Jackman, W.M, X Wang, KJ Friday et al. Catheter ablation of accessory atrioventricular pathways (Wolff–Parkinson–White syndrome) by radiofrequency current. New England Journal of Medicine 1991; 32: 1605-11.
6. Page, R.L, JA Joglar, MA Caldwell et al., 2015 ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2016; 67: 27-115
7. Ranjan KT, George JK, Raymond Y. Radiofrequency catheter ablation in patients with Wolff-Parkinson-White syndrome. Can Med Assoc J 1994; 151: 771-76
8. Gaita F, Riccardi R, Hocini M et al. Safety and efficacy of cryoablation of accessory pathways adjacent to the normal conduction system. J Cardiovasc Electrophysiol 2003; 14: 825-29
9. Arruda MS, McClelland JH, Wang X et al. Development and validation of an ECG algorithm for identifying accessory pathway ablation site in Wolff-Parkinson-White syndrome. J Cardiovasc Electrophysiol 1998; 9: 2-12.
10. Calkins H, Yong P, Miller JM et al. Catheter ablation of accessory pathways, atrioventricular nodal reentrant tachycardia, and the atrioventricular junction: final results of a prospective, multicenter clinical trial. The Atakr Multicenter Investigators Group. Circulation 1999; 99: 262–70.
11. Spector P, Reynolds MR, Calkins H et al. Metaanalysis of ablation of atrial flutter and supraventricular tachycardia. Am J Cardiol 2009; 104: 671–77.
12. Packer DL. Three-dimensional mapping in interventional electrophysiology: techniques and technology. Journal of Cardiovascular Electrophysiology 2005; 16: 1110–16.
13. Bhakta D, & Miller, J. M. Principles of electroanatomic mapping. Indian Pacing and Electrophysiology Journal 2008; 8: 32-50
14. J Romero, F Lupercio, D Goodman-Meza et al. "Electroanatomic mapping systems (CARTO/EnSite NavX) vs. conventional mapping for ablation procedures in a training program", J Interv Card Electrophysiol 2016; 45: 71-80
15. Al-Khatib SM, Arshad A, Balk EM et al. Risk stratification for arrhythmic events in patients with asymptomatic pre-excitation: a systematic review for the 2015 ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia: a report of the American College of Cardiology/ American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2016; 67: 1617–29.
16. Al-Khatib SM, Pritchett EL. Clinical features of Wolff-Parkinson-White syndrome. Am Heart J 1999; 138: 403-13.
17. Pappone C, Santinelli V, Rosanio S et al. Usefulness of invasive electrophysiologic testing to stratify the risk of arrhythmic events in asymptomatic patients with Wolff-Parkinson-White pattern: results from a large prospective long-term follow-up study. J Am Coll Cardiol 2003; 41: 239-44.
18. Pappone C, Vicedomini G, Manguso F et al. Wolff-Parkinson-white syndrome in the era of catheter ablation: insights from a registry study of 2169 patients. Circulation 2014; 130: 811-19.
19. Brembilla-Perrot B, Holban I, Houriez P et al. Influence of age on the potential risk of sudden death in asymptomatic Wolff-Parkinson-White syndrome. Pacing Clin Electrophysiol 2001; 24: 1514–18.

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Original Article

The relationship between coronary arterial dominance and the QRS axis

Koroner arteriyel baskınlık ve QRS ekseni arasındaki ilişki

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ABSTRACT

Aim: Coronary artery dominance influences the amount and anatomic location of myocardium that is perfused by the left or right coronary circulation. However, the association between coronary arterial dominance and the QRS axis on 12-lead surface electrocardiography (ECG) was not investigated. The present study aims to evaluate the relationship between coronary arterial dominance and the QRS axis on ECG in patients without significant coronary artery and structural cardiac disease.

Material and Methods: Overall, 133 patients, without significant CAD and who met the inclusion criteria, participated in this study. A standard surface 12-lead ECGs were performed in all study patients. QT interval, QTc interval, QRS duration, PR interval, P wave and QRS axis were determined. Based on the origin of the posterior descending coronary artery, coronary circulation was categorised into left, right, and balanced coronary dominance.

Results: There were 133 subjects with 56 right dominant (42%), 39 left dominant (29%) and 38 codominant (29%) pattern. QRS axis value was found to be significantly higher in the left dominant group when compared with the codominant and right dominant group ($p<0.05$). No significant difference was observed between the codominant and right dominant groups regarding QRS axis values. The axis of (+30)-(+90) ratio in the left dominant group was found to be significantly higher when compared with the codominant and right dominant group ($p<0.05$). No significant difference was observed between the codominant and right dominant groups regarding the axis of (+30)-(+90) ratio.

Conclusion: Our findings suggested that the QRS axis may be related to coronary artery dominance.

Keywords: coronary artery dominance; QRS axis

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ÖZ

Amaç: Koroner arter baskınlığı, sol veya sağ koroner dolaşım tarafından perfüze edilen miyokardın miktarını ve anatomik konumunu etkiler. Ancak, koroner arter baskınlığı ile 12-lead yüzey elektrokardiyografisindeki (EKG) QRS ekseni arasındaki ilişki araştırılmamıştır. Bu çalışma, ciddi koroner arter ve yapısal kardiyak hastalığı olmayan hastalarda koroner arter baskınlığı ile yüzey EKG' deki QRS ekseni arasındaki ilişkiyi değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntemler: Ciddi koroner arter hastalığı olmayan ve dahil etme kriterlerini karşılayan tam olarak 133 hasta bu çalışmaya katılmıştır. Tüm çalışma hastalarında standart yüzey 12-lead EKG çekildi. QT aralığı, QTc aralığı, QRS süresi, PR aralığı, P dalgası ve QRS ekseni belirlendi. Posterior inen koroner arterin kökenine göre koroner dolaşım, sağ, sol ve dengeli (kodominant) koroner dominant olarak sınıflandırıldı.

Bulgular: 56 sağ dominant (% 42), 39 sol dominant (% 29) ve 38 kodominant (% 29) paternli 133 hasta vardı. Kodominant ve sağ dominant grup ile karşılaştırıldığında, QRS ekseni değeri sol dominant grupta anlamlı olarak daha yüksek bulundu ($p<0.05$). Kodominant ve sağ dominant gruplar arasında QRS ekseni değerleri açısından anlamlı fark saptanmadı. Sol dominant grupta QRS ekseni (+30) - (+ 90) oranı, kodominant ve sağ dominant grup ile karşılaştırıldığında anlamlı derecede yüksek olduğu bulundu ($p<0.05$). Kodominant ve sağ dominant gruplar arasında QRS ekseni (+30) - (+ 90) oranları arasında anlamlı bir fark gözlenmedi.

Sonuç: Bulgularımız QRS ekseninin koroner arter baskınlığı ile ilişkili olabileceğini düşündürmektedir.

Anahtar kelimeler: koroner arter baskınlığı; QRS ekseni

Introduction

Anatomical coronary dominance is defined by the origin of the posterior descending artery (PDA), which supplies the posterior portion of the interventricular septum. In a right-dominant (RD) circulation, the right coronary artery (RCA) gives off the PDA, while in a left-dominant (LD) circulation the left circumflex (LCX) artery supplies this territory. In a codominant circulation, the supply of the posterior interventricular septum is shared by the RCA and LCX. RD is the most prevalent pattern of coronary circulation, which is found in 72–90% of individuals, while the prevalence of LD and balanced coronary dominance (BD) is reported to be 8–33% and 3–7%, respectively [1].

Studies have been conducted regarding the prognostic significance of coronary artery dominance in patients with CAD. A left dominant system has been shown to be an independent risk factor of morbidity and mortality in patients who underwent both surgical and percutaneous revascularization, particularly in patients with ST-segment elevated myocardial infarction (STEMI) [2-4]. In addition, LD is shown to be an independent predictor of increased all-cause death and MACE in patients with chronic total occlusion (CTO) [5]. Therefore, an assessment of coronary vessel dominance by angiography could contribute to risk stratification in patients with coronary artery disease. However, so far interaction of coronary arterial dominance and the QRS axis on 12-lead surface electrocardiography (ECG) was not investigated thoroughly. The present study aims to evaluate the relationship between coronary arterial dominance and the QRS axis on ECG in patients without significant coronary artery and structural cardiac disease.

Material and Methods

Patients with chest pain, or other signs and symptoms suggestive of CAD referred for elective coronary angiography were screened for the enrollment in this study. Overall, 133 patients, without significant CAD and who met the inclusion criteria, participated in this study.

Patients were excluded if they had known history of CAD, acute coronary syndrome, chronic kidney disease, advanced liver disease, cancer, infection, hyper-or hypothyroidism, left ventricular (LV) systolic dysfunction (LV ejection fraction <50%), or any congenital heart disease. In addition, patients with a history of myocardial infarction and/or left ventricular hypertrophy based on echocardiography and ECG findings were also excluded. Any rhythm disturbance other than sinus (including permanent pacemakers, atrial fibrillation; bundle branch block; and patients taking the class I or class

III antiarrhythmic drugs) were not included. Furthermore, the young, thin, elderly and obese population were excluded from this study due to normal variants right or left QRS axis deviation.

A standard surface 12-lead ECGs were performed in all study patients. QT interval, QTc interval, QRS duration, PR interval, P wave and QRS axis were determined. Despite the fact that a real consensus on the normal values of the QRS axis has not been made yet, values of -30 and +90° of QRS axis were accepted as normal based on recommendations of the ACC/AHA ECG guidelines published in 2009 [6]. The QRS axis is computed by the hexa-axial reference system. There are several different ways for determining the QRS axis. In addition to computer software, studies have also pointed out that there is a high correlation between the QRS axes computed by inspection, computer, or the vector method [7]. Thus, for practical purposes, computer software was chosen for this study.

Images of the coronary angiography were obtained using standardized angiographic projections according to the guidelines of the American College of Cardiology/American Heart Association and stored digitally [8]. All images were retrospectively reviewed for the coronary dominance by two experienced observers. The coronary artery system was classified as right dominant if the RCA, as left dominant if the LCX, or as balanced if the RCA and LCX gave rise to the PDA. Significant CAD was defined as ≥50% narrowing of the luminal diameter in at least one projection of at least one major epicardial artery and was excluded.

The local ethics committee approved the study protocol, and informed consent was obtained from all of the patients. Local ethics committee approved the study and informed consent was obtained from participant(s)

Statistical analysis

Data were analyzed using SPSS software version 22.0 for Windows (SPSS Inc, Chicago, IL, USA). The Kolmogorov-Smirnov test was used to test the normality of the distribution of the continuous variables. The continuous variables were presented as mean±standard deviation or as median and interquartile ranges, and categorical variables were given as counts and percentages. Categorical variables were compared with chi-square test. The Kruskal-Wallis and Mann-Whitney U tests were used to compare non-normally distributed parametric data. For all tests, a 2-tailed P<0.05 was considered significant.

Results

Baseline characteristics and electrocardiographic findings of the patient are listed in Table 1.

Table 1. Baseline characteristics of study patients

		Min-Max	Median	Mean.±s.d./n-%
Age,(years)		23.0-76.0	55.0	52.1±12.0
Sex	Female			69-51.9%
	Male			64-48.1%
Weight, (kg)		50.0-110.0	64.0	63.7±12.4
Height,(m)		1.5-1.9	1.6	1.6±0.1
BMI		20.3-29.8	25.2	25.7±3.0
HT	No			68-51.1%
	Yes			65-48.9%
DM	No			100-75.2%
				33-24.8%
Smoking	No			97-72.9%
	Yes			36-27.1%
P axis		-30.0-132.0	47.0	47.6±22.9
QRS axis		-25.0-85.0	22.0	28.2±28.3
T axis		-40.0-90.0	35.0	36.1±25.6
PR, (msn)		112.0-192.0	148.0	148.4±13.5
QT,(msn)		350.0-450.0	390.0	396.3±24.9
QRS axis		(-30)-(+30)		76-57.1%
		(+30)-(+90)		57-42.9%

BMI; body mass index, DM; diabetes mellitus, HT; hypertension, s.d; standard deviation

There were 133 subjects with 56 right dominant (42%), 39 left dominant (29%) and 38 codominant (29%) pattern. No significant difference was observed between the codominant, right dominant and left dominant groups regarding age, sex distribution, weight, height, and BMI values (p> 0.05)(Table 2). There was also no significant difference in the codominant, right dominant, left dominant group in terms of HT, DM, and smoking rates (p> 0.05) (Table 2). The P-wave axis, T-wave axis, PR, QRS, and QT values were not significantly different in the codominant, right dominant and left dominant groups (p>0.05) (Table 3). QRS axis value was found to be significantly higher in the left dominant group when compared with the codominant and right dominant group (p<0.05). No significant difference was observed between the codominant and right dominant groups regarding QRS axis values. The axis of (+30)-(+90) ratio in the left dominant group was found to be significantly higher when compared with the codominant and right dominant group (p<0.05). No significant difference was observed between the codominant and right dominant groups regarding the axis of (+30)-(+90) ratio.

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Table 2. Baseline demographics of the study population by coronary dominance

		Co-dominant (n:38)		Right dominant (n:56)		Left dominant (n:39)		p
		Mean.±s.d./n-%Median	Median	Mean.±s.d./n-%Median	Median	Mean.±s.d./n-%Median	Median	
Age		52.1±12.7	55.0	54.0±9.9	55.5	49.4±13.8	52.0	0.358[K]
Sex	Female	20-52.6%		27-48.2%		22-56.4%		0.730[x2]
	Male	18-47.4%		29-51.8%		17-43.6%		
Weight,kg		65.5±12.6	63.3	67.2±11.9	64.8	69.0±12.9	64.0	0.366[K]
Height,m		1.6±0.1	1.6	1.6±0.1	1.6	1.6±0.1	1.6	0.347[K]
BMI		25.5±2.9	25.4	25.6±3.2	25.1	26.1±3.0	25.4	0.675[K]
HT	No	22-57.9%		27-48.2%		19-48.7%		0.613[x2]
	Yes	16-42.1%		29-51.8%		20-51.3%		
DM	No	30-78.9%		41-73.2%		29-74.4%		0.811[x2]
	Yes	8-21.1%		15-26.8%		10-25.6%		
Smoking	No	26-68.4%		42-75.0%		29-74.4%		0.758[x2]
		12-31.6%		14-25.0%		10-25.6%		

BMI; body mass index, DM; diabetes mellitus, HT; hypertension, kg; kilogram, m; meter, s.d; standard deviation, [K]; Kruskal-wallis (Mann-whitney u test), [x2]; Chi-square test

Table 3. Baseline electrocardiographic findings and QRS axis of the study population by coronary dominance

		Co-dominant (n:38)		Right dominant (n:56)		Left dominant (n:39)		p
		Mean.±s.d./n-%Median	Median	Mean.±s.d./n-%Median	Median	Mean.±s.d./n-%Median	Median	
P axis		42.4±20.4	40.0	51.1±26.3	50.0	48.9±19.6	47.0	0.133[K]
QRS axis		22.2±27.2	15.5	24.9±27.4	21.0	38.6±28.6	21.0	0.019[K]
T axis		37.0±20.7	41.0	34.8±26.4	34.0	37.0±29.0	36.0	0.587[K]
PR, msn		148.9±13.0	149.0	148.3±14.7	148.0	148.0±12.+6	148.0	0.943[K]
QT, msn		398.9±25.7	398.0	390.7±23.2	390.0	401.8±25.4	400.0	0.062[K]
QRS axis	(-30)-(30)	26-68.4%		35-62.5%		15-38.5%		0.017[x2]
	(30)-(90)	12-31.6%		21-37.5%		24.61.5%		

[K]; Kruskal-wallis (Mann-whitney u test), s.d; standard deviation, [x2]; Chi-square test

Discussion

In this study, it was determined that coronary artery dominance appears to affect the QRS axis in patients without significant coronary artery disease. The QRS axis significantly moves to 30-90 degrees in left coronary artery dominance patients.

The QRS axis moves leftward throughout childhood and adolescence, and this continues into adulthood. At birth, the normal QRS axis lies between +30 degrees and +190 degrees. Between the ages of 8 and 16 years, the axis moves leftward, normally lying between 0° degrees to +120 degrees. The normal adult QRS axis is between -30 degrees and +90 degrees, which is directed downward and to the left. This adult range is sometimes extended from -30 degrees to +100 degrees [9].

When studies relating to QRS axis are evaluated, in clinical practice a QRS axis shift may be related to coronary artery disease (CAD). Recent reports have pointed out that an exercise- induced QRS axis shift may be related to CAD [10-15]. In a different study, the role of QRS axis change was evaluated in assessing the efficacy of thrombolytic therapy and in determining prognostic infarct size [16]. Also, the change in QRS axis after mitral balloon valvuloplasty was shown to be associated with hemodynamic improvement [17]. We think that if there is a relationship between the QRS axis and coronary artery dominance, may be future risk prediction for coronary atherosclerosis could be done considering some earlier studies [3,18-21]. Our study demonstrated that there was a significant difference in QRS axis between left coronary arterial dominance and other groups.

Previous data have indicated that RCA is dominant in 85% of the patients, while about half of the remaining 15% appear to have left coronary artery dominancy and the other half has a balanced (codominant) circulation [22]. Several studies in the past have reported that age, sex, heart weight, left ventricular wall thickness, and other risk factors were not correlated with coronary dominance [23-25]. Moreover, in these trials, left-dominant circulation is not a predisposition

for coronary atherosclerosis, and the dominant coronary artery pattern does not affect atherosclerosis. In some studies coronary dominance has not been shown to be related with presence and extent of coronary atherosclerosis. In contrast, Vasheghani-Farahani A et al have claimed a significantly higher predisposition to the three-vessel disease in right-dominant patients [21]. Considering these ambiguous findings, patients with CAD were not included in this study.

Although the available data are not clear, previous studies in patients who underwent PCI demonstrated that LD was associated with increased risk of death or re-infarction during long-term follow-up [3, 18, 26]. Similarly, patients with a left dominant or codominant coronary artery system had lower LVEF early after STEMI [27-28]. A left dominant coronary artery tree may have a less well-balanced circulation than other systems, resulting in a larger area of myocardium at risk during acute coronary syndromes. Therefore earlier noninvasive identification of left dominant system may imply better prognosis after a coronary incident with more intensive treatment. In our study, the electrocardiographic QRS axis was found to be related to coronary artery dominancy. In the left-dominant coronary artery group, the QRS axis was found to be between (+30)-(+90) degrees, which was statistically significant. Therefore simple ECG tracing may aid determining coronary dominance.

Our study had several limitations. The first limitation is regarding the number of the patients. To increase the statistical strength of this study, more patients should be included. The second limitation of our study is that the utilization of a software program on the ECG machine to estimate the QRS axis of patients, direct measurement of QRS axis might be more appropriate. The last one only one ECG was evaluated.

Conclusion

Our findings suggested that the QRS axis may be related to coronary artery dominance. We found that the QRS axis is significantly different with left coronary arterial dominancy as compared to right and codominant pattern. However, the reasons for these relationships are not clear. Due to small proportion of left and codominant coronary arterial system in general population our findings should be confirmed with larger and sufficiently powered studies.

Declaration of conflict of interest

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References

1. Allwork SP. The applied anatomy of the arterial blood supply to the heart in man. J Anat 1987; 153: 1–16.
2. Omerbasic E, Hasanovic A, Omerbasic A, Pandur S. Prognostic value of anatomical dominance of coronary circulation in patients with surgical myocardial revascularization. Med Arch 2015; 69: 6-9
3. Lam MK, Tandjung K, Sen H et al. Coronary artery dominance and the risk of adverse clinical events following percutaneous coronary intervention: insights from the prospective, randomised TWENTE trial. EuroIntervention 2015; 11: 180-87
4. Veltman CE, van der Hoeven BL, Hoogslag GE et al. Influence of coronary vessel dominance on short- and long-term outcome in patients after ST-segment elevation myocardial infarction. Eur Heart J 2015; 36: 1023-30
5. Gebhard C, Gick M, Ferenc M et al. Coronary dominance and prognosis in patients with chronic total occlusion treated with percutaneous coronary intervention. Catheter Cardiovasc Interv 2017; 91: 669-78
6. Surawicz B, Childers R, Deal BJ et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part III: intraventricular conduction disturbances: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. J Am Coll Cardiol 2009; 53: 976-81
7. Spodick DH, Frisella M, Apiyassawat S. QRS axis validation in clinical electrocardiography. Am J Cardiol 2008; 101: 268-69.
8. Scanlon PJ, Faxon DP, Audet AM et al. (ACC/AHA guidelines for coronary angiography. A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee on Coronary Angiography). Developed in collaboration with the Society for Cardiac Angiography and Interventions. J Am Coll Cardiol 1999; 33: 1756–824.
9. Kashou AH, Kashou HE. Electrical Axis (Normal, Right Axis Deviation, and Left Axis Deviation). StatPearls. Treasure Island (FL): StatPearls Publishing; 2018 Jan-2017 Dec 12.
10. Bobba P, Salerno JA, Casari A. Transient left posterior hemiblock--report of four cases induced by exercise test. Circulation 1972; 46: 931-38.

11. Hegge FN, Tuma N, Burchell HB. Coronary arteriographic findings in patients with axis shifts or S-T-segment elevations on exercise-stress testing. Am Heart J 1973; Nov;86:603-15
12. Kulbertus HE. Transient hemiblock: An abnormal type of response to the Master two-step test. Am Heart J 1972; 83: 574-76.
13. Olivems RA, Seaworth J, Weiland FL, Boucher CA. Intermittent left anterior hemiblock during treadmill exercise test correlation with coronary arteriogram. Chest 1977; 72: 492-94
14. Takayama Y, Seki A, Imataka K, Fujii J. Exercise-induced QRS axis shift and its clinical significance. Jpn Heart J 1986; 27: 17-23.
15. Ogino K, Fukugi M, Hirai S et al. The usefulness of exercise-induced QRS axis shift as a predictor of coronary artery disease. Clin Cardiol 1988; 11: 101-104.
16. Karakas MF, Bilen E, Kurt M et al. The Correlation between Infarct Size and the QRS Axis Change after Thrombolytic Therapy in ST Elevation Acute Myocardial Infarction. Eurasian J Med 2012; 44: 13-17
17. Chandrasekar B, Loya YS, Sharma S, Paidhungat JV. Acute effect of balloon mitral valvotomy on serial electrocardiographic changes and their haemodynamic correlation. Indian Heart J 1998; 50: 179-82.
18. Goldberg A, Southern DA, Galbraith PD, Traboulsi M, Knudtson ML, Ghali WA. Coronary dominance and prognosis of patients with acute coronary syndrome. Am Heart J 2007; 154: 1116-22.
19. Veltman CE, de Graaf FR, Schuijf JD et al. Prognostic value of coronary vessel dominance in relation to significant coronary artery disease determined with non-invasive computed tomography coronary angiography. Eur Heart J 2012; 33: 1367-77.
20. Gebhard C, Fuchs TA, Stehli J et al. Coronary dominance and prognosis in patients undergoing coronary computed tomographic angiography: Results from the CONFIRM (coronary CT Angiography EvaluatioN For Clinical Outcomes: An International Multicenter) registry. Eur Heart J Cardiovasc Imaging 2015; 16: 853–62.
21. Vasheghani-Farahani A, Kassaian SE, Yaminisharif A et al. The association between coronary arterial dominancy and extent of coronary artery disease in angiography and paraclinical studies. Clin Anat 2008; 21: 519–23.
22. Zipes DP, Libby P, Bonow RO. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. 7th ed. Philadelphia: W.B.Saunders; 2005
23. Kaimkhani ZA, Ali MM, Faruqi AM. Pattern of coronary arterial distribution and its relation to coronary artery diameter. J Ayub Med Coll Abbottabad 2005; 17: 40-43.
24. Virmani R, Chun PK, Robinowitz M, Goldstein RE, McAllister HA. Length of left main coronary artery. Lack of correlation to coronary artery dominance and bicuspid aortic valve: An autopsy study of 54 cases. Arch Pathol Lab Med 1984; 108: 638–641.
25. Balci B, Yilmaz O. Atherosclerotic involvement in patients with left or right dominant coronary circulation. Kardiol Pol 2004; 60: 564-66.
26. Abu-Assi E, Castineira-Busto M, Gonzalez-Salvado V et al. Coronary Artery Dominance and Long-term Prognosis in Patients With ST segment Elevation Myocardial Infarction Treated With Primary Angioplasty. Rev Esp Cardiol (Engl Ed) 2016; 69: 19–27.
27. Parikh NI, Honeycutt EF, Roe MT et al. Left and codominant coronary artery circulations are associated with higher in-hospital mortality among patients undergoing percutaneous coronary intervention for acute coronary syndromes: report From the National Cardiovascular Database Cath Percutaneous Coronary Intervention (CathPCI) Registry. Circ Cardiovasc Qual Outcomes 2012; 5: 775-82.
28. Veltman CE, Hoogslag GE, Kharbanda RK et al. Relation between coronary arterial dominance and left ventricular ejection fraction after ST-segment elevation acute myocardial infarction in patients having percutaneous coronary intervention. Am J Cardiol 2014; 114: 1646-50

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Original Article

The effect of "patient blood management" education on the number of red blood cell transfusions in patients undergoing cardiac surgery: a 5-year retrospective study

Kardiyak cerrahi geçiren hastalarda "hasta kan yönetimi" eğitiminin kırmızı kan hücresi transfüzyon sayısı üzerine etkisi: 5 yıllık retrospektif çalışma

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ABSTRACT

Aim: Red blood cell transfusion may be inevitable in cardiac surgery due to both blood loss and hemodilution secondary to cardiopulmonary bypass. Transfusion strategies may change over time owing to technological advances. The aim of this study was to evaluate the effect of the patient blood management education applied to healthcare staff on the number of red blood cell transfusions and clinical outcomes of the patients undergoing cardiac surgery.

Material and Methods: Patients were included to the study if they had undergone coronary artery bypass grafting and/or heart valve surgery at the cardiovascular surgery clinic of tertiary training and research hospital during the five-year period between January 1, 2013 and December 31, 2017. Age, sex, number of RBC transfusions, Euroscore II, type of surgery, duration of mechanical ventilation, length of intensive care unit (ICU) stay, length of hospital stay, and in-hospital mortality of the patients were recorded. As the intervention, a patient blood management course was held for anesthesia and intensive care unit staff the department of cardiovascular surgery in December 2015. Patient blood management program was started as of 1st January of 2016 during perioperative period in cardiac surgery patients. Patients were divided into two groups as those undergoing cardiac surgery before January 2016 (Group I, the control group) and those having the surgery after January 2016 (Group II, the intervention group). The groups were compared in terms of sex, age, Euroscore II, duration of mechanical ventilation at intensive care unit, length of stay at intensive care unit and hospital, and in-hospital mortality.

Results: A total of 691 patients were found to meet inclusion criteria. The patients in Group I and Group II were statistically similar in age, sex, and Euroscore II. Mean number of RBC transfusions were 3.55 ± 1.49 in Group I and 2.77 ± 1.64 in Group II ($p<0.001$). The duration of mechanical ventilation in Group I (6.56 ± 1.18 days) was significantly longer than that in Group II (5.93 ± 14.1 days), ($p<0.001$). There was no statistically significant difference between the groups in terms of length at ICU and hospital ($p=0.255$ and $p=0.823$, respectively). The mortality rate was 3.0% in Group I and 3.5% in Group II, where the difference was not statistically significant ($p=0.736$).

Conclusion: The training of healthcare personnel about current "patient blood management" protocols was associated with reduced number of perioperative RBC transfusions and partially improved clinical outcomes in patients undergoing cardiac surgery.

Keywords: cardiac surgery; red blood cell; transfusion training, mortality.

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ÖZ

Amaç: Kardiyak cerrahide hem kan kaybı hem de kardiyopulmoner baypas uygulamasına bağlı hemodilüsyon nedeniyle kırmızı kan hücresi transfüzyonu zorunlu hale gelebilir. Teknolojik gelişmeler sayesinde transfüzyon stratejileri zaman içinde değişiklik gösterebilir. Bu çalışmanın amacı kardiyak cerrahi geçiren hastalarda, güncel bilgilerin kullanılması ile kırmızı kan hücresi transfüzyon yaklaşımındaki değişikliklerin ortaya konmasıdır.

Gereç ve Yöntemler: Üçüncü basamak eğitim ve araştırma hastanesi kardiyovasküler cerrahi kliniğinde 1 Ocak 2013 ile 31 Aralık 2017 tarihleri arasında 5 yıllık periyotta koroner arter baypas greftleme ve/veya kalp kapak cerrahisi geçiren hastalar çalışma kapsamına alındı. Tüm hastaların yaş, cinsiyet, kırmızı kan hücresi transfüzyonu sayısı, Euroscore II, ameliyat tipi, mekanik ventilasyon süresi, yoğun bakım ünitesinde yatış süresi, hastanede yatış süresi, hastane içi mortalite durumu kaydedildi. Aralık 2015'te kalp ve damar cerrahisinde çalışan anestezi ve yoğun bakım çalışanlarına "hasta kan yönetimi" kursu düzenlendi. 1 Ocak 2016 tarihinden itibaren hasta kan yönetimi programı, kardiyak cerrahi uygulanan hastalara perioperatif dönemde uygulanmaya başlandı. 1 Ocak 2016 dan önce (Grup I) ve sonra (Grup II) kardiyak cerrahi geçiren hastalar iki gruba ayrıldı. Hastaların karakteristik özellikleri yanı sıra yoğun bakım ünitesinde mekanik ventilasyon süresi, yoğun bakım yatış süresi, hastanede yatış süresi ve hastane içi mortalite durumu açısından bu iki grup karşılaştırıldı.

Bulgular: Toplam 691 hasta çalışmaya dahil edildi. Grup I'deki (kontrol grubu) hastalar ile Grup II'deki (çalışma grubu) hastalar istatistiksel olarak yaş, cinsiyet, Euroscore II açısından benzer idi. Transfüzyon yapılan kırmızı kan hüresi sayısı Grup I de 3.55 ± 1.49 iken Grup II'de 2.77 ± 1.64 idi (P<0.001). Mekanik ventilasyon süresi Grup I'de (6.56± 1.18 gün) Grup II'ye (5.93 ± 1.14 gün) göre daha uzun idi (P<0.001). Hem yoğun bakımda hem de hastanede yatış süresi açısından iki grup arasında istatistiksel olarak fark yoktu (P=0.823). Mortalite oranı Grup I'de %3 iken Grup II'de %3.5 idi ve bu fark istatistiksel olarak önemli değil idi (P=0.736).

Sonuç: Sağlık personelinin mevcut "hasta kan yönetimi" protokolleri hakkındaki eğitimi, kalp cerrahisi geçiren hastalarda perioperatif kırmızı kan hücresi transfüzyonlarının azalması ve kısmen iyileşmiş klinik sonuçlarla ilişkili bulunmuştur.

Anahtar kelimeler: kardiyak cerrahi; kırmızı kan hücresi; transfüzyon eğitimi, mortalite.

Introduction

In cardiac surgery, a high rate of allogeneic blood transfusion is performed conventionally. In a multi-center study involving 82,446 cases undergoing on-pump coronary artery bypass grafting (CABG), use of red blood cell (RBC) transfusion was reported to vary from 7.8% to 92.8% [1]. Such wide range of RBC transfusion rate suggests no standardized strategy of RBC transfusion. The primary goal of RBC transfusion is to maintain a normal level of oxygen delivery to the tissues and thus provide adequate tissue oxygenation. If an adequate tissue perfusion can be achieved with fewer number of RBC transfusions, a lower target of hemoglobin level may be considered. This may facilitate improved patient outcomes and reduced costs. Allogenic blood transfusions may be associated with such complications as hemolytic transfusion reactions, graft-versus-host disease, circulatory overload, anaphylaxis, and post-transfusion purpura [2]. For this reason, it is necessary to appropriately determine whether a patient really needs blood transfusion. Reducing unnecessary use of blood components will reduce the risks associated with transfusion. In recent years, some reports have been published on strategies to reduce perioperative use of blood products, including perioperative iron therapy, intraoperative tranexamic acid treatment, cell salvage, maintenance of lower target hemoglobin levels, and combinations thereof.

In patients undergoing cardiac surgery, those who were managed with restrictive hemoglobin transfusion strategy were reported to receive less RBC transfusion and have lower incidence of transfusion-associated adverse events compared with that in those managed with liberal hemoglobin transfusion strategy [3]. However, information on optimal blood transfusion management is scarce. Therefore, "patient blood management" guideline was developed and associated training programs were planned [4,5]. Studies so far reported

widely varying target hemoglobin levels, where the number of RBC transfusions also showed variations between centers [6-9]. Unfortunately, there is still controversy about how much RBC transfusion should be done. Furthermore, the clinical implications of providing healthcare staff with patient blood management training are also not known.

The aim of this study was to determine whether the number of RBC transfusions and clinical outcomes were changed by training healthcare staff about patient blood management training in patients who underwent cardiac surgery and subsequently managed in the intensive care unit (ICU).

Material and methods

After the local ethics committee approval of the study, the patients who underwent CABG and/or heart valve surgery in the cardiovascular surgery clinic of tertiary training and research hospital during the 5-year period between January 1, 2013 and December 31, 2017 were included in the study. Data on patients' age, sex, number of RBC transfusions, Euroscore II, type of surgery, duration of mechanical ventilation, length of stay at ICU, length of hospital stay, and in-hospital mortality were collected from institutional database of medical records. The patients who had ≥10 RBC transfusionsor preoperative lung disease were excluded from the study.

In December 2015, anesthesia and intensive care staff in the cardiovascular surgery department of tertiary training and research hospital were given a 1-hour course of patient blood management training by an anesthesiologist according to most up-to-date clinical guidelines and other evidence-based materials [3,4,10]. Beside restrictive transfusion strategy, the course endorsed recommendations about administering iron treatment if preoperative iron deficiency was present, or using tranexamic acid as systemic hemostatic agent and hemostatic sealants and anti-fibrinolytic agents as topical hemostatic agents in the intraoperative period [11,12]. The patients were divided into two groups in order to compare outcomes before and after 1 January 2016. While Group I (control group) consisted of those undergoing heart surgery between January 1, 2013 and December 31, 2015; Group II (intervention group) consisted of those undergoing heart surgery between 1 January 2016 and 31 December 2017. Local ethics committee approved the study and informed consent was obtained from participant(s)

Statistical Analysis

All analyses were performed through IBM SPSS Statistics for Windows [13]. While describing the data in each study group, we reportedmean ± standard deviation (median, minimum - maximum) for continuous variables and frequency (%) for categorical variables. We applied Shapiro-Wilk and Levene's tests to check normality and variance homogeneity assumptions, respectively. Independent t-test was used to compare the study groups with respect to continuous variables. Pearson Chi-square test was utilized for comparison of the study groups in terms of categorical variables. A two-sided p-value ≤ 0.05 was considered as statistically significant.

Results

A total of 691 patients were found to meet inclusion criteria between January 2013 and December 2017. While 432 patients who had undergone heart surgery were in Group I, remaining 259 patients with heart surgery between 1 January 2016 and 31 December 2017 were included to the Group II. Mean age of the patients in Group I (57.1± 12.8 years) and Group II (58.0 ± 10.8) were similar (p=0.324). The percentages of male patients in Group I (72.2%) and Group II (74.1%) were also similar (p=0.585). Mean Euroscore II did not differ between Group I and Group II (1.49 ± 0.71 and 1:46 ± 0.67, respectively; p=0.624), (Table 1).

Table 1. Characteristics of study groups.

		Group I (n=432)	Group II (n=259)	P-value
Age (years)		57.1± 12.8 (58, 17- 85)	58.0± 10.8 (59, 19- 83)	0.324[a]
Sex	Female	120 (27.8)	67 (25.9)	0.585[b]
	Male	312 (72.2)	192 (74.1)	
EuroScore II		1.49 ± 0.71 (1.23, 0.63 - 5.84)	1.46 ± 0.67 (1.23, 0.78 - 3.88)	0.624[a]

Note: Results were demonstrated as mean ± standard deviation (median, min - max) for continuous variables and as frequency (%) for categorical variables.a, b: p-values are obtained via independent t-test and Pearson Chi-square test, respectively.

Mean number of RBC transfusions were 3.55 ± 1.49 in Group I and 2.77 ± 1.64 in Group II (p<0.001). The duration of mechanical ventilation in Group I (6.56 ± 1.18 days) was significantly longer than that in Group II (5.93 ± 14.1 days),(p<0.001). There was no statistically significant difference between the groups in terms of length of stay at ICU (p=0.255). The groups were also similar

for length of hospital stay (p=0.823).The in-patient mortality rate was 3.0% in Group I and 3.5% in Group II, where the difference was not statistically significant (p=0.736), (Table 2).

Table 2. The variables regarding intensive care unit.

		Group I (n=432)	Group II (n=259)	P-value
Duration of mechanical ventilation, hours		6.56± 1.18 (6, 2 - 11)	5.93± 1.14 (6, 1 - 9)	<0.001a
RBC, n		3.55 ± 1.49 (4, 0 - 9)	2.77 ± 1.64 (3, 0 - 8)	<0.001a
Length of stay at ICU, hours		43.3 ± 11.9 (40, 30 - 72)	44.4 ± 12.0 (40, 30 - 74)	0.255a
Length of stay at hospital, days		5.78 ± 0.98 (5, 5 - 8)	5.76 ± 0.96 (5, 5 - 8)	0.823a
Mortality	**Deceased**	13 (3.0)	9 (3.5)	0.736[b]
	Alive	419 (97.0)	250 (96.5)	

Note: Results were demonstrated as mean ± standard deviation (median, min - max) for continuous variables and as frequency (%) for categorical variables.a, b: p-values are obtained via independent t-test and Pearson Chi-square test, respectively.

Discussion

In this study, the "patient blood management" education was shown to be associated with a 22% lesser number of perioperative RBC transfusions (p<0.001) and about 10% shorter duration of postoperative mechanical ventilation (p<0.001) in patients who underwent heart surgery. No statistically significant difference was detected in terms of length of ICU or hospital stay, or in-patient mortality after the intervention compared to the baseline. Despite numerous studies regarding RBC transfusion strategy in heart surgery, no consensus has been achieved yet. It is important to follow up most up-to-date information and to support healthcare professionals with training activities according to the evidence-based medicine principles. The effectiveness of these trainings and their reflection on clinical outcomes should also be measured.

Target hemoglobin levels show variation in studies where the efficacy of restrictive transfusion was investigated in patients undergoing cardiac surgery. Shehata et al.[14] reported that they targeted intraoperative hemoglobin as 7 g/dL and postoperative hemoglobin as 7.5 g/dL in cardiac surgery.On the other hand, Slight et al. [8] determined a target hemoglobin rangeof 7.2 to 8.5 both in intraoperative and postoperative setting. Lilly et al. [15] reported to choose the target 7 g/dL for both intraoperative and postoperative hemoglobin. Bracey et al. [6] reported that they determined postoperative hemoglobin target to be 8 g/dL. Mazer et al. [16], in their multi-center randomized study of 5243 patients who underwent cardiac surgery, reported intraoperative target hemoglobin level as 7.5 g/dL in the restrictive transfusion group. These studies suggest that a definite hemoglobin target value in the restrictive transfusion strategy is still controversial. In our study, we recommended the participants to use a hemoglobin threshold value of 7.5 g/dL for RBC transfusion in both intraoperative and postoperative periods as part of the patient blood management training.

Koch et al. compared patients who did and did not receive RBC transfusion among 11,963 patients who underwent CABG. They reported prolonged ventilatory support (OR, 1.79; 95%CI, 1.72-1.86; p<0.0001) in the RBC transfusion group [17]. The study by Mazer et al. included cardiac surgery patients, where median duration of postoperative mechanical ventilation was 0.38 days (interquartile range, 0.22 to 0.75) in the restrictive RBC transfusion strategy group compared to 0.36 days (interquartile range, 0.22 to 0.71) in the liberal strategy group with a hazard ratio of 94% (0.89-1.00) [16]. On the contrary, we found the duration of mechanical ventilation as 6.56 ± 1.18 hours before the intervention and 5.93 ± 1.14 hours after the intervention, which constituted a statistically significant difference (p<0.001).

In their study of 8598 patients undergoing cardiac surgery, Murphy et al. reported that the length of stay at ICU and hospital were about 30% and 35% shorter, respectively, in patients who were not transfused RBCs compared to that in those receiving RBC transfusions (p<0. 0001)[18]. Mazer et al. reported that there was no difference of length of ICU or hospital stay between patients in whom a restrictive or liberal RBC transfusion strategy was applied in the study involving cardiac surgery patients [16]. Similarly, Hajjar et al. reported no difference between patients receiving restrictive or liberal RBC transfusions in terms of length of stay at ICU or hospital (p=0.45) [9]. The groups in our study also did not differ according to the intervention in terms of duration of stay at ICU or hospital.

Murphy et al. reported 6-fold higher 30-day mortality in cardiac surgery patients who received RBC transfusion compared to those who were not RBC-transfused [18]. Several other studies were also published, comparing liberal and restrictive transfusion strategies in patients who underwent heart surgery. Some of these studies reported no statistically significant difference in mortality between these two strategies [6,7,9]. We also did not find any significant difference of mortality between the study groups. On the contrary, there were also studies reporting reduced mortality by restrictive RBC transfusion compared to that by liberal approach [18,19].

In recent years, studies have been carried out on the development of various RBC transfusion protocols. Obtaining information about new transfusion guidelines is a very critical issue in this manner. Not only hematologists, but also physicians and other healthcare personnel from different disciplines should also follow new transfusion protocols. Institutional continuous training activities should be organized for clinicians, medical residents, and medical students about updated transfusion guidelines. By translating this information into clinical practice, blood transfusion reactions can be reduced and improved patient outcomes can be achieved.

The limitation of the study is that no further detailed data could be obtained due to its retrospective design.

In conclusion, the number of perioperative RBC transfusions in patients undergoing cardiac surgery was reduced by a training about current patient blood management protocols. While the duration of postoperative mechanical ventilation was shortened by the training, the mortality rate remained unchanged.

Declaration of conflict of interest

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References

1. Bennett-Guerrero E, Zhao Y, O'Brien SM et al. Variation in use of blood transfusion in coronary artery bypass graft surgery. JAMA 2010; 304: 1568-75.
2. Demirok M, Askin D, Emin I. Autologous blood transfusions during the bypass and valve operations. Turk Gogus Kalp Dama 2005; 13: 193-96.
3. Curley GF, Shehata N, Mazer CD, Hare GM, Friedrich JO. Transfusion triggers for guiding RBC transfusion for cardiovascular surgery: a systematic review and meta-analysis. Crit Care Med 2014; 12: 2611-24.
4. National Blood Transfusion Committee. Patient Blood Management: An evidence-based approach to patient care https://www.transfusionguidelines.org/uk-transfusion-committees/national-blood-transfusion-committee/patient-blood-management.
5. National Blood Authority. Patient Blood Management Guidelines: Module 2: Perioperative https://www.blood.gov.au/system/files/documents/pbm-module-2.pdf
6. Bracey AW, Radovancevic R, Riggs SA et al. Lowering the hemoglobin threshold for transfusion in coronary artery bypass procedures: Effect on patient outcome. Transfusion 1999; 39: 1070–77.
7. Slight RD, Fung AK, Alonzi C et al. Rationalizing blood transfusion in cardiac surgery: Preliminary findings with a red cell volume-based model. Vox Sanguinis 2007; 92: 154–56.
8. Slight RD, O'Donohoe P, Fung AK et al. Rationalizing blood transfusion in cardiac surgery: The impact of a red cell volume-based guideline on blood usage and clinical outcome. Vox Sang 2008; 95: 205–10.
9. Hajjar LA, Vincent JL, Galas FR et al. Transfusion requirements after cardiac surgery: The TRACS randomized controlled trial. JAMA 2010; 304: 1559–67.

10. Goodnough LT, Shander A. Patient blood management. Anesthesiology 2012; 116: 1367-76.

11. Carless PA, Henry DA, Anthony DM. Fibrin sealant use for minimising peri-operative allogeneic blood transfusion. Cochrane Database Syst Rev 2003; 2: 4171.

12. Abrishami A, Chung F, Wong J. Topical application of antifibrinolytic drugs for on-pump cardiac surgery: a systematic review and meta-analysis. Can J Anaesth 2009; 56: 202–12.

13. IBM Corp. (2015). IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.

14. Shehata N, Burns LA, Nathan H et al. A randomized controlled pilot study of adherence to transfusion strategies in cardiac surgery. Transfusion 2012; 52: 91–99.

15. Lilly CM, Badawi O, Liu X, Christine S G, Harris I. Red Blood Cell Product Transfusion Thresholds and Clinical Outcomes. J Intensive Care Med 2018; 1: 885066618762746.

16. Mazer CD, Whitlock RP, Fergusson DA et al. TRICS Investigators and Perioperative Anesthesia Clinical Trials Group. Restrictive or Liberal Red-Cell Transfusion for Cardiac Surgery. N Engl J Med 2017; 30: 2133-44.

17. Koch CG, Li L, Duncan AI et al. Morbidity and mortality risk associated with red blood cell and blood-component transfusion in isolated coronary artery bypass grafting. Crit Care Med 2006; 34: 1608-16.

18. Murphy GJ, Reeves BC, Rogers CA et al. Increased mortality, postoperative morbidity, and cost after red blood cell transfusion in patients having cardiac surgery. Circulation 2007; 116: 2544–52.

19. Paone G, Brewer R, Theurer PF et al. Michigan Society of Thoracic and Cardiovascular Surgeons. Preoperative predicted risk does not fully explain the association between red blood cell transfusion and mortality in coronary artery bypass grafting. J Thorac Cardiovasc Surg 2012; 143: 178–85.

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Derleme

Normokalsemik hiperparatiroidiye farklı bakış: Kardiyak sorunların gözden geçirilmesi

A different view of normocalcemic hyperparathyroidism: The examination of cardiac problems

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ÖZ

Hiperparatiroidizmde renal komplikasyonlar ve osteoporoz gibi yan etkiler klinisyenler tarafından çok iyi bilinerek sıkı takip edilmektedir. Bununla birlikte yapılan çeşitli çalışmalarda hiperparatiroidiye bağlı hipertansiyon, diastolik disfonksiyon, endotel disfonksiyonu, kalp kapak kalsifikasyonu, aritmi, kardiyak hipertrofi gibi yan etkiler belirtilmiştir. Bazı çalışmalar hiperparatiroidide kardiak mortalite artışı olduğunu işaret etmektedir. Bu derlemede primer hiperparatiroidide rastlanan kardiyak sorunlara dikkat çekmek amaçlanmıştır.

Anahtar kelimeler: Hiperparatiroidi; kardiyak etkiler; hipertansiyon

ABSTRACT

While hyperparathyroidism is well known among the clinicians, such side effects as renal complications and osteoporosis are closely monitored. Besides various conducted studies have found out several side effects such as hypertension, diastolic dysfunction, endothelial dysfunction, heart valve calcification, arythmia, cardiac hypertropy. Even some studies have pointed to increase in cardiac mortality is correlated with hyperparathyroidizm. İn this review, it is intended to raise a concern about cardiac complications occuring in primary hyperparathyroidism.

Keywords: Hyperparathyroidism; cardiac effects; hypertension

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Giriş

Hiperparatiroidi yalnızca kemik metabolizmasını etkileyen bir endokrinolojik hastalık değildir. Primer hiperparatiroidili (PHPT) hastalar erken tanı nedeniyle asemptomatik ya da normokalsemik evrede yakalanmakta ve çoğu zaman paratiroidektomi geçirmeden yıllarca medikal tedaviyle ya da tedavisiz izlenmektedir [1]. Klinisyenlerin çoğu normokalsemik ya da asemptomatik primer hiperparatiroidi takibinde genellikle renal komplikasyonlara ya da osteoporoza odaklanmakta kardiyak sorunlar göz ardı edilmektedir [2]. Son yıllarda yapılan çalışmalar çelişkili olsa da hiperparatiroidinin kardiyak mortaliteyi artırdığı endişesi devam etmektedir. Kardiyak mortalite artışı beklenenin aksine hasta paratiroidektomi geçirse bile devam etmektedir [3]. Yine primer hiperparatiroidide görülen hiperkalsemi ve hipofosfatemi de kardiyak sorunlara yol açabilmektedir [4]. Normokalsemik hiperparatiroidizmde ise bu iki elektrolit düzeyleri normal sınırlarda izlendiğinden kardiyak komplikasyonlardan hangi mekanizmaların sorumlu olduğu çok açık değildir.

Kardiyak sorunların başında ilk dikkat çeken hipertansiyon insidansındaki artış olmuştur [2,5,6]. Ancak daha sonraki veriler yaşa göre eşleştirildiğinde hiperparatiroidide hipertansiyon sıklığının artmadığı yönündedir [1,7-9]. Primer hiperparatiroidili hastalarda ayrıca kalp kapaklarında kalsifikasyon, sol ventrikül hipertrofisi, miyokardial kalsifikasyon, koroner mikrovaskuler disfonksiyon nedeni ile kardiyovasküler hastalık riskinde artma [7], kalp yetmezliği, serebrovasküler hastalıklar, periferik arter hastalıkları, abdominal aort kalsifikasyonu, aritmi ve ani kardiyak ölümler görülebilmektedir [8,9]. Ayrıca primer hiperparatiroidili hastalarda dislipidemi, obezite, glukoz toleransında bozulma, hiperlipidemi, hipertansiyon gibi metabolik sendrom parametrelerinin artmış sıklığı kardiyak sorunlara eklenmektedir [10]. Normokalsemik ya da asemptomatik hiperparatiroidizmli hastalarda konu hala çok net değildir. Bu derlemede primer hiperparatiroidide rastlanan kardiyak sorunlara dikkat çekmek amaçlanmıştır.

Paratiroid hormon ve sol ventrikül hipertrofisi

Son günlerde yapılan çalışmalar düşük kemik kitlesi ile kardiyak mortalite arasında bir ilişki olduğunu ileri sürmekte ve bu konuda özellikle paratiroid hormon (PTH) ve vitamin D suçlanmaktadır [11,12]. PTH'in serumda artışı yaşlı erkeklerde kardiovaskuler mortalite için bir prediktördür [13]. PTH'ın aşırı artışının kalp ve arter duvarını etkilediği hem yapısal hem de fonksiyonel bozukluklarla ilişkili olduğu anlaşıldıktan sonra bu konuda yapılan çalışmalar sıklaşmıştır [8,13,14]. Soares ve arkadaşları [15] 80 yaş üzerindeki yaşlı ama sağlıklı kişilerde yaptıkları çalışmalarında PTH artışının konsantrik sol ventrikül hipertrofisi ile ilişkili bulurken, arteriel duvarın yapı ve fonksiyonu, karotid arter elastisitesi ile bir ilişki saptamadılar. Walker ve ark [16] yaptığı bir başka çalışmada hafif hiperparatiroidili hastalarda subklinik karotid arter anormallikleri, aortik kapak kalsifikasyonlarında artış saptanırken sol ventrikul kitle indeksi ve kardiyak fonksiyonlar normal bulundu.

Hiperkalsemi kardiak hipertrofiye sebep olabilir [8]. Ancak hiperkalsemi olmasa da PTH'ın kendisinin kardiyak miyositlerde ve damar düz kaslarında hipertrofiye yol açtığı artık bilinmektedir [8,15,16]. Gençlerde yapılmış çalışmalarda da PTH artışı ile orantılı olarak sol ventrikül hipertrofisi gösterilmiştir [17]. Hatta PTH normalin üst sınırında olsa bile özellikle yaşlı erkeklerde kardiyak mortalite artışına neden olduğu gösterilmiştir [18]. Mekanizması tam olarak anlaşılamasa da PTH kardiyak miyositlere direkt hipertrofik bir etki gösteriyor olabilir. İntraselluler kalsiyum artışı yüzünden protein kinaz C yolağının aktive olması ile MEK/ERK/1/2 aktivasyonu gerçekleşmekte ve hücresel proteinlerde hem de kardiyak ventrikül kitlesindeki artış ile sonuçlanabilmektedir [8,19-21]. Buradaki sorun PTH artışının ne kadar sürede ve hangi şiddette bu tür yeniden düzenlenmeyi tetikleyeceğinin çok açık olmamasıdır. Soares ve arkadaşları [15] PTH düzeyleri yüksek olan kişilerde E dalga deselerasyon zamanında kısalma olduğunu, sol ventrikül stiffnesinin ve sol atrial afterloadunun artarak sol atriumda genişlemeye neden olduğunu gösterdiler. PTH aynı zamanda inotropik etkilerle kalp hızını ve koroner kan akımını artırıyor olabilir [22]. Diğer bir mekanizma ise arteriel stifness artışının PTH tarafından induklenerek kardiyak afterloadu artırarak LVH yaratmasıdır [23].

McMahon ve arkadaşlarının [24] yaptığı 15 çalışmanın metaanalizinde primer hiperparatiroidili hastalarda paratiroidektominin sol ventrikül myokard indeksinde 11.6 g/m2 azalmaya yol açtığı gösterilmiştir. Preoperatif PTH düzeyindeki artış şiddeti ile LV kitlesi arasında ilişki varken kalsiyum düzeyleri ile orantılı bir ilişki görülmemiştir [24]. Hiperkalsemili kişilerde kardiyak relaksasyonun bozulduğu eskiden beri bilinmektedir [25]. Ancak bu metaanalizde kalsiyum yüksekliğinden ziyade PTH yüksekliğinin LVH'ne yol açan bir faktör olabileceği ileri sürülmüştür [24]. Bazı çalışmalarda ise paratiroidektomi sonrasında LV kitlesinde herhangi bir azalma gösterilememiş olması kısa gözlem süreli çalışmalarda bias olduğunu düşündürmüştür [24].

Primer hiperparatiroidili hastalarda yapılan ekokardiografik değerlendirmelere göre sistolik fonksiyonlar genellikle normal bulunurken E/A oranları ve izovolumetrik relaksasyon zamanında uzama gibi diastolik disfonksiyonu gösteren parametrelerde bozulma olduğu bildirilmişse de normal olduğunu gösteren çalışmalar konuyu daha tartışmalı hale getirmiştir [8,24]. Özdemir D ve arkadaşlarının [8] yaptığı bir çalışmada çok ilginç olarak M-mod ve pulsed-wave Doppler ekokardiyografik bulgular normal bulunmuş ancak primer hiperparatiroidili hasta gruplarında daha ileri bir yöntem olan tissue doppler imaging ve strain rate ekokardiyografisi ile değerlendirme yapıldığında hem sistolik hem de diastolik fonksiyon kusurları oluştuğu ve subklinik yapısal bozuklukların geliştiği raporlandı. Büyük olasılıkla kalsiyum yüküne sekonder intraselluler Ca artışı kalpte relaksasyonu azaltarak diastolik disfonksiyona sebep oluyor gibi görünmektedir [27]. Yine Özdemir ve arkadaşları [8] aynı çalışmada tissue doppler ekokardiyografi kullanarak miyokardial performans indeksini primer hiperparatiroidili hastalarında yüksek ölçtüler.

Diğer yandan Sin ve arkadaşları [28] Kore'li son dönem böbrek yetmezliği olan sekonder hiperparatiroidili hastalarda kalsiyum sensör reseptörüne etki eden cinecalcet'in kalsiyum, fosfor ve PTH düzeylerini normale getirmekle birlikte kardiyovaskuler mortaliteyi azaltmadığını gösterdi. Ancak daha önce yapılmış bazı çalışmalarda kronik böbrek yetersizliğine bağlı sekonder hiperparatiroidide paratiroidektomi sonrası kardiyak fonksiyonların düzeldiği gösterilmiştir [29]. Nanosato ve ark. [30] son dönem böbrek yetersizliği olan sekonder hiperparatiroidili bir kadında lokal minimal invaziv paratiroidektomi sonrası kardiyak performansı New York Heart Association'a göre klas 3'den klas 1'e gerilediğini ve ekokardiyografik parametrelerin düzeldiğini gözlemlediler. Ancak kronik böbrek yetmezliğinin son evresindeki sekonder hiperparatiroidili hastalarda hipertansiyon, volüm ve basınç yükünün artması ve organik miyokardial hasar sol ventrikül disfonksiyonunda sorumlu diğer faktörler olduğundan (30) primer hiperparatiroididen biraz daha kompleks kardiyak sorunlar doğurması kaçınılmazdır. Kronik olarak yüksek PTH'a maruz kalma mitokondriumda carnitine palmitoil transferase 1 aktivitesini azaltarak yağ asitlerinin beta oksidasyonunu bozmakta ve miyokard fonksiyonlarını azaltmaktadır [30,31].

Hiperparatiroidi kan basıncını artırır mı?

Hem primer hem de sekonder hiperparatiroidide hipertansiyon sıklığında bir artış olduğu görüşü çelişkilidir [32]. Özellikle normokalsemik hiperparatiroidi gibi hastalığın daha subklinik seyrettiği durumlarda hipertansiyonun düşük fosfor düzeyleri ile de ilişkili olabileceği ileri sürülmektedir [33].

Diğer ilginç ve beklenmeyen bir mekanizma primer hiperparatiroidili hastalarda Brunauld ve ark. tarafından [8,21] gözlenen aldosteron artışıdır. Hiperaldosteronizm de kan basıncı artışına katkı sağlıyor olabilir. Paratiroidektomiden sonra hem aldosteron düzeyleri hem de kan basıncı azalmaktadır. PTH baroreseptörlerden bağımsız olarak direkt zona glomerulozaya etki ederek PTH/PTHRP reseptörlerine bağlanmakta sitozolik kalsiyum artışına neden olmakta ve ayrıca renin salınımını direkt artırarak hiperaldosteronizme ve hipertansiyona sebep olmaktadır [2,34-36]. Aynı zamanda diğer vazopresörlere sensitivite artmaktadır [2]. Yine primer hiperparatiroidili hastalarda atheroskleroz ile yakın ilişkisi olduğu bilinen karotis intima media kalınlığı ve plak kalınlıklarındaki artış ile karotis stifnessi artmaktadır [16]. Paratiroidektomiden sonra bu bulgularda gerileme olur [16]. Ancak çalışmaların bir çoğu bu konuda çelişkili sonuçlanmıştır. İlginç olarak PTH infüzyonu hipertansif hastalarda kan basıncını düşürürken, normotansif hastalarda kan basıncını artırmaktadır. PTH damar düz kas hücrelerinde ca influxunu ve hücre içi cAMP artışını sağlayarak vazodilatasyona yol açtığı, uzun süreli PTH uyarısının ise reseptörerde desensitizasyon yarattığı sanılmaktadır. Kan basınçları yanıtları kişiden kişiye ve hiperparatiroidi süresine göre değişken olabilir [2,37,38].

Hiperparatiroidi ve aritmi

Primer hiperparatiroidide gelişen hiperkalsemi klasik bilgi olarak QT intervalinde kısalmaya, ST segmentinde azalmaya, PR ve QRS intervallerinde ise hafif uzamaya sebep olmaktadır [39]. T dalgası düzleşebilir ya da tersine döner, çeşitli derecelerde kalp blokları gelişebilir [40]. QT kısalması nedeniyle refraktör periyotun kısalması kompleks ventriküler aritmilere ya da ani ölümlere yol açabilmektedir [39]. Hafif düzeyde hiperkalsemi ile seyreden primer hiperparatiroidili hastalarda paratiroidektomiden sonra kardiyak ventriküler depolarizasyonda kısalma olmasına rağmen, EKG değişiklikleri hiperkalseminin derecesi önceden belirlenemez. Primer hiperparatiroidili ve hafif hiperkalsemili hastalarda kardiyak aritmiler oldukça nadir görülmektedir. Rosenqvist ve arkadaşları [39] orta düzeyde hiperkalsemisi olan primer hiperkalsemili kişilerde repolarizasyon fazı kısalsa bile klinik olarak belirgin bir kardiyak iletim defekti görülmediğini 20 vaka üzerinde gösterdiler. Dokupiliva A ve ark. [40] PHPT'li hastalarda 24 saatlik EKG monitorizasyonunun QT kısalsa bile aritmilerin tespitinde ek yarar getirmediğini gösterdiler.

Hiperparatiroidi ve oksidatif stres

Primer hiperparatiroidili hastalarda endotel fonksiyonlarında bozulma olduğu eskiden beri bilinmektedir. Reaktif oksijen ürünlerinde artma ve endojen antioksidan kapasitede azalma kalsiyum yükü ile ilişkilendirilmiştir. Bazı çalışmalarda kalsiyumdan çok yüksek PTH düzeyleri ile endotel disfonksiyonu arasında direkt ilişki bildirilmiştir [8,41,42].

Serum vitamin D düzeyleri ve kardiyak bozukluklar

Genellikle PTH yüksekliği serum 25-OH Vitamin D düzeyleri ile negatif korelasyon gösterir [43]. Vitamin D endotelde reseptörlerine bağlanarak düz kas hücre proliferasyonunu ve migrasyonunu inhibe etmektedir [8,44,45]. Bu durum primer hiperparatiroidili olgularda artmış atheroskleroz riskini biraz da olsa açıklayabilir. Vitamin D eksikli ile renin ve aldosteronda artma, glukoz intoleransı, proinflamatuar sitokinlerin artması gibi diğer katkı sağlayan mekanizmalar da rol oynayabilir [44]. Vitamin D eksikliği kalp yetmezliği olan kişilerin klinik durumunun kötüleşmesine sebep olan diğer bir faktör olarak ileri sürülmektedir [43]. Yaşlı hastalarda vitamin D eksikliği ve beraberinde gelişen sekonder hiperparatiroidi kalp yetmezliğinin şiddetlenmesine ve uzun dönem survive'ın bozulmasına hastane yatışlarının artmasına ve NT-proBNP artışına sebep olamaktadır [46]. Invitro çalışmalar fizyolojik dozda uygulanan aktif vitamin D'nin vaskuler düz kas sitostazını sağlayarak ve makrofaj scavanger reseptörlerinin expresyonunu kısıtlayarak atherosklerozisi kontrol ettiğini düşündürmektedir [43,47]. Ayrıca Vitamin D reseptör knockout edilmiş farelerde renin anjiotensin sistemi aktive olmakta kardiyak kitlede ve miyokard kalınlığında artışa sebep olmaktadır [43]. Bu nedenle PHPT'li hastalarda hiperkalsemiyi tetikleyeceği endişesi ile vitamin D vermekten kaçınmak kalp yetmezliği olan hastalarda kardiyak sorunları artırabilir.

Paratiroidektomi sonrası kardiyak disfonksiyon düzelir mi?

Primer hiperparatiroidili hastaların çoğu asemptomatik dönemde tesadüfen saptanmakta ve şu anda kabul gören 4. Workshop kriterlerine göre [48] operasyon endikasyonu olmayan hastalar yıllarca takip edilmektedir. Hali hazırdaki kılavuz kardiyak disfonksiyonu operasyon endikasyonu olarak değerlendirmemektedir. Yıllarca takip edilen hastalarda kardiyak sorunların ilerleyip ilerlemeyeceği de bilinmemektedir. Walker TR ve ark [16] yaptığı bir çalışmada Ca seviyesi 12 mg/dL'nin altındaki hafif PHP'li hastalarda subklinik karotis vaskuler anormallikleri, artmış aortik kapak kalsifikasyonlarını gösterdiler. Karotis intima/ media kalınlığı oranı ve plak kalınlığı ile karotis stiffnessi de artmıştır [16]. Paratiroidektomi sonrası 2 yıl takip ettikleri hastalarında paratiroidektominin bazı kardiyak bulguları düzelttiğini bazılarının ise değişmeden sebat ettiğini gösterdiler. Paratiroidektomiden sonra özellikle karotis stifnesinde belirgin azalma olduğunu bildirdiler [16]. Bazı çalışmalar paratiroidektomi sonrası sol ventrikül kitlesinde azalma bildirse de Walker ve ark [16] yaptıkları çalışmada kardiyak indekslerde düzelme olmadığını gözlemlediler. Diastolik disfonksiyonda da genellikle düzelme olmamaktadır [16]. Hafif hiperparatiroidili hastalarda diyastolik fonksiyonlar ve sol ventrikül kitlesinde genellikle artış görülmemektedir. Aortik valv kalsifikasyonları da paratiroidektomi sonrası irreversibl olan bir bulgudur.

Sonuç olarak; asemptomatik hiperparatiroidili ve normokalsemik hiperparatiroidili hastaların yıllar süren uzun süreli klinik takiplerinde kardiyak bozuklukların da dikkatle izlenmesi gerekmektedir. Kılavuzlarda henüz yeterince yer almasa da veriler PHPT'li hastalarda kardiyak açıdan yeni bir bakış açısının olması gerektiğini işaret etmektedir. Fizyopatolojilerin daha net anlaşılabilmesi bu konuda ileri çalışmaların yapılması ile gerçekleşecektir.

Maddi Destek ve Çıkar İlişkisi

Çalışmayı maddi olarak destekleyen kişi/kuruluş yoktur ve yazarların çıkara dayalı bir ilişkisi yoktur.

Kaynaklar

1. Andersson P, Rydberg E, Willenheimer R. Primary hyperparathyroidism and heart disease--a review. Eur Heart J 2004; 25: 1776-87.
2. Kalla A, Krishnamoorthy P, Gopalakrishnan A, Garg J, Patel NC, Figueredo VM. Primary hyperparathyroidism predicts hypertension: Results from the National Inpatient Sample. Int J Cardiol 2017; 227: 335-37
3. Heath III, Hunter, Stephen F. Hodgson, Margaret A. Kennedy. "Primary hyperparathyroidism: incidence, morbidity, and potential economic impact in a community." Nejm 1980; 302: 189-93.
4. Amanzadeh J, Reilly RF Jr. Hypophosphatemia: an evidence-based approach to its clinical consequences and management. Nat Clin Pract Nephrol 2006; 2: 136-48.
5. Fardella C, Rodriguez-Portales JA. Intracellular calcium and blood pressure: comparison between primary hyperparathyroidism and essential hypertension. J Endocrinol Invest 1995; 18: 827-32.
6. Gennari C, Nami R, Gonnelli S. Hypertension and primary hyperparathyroidism: the role of adrenergic and renin-angiotensin-aldosterone systems. Miner Electrolyte Metab 1995; 21: 77-81.

7. Osto E, Fallo F, Pelizzo MR et al. Coronary microvascular dysfunction induced by primary hyperparathyroidism is restored after parathyroidectomy. Circulation 2012; 126: 1031-39.
8. Ozdemir D, Kalkan GY, Bayram NA et al. Evaluation of left ventricle functions by tissue Doppler, strain, and strain rate echocardiography in patients with primary hyperparathyroidism. Endocrine 2014; 47: 609-17.
9. J.L. Anderson, R.C. Vanwoerkom, B.D. Horne, T.L. Bair, H.T. May, D.L. Lappé, J.B. Muhlestein, Parathyroid hormone, vitamin D, renal dysfunction, and cardiovascular disease: dependent or independent risk factors? Am. Heart J 2011; 162: 331-39.
10. D. Han, S. Trooskin, X. Wang, Prevalence of cardiovascular risk factors in male and female patients with primary hyperparathyroidism. J. Endocrinol. Invest 2012; 35: 548-52.
11. Stefenelli T, Abela C, Frank H et al. Cardiac abnormalities in patients with primary hyperparathyroidism: implications for follow-up. J Clin Endocrinol Metab 1997; 82: 106-12.
12. Palmer M, Adami HO, Bergström R, Jakobsson S, Akerström G, Ljunghall S. Survival and renal function in untreated hypercalcaemia. Population-based cohort study with 14 years of follow-up. Lancet 1987; 1: 59-62.
13. Hagstrom M, Hellman EP, Larsson TE et al. Plasma parathyroid hormone and the risk of cardiovascular mortality in the community. Circulation 2009; 119: 2765-71.
14. Buizert PJ, van Schoor NM, Simsek S et al. PTH: a new target in arteriosclerosis? J Clin Endocrinol Metab 2013; 98: 1583-90.
15. Soares AA et al. "Enhanced parathyroid hormone levels are associated with left ventricle hypertrophy in very elderly men and women." J Am Society Hypertens 2015; 9: 697-704.
16. Walker MD, Rundek T, Homma S et al. Effect of parathyroidectomy onsubclinical cardiovascular disease in mild primary hyperparathyroidism. Eur J Endocrinol 2012; 167: 277-85.
17. Johnstone LM, Jones CL, Grigg LE, Wilkinson JL, Walker RG, Powell HR. Left ventricular abnormalities in children, adolescents and young adults with renal disease. Kidney Int 1996; 50: 998-1006.
18. Taylor EN, Curhan GC, Forman JP. Parathyroid hormone and the risk of incident hypertension. J Hypertens 2008; 26: 1390–94.
19. Schlüter KD, Weber M, Piper HM. Parathyroid hormone induces protein kinase C but not adenylate cyclase in adult cardiomyocytes and regulates cyclic AMP levels via protein kinase C-dependent phosphodiesterase activity. Biochem J 1995; 310: 439-44.
20. X. Liu, R. Xie, S. Liu, Rat parathyroid hormone 1-34 signals through the MEK/ERK pathway to induce cardiac hypertrophy. J Int Med Res 2008; 36: 942-50.
21. L. Brunaud, A. Germain, R. Zarnegar et al. Serum aldosterone is correlated positively to parathyroid hormone (PTH) levels in patients with primary hyperparathyroidism. Surgery 2009; 146: 1035-41.
22. Ogino K, Burkhoff D, Bilezikian JP. The hemodynamic basis for the cardiac effects of parathyroid hormone (PTH) and PTH-related protein. Endocrinology 1995; 136: 3024-30.
23. Pirro M, Manfredelli MR, Helou RS et al. Association of parathyroid hormone and 25-OH-vitamin D levels with arterial stiffness in postmenopausal women with vitamin D insufficiency. J Atheroscler Thromb 2012; 19: 924-31.
24. McMahon DJ, Carrelli A, Palmeri N et al. Parathyroidectomy upon left ventricular mass in primary hyperparathyroidism: A meta-analysis. J Clin Endocrinol Metab 2015; 100: 4399-407.
25. Nappi S, Saha H, Virtanen V et al. Left ventricular structure and function in primary hyperparathyroidism before and after parathyroidectomy. Cardiology 2000; 93: 229-33.
26. Barletta G, De Feo ML, Del Bene R et al. Cardiovascular effects of parathyroid hormone: a study in healthy subjects and normotensive patients with mild primary hyperparathyroidism. J Clin Endocrinol Metab 2000; 85: 1815-21.
27. S.A. Camacho, R. Brandes, V.M. Figueredo, M.V. Weiner, Ca2 + transient decline and myocardial relaxation are slowed during low flow ischemia in rat hearts. J Clin Invest 1994; 93: 951-57.
28. Sin HY. Prospective cohort study: Cinacalcet-mediated lowering of PTH level and cardiovascular disease mortality in younger Korean patients with stage 5 CKD at a Korean secondary hospital. J Clin Pharm Ther 2017; 5: 607-14
29. Nagashima M, Hashimoto K, Shinsato T et al. Marked improvement of left ventricular function after parathyroidectomy in a hemodialysis patient with secondary hyperparathyroidism and left ventricular dysfunction. Circ J 2003; 67: 269-72.
30. Nanasato M, Goto N, Isobe S et al. Restored cardiac conditions and left ventricular function after parathyroidectomy in a hemodialysis patient. Parathyroidectomy improves cardiac fatty acid metabolism assessed by 123I-BMIPP. Circ J 2009; 73: 1956-60.
31. Smogorzewski M, Perna AF, Borum PR, Massry SG. Fatty acid oxidation in the myocardium: Effects of parathyroid hormone and CRF. Kidney Int 1988; 34: 797-803.
32. Schiffl H, Lang SM. Hypertension Secondary to PHPT: Cause or Coincidence? Int J Endocrinol 2011; 2011: 974647.

33. Kizilgul M, Beketaev I, Dolapoglu A. Letter to the Editor: Could Low Phosphate Level Be the Reason for High Risk of Hypertension in Normocalcemic Primary Hyperparathyroidism? J Clin Endocrinol Metab 2015; 100: 39.
34. Tomaschitz A, Ritz E, Pieske B et al. Aldosterone and parathyroid hormone: a precarious couple for cardiovascular disease. Cardiovasc Res 2012; 94: 10-19.
35. Zia AA, Kamalov G, Newman KP et al. From aldosteronism to oxidative stress: the role of excessive intracellular calcium accumulation. Hypertens Res 2010; 33: 1091-101.
36. Bernini G, Moretti A, Lonzi S, Bendinelli C, Miccoli P, Salvetti A. Renin-angiotensin-aldosterone system in primary hyperparathyroidism before and after surgery. Metabolism 1999; 48: 298-300.
37. D. Fliser, E. Franek, P. Fode et al. Subacute infusion of physiological doses of parathyroid hormone raises blood pressure in humans. Nephrol Dial Transplant 1997; 12: 933-38.
38. B. Jespersen, A. Randlov, J. Abrahamsen et al.The altered pattern of reactivity may counteract raised blood pressure Am J Hypertens 1997; 10: 1356-67.
39. Rosenqvist M, Nordenström J, Andersson M, Edhag OK. Cardiac conduction in patients with hypercalcaemia due to primary hyperparathyroidism. Clin Endocrinol (Oxf) 1992; 37: 29-33.
40. Dokupilova A, Payer J. 24-hour outpatient ECG as a screening method in patients with primary hyperparathyroidism. Bratisl Lek Listy 2016; 117: 495-500.
41. C. Bosworth, M.C. Sachs, D. Duprez et al. Parathyroid hormone and arterial dysfunction in the multi-ethnic study of atherosclerosis. Clin. Endocrinol (Oxf) 2013; 79: 429-36.
42. Ekmekci A, Abaci N, Colak ON et al. Endothelial function and endothelial nitric oxide synthase intron 4a/b polymorphism in primary hyperparathyroidism. J Endocrinol Invest 2009; 32: 611-16.
43. Izumi G, Inai K, Shimada E, Nakanishi T. Vitamin D Kinetics and Parathyroid Gland Function in Patients with Congenital Heart Disease. Congenit Heart Dis 2016; 11: 700-706.
44. Y.C. Ku, M.E. Liu, C.S. Ku, T.Y. Liu, S.L. Lin, Relationship between vitamin D deficiency and cardiovascular disease. World J Cardiol 2013; 5: 337-46.
45. Wang L, Song Y, Manson JE et al. Circulating 25-hydroxy-vitamin D and risk of cardiovascular disease: a meta-analysis of prospective studies. Circ Cardiovasc Qual Outcomes 2012; 5: 819-29.
46. Loncar G, Bozic B, Cvetinovic N et al. Secondary hyperparathyroidism prevalence and prognostic role in elderly males with heart failure. J Endocrinol Invest 2017; 40: 297-304.
47. Suematsu Y et al. Effect of 1,25-dihydroxyvitamin D3 on induction of scavenger receptor and differentiation of 12-O-tetradecanoylphorbol-13-acetate-treated THP-1 human monocyte like cells.Journal of cellular physiology 1995; 165: 547-55.
48. Wilhelm SM, Wang TS, Ruan DT et al. The american association of endocrine surgeons guidelines for definitive management of primary hyperparathyroidism. JAMA Surg 2016; 151: 959-68.

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Case Report

A case report: A young patient with inferior ST elevation accompanying resiprocal ST depresion

Resiprokal ST depresyonu ile birlikte inferior ST elevasyonu olan genç hasta: Olgu sunumu

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ABSTRACT

In patients admitting to the emergency department with chest pain and ST-segment elevation, the first diagnosis to be considered is acute myocardial infarction. Urgent differential diagnosis and immediately referral to catheter laboratory to perform coronary angiography is life-saving. The electrocardiography is a vital tool in the differential diagnosis of chest pain. Although the electrocardiographic findings of acute myocardial infarction and acute myocarditis are generally different, rarely two diseases can mimic each other. We presented a 21-year-old male patient who had admitted our emergency with acute typical chest pain and ST-segment elevation in D2, D3, AVF leads accompanying with reciprocal ST depression in DI and AVL leads.

Keywords: ST elevation myocardial infarction; myocarditis; electrocardiography

ÖZ

Acil servise göğüs ağrısı ve ST segment elevasyonu ile başvuran hastalarda akut miyokart infarktüsü ilk akla gelen tanıdır. Acil ayırıcı tanı ve katater laboratuvarına koroner anjiyografi için hemen refere edilmesi hayat kurtarıcıdır. Elektrokardiyografi göğüs ağrısının ayırıcı tanısında çok önemli bir araçtır. Akut miyokard enfarktüsü ve akut miyokardit elektrokardiyografik bulguları genel olarak farklı olsa da, nadiren bu iki hastalık birbirini taklit edebilir. Acil servisimize akut başlangıçlı tipik göğüs ağrısı ile başvuran, D2,D3,AVF derivasyonlarında ST elevasyonu ile birlikte DI ve AVL derivasyonlarında resiprokal ST depresyonu görülen 21 yaşında erkek hasta vakası sunduk.

Anahtar kelimeler: ST elevasyonlu miyokard infarktüsü; miyokardit; elektrokardiyografi

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Introduction

Acute myocardial infarction and acute myocarditis are the most common causes of chest pain in patients admitting to the emergency department. First evaluation of patients with chest pain is identifying the chest pain characteristics with electrocardiographic (ECG) findings and cardiac-specific enzymes and then the patient usually can be diagnosed. But in some cases it is very difficult to diagnose the case with those findings. Although the first diagnosis that comes to mind in a patient with chest pain and ST segment elevation is ST-Elevation Myocardial Infarction (STEMI) , also other diagnoses such as pericarditis, myocarditis, prinzmental angina should be considered as differential diagnosis. ECG is essential to decide to emergency coronary angiography.

Case report

We present a 21-year-old patient admitted to our emergency department at first contact with chest pain and dyspnea of one day history with ST segment elevation in D2,D3,AVF leads (inferior derivations) and resiprocal ST depression in DI and AVL leads in 12-lead electrocardiogram . Inspite of these ECG abnormalities being in favor of acute inferior myocardial infarction, myopericarditis were diagnosed due to detecting normal coronary arteries in coronary angiography . In the literature, it has been reported that in very rare cases ST elevation and reciprocal ST depression is observed together in myopericarditis.

Our patient had no risk factors for atherosclerosis such as hypertension, diabetes, dyslipidemia, cocaine usage and family history except smoking. He had influenza ten days ago and treated with symptomatic medication. On admission, her blood pressure was 120/76mmHg, his heart rate was 67 beats/minute and sinus rhytm and body temperature was 35.6ºC. The room air oxygen saturation was 98%. The chest wall examination revealed no rhonchi or rales. The findings of abdominal examination were unremarkable. On cardiac auscultation, S1 and S2 were normal, an S3 gallop was revealed, pathologic murmur and pericardial friction sound were not observed. ≥ 1 mm ST segment elevation in the inferior derivations and resiprocal ST depression in DI and AVL leads, and absence of R wave progression in anterior leads was observed in first ECG. (figure1) In second ECG at fifth minute ≥ 1 mm ST segment elevation in V5-V6 leads was also added. (figure 2) He was considered as acute coronary syndrome and was given aspirin 300 mg, ticagrelor 180 mg and standart heparin. Coronary angiogram (CAG) was immediately done in view of history of chest pain and ECG findings consistent with STEMI . But, it didn't show any significant coronary stenosis or vascular obstruction. 2D Echocardiography (ECHO) showed no segmental wall abnormality. Local ethics committee approved the study and informed consent was obtained from participant(s)

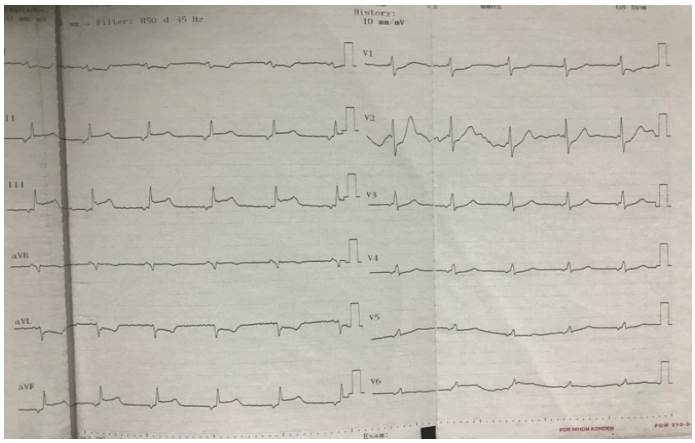

Figure1: Initial ECG

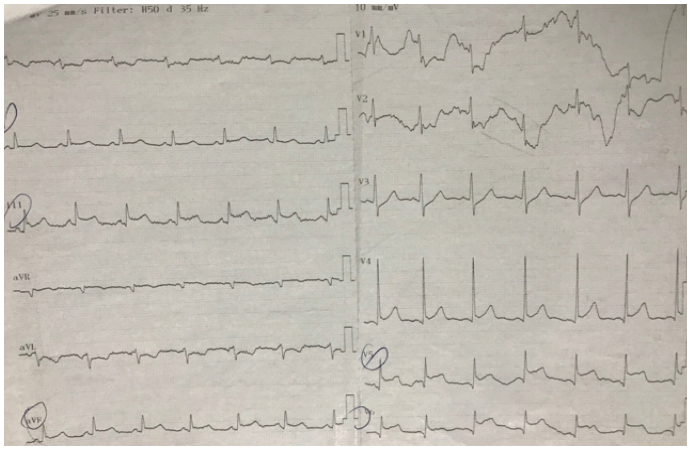

Figure 2 ECG in fifth minute

Creatine phosphokinase-MB isoenzyme was measured as 205.3 ng/ml and troponin T as 2.53 ng/ml. White blood cell count, erythrocyte sedimentation rate, C-reactive protein were 10,09 109, 51mm/h, 101.85 mg/l respectively. He had neutrophilia. Levels of serum electrolytes, glucose, blood urea and creatinine and thyroid function tests within normal limits. Liver function tests were slightly increased. During in hospital-follow up, electrocardiographic changes were resolved (Figure 3 and Figure 4).The discharge ECG demonstrated any ST segment elevation or depression (Figure 5).

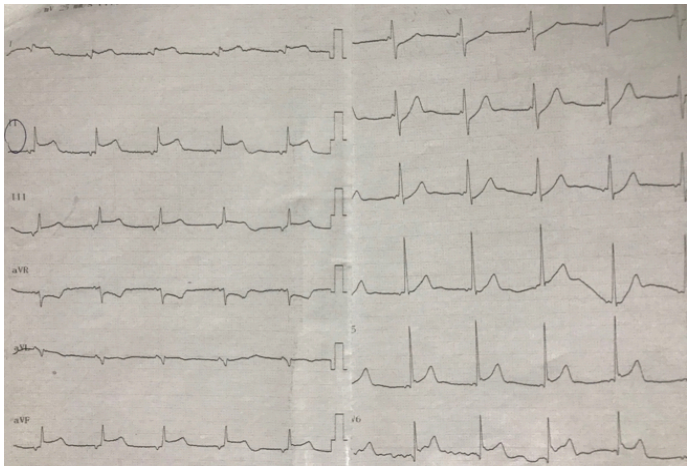

Figure 3 ECG after coronar angiography

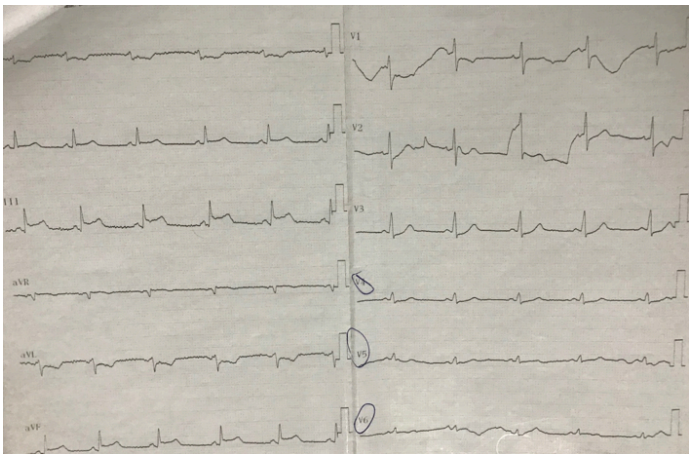

Figure 4 ECG at 24 hour

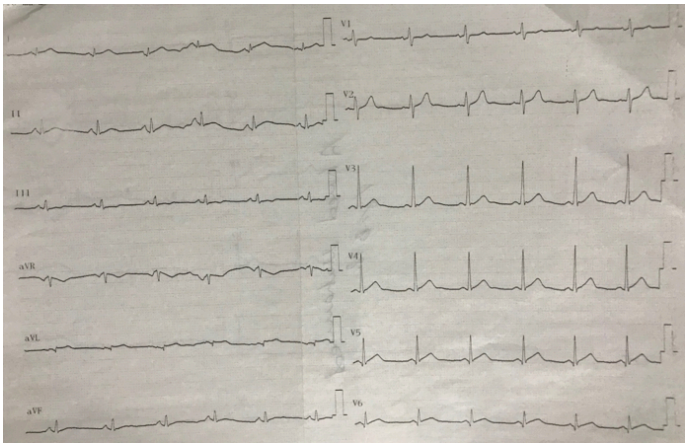

Figure 5 ECG at 7th day during discharge

Discussion

Initial evaluation of patients admitted with chest pain is firstly made with physical examination, electrocardiography and cardiac specific enzymes and we often can diagnose. But in some cases it is challenging to diagnose.1

In STEMI, ST segment elevation in at least two successive leads other than V2-V3 belonging to related vessel is observed as ≥ 1 mm convex ST elevation in the absence of left ventricular (LV) hypertrophy or left bundle branch block LBBB and there may also be a reciprocal ST depression.2 In vasospastic angina, ECG is encountered with the same findings as in myocardial infarction.3,4

Classic changes in acute pericarditis include widespread concave upward ST-segment elevation and PR-segment depression without T-wave inversions.5,6,7 In contrast to acute pericarditis, pathologic Q waves, regional convex ST-segment elevations, and reciprocal changes commonly occur with myocardial ischemia or infarction.7

The first diagnosis that came to mind when considering his age, risk factors and history was myopericarditis but reciprocal ST segment depression in ECG and being a compressive pain in central part of the chest and not responding to non-steroidal anti-inflammatory drugs; acute coronary syndrome was suggested. The most important feature of our case was observation of such a severe pain and unexpected reciprocal ST depression in lateral(I and AVL) leads which was seen only in few cases in the literature. So electrocardiography act as an acute inferior myocardial infarction with reciprocal ST depression in the lateral leads.

References

1. Nisbet BC, Breyer M. Acute myopericarditis with focal ECG findings mimicking acute myocardial infarction. J Emerg Med 2010; 39:153-8
2. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, Writing Group on the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction, Thygesen K, Alpert JS, White HD, Jaffe AS, Katus HA, Apple FS, Lindahl B, Morrow DA, Chaitman BA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky BF, Steg PG, Wijns W, Bassand JP, Menasche P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Simoons ML, Januzzi JL, Nieminen MS, Gheorghiade M, Filippatos G, Luepker RV, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon JL, Robertson RM, Weaver D, Tendera M, Bove AA, Parkhomenko AN, Vasilieva EJ, Mendis S, ESC Committee for Practice Guidelines. Third universal definition of myocardial infarction. Eur Heart J 2012;33(20):2551–2567.
3. Pitts SR, Niska RW, Xu J, Burt CW, US Dept of Health and Human Services National hospital ambulatory medical care survey: 2006 emergency department summary. Natl Health Stat Report. 2008; 6: 1-38.
4. Kusama Y1, Kodani E, Nakagomi A, Otsuka T, Atarashi H, Kishida H, Mizuno K. Variant angina and coronary artery spasm: The clinical spectrum,pathophysiology, and management. J Nippon Med Sch 2011; 78: 4-12
5. Ariyarajah V, Spodick DH. Acute pericarditis: diagnostic cues and common electrocardiographic manifestations. Cardiol Rev. 2007;15(1):24–30.
6. Lange RA, Hillis LD. Clinical practice. Acute pericarditis [published correction appears in N Engl J Med. 2005;352(11):1163]. N Engl J Med. 2004;351(21):2195–2202.
7. Marinella MA. Electrocardiographic manifestations and differential diagnosis of acute pericarditis. Am Fam Physician. 1998;57(4):699–704.

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Olgu Sunumu

Sessiz mastoidit: İki olgu sunumu

Silent mastoiditis: Two case reports

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ÖZ

Sessiz mastoidit mastoid hücrelerin kemik yapılarında ve mukozal tabakadaki subklinik enfeksiyöz enflamatuar süreci tanımlamaktadır. Hayatının belli döneminde akut otitis media (AOM) geçiren ve yanlış antibiyotik tercihi veya yetersiz dozda antibiyotik kullanımı sonucunda hastaların kliniğinde gerileme olmasına rağmen; bakterilerin eredike olmaması sonucunda sessiz mastoidit gelişmektedir. Bu hastaların kliniğinde genellikle hiçbir semptom olmamakla birlikte bazı hastalarda baş ağrısıyla karışan kulak ağrısı, mastoid bölgede duyarlılık, işitme kaybı, kulakta dolgunluk hissi ve subfebril ateş gibi semptomlar olabilmektedir. Sessiz mastoidit subklinik seyirli olması ve fizik muayenede tipik bulgusunun olmaması sebebiyle gözden kaçmakta ve hastalarda yaşam kalitesini bozan şikayetler oluşturmaktadır. Bu çalışmadaki amacımız kliniğimizde sessiz mastoidit tanısı konularak tedavileri gerçekleştirilen iki olgunun literatür eşliğinde tartışılması ve sessiz mastoiditin öneminin vurgulanmasıdır.

Anahtar kelimeler: maskelenmiş mastoidit; mastoidektomi; otitis media; sessiz mastoidit; sintigrafi

ABSTRACT

Silent mastoiditis describes the subclinical infectious inflammatory process in the bone structures of the mastoid cells and the mucosal layer. In the diagnosis of acute otitis media (AOM), despite the decrease in the the patients' clinic status, as a result of the wrong antibiotic preference or inadequate dose of antibiotics, silent mastoiditis develops due to the fact that the bacteria are not eradicated.Although there are usually no symptoms in these patients, some patients may have symptoms such as ear pain feeling like headache, sensitivity in mastoid region, hearing loss, ear fullness and subfebrile fever. Silent mastoiditis is overlooked because of its subclinical course and the lack of typical findings in physical examination. and causes complaints that impair quality of life in patients. The aim of this study is to emphasize the importance of silent mastoiditis and discuss, two cases of silent mastoiditis which diagnosed and treated in our clinic,with the literature.

Keywords: masked mastoiditis; mastoidectomy; otitis media; silent mastoiditis; scintigraphy

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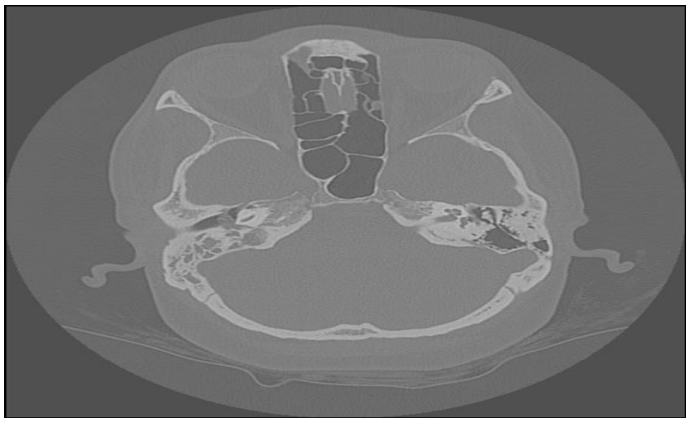
Giriş

Antibiyotik öncesi dönemde akut otitis media olgularında akut mastoidit ve akut mastoidite bağlı gelişen intrakranial komplikasyonlar sık görülürdü [1]. Günümüzde geniş spektrumlu antibiyotik kullanımının yaygın olmasına bağlı olarak klasik mastoidit sıklığı giderek azalmıştır. Klasik mastoidit yerine subklinik seyrederek gözden kaçabilen ve ciddi komplikasyonlar yaratabilen sessiz mastoidit sıklığı artmıştır [2]. Sessiz mastoidit; mastoid hücrelerin kemik yapılarında ve mukozal tabakalarındaki subklinik enflamatuar süreci tanımlamaktadır [3]. Sessiz mastoiditte orta kulak boşluğu sağlıklıdır [4]. Literatürde latent mastoidit ve maskelenmiş mastoidit olarak da adlandırılmaktadır [3,5]. Sessiz mastoidit ciddi otojenik komplikasyonlar oluşturma potansiyeli nedeniyle erken tanı konulmalı ve geciktirilmeden tedavi edilmelidir [4].

Bu çalışmadaki amacımız kliniğimizde sessiz mastoidit tanısı konularak tedavileri yapılan iki olguyu literatür eşliğinde tartışarak sessiz mastoidit'in önemini vurgulamaktır.

Olgu 1

Otuz sekiz yaşında kadın hasta; polikliniğimize yaklaşık on aydır başın sağ yarımında ağrı ve yine aynı bölgede son yirmi gündür süren uyuşukluk şikayetiyle başvurdu. Hastanın yaklaşık bir yıl önce sağ akut otitis media nedenli dış merkezde antibiyotik tedavisi aldığı ve şikayetlerinin gerilediği öğrenildi. Bu enfeksiyon sonrasında aynı kulağında hafif bir işitme kaybı şikayeti de başlamış. Özgeçmişinde üç yıldır hipertansiyon nedenli ilaç kullanım öyküsü ve üç kez sezeryan öyküsü mevcuttu. Hastanın yapılan kulak burun boğaz fizik muayenesinde patolojik bulguya rastlanmadı. Yapılan odyometrik incelemede sağ kulakta hafif derecede iletim tipi işitme kaybı mevcuttu. Bu bulgularla hastadan temporal kemik bilgisayarlı tomografisi (BT) ve difüzyonlu temporal kemik manyetik rezonans görüntüleme (MRG) yöntemi istendi. Temporal kemik BT'sinde mastoid antrum ve mastoid hücrelere uzanan yumuşak doku değerleri izlendi (Resim 1). Temporal kemik MRG'de difüzyon kısıtlanması göstermeyen mastoid antrum ve mastoid hücrelere uzanan yumuşak dokular izlendi. Öykü, fizik muayene ve radyolojik tetkikler sonucunda ön tanı olarak sessiz mastoidit'ten şüphelenilen hastadan üç fazlı kemik sintigrafisi istendi. Teknesyum-99 (Tc99m) ile yapılan sintigrafik incelemede üçüncü saatteki görüntülerde sağ mastoid bölgede sol mastoid bölgeye göre artmış tutulum saptandı. Bu bulgularla hastaya genel anestezi altında sağ kortikal mastoidektomi yapıldı. Operasyon esnasında mastoid kavite içerisinde granülasyon dokularına rastlandı. Postoperatif takiplerinde şikayetlerinde tamamen düzelme olan hasta takibimize alındı.



Resim 1: Birinci olgunun Temporal BT'sinde mastoid antrum ve mastoid hücrelere uzanan yumuşak doku değerleri

Olgu 2

Otuz yaşında kadın hasta; dört ay önce üst solunum yolu enfeksiyonu sonrasında sağ kulağında ağrı şikayeti olması üzerine dış merkeze başvurmuş. Dış merkezde üst solunum yoluna ikincil gelişen sağ akut otitis media tanısı konularak medikal tedavi başlanmış ve medikal tedavi sonrasında hastanın sağ kulak ağrısı gerilemiş. Hasta kulak ağrısı gerilediği için antibiyotik tedavisini tamamen bitirmediğini belirtiyor. Medikal tedavi bitiminden iki hafta sonra sağ kulak ağrısı tekrar başlayan hastanın yine aynı kulağından üç gün boyunca kanlı kulak akıntısı olmuş. Akıntı sonrasında sağ kulağında işitme kaybı da başlamış. Bu şikayetlerle dış merkeze başvuran hastaya lokal anestezi altında sağ ventilasyon tüpü tatbiki yapılmış. Operasyondan sonra sağ kulak bölgesinde ve çevresinde zonklayıcı tarzda baş ağrısı azalan ancak tamamen geçmeyen hasta kliniğimize başvurdu. Hastanın yapılan kulak burun boğaz fizik muayenesinde sağ dış kulak yolunda ventilasyon tüpü mevcuttu ve ventilasyon tüpü mikroskop altında poliklinik şartlarında çıkarıldı. Her iki timpanik membran intakt olarak izlendi. Sağ mastoid kemik üzerinde palpasyonla hassasiyeti mevcuttu. Yapılan odyometrik incelemede her iki kulakta anormal bulguya rastlanmadı. Hasta kliniğimize yatırılarak intravenöz anaerop ve aerop etkili antibiyoterapi tedavisine başlandı. Hastanın Temporal kemik BT' sinde sağ mastoid bölgede yumuşak doku yoğunluğu saptandı (Resim 2). Difüzyon temporal kemik MRG'de sağ mastoid bölgede difüzyon kısıtlamayan yumuşak doku yoğunluğu izlendi. Klinik değerlendirme sonucunda ön tanı olarak sessiz mastoidit düşünülen hastadan üç fazlı kemik sintigrafisi istendi. Teknesyum-99 (Tc99m) ile yapılan sintigrafik incelemede üçüncü saatte (geç metabolik fazda) alınan görüntülerde sağ mastoid bölgede sol mastoid bölgeye göre osteoblastik aktivite artışı ile uyumlu görünüm saptandı. Sessiz mastoidit tanısı konulan hastaya genel anestezi altında sağ kortikal mastoidektomi yapıldı. Operasyon esnasında mastoid kavite içerisinde

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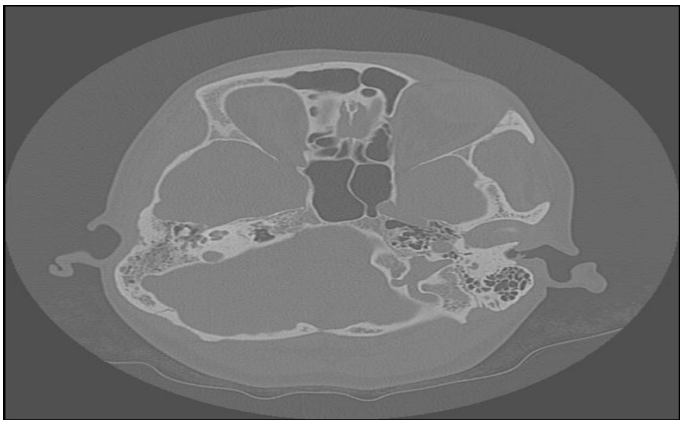
granülasyon ve yumuşak dokulara rastlandı. Mastoid hücreler arası kemik dokunun yumuşaklığı da dikkati çekmiştir. Operasyon sonrasında ve kontrol muayenelerinde ağrı şikayeti gerileyen hasta takibe alındı. Çalışma için yerel etik kurul onayı alındı. Hasta onam formları imzalatıldı.



Resim 2 : İkinci olgunun Temporal BT' sinde sağ mastoid bölgede yumuşak doku yoğunluğu değerleri

Tartışma

Sessiz mastoidit genellikle akut otitis media sonrasında meydana gelen nadir görülen klinik bir tablodur. Akut otitis media tedavisinde yanlış antibiyotik seçimi veya doğru antibiyotik seçimine rağmen yetersiz dozda antibiyotik kullanımı sonrasında hastaların şikayetlerinde gerileme olur ancak bakterilerin tam eredike edilememesi sonucu mastoid kemik ve mukozal dokularda subklinik inflamatuar tablo devam eder [3,5,6]. Sessiz mastoidit subklinik seyirli olması ve fizik muayenede tipik bulgusunun olmaması sebebiyle gözden kaçmakta ve hastalarda yaşam kalitesini bozan şikayetler oluşturmaktadır.

Sessiz mastoidit'in klinik önemi ilk defa Amerika Birleşik Devletleri'nde ortaya çıkan Neisseria menenjiti salgını sonrasında ortaya çıkmıştır. Menenjit nedeniyleölen çocukların otopsilerinde; menenjit kaynağının orta kulak ve mastoid içerisinde olduğu histopatolojik çalışmalar sonrasında kanıtlanmıştır. 1963 yılında Mawson ve 1979 yılında Goodhill akut otitis mediada antibiyotik kullanımı sonrasında yeni bir komplikasyon sürecinin ortaya çıktığını bildirmişlerdir [6].

Sessiz mastoidit olgularında klinik olarak hiçbir semptom olmayabilir. Semptomatik olgularda işitme kaybı, baş ağrısı ile karışan kulak ağrısı, kulakta dolgunluk hissi, hafif ateş ve kulak arkasında hassasiyet görülebilir [1,3,6]. Çocuk olgularda ise iştah kaybı, halsizlik, kronik ya da rekurren ateş gibi nonspesifik semptomlar görülür [3]. Komplikasyon gelişen olgularda ise ciddi kulak ve baş ağrıları, çınlama, bulantı, kusma, baş dönmesi, titreme, ateş ve meningeal irritasyon bulguları gibi şikayetler görülebilir [3]. Sunduğumuz olgularda kulak ağrısı şikayeti ön plandaydı. İlk olguda kulak ağrısına ek olarak hafif derecede işitme kaybı şikayeti de mevcuttu.

Sessiz mastoidit olgularının özgeçmişinde genellikle geçirilmiş akut otitis media öyküsü mevcuttur [3,6]. Bu enfeksiyon sırasında yanlış antibiyotik seçimi, doğru ancak yetersiz dozda antibiyotik kullanımı veya bakteriyel dirence bağlı olarak bakteriler tam olarak eredike edilemez. Ancak olguların otitis media'ya bağlı gelişen akut klinik şikayetleri geriler [3,5]. Bu olgularda AOM'nın gerilemiş olduğu kabul edildiği için olgular intratemporal veya intrakranial komplikasyonlar gelişene kadar gözden kaçarlar veya hasta olarak kabul edilmezler [6]. Tam eredike edilemeyen bakteriler mastoid mukozası ve kemik dokularda varlığını sürdürmekte ve bu dokularda histopatolojik değişikliklere neden olmaktadır [6]. Mastoid kavite içerisinde inflamatuar reaksiyon, granülasyon dokusu, osteit ve ilerleyen dönemde osteolizis gibi histolojik değişiklikler devam etmektedir [3,6]. Sonuç olarak patogenez oluşum mekanizmasında yetersiz tedavi edilen AOM sonucu mukozal ödem ve granülasyon dokusu oluşumuna inanılmaktadır [4]. Çalışmamızdaki her iki olgunun da daha önceden geçirilmiş AOM öyküsü mevcuttur. İkinci olgunun yetersiz dozda antibiyotik kullanım öyküsü de mevcuttur.

Sessiz mastoidit tanısı dikkatli ve ayrıntılı bir anamnez, ayrıntılı otolojik muayene ve radyolojik yöntemlerle konulabilir [5]. Anamnezde daha önceden geçirilmiş ve yetersiz tedavi alınmış AOM öyküsü sorgulanmalıdır. Kulak burun boğaz fizik muayenesinde çoğunlukla timpanik membran intakt olarak saptanır. Bazen timpanik membranda kalınlaşma, pars flaksida bölgesinde lokalize hiperemi, mastoid kemik üzerinde palpasyonla hassasiyet saptanabilir [5]. Sessiz mastoidit olgularında radyolojik yöntemler tanıda önemlidir. Temporal kemiğin Bilgisayarlı Tomografi (BT)ile görüntülenmesinde mastoid hücrelerde havalanma kaybı, mastoid hücre aralığında kemik doku artışı, attik ve mastoid bölgelerde yumuşak doku artışı görülmektedir [6]. Ancak bu bulgular sessiz mastoidite özgü değildir. Bilgisayarlı Tomografide osteolizisin gösterilebilmesi için kemik matriksin %30-50 oranında tahrip olması gereklidir [7]. Bu durum sessiz mastoidit olgularında tanıda gecikme yaratabilir. Bilgisayarlı Tomografinin sessiz mastoidit tanısı açısından dezavantajı budur. Teknesyum-99 ile yapılan sintigrafik çalışmalar tanıda önemlidir. Teknesyum-99 yeni kemik oluşumu olan dokularda tutulan bir maddedir. Enfeksiyona bağlı gelişen yeni kemik oluşumunda ise Tc99m normale göre %15 daha fazla tutulmaktadır [6,7]. Bu tutulum sayesinde kemik dokulardaki artmış osteoblastik aktivite saptanmaktadır. Çalışmamızdaki olgularda patolojik fizik muayene bulgusu olarak sadece ikinci olguda sağ mastoid kemikte palpasyonla hassasiyet saptanmıştır. Her iki olgunun temporal kemik BT'nde mastoid bölgede yumuşak dokular saptanmıştır. Her iki olguda da Tc99m ile yapılan sintigrafik incelemelerde patolojinin

olduğu mastoid kemikte geç fazda artmış osteoblastik aktivite saptanmıştır. Teknesyum-99 ile yapılan sintigrafik çalışmalar günlük pratikte rutin olarak yapılan tetkikler değildir. Sessiz mastoidit şüphesi olan olgularda mutlaka istenmeli; özellikle geç metabolik faz değerlendirilmelidir.

Sessiz mastoidit ciddi otojenik komplikasyonlar oluşturma potansiyeli nedeniyle erken tanı konulmalı ve geciktirilmeden tedavi edilmelidir [4]. Sessiz mastoidit olgularında öncelikle aerobik ve anaerobik etkili intravenöz antibiyotik tedavisi başlanmalıdır [6]. Sessiz mastoidit olgularının tedavisinde mastoidektominin mutlak gerekli olduğu ve zamanlama olarak genel durumu müsait olunan en kısa sürede cerrahi işlem yapılmalıdır [3,5]. Komplikasyon gelişen olgularda ise komplikasyonlara yönelik tedaviler ve sessiz mastoidite yönelik cerrahi tedavi uygulanmalıdır.

Tedavi edilmeyen sessiz mastoidit olgularında ağrı, ateş, kulak akıntısı gibi uyarıcı semptom ve bulgular olmadan bile hayatı tehdit edici ciddi komplikasyonlar gelişebilir [5]. İntrakraniyal komplikasyonlar menenjit, beyin absesi, lateral sinüs tromboflebiti, kortikal sinüslerde tıkanma ve ensefalittir [6]. Sessiz mastoiditte intrakranial komplikasyonlar çoğunlukla tek bir odak halinde görülürken, literatürde multiple intrakranial komplikasyonla seyreden sessiz mastoidit olguları da bildirilmiştir [4]. İntratemporal komplikasyonlar ise sensörinöral tip işitme kaybı, fasial paralizi ve tinnitustur [6]. Çalışmamızdaki olgularda klinik ve radyolojik incelemelerde komplikayon bulgularına rastlanmamıştır.

Sonuç

Akut otitis media tanısı konulan hastalara doğru ve etkin antibiyoterapi başlanılmalı ve hastalara antibiyotikleri düzenli kullanmaları gerektiği özellikle belirtilmelidir. Takiplerinde işitme kaybı, hafif kulak ağrısı, kulakta dolgunluk hissi, kulak arkasında duyarlılık gibi belirgin olmayan kulak şikayetleri devam eden hastalarda, ciddi komplikasyonlar oluşturma potansiyeli nedeniyle sessiz mastoidit tanısı akılda tutulmalıdır. Şüphelenilen olgularda temporal kemiğin BT incelemesi ve sintigrafik incelenme ile tanı doğrulanmalı ve en kısa sürede tedavi edilmelidir.

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Kaynakça

1. Tsai TC, Yu PM, Tang RB, Wang HK, Chang KC. Otorrhea as a sign of medical treatment failure in acute otitis media: two cases with silent mastoiditis complicated with facial palsy. Pediatrics & Neonatology 2013; 54: 335-38.
2. Martin-HirschDP, Habashi S, Page R, Hinton AE. Latent mastoiditis: no room for complacency. The Journal of Laryngology & Otology 1991; 105: 767-68.
3. Şahin B, Karavuş A, Şapçı T, Akbulut UG. İntrakranyal komplikasyonlarla seyreden silent mastoidit: olgu sunumu. Turk Arch Otolaryngol 2003; 41: 232-38.
4. Voudouris C, Psarommatis I, Nikas I, Kafouris D, Chrysouli K. Pediatric masked mastoiditis associated with multiple intracranial complications. Case Rep Otolaryngol 2015: 1-4
5. Toprak M, Yener M. Subakut veya Sessiz Mastoidit. In: Dış ve Orta Kulak Cerrahisi, Devranoglu İ (ed). 1st ed. İstanbul: Deomed; 2011: 119-20
6. Akyıldız N. Kulak hastalıkları ve mikrocerrahisi. Bölüm 5. Ankara: Bilimsel Tıp Yayınevi 1998; 332-34.
7. Tovi F, Gatot A. Bone scan diagnosis of masked mastoiditis. Ann Otol Rhinol Laryngol 1992; 101: 707-9.

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Case Report

Surgical managment of "forgotten" goiter in a patient with the history of coronary artery bypass grafting.

Koroner arter bypass greftleme öyküsü olan bir hastada "gizli" guatrın cerrahi tedavisi

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ABSTRACT

Forgotten goiter is a rare condition and it is surgically managed through cervical approach in most cases. Extracervical management could be necessary in rare cases. We report a case of a forgotten goiter managed with thyroidectomy through a mini-resternotomy combined with a transcervical approach as the patient underwent previous cardiac surgery.

Keywords: retrosternal guatr, resternotomy, minimal invasive surgery

ÖZ

Gizli guatr nadir karşılaşılan bir durum olmasına rağmen servikal bölgeye yapılan kesilerle cerrahi olarak tedavi edilebilmektedir. Ekstraservikal yaklaşık istisnai durumlarda başvurulan bir yöntemdir. Biz bu olgu sunumunda daha önce kardiyak cerrahi geçirmiş, gizli guatrı olan bir hastada tiroidektomi için transservikal yaklaşım ile mini-sternotomiyi nasıl kombine ettiğimizi anlatmak istedik.

Anahtar Kelimeler: retrosternal guatr, resternotomi, minimal invazif cerrahi

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Introduction

Retrosternal goiter was described for the first time in 1749 by Haller [1]. Massard et al, in 1992, first described the term "forgotten goiter" that means a mediastinal mass diagnosed after a cervical total thyroidectomy [2]. Forgotten goiter is a rare condition with an incidence of 2%-16% [3]. The main reasons for this issue to occur are; incomplete removal of a cervico-mediastinal goiter during initial cervical thyroidectomy or an undiagnosed mediastinal goiter which has no connection to the cervical mass [4]. Surgical management in forgotten goiter varies from patient to patient however in most cases cervical approach is sufficient for the removal of the retrosternal goiter [5]. In the literature, the requirement of extracervical approach is suggested to be 2%-11%, either through sternotomy for anterior mediastinal mass or through thoracotomy for posteriorly located masses [5].

Herein, we report a case of a patient managed with thyroidectomy through a mini-resternotomy combined with a transcervical approach since she had a past history of cervical total thyroidectomy 20 years ago and a coronary artery bypass graft operation 3 years ago.

Case

A 67-year-old female patient with a past medical history of total cervical thyroidectomy for multinodular goiter was admitted to endocrine surgery department with mild dyspnea. In her previous thyroidectomy, the surgeon reported that a total cervical thyroidectomy was carried on without any complication. She was on levothyroxine sodium treatment since her initial operation that was 20 years ago. Additionaly, the patient underwent a coronary artery bypass graft surgery for left anterior descending artery (LAD) lesion through a median sternotomy and a left internal thoracic artery (LITA) to LAD anastomosis was performed 3 years ago.

Her physical examination on her admission to endocrine surgery department was normal and there was no palpable cervical thyroid. She was euthyroid with normal serum levels of Free T4 and TSH (1.38 ng/dl (0.87-1.7 ng/dl) and 0.646 µU/ml (0.27-4.2 µU/ml) respectively). Her chest X-ray revealed a significant deviation of the trachea to the right side (Figure1a). Computed tomography of neck and chest revealed a mass with a diameter of 64x51mm located on superior mediastinum leading to a rightward deviation of both trachea and left carotid artery and compressing both left internal jugular and brachiocephalic veins (Figure 1b). Thyroid scintigraphy demonstrated hyperplasia of the left thyroid lobe and a nodule that was located retrosternally showing a heterogenous activity (Figure 1c). As the patient had a history of CABG and a "forgotten" goiter, endocrine surgeons consulted us, as cardiovascular surgeons, for requirement of a sternotomy. Her coronary angiography revealed a patent LITA-LAD anastomosis (Figure1d).

Figure 1a

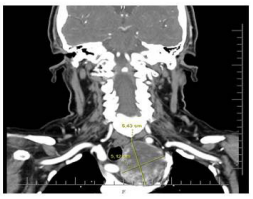

Figure 1b

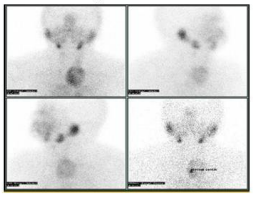

Figure 1c

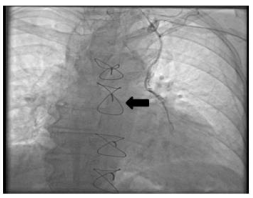

Figure 1d

Figure 1: 1a; preoperative chest X-ray, white arrow showing the tracheal deviation. **1b;** preoperative computed tomography of the patient showing the retrosternal goiter that deviated trachea to the right. **1c;** thyroid scintigraphy. 1d; coronary angiography, black arrow showing the patent LITA-LAD anastomosis.

Initially, the patient underwent a transcervical approach for the removal of the mass. Thyroid gland with a diameter of 1x1cm was explored and removed. A neural integrity monitor (NIM) was used during the procedure to identify the left recurrent laryngeal nevre. Due to the patient's previous CABG surgery we thought that there could be massive fibrous adhesions around the mediastinal mass that may lead to an uncontrollable bleeding when trying to deliver the mass through the cervical incision, and decided to perfom a mini resternotomy (Figure 2a). The nodule was removed with its capsule successfully without a vascular complication (Figure 2b). The patient's recovery was uneventful and discharged on 3rd postoperative day.

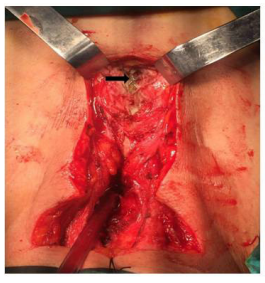

Figure 2a

Figure 2b

Figure 2: 2a; mini resternotomy combined with cervical incision, black arrow showing sternal wires, **2b;** thyroid gland.

Local ethics committee approved the study and informed consent was obtained from participant(s)

Discussion

Retrosternal goiter is the extension of thyroid gland in the me-

diastinum. It is called primary when there is an ectopic thyroid gland in the mediastinum that is fed by mediastinal vessels and it is called secondary when the cervical thyroid gland extends to the mediastinum either posteriorly or anteriorly and fed by neck vessels. Forgotten goiter is a condition that defines a mediastinal mass diagnosed after a total cervical thyroidectomy [2]. Most forgotten goiters are asymptomatic and diagnosed incidentally [5]. Surgery is indicated whether the goiter is symptomatic or not. Complete delivery of "forgotten" goiter through a standard cervical approach is mostly sufficient. However, extracervical approach either sternotomy or thoracotomy could be required in rare cases. Recently, video-assisted thoracoscopic surgery (VATS) and the da Vinci robotic surgery approaches are started to use in retrosternal goiters to avoid the complications of thoracotomy or sternotomy. These minimal invasive approaches lead to shorter hospital stays, reduced pain and also better cosmetic results, however these are expensive systems [5].

We performed standard cervical incision combined with a mini re-sternotomy in this case to avoid troublesome bleeding, injury to recurrent laryngeal nerve and also to avoid incomplete removal of the mediastinal mass. In the literature, there are cases that report standard cervical incision combined with a sternotomy for retrosternal goiters. What makes the things complex and interesting in our case is that the patient underwent a CABG operation 3 years ago through a median sternotomy and resternotomy was necessary. To the best of our knowledge this case is the first case report that required resternotomy for a forgotten goiter excision.

Conclusion

Surgical resection of forgotten goiter even asymptomatic is the gold standard. Sternotomy combined with transcervical approach is necessary in rare cases. We conclude that even resternotomy can be performed safely in retrosternal goiters who underwent a median sternotomy for a cardiac surgery.

Declaration of conflict of interest

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References

1. Haller A. Disputationes Anatomica Selectae. Gottingen: Vandenhoeck 1749: 96.
2. Massard G, Wihlm JM, Jeung MY, Roeslin N, Dumont P, Witz JP. Forgotten mediastinal goiter: seven cases. Ann Chir 1992; 46: 770–73.
3. Calò PG, Tatti A, Medas F, Petruzzo P, Pisano G, Nicolosi A. Forgotten goiter. Our experience and a review of the literature. Ann Ital Chir 2012; 83: 487-90.
4. Riquet M, Deneuville M, Debesse B, Chretien J, Autonomous intrathoracic goiter: apropos of 2 new cases, Rev Pneumol Clin 1986; 42: 267–73.
5. Tsilimigras DI, Patrini D, Antonopoulou A, Velissaris D, Koletsis E, Lawrence D, et al. Retrosternal goitre: the role of the thoracic surgeon. J Thorac Dis 2017; 9: 860-63.

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Case Report

Talon cusps: Two case reports

Talon tüberkülü: İki olgu sunumu

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ABSTRACT

The talon is an accessory, irregular cusp on incisors and canines, involving in enamel and dentine with or without pulp tissue.It was also reported in association with syndromes, for example, Mohr Syndrome, Incontinenta pigmentii Achromians, Ellis-van Creveld Syndrome, Struge Weber Syndrome, Rubinstein Taybi Syndrome, and Alagille's Syndrome. The aim of this paperwas to describe talon tubercules in two cases. In first case the talon cusp is seen on lingual surface of the maxillary left central tooth and there is a specific talon tubercle which extending from the incisal edge to the cervical edge, perpendicular to the mesiodistal surface of the tooth. In second case bilateral talon tubercles were detected extending from the cervical region less than half of the incisal margin on the lingual surface of the maxillary central and lateral teeth. This present two case reports radiograph gives a v-shaped radiopaque image.Talon tubercle is a dental anomaly we rarely encounter. Consequently this anomaly may occur with a systemic syndrome Therefore, clinicians should have adequate knowledge of this anomaly.

Keywords: talon cusp; accessory cusp; maxillary permenant incisor

ÖZ

Talon tüberkülü kesici ve kanin dişlerde görülen, mine ve dentin dokusundan oluşan, bazen pulpa uzantılarının da içerisinde bulunduğu aksesuar bir tüberkül olarak tanımlanır. Bu durum Mohr Sendromu, Incontinenta pigmenti Achromians, Ellis-van Creveld Sendromu, Struge Weber Sendromu, Rubinstein Taybi Sendromu ve Alagille Sendromu gibi sendromlarla birlikte de bildirilmiştir. Bu makalenin amacı iki ayrı vakada görülen talon tüberkülünü tanımlamaktadır. Birinci vakada talon tüberkülü, maksiller sol santral dişin lingual yüzeyinde görülmektedir ve servikal kenardan insizal kenara uzanan, dişin mesiodistal yüzeyine dik olarak konumlanan spesifik bir talon tüberkülü bulunmaktadır. İkinci vakada da maksiller santral ve lateral dişin lingual yüzeyinde, dişin servikal kenarından insizal kenarının yarısına kadar uzanan bilateral talon tüberkülü saptanmıştır. Bu iki vaka raporunda, radyografinin de V-şeklinde radyopak bir görüntü verdiğini saptanmıştır. Sonuç olarak talon tüberkülü nadiren karşılaştığımız bir dental anomalidir. Bu anomali sistemik sendromlar ile birlikte görülebilmektedir; Bu nedenle, klinisyenler bu anomaliye ilişkin yeterli bilgiye sahip olmalıdır.

Anahtar kelimeler: talon tüberkülü; aksesuar tüberkül; maksiller üst kesici

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Introduction

The talon is an accessory, irregular cusp onincisors and canines, involving in enamel and dentine with or without pulp tissue.Talon cusp is a rare developmental anomaly in which from the cemento-enamel junction of the upper or lower anterior teeth in either primary or permanent dentition and extending to at minimal half of the distance to the incisal margin of the anterior teeth. Mitchell was the first to describe a talon cusp in 1892. It was named as talon cuspby Ripa and Mellor due to its view as eagle's talon when viewed from incisal margin[1].

The talon is also named such as the names; accessory cusp, addition cusp, anterior dens evaginatus, cusp-like hyperplasia, prominent accessory cusp like structure, supernumerary cusp, interstitial cusp, odontoma of the axial core type, evaginated odontoma, occlusal enamel pearl, occlusal anomalous tubercle[2].The maxillary lateral incisors are the most often involved, followed by the maxillary central incisors and canines [3]. Talon cusps are most frequently located on the lingual faces of the teeth; a few case reports of labial cases are given information in the literature [1]. Males show a upper frequency than females[2] and talon cusps are reported ussually unilateral; rarely are bilateral [4].

The aetiology of the teeth anomaly is unknown. It arises during the morphodifferentiation stage of tooth development[5]. It was also reported in association with syndromes, for example, Mohr syndrome, Incontinenta pigmentii Achromians, Ellis van creveld syndrome, Struge Weber syndrome, Rubinstein Taybi syndrome, and Alagille's syndrome[6].

The presence of this talon cusp is not forever an indication for dental cure unless it is associated with clinical problem. The problems of talon cusp are functional , pathological, diagnostic and esthetics[1, 6]. This report showes two cases of talon cusp, one on a maxillary bilateral central and lateral incisor and another on a maxillary central tooth. Informed constent form was approved both two patients.

Case 1

23 years old Turkish male applied to the Kırıkkale University Faculty of Dentistry Department of Restorative Dentistry with a chief complaint of a due to decay teeth. No systemic disease of the patient was detected in the received anamnesis. Oral examination all permanent teeth were exist and hypoplasia and coloration in the anterior teeth. Examination revealed talon cusps on the lingual surfaces of maxillary left central incisor and this tooth is protruzive (Figure 1a). This anomaly was not found in family history. Maxillary left central incisor had a specific talon cusp so that covering from the cervical region towards the incisal margin.The cusp determined and perpendicularly localized to the mesiodistal surface of the crown. The shape of the talon cusp were hornlike, and can be described as conical (Figures 1b). Replies of the affected teeth during the palpation,percussion and pulpal tests were normal. The talon cusps had no unfavourable influence on the tongue along speaking and mastication. Radiographic (periapical and panoramic) examination showed a "V"-shaped radiopaque structure but did not clearly define this formation associate with to the pulp chamber (Figures 1c and 1d). Therefore, we considered no treatment needed.

FIGURE 1a. Occlusal image of the teeth.

FIGURE 1b. Incisal image of the teeth.

FIGURE 1c. Panoramic radiography of the teeth.

FIGURE 1d. Periapical radiography of the teeth.

Case 2

22 years old Turkish female applied to the Kırıkkale University Faculty of Dentistry Department of Restorative Dentistry with a chief complaint of a due to decay teeth. No systemic disease of the patient was detected in the received anamnesis. Intraoral examination all permanent teeth were exist and clinical examination of this patient indicated additional cusps located on the palatal plane of the upper centrals and laterals bilaterally, extending from the cemento enamel junction less than half the distance to the incisal margin. The type of the cusps was semi-talon (Figure 2a). The four affected teeth replied positively to palpation,percussion and thermal tests. The color of teeth which talon cusp was normal. The cusps did'nt interfere on occlusion; neither the centrals nor the laterals were carious. In the panoramic radiograph was spied on the talon cusps as "V" formed radiopaque structures on the both centrals and laterals (Figure 2b). Therefore, we considered no treatment needed.

FIGURE 2a. Incisal image of the teeth

FIGURE 2b. Panoramic radiography of the teeth

Local ethics committee approved the study and informed consent was obtained from participant(s)

Discussion

Talon cusp reported as a very uncommon dental anomaly. Hattab et al. defined a classification system for these abnormal cusps on the foundation of the degree of cusp size, formation and location [7]. This is shown in table 1.

Table 1. Classification of talon cusp based on the degree of formation and extension

Type 1 Talon	A morphologically well-delineated additional cusp that prominently projects from the lingual surface of a primary or permanent anterior tooth and extends at least half the distance from the cemento enamel junction to the incisal marginal.
Type 2 Semi Talon	An additional cusp of a millimeter or more extending less than half the distance from the cemento enamel junction to the incisal marginal. It may blend with the palatal surface or stand away from the rest of the crown.
Type 3 Trace Talon	Enlarged or prominent cingula and their variations, i.e. conical, bifid, or tubercle like. Radiographically, it may appear typically as a V-shaped radiopaque structure, as in true talon and semi talon, or be tubercle-like, originating from the cervical third of the root.

Hsu Chin-Ying et al.defined this as major, minor, and trace talon. When examined from incisal margin, the morphology seem as either "T," "Y,"or "π" shape for major, minor, or bifid talon cusp.[6] In case 1, the talon cusp classification is type 1 (true talon), whereas in case 2, the type 2 (semi talon) talon cusp classification is included.

Ekambaram et al. [8],Topaloğlu et al.[9] and Abbott et al.[10] showed vestibül and lingual talon cusps on the same tooth.In present report, Case 1 was unilateral. Balcıoğlu et al.[4] , Güngör et al.[11] , reported bilateral talon cusp. In the present report, Case 2 was bilateral.

When the literature is examined; talon cusps arethe maxillary lateral incisors (%67) are the most often arises, followed by the maxillary central incisors (%24) and canines (%9) [3].Segura JJ and Jiménez- Rubio et al. the cause as this event may be consist the pressure of the tooth germ of the lateral teeth by the central and the canine tooth; because the central incisor and the canine develop seven months earlier than the lateral incisor.Increased pressure on a tooth germ can cause outfolding of the dental lamina along the morpho-differentiation stage [4]. Talon cusp, Case 1 occurred at the maxillary central incisor tooth; Case 2 occurred in both the maxillary central and lateral teeth.

The talon cusp is including normal enamel, dentin, and varying extensions of pulp tissue, however; its composition is difficult to determine because of the cusps superposed on the pulp chamber [1]. In the present cases did not clearly define this formation associate with to the pulp chamber.Radiographically, a talon cusp typically seems as a "V"-shaped radiopaque structure [1, 2]. This radiographic image was seen in two cases.

The frequency of talon cusp ranges from 0.06% to 7.7% in the literature[1, 4]. The reported frequency is 2.4% in Jordanians, 2.5% in Hungarians, 0.06% in Mexicans, 5.2% in Malaysians, 0.97% and 0.58%in Indians[12]. Arfat et al.[13] talon cusps found prevalence to be 1.2% Turkish population while Güven et al.[12] talon cusps were found in 0.34%.

Kayalvizhi et al.[14] and Segura JJ et al.[3] reported dens invaginatus with associated talon cusp. In the present report; No dental anomalies associated with talon cusp were found and none of the two case repots reported here had any systemic syndrome.

Talon cusp may reason a variety of clinical problems; such as occlusal interference, irritation of tongue and oral tissues, pulpal disorder, decay, attrition, periodontal problems, displacement of the affected tooth, esthetic problems, accidental cusp fracture, and even temporomandibular disorders. Treatment of talon cusp may vary depending on each case [4]. Early diagnosis of talon is very important. If the grooves are carious, the lesion must be removed and the cavity restored with glass ionomer restorative material [15] or composite resin [1]. If premature contact and occlusal interference have the talon cusp should be reduced gradually on consecutive visit over 6 to 8week intervals to allow time for deposition of reperative dentine for pulpal preservation. After each procedure the tooth surface must be covered with a desentisizing agent or fluoride varnish[16]. Sometimes,less conservative methods can be used, including complete reduction of cusp followed by calcium hydroxide/ mineral trioxide aggregate pulpotomy or canal therapy or extraction followed by orthodontic correction and prosthetic rehabilitation [6].

Talon cusp is not always a need for dental treatment, unless the cusp is associated with issue such as compromised esthetics, occlusal interference, tooth displacement, caries, periodontal problems, or irritation of during speech or mastication[1].

In the 1th case described here, the maxillary talon cusp defined on the lingual surface of the central tooth.In the 2th case described here, the maxillary talon cusp bilaterally defined on the lingual surface of both the central and lateral teeth. The margins of the talon cusp were regular and did not cause any irritation to the surface of the tongue. Caries didn't define and no functional and occlusal interference or aesthetic problems were present. Hence, no treatment was applied.

Conclusion

In conclusion, the cases described in this paper contains an asymptomatic dental anomaly that did not reason any other variation in the tooth or arch.Clinicians should have a wide knowledge about developmental anomalies, their variations and the clinical conclusions.Early diagnosis of talon cusps aids in choosing the correct treatment and avoiding complications.

Declaration of conflict of interest

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References

1. Yazıcıoğlu O, Ulukapı H. Management of a facial talon cusp on a maxillary permanent central incisor: A case report and review of the literature. J Esthet Restor Dent 2014; 26: 374-81.
2. Dankner E, Harari D, Rotstein I, Dens evaginatus of anterior teeth: literature review and radiographic survey of 15,000 teeth. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996; 81: 472-75.
3. Segura-Egea JJ, Jimenez-Rubio A, Rios-Santos JV, Velasco-Ortega E, Dens evaginatus of anterior teeth (talon cusp): Report of five cases. Quintessence Int 2003; 34: 272-77.
4. Balcioğlu H, Keklikoğlu N, Kökten G, Talon cusp: a morphological dental anomaly. Rom J Morphol Embryol 2011; 52: 179-81.
5. Nadkarni U, Munshi A, Damle S, Unusual presentation of talon cusp: two case reports. Int J Paediatr Dent 2002; 12: 332-35.
6. Nuvvula S, Raja Gaddam K, Jayachandra B, Kumar MallineniS, A rare report of mandibular facial talon cusp and its management. J Conserv Dent 2014; 17: 499-502.
7. Hattab F, Yassin O, Al-Nimri K, Talon cusp in permanent dentition associated with other dental anomalies: review of literature and reports of seven cases. ASDC J Dent Child 1995; 63: 368-76.

8. Ekambaram M, Yiu CKY, King NM, An unusual case of double teeth with facial and lingual talon cusps. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008; 105: 63-67.
9. Topaloğlu Ak A, Eden E, Ertuğrul F, Sütekin E , Supernumerary primary tooth with facial and palatal talon cusps: a case report. J Dent Child 2008; 75: 309-12.
10. Abbott PV, Labial and palatal "talon cusps" on the same tooth: A case report. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998; 85: 726-30.
11. Güngör HC, Altay N, Kaymaz FF, Pulpal tissue in bilateral talon cusps of primary central incisors: report of a case. Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 2000; 89: 231-35.
12. Guven Y, Kasimoglu Y, Tuna EB, Gencay K, Aktoren O, Prevalence and characteristics of talon cusps in Turkish population. Dent Res J (Isfahan) 2016; 13: 145-50.
13. Arfat B, Çolak H, Çelebi AA, Uzgur R, Turkal M, Hamidi MM, The frequency and characteristics of talon cusps in a Turkish population. Eur J Gen Dent 2012; 1: 39-43.
14. Kayalvizhi G, Neeraja R, Co-occurrence of bilateral coronal Dens invaginatus and true Talon. Pediat Dent J 2010; 20: 110-13.
15. Hattab FN, Mok NY, Agnew EC, Artificially formed carieslike lesions around restorative materials. J Am Dent Assoc 1989; 118: 193-97.
16. Hattab F, Wei S, Chan D, A scanning electron microscopic study of enamel surfaces treated with topical fluoride agents in vivo. ASDC J Dent Child 1987; 55: 205-209.

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Olgu Sunumu

Kinolon ilişkili nadir bir komplikasyon: Uzun QT sendromu

A rare quinolone-associated complication: Long QT sydrome

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ÖZ

Enfekte diyabetik ayak ülserlerinin tedavisinde antibiyotikler sık kullanılan tedavi ajanları arasında yer almaktadır. Ancak antibiyotiklere bağlı bazen hayatı tehdit edebilecek boyutta ciddi yan etkiler görülebilir. Bu yazıda enfekte diyabetik ayak ülseri nedeniyle kinolon grubu antibiyotik tedavisi başlanan bir hastada bu tedaviyi takiben gelişen uzun QT sendromu ve devamında kardiyopulmoner arrest gelişen ve defibrilasyon tedavisi ile reanimasyonu sağlanan oldukça nadir bir vaka tartışılarak nadir görülen komplikasyon üzerine dikkat çekmeyi amaçladık.

Anahtar kelimeler: uzun QT sendromu, antibiyotik, kinolon

ABSTRACT

In the treatment of infected diabetic foot ulcers, antibiotics are frequently used as treatment agents. However, serious adverse effects may be seen on antibiotics, which can sometimes be life-threatening. In this article, we aimed to draw attention to a rare complication in a patientwhowastreatedwithquinoloneantibioticsduetoinfecteddiabeticfootulcer, a rare long QT syndrome following this treatment, subsequent cardiopulmonary arrest and reanimation with defibrillation therapy.

Keywords: long QT syndrome; antibiotic; quinolone

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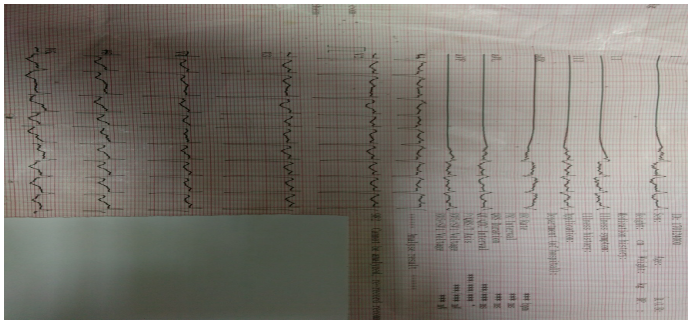
Giriş

Uzun QTsendromları EKG'de uzamış QT mesafesi ile karakterize olan kardiyak repolarizasyon bozukluklarıdır. Doğumsal veya edinsel nedenlere bağlı olarak ortaya çıkabilmektedir. QT değerinin kalp hızına göre düzeltilmiş değeri için (QTc) 350-420 msn arası değerler normal, 420-440 msn arasındaki değerler sınırda, 440 msn üzerindeki değerler ise yüksek olarak kabul edilmektedir [7]. EKG'de uzamış QT aralığı ve T dalgası değişiklikleri ile özellikle sempatik aktivitenin arttığı egzersiz veya emosyonel durumlarda yaşamı tehdit eden torsade de pointes(TdP) tipi ventriküler taşikardiler sonucu, senkop atakları ve/veya ani kardiyak ölüm karakteristik bulgulardır[1-3]. Uzun QT sendromunun edinsel tipi doğumsal tipinden daha sıktır, kadınlarda daha sık görülür ve tipik olarak QT mesafesini uzatan elektrolit bozukluklarıveilaçlarla tedavinin bir komplikasyonu olarak ortaya çıkar [4]. QT aralığının uzaması kinidin, sotalol, amiodaron, prokainamid gibi antiaritmik ilaçlar ile birlikte görülebilmekle beraber antiaritmik kardiyak ilaçlar dışında diğer grup ilaçlarda bu duruma neden olabilir[6]. Edinsel uzun QT sendromunun nedeni tam olarak bilinmemektedir. Bir hipoteze göre, iyon kanalları ya da diğer genlerdeki subklinik mutasyonlar uygun ortamlarda hastayı aşırı QT uzamasına yatkın hale getirebilir [5]. Bu yazıda diyabetik ayak enfeksiyonu nedeni ile florokinolon grubu bir antibiyotik olan moksifloksasin başlanan ve takibinde edinsel uzun QT sendromuna bağlı kardiyak arrest gelişen bir olgu sunulmuştur.

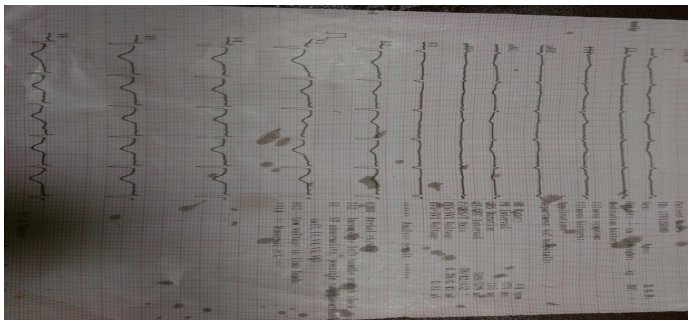
Literatürde antibiyotik alımından birkaç gün sonra QTc mesafesi uzayan vakalar bildirilmekle birlikte tek doz sonrası görüldüğüne dair bir makale görülmedi. Bu yönüyle de bu vaka sunulmaya değer görülmüştür.

Olgu

İki yıldır bilinen tip 2 diabetes mellitus tanısı olan ve oral antidiyabetik kullanan 65 yaşında kadın hasta, kan şekeri regülasyon bozukluğu ve sağ ayakta diyabetik ayak ülseri ile başvurdu. Hastanın fizik muayenesinde ayak bileğine kadar uzanankızarıklık, ödem, hassasiyet, ısı artışı ve anaerobik koku mevcuttu. Ayak falankslarında lokalize nekroz bulunan bu yara Wagner evre 4 olarak değerlendirildi. Laboratuvar değerlerinde CRP: 170 mg/l (0,15-5 mg/l), eritrosit sedimentasyon hızı: 84 mm/saat (0-20mm/saat), beyaz küre: 27.130 /mm3(4400-11300 /mm3),trombosit: 434.000/mm3(150000-500000 / mm3),hemoglobin: 10,2g/dl (10-18 g/dl), kalsiyum: 8,09 mg/dl (düzeltilmiş kalsiyum: 8,88 mg/dl)(8,8-10,2 mg/dl), potasyum: 3,96 mmol/l (3,5-5,1mmol/l), magnezyum: 2,10 mg /dl (1,9-2,55 mg/dl), albumin: 3,01g/dl (3,5-5,2 g/dl) idi ve diğer laboratuvar değerlerinde belirgin bozukluk yoktu. Hastanın başvuru anındaki EKG'si (Resim 1) normal sinüzal ritm idi. Hastaya diyabetik ayak enfeksiyonu için enfeksiyon hastalıklarının önerisiyle moksifloksasin 400 mg 1x1/gün ile birlikte piperasilin-tazobaktam 3x4,5 gr/gün başlandı. Tedavisinin ikinci günü baş dönmesi,bulantışikayetleri oldu, ardından hasta mönitorize edildi, çekilen EKG'sinde (Resim 2) kalp hızı dakikada 64 atım, Bazett formülüne göre düzeltilmiş QT mesafesinin 496 msn ile uzamışolduğu tespit edildi. Kardiyoloji konsültasyonusonucu hastada bu durumun primer kardiyak bir problemden ziyade kullanmış olduğu kinolon grubu antibiyotik (moksifloksasin) tedavisine bağlı olduğu düşünüldü ve bu antibiyotiği kesildi. Ancakbu sırada genel durumu bozulmuş olan hastada yaklaşık 1 saat sonra kardiyopulmoner arrest gelişti. Kardiyopulmoner resusitasyona başlanıp entübe edilen hastada kardiyak ritm olarak ventiküler fibrilasyon gözlendi ve150 joule ile defibrilasyon uygulandı. Normal sinüs ritmine dönenhasta yoğun bakıma alınıp mekanik ventilatöre bağlandı. Enfeksiyon hastalıklarının önerisi ile kesilmiş olan moksifloksasin yerine tedavisine teikoplanin 400 mg 1x1/gün eklendi. Genel durumu gün içinde hızla düzeldi ve ertesi gün ekstübe edildi, birkaç günlük yoğun bakımda yakın takibin ardından genel durumu daha da düzelen hasta servise alındı. Sonrasında ayağındaki enfeksiyon gerilemeyen hastaya ortopedi bölümünce sağ bacak diz altı amputasyon uygulandı. Hastanın takiplerinde genel durumu düzeldi, tedavisi düzenlenen hasta önerilerle taburcu edildi.



Resim1: Başvuru anındaki EKG.



Resim2: QT mesafesi uzamış EKG.

Çalışma için yerel etik kurul onayı alındı. Hasta onam formları imzalatıldı.

Tartışma

Yeni nesil fluorokinolonlar halen kullanılmakta olan en aktif ve geniş spektrumlu oral antibakteriyelleri içermektedir [12-13].

Florokinolon grubu antibiyotikler doz bağımlı olarak gecikmiş düzenleyici potasyum akımının hızlı bileşenini bloke ederler ve bu etkileri ile QT mesafesinde uzamaya ve TdP'ye neden olabilirler [6]. Mevcut kanıtlar QTc aralığının uzatılmasının florokinolonların sınıf etkisi olduğunu ancak bu grubun çeşitli üyeleri arasında geniş farklar olduğunu göstermektedir [11]. Halen piyasaya sürülen fluorokinolonlar dikkat çekici bir güvenlik profiline sahiptirler. Kinolonların izlem yapılmaksızın kullanımı büyük olasılıkla güvenilirdir ve proaritmi riski düşüktür [14-16]. Bununla birlikte, birkaç florokinolon (grepafloksasin ve son zamanlarda sparfloxacindahil) TP'nin belgelendirilmiş raporlarını takiben piyasadan çekilmiştir. Yapılan araştırmalarda moksifloksasin standart oral veya intravenöz dozda sırasıyla 6'ya 12 ms'likQTc uzamasına neden olmuştur[8]. 1111 hastadan elde edilen FDA verilerine göre, bu QT uzaması, klaritromisin ile karşılaştırıldığında, oral moksiflaksasin (200 veya 400 mg), 4±3 ms ve 5±12 ms ile en az iki kat daha fazladır, 2±12. [9]. Yeni bir klinik araştırmada, sağlıklı gönüllülere tek doz(1,5 kat) moksifloksasin, levofloksasin ve siprofloksasin (~4 ms) ile karşılaştırıldığında QTc aralığının (yaklaşık 17 ms) dört misli uzamasına neden oldu [10].

Bizim hastamızda uzun QT sendromuna neden olabilecek moksifloksasin kullanımı dışında durum mevcut değildi. Hastamızda diyabetik ayak enfeksiyonu nedeni ile verilen moksifloksasinin ilk ve tek intravenöz 400mg doz sonrasında bazal EKG de 433msn ile sınırda olan QTc mesafesinde 63msn uzama meydana gelerek QTc mesafesi496msn olmuştur. Sonrasında kardiyak arreste neden olmuştur. Bu sendromun ortaya çıkması önceden öngörülememekle birlikte ilaç kullanımı sonrası ortaya çıkabilen uzun QT sendromunu önceden gösterebilecek bir parametre yoktur. Bununlabirlikte yine de nadir ancak önemli bukomplikasyon akıldan çıkarılmamalıdır.

Kronik iskemik kalp hastalığı ve korunmuş sol ventrikül fonksiyonu olan hastalarda, tüm kinolonlar EKG izlemesi yapılmaksızın kullanılabilir. Uzun QT sendromu vakalarında veya QT uzamaya eğilimli koşullara sahip hastalarda özel dikkat gösterilmelidir. Konjestif kalp yetmezliği, bradikardi, hipokalemi veya hipomagnezemi varlığında ve Sınıf Ia ve Sınıf III antiaritmik ajanlar gibi bağımsız olarak QTc aralığını uzatan ilaçların kullanılması durumunda, tedavinin başlangıcında kinolon tedavisi EKG monitörizasyonu ile tercih edilmelidir.

Maddi Destek ve Çıkar İlişkisi

Çalışmayı maddi olarak destekleyen kişi/kuruluş yoktur ve yazarların çıkara dayalı bir ilişkisi yoktur.

Kaynaklar

1. Moss AJ. Long QT syndrome. JAMA 2003; 289: 2041-44.
2. Vincet GM. Themoleculargenetic of thelong QT syndrome: Genes causing fainting and sudden death. Annu Rev Med 1998; 49: 263-74.
3. Vincent GM. Long QT syndrome. Cardiology Clinics 2000; 18: 309-25.
4. Roden DM. Takingthe 'idio' out of 'idiosyncratic'. Predicting torsades de pointes. Pacing Clin Electrophysiol 1998; 21: 1029-34.
5. Donger C, Denjoy I, Berthet M et al. KVLQT1 C terminal missense mutation causes a forme fruste long QT syndrome. Circulation 1997; 96: 2778-81.
6. Wang WX, Ebert SN, Liu XK et al. "Conventional" antihistamines slow cardiac repolarization in isolated perfused (Langendorff) feline hearts. J Cardiovasc Pharmacol 1998; 32: 123-28.
7. Reardon M, Malik M. QT interval change with age in an overtly healthy older population. Clin Cardiol1996; 19: 94952.
8. Fogarty C, Grossman C, Williams J et al. Efficacy and safety of moxifloxacin vs. clarithromycin for community-acquiredpneumonia. Infect Med 1999; 16: 748 – 63.
9. Korvick J. QT and quinolones: recent regulatory actions. Office of Drug Evaluation IV. Division of Special Pathogens FDA 5/23/01.
10. Noel GJ, Natarajan J, Chien S et al. Effects of three fluoroquinolones on QT interval in healthy adults after single doses. Clin Pharmacol Ther 2003; 73: 292 – 303.
11. Stahlmann R, Schwabe R. Safetyprofile of grepafloxacin compared with other fluoroquinolones. J Antimicrob Chemother 1997; 40: 83 – 92.
12. Owens RC Jr, Ambrose PG. Clinical use of the fluoroquinolones. Med Clin North Am 2000; 84: 1447 – 96.
13. Appelbaum PC, Hunter PA. The fluoroquinolone antibacterials: Past, present and future perspectives. Int J Antimicrob Agents 2000; 16: 5 – 15.
14. Stahlman R, Lode H. Toxicity of quinolones. Drugs 1999; 58: 37 – 42.
15. Bertino J, Fish D The safety profile of the fluoroquinolones Clin Ther 2000; 22: 798 – 817.
16. Ball P. Future of the quinolones. Semin Respir Infect 2001; 16: 215 – 24.

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Olgu Sunumu

Erişkin atipik kızamık olgusu

Adult atypical measles case

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ÖZ

Atipik kızamık ilk kez 1965 yılında Rauh ve Schmidth tarafından tanımlanmıştır. Atipik kızamık, daha önce ölü kızamık aşısı ile aşılanmış bireylerin kızamık virüsüyle karşılaşmasıyla ortaya çıkan, tipik kızamıktan farklı klinik tablo olarak tanımlanır. Bu durum nadiren canlı aşıya bağlı olarak da bazı bireylerde görülebilir. Bu yazıda, daha önce kızamık aşısı anamnezi bilinmeyen, 37 yaşında bir kadın hastada yüksek ateş, ekstremitelerden başlayıp gövdeye ve yüze yayılan makülopapüler döküntülerle karakterize bir atipik kızamık olgusu sunduk.

Anahtar kelimeler: erişkin; atipik kızamık; klinik seyir

ABSTRACT

Atypical measles was first recognized by Rauth and Schmidt. Atypical measles has been described in persons who were exposed to wildmeasles virus several years after they were vaccinated with killed measles vaccine and it is defined as different clinical picture from typical measles. This condition also occurs, but rarely, in some individuals vaccinated with attenuated virüs vaccine. In this report, we presented 37 years of female patient with a unknown history of measles vaccination, who presented with high fever, maculopapular rash starting on the extremities and spreading to the body and face.

Keywords: adult; atypical measles; clinical course

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Giriş

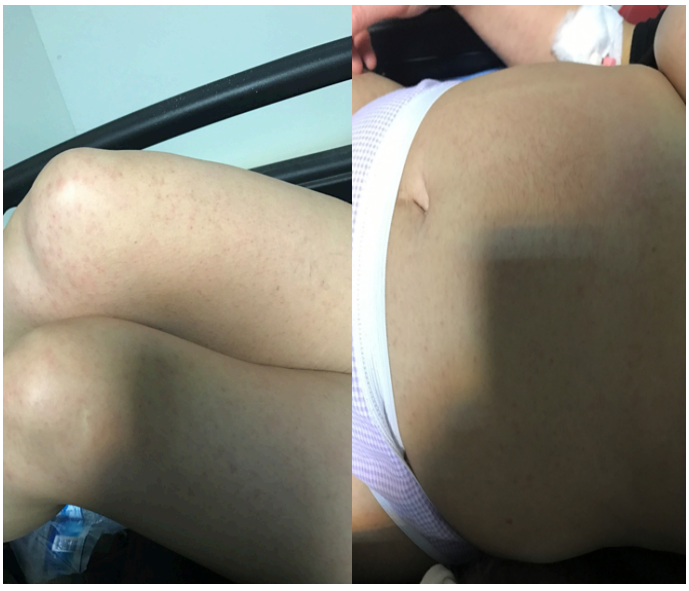
Atipik kızamık, daha önce ölü kızamık aşısı ile aşılanmış bireylerin vahşi tip kızamık virüsüyle karşılaşmasıyla veya nadiren de canlı aşıya bağlı olarak ortaya çıkan, tipik kızamıktan farklı klinik tablo olarak tanımlanır [1,2]. Atipik kızamıkta ateş ve bir iki gün süren ağrılı prodromdan sonra döküntü ortaya çıkar. Klasik kızamığın aksine döküntüler periferden başlar, döküntüler ürtikeriyal, makülopapüler, hemorajik,veziküler veya bunların kombinasyonu şeklinde olabilir [2].

Bu yazıda, daha önce kızamık aşısı öyküsü bilinmeyen,37 yaşında bir kadın hastada yüksek ateş, ekstremitelerden başlayıp gövdeye yayılan makülopapüler döküntülerle karakterize bir atipik kızamık olgusu sunuldu.

Olgu

Otuzyedi yaşında kadın hasta 3 gün önce başlayan 39^{0}C'ye kadar yükselen ateş, boğaz ağrısı ve vücutta döküntü yakınmaları ile acil servise başvurdu. Anamnezinden döküntülerin kollarından ve bacaklarından başlayıp tüm vücuda yayıldığı, acil servise başvurusundan önce ateşi için birkaç gün süreyle parasetamol ve ibuprofen kullandığı öğrenildi. Öz geçmişinde yurt dışı seyahat, hayvan besleme ve evde benzer şikayeti olan aile bireyi yoktu. Soygeçmişinde özellik saptanmadı.

Hasta ateş ve döküntü nedeni araştırılmak üzere enfeksiyon hastalıkları kliniğine yatırıldı. Fizik muayenesinde; ateş: 37.5 ^{0}C, kan basıncı: 100/60 mmHg, bilinci açık, orofarenks hiperemikti. Ekstremiteler, gövde ve yüzde makülopapüler tarzda nadiren veziküler döküntüler mevcuttu (Resim 1-2). Hastadan resimlerin yayınlanması için yazılı izin alındı.



Resim 1. Ekstremiteler ve gövdedeki makülopapüler döküntü

Resim 2. Hastanın yüz bölgesindeki makülopapüler döküntüsü

Orofarenkste Koplik lekesi görülmedi. Diğer sistem muayeneleri normaldi.Laboratuvar testlerinde; lökosit sayısı: 6.600/mm3, CRP: 30 mg/L (normali:0-5 mg/L), sedimentasyon hızı: 22 mm/saat, AST:137 IU/L (normali: ≤ 31U/L) , ALT: 149 IU/L (normali: ≤ 33U/L) , GGT: 206 U/L (normali: <=42), diğer tetkikleri normaldi. Abdominal ultrasonografisinde patoloji saptanmadı. Postero-anterior akciğer grafisi normaldi. Anti-HVA-IgM: negatif, Anti-HCV: negatif, HBsAg: negatif, HBcIgM:negatif, Anti-HIV: negatif, AntiCMV-IgM: negatif, EBNA-VCA IgM:negatifti. Yatışının ilk günü konjuktivada hiperemi saptanan hastaya göz hastalıkları kliniği tarafından topikal göz damlası önerildi. Ateşli dönemde hastadan kan, boğaz ve idrar kültürleri alındı. Kültürlerinde üreme olmadı. Dermatoloji kliniğine konsülte edilen hastada atipik kızamık, ilaç erüpsiyonu ön tanıları düşünüldü. Yatışının ilk iki günü ara ara 37.5 C-38C arası ateşi olan hastaya semptomatik tedavi uygulandı, yatışının üçüncü gününde döküntüleri geriledi ve ateşi olmadı. Hastadan istenen Rubeola-IgM ELISA testi sonucu pozitif olarak saptandı.Yatışının beşinci gününde hasta kontrole gelmek üzere taburcu edildi. İki hafta sonraki kontrol tetkiklerinde AST, ALT ve GGT değerlerinin normal sınırlarda olduğu saptandı.Sunduğumuz olguda hepatit virüslerinin negatif olması ve toksik ilaç maruziyeti olmaması nedeniyle hepatitin atipik kızamığa bağlı olabileceğini düşündük. Çalışma için yerel etik kurul onayı alındı. Hasta onam formları imzalatıldı.

Tartışma

Kızamık (Rubeola, measles), sıklıkla çocukluk çağında görülen,

ateş ve döküntüyle seyreden, aşıyla önlenebilen bir infeksiyon hastalığıdır. Hastalığın etkeni Paramyxoviridae ailesinin Morbili virüs cinsinde yer alan, tek iplikli, seğmenter yapı göstermeyen Rubeola virüstür. Tipik kızamık tablosu yüksek ateş, öksürük, burun akıntısı ve konjuktivit semptomları ile başlar. Prodromal dönemden sonra başlayıp perifere yayılan (sentrifugal) makülopapüler tarzda döküntüler görülür. Döküntüler birleşme eğilimindedir. Ağız mukozasında sıklıkla molar diş hizasında görülen, bazen yanak mukozasının diğer kıısmlarına da yayılabilen,küçük parlak kırmızı renkte lekenin içerisinde beyaz renk beneklerle karakterize enatem Koplik lekesi olarak isimlendirilir ve hastalık için patognomiktir. Koplik lekesi döküntülerin başlamasından önceki iki gün içerisinde ortaya çıkar, 12-18 saat sonra hızla kaybolur [1-3]. Atipik kızamık, tipik kızamıktan klinik olarak farklılık gösteren bir tablo olup,ilk kez 1965 yılında tanımlanmıştır [1,3]. Atipik kızamık olgularında ateşle birlikte atipik döküntü, döküntülerin vücuda yayılım şeklinde farklılık, ekstremitelerde ödem, akciğerlerde intertisiyel infiltratlar ,hepatit ve bazen plevral efüzyon görülebilir [1,2,4]. Atipik kızamıkta döküntüler tipik kızamığın aksine periferden başlar (sentripedal) merkeze doğru yayılır. Sunduğumuz olguda da döküntüler ekstremitelerden başlayıp gövdeye yayılmıştı. Döküntüler ürtikeriyal, makülopapüler, hemorajik,veziküler veya bunların kombinasyonu şeklinde olabilir [2]. Olgumuzda döküntüler ağırlıklı olarak makülopapüler tarzda olmakla birlikte nadirde olsa veziküler tarzda döküntüler de mevcuttu. Demirdağ ve ark.[1] 36 yaşında bir kadın hastada avuç içinden başlayıp tüm vücuda yayılan makülopapüler döküntü, kuru öksürük ve dispine yakınmaları olan bir atipik kızamık olgusu bildirimişlerdir.Olguda akciğer grafiside intertisiyel tutulum, toraks bilgisayarlı tomografisinde ise akciğerlerde nodüler opasiteler saptanmıştır. Olguda solunum sıkıntısının atipik kızamık seyrinde görülebilen akciğer tutulumuna bağlı olabileceği bildirilmiştir. Kızamıkla birlikte hepatit görülebilir ve sıklıkla asemptomatiktir. Kızamık seyrinde görülen hepatit iki formda görülebilir. İlk form erken ortaya çıkar ve birkaç gün içinde düzelir. İkinci form kolestaz ve sarılıkla birliktedir Bu form kızamık gerilemeye başladığında hepatit belirgin hale gelir ve hepatit iki hafta ve daha fazla sürebilir [5]. Pasha ve ark.[6] 284 kızamık olgusunu retrospektif olarak değerlendirdikleri çalışmasında 138 olguda (%48.6) karaciğer disfonksiyonu bildirmişlerdir. Aynı çalışmada ateş ve döküntü tüm olgularda saptanırken, Koplik lekesi %38'inde, akciğerlerde patolojik dinleme bulgusu ise %76'sında saptanmıştır. Khatib ve ark.[5] kızamığa bağlı hepatit gelişen 27 olguyu değerlendirdikleri çalışmada olguların 7'sinin atipik kızamık olgusu olduğunu bildirmişlerdir.Olguların sadece 3'ünde kızamık kolestaz ve sarılıkla seyrederken, diğerlerinde ise asemptomatik hepatit şeklinde seyretmiştir. Erişkin hastalarında kızamık seyrinde görülen hepatitin prognozu iyidir.Karaciğer biyopsisinde kızamık virüsü RNA'sı polimeraz zincir reaksiyonu ile gösterilerek tanı doğrulanabilir [7,8].Giladi ve ark.[9] kızamık olgularında hepatit sıklığını %71-89 arasında, Tartar ve ark. [8] ise %63 oranında bildirmişlerdir. Sunduğumuz olguda karaciğer transaminaz değerlerindeki yüksekliğin hepatit markerlarının negatif olması, toksik ilaç kullanımı öyküsü olmaması, hepatobiliyer USG'sinin normal olması ve transaminaz değerlerinin normal değerlere dönmesi nedeniyle atipik kızamığa bağlı hepatit olabileceğini düşündük. Olgumuzda hepatitle birlikte kolestaz ve sarılık görülmemiştir. Koplik lekeleri döküntüden önceki iki gün içerisinde ortaya çıkıp hızla kaybolduğundan olgumuzda Koplik lekelerinin saptanmama nedeni döküntüler başladıktan sonra hastanın kliniğimize başvurması nedeniyle olabilir. Tartar ve ark.[8] 19 erişkin kızamık hastasını değerlendirdikleri çalışmalarında en sık görülen belirtileri yüksek ateş (18 olguda), döküntü (19 olguda) ve öksürük (15 olguda), en sık görülen fizik muayene bulgusunu ise makülopapüler döküntü (19 olguda) ve Koplik lekesi (11 olguda) ve olarak belirlemişlerdir. Olguların laboratuvar bulgularında; 11'inde (%57.8) AST yüksekliği,10'unda (%52.6) ALT yüksekliği ,13'ünde (%68.4) lökopeni bildirmişlerdir. Sunduğumuz olguda lökopeni saptanmazken, ALT ve AST değerlerinde normalin yaklaşık 4 katı yükseklik saptandı.

Turhan ve ark.[3] 21 yaşında bir erkek hastada periferden başlayıp merkeze doğru yayılan, el ayası ve ayak tabanında da görülen, ürtikeriyal, hemorajik ve veziküler tarzda döküntü, pnömoni ve hepatit ile karakterize atipik kızamık bildirmişlerdir. Olgumuzda da döküntünün yayılma şekli, hepatit görülmesi ve Koplik lekesinin görülmemesi nedeniyle Turhan ve ark. olgusuyla benzerlik göstermektedir.

Atipik kızamık olguları suçiçeği, kayalık dağlar benekli ateşi, Henoch-Schönlein purpurası , ilaç erüpsiyonu, veya toksik şok sendromu ile karışabilir [1,2].Sunduğumuz olguda ayırıcı tanı olarak ilaç erüpsiyonu düşünülmüş, ancak; Rubeola IgM ELISA testinin pozitif saptanması ile atipik kızamık tanısı kesinleştirilmiştir.

Atipik kızamık tipik kızamıktan daha uzun seyir göstermesi nedeniyle daha ciddi seyir gösterme eğilimindedir. Olgumuzda ciddi seyir görülmedi, hasta semptomatik tedavi ile tamamen düzeldi. Atipik kızamıklı hastalar başlangıçta saptanamaz veya çok düşük düzeyde antikor seviyesine sahiptir. Bundan sonra

kızamığın beklenmedik bulgularından sonra oldukça yüksek titrede antikor titresi ortaya çıkar. Atipik kızamık hastalarından virüs izole edilmez ve diğer hastalara bulaş olmaz. Bu sendromun patogenezinin kızamığa karşı kismi yanıt veren konakta hipersensitiviteye bağlı olduğu düşünülmektedir. Atipik kızamığın rekürrensi de bildirilmemiştir [2].

Atipik kızamık olguları kızamık aşısının uygunsuz transportu, uygunsuz şartlarda depolanmaması, soğuk zincir koşullarına uygun muhafaza edilmemesi durumunda sağlıklı bireylere uygulanması sonucunda da ortaya çıkabilir [3].

Sonuç

Sunduğumuz olguda da olduğu gibi kızamık aşısı öyküsü bilinmeyen, yüksek ateş, atipik seyirli makülopapüler döküntü ile başvuraran erişkin hastalar atipik kızamık açısından araştırılmalıdır.

Kaynaklar

1. Demirdal T, Sarı ÜS, Kaptan F, Türker N, Örmen B, Sezak N. Nadir görülen bir olgu: atipik kızamık. Med Bull Haseki 2016; 54: 50-52.
2. Gershon AA. Measles virüs (Rubeola). In: Bennett JE, Dolin R, Blaser MJ, eds. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 8th ed. Philadelphia, PA: Elsevier Saunders; 2015; 106: 1318-27.
3. Turhan V, Adam E, Gül HE, Beşirbelioğlu AB, Pahsa A. Atipik kızamık sendromu (Bir olgu nedeniyle) Flora 2007; 12: 157-60.
4. Frey HM, Krugman S. Atypical measles syndrome: unusual hepatic, pulmonary, and immunologic aspects. Am J Med Sci. 1981; 281: 51-55.
5. Khatib R, Siddique M, Abbass M. Measles associated hepatobiliary disease: an overview.Infection 1993; 21: 112-14.
6. Pahsa A, Özsoy MF, Altunay H,ve ark. Erişkinlerde Kızamık: 284 Olgunun Retrospektif Değerlendirilmesi. Flora 1999; 4: 200-205.
7. Satoh A, Kobayashi H, Yoshida T at al. Clinicopathological study on liver dysfunction in measles, Intern Med 1999; 38: 454-57.
8. Tartar AS, Balin ŞÖ, Kırık Y, Akbulut A, Demirdağ K. Erişkin yaş grubunda kızamık vakalarının irdelenmesi. ANKEM Derg 2016; 30: 91-96.
9. Giladi M, Schulman A, Kedem R, Danon YL. Measles in adults: a prospective study of 291 consecutive cases, Br Med J (Clin Res Ed) 1987; 295: 1314.

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Technical Art

Simple distraction method for ankle arthroscopy

Ayak bileği artroskopisinde basit distraksiyon yöntemi

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ABSTRACT

Ankle arthroscopy has been a frequently used procedure in settings such as osteochondral lesions of the talus (OLT), anterolateral ankle impingement, arthroscopic-assisted arthrodesis and removal of loose bodies. Tibiotalar joint is a joint too narrow for camera entry or using instruments. Therefore, these procedures, particularly the treatment of the OLT, requires a non-invasive and simple method of distraction more suitable to obtain a clear visualization. In this technical note, we aimed to describe a novel, easy to install and useful non-invasive distraction method designed to meet these requirements in anterior ankle arthroscopy under operating room conditions.

Keywords: ankle; arthroscopy of the ankle; distraction; non-invasive distraction

ÖZ

Ayak bileği artroskopisi Talusun Osteokondral Lezyonu (TOL), anterolateral ayak bileği sıkışması, artroskopik yardımlı artrodez ve serbest cisim çıkarılması gibi durumlarda sıklıkla kullanılagelmiş bir prosedürdür. Tibiotalar eklem genellikle kamera girişi ve enstrümanların çalışması için oldukça dar bir eklemdir. Bu durumdan dolayı; bu işlemler, özellikle TOL'ün tedavisi, net bir görüş sağlamak için daha uygun, non-invaziv ve kolay bir distraksiyon metoduna ihtiyaç duyarlar. Biz de bu teknik notta, anterior ayak bileği artroskopisindeki bu ihtiyacı ameliyathane şartlarında kolaylıkla karşılamak için tasarladığımız yeni, kurulumu kolay ve kullanışlı bir non-invaziv distraksiyon yöntemini tarif etmeyi amaçladık.

Anahtar kelimeler: ayak bileği; ayak bileği artroskopisi; distraksiyon; non-invaziv distraksiyon

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Introduction

The ankle is a special joint due to its unique anatomy. As already discussed, the ankle joint is a rather narrow joint to use camera and instruments. In order to eliminate this problem, invasive and non-invasive distraction methods have been described in the literature. In order to reduce the rate of complication, the approach evolved from invasive methods to continuous soft tissue distraction [1]. In light of this aim; many distraction methods have been described, such as using kyphoplasty balloon [2], using gauze roll [3], using bandage [4], using special tools and traction table [5,6].

Technique

While the patient is lying on supine position, the same side is supported with a sheet or pillow behind the hip to see the ankle on the actual anteroposterior plane and master the anatomical structure. A tourniquet is applied on the proximal thigh. After applying general or regional anesthesia, the patient is prepared for surgery using sterile skin paint and the important structures on the ankle are drawn and marked. First, a 3-meter-long gauze roll is folded in half (Figure 1). Then, a loop is formed by crossing the bandage and the bandage on the upper side is crossed under the other once more to remove it from the loop (Figures 2, 3, 4). Thus, 2 loops are obtained (Figure 5). Once the loops are tightened, one of them is taken from the anterior to the posterior of the foot so the ankle is placed in the mid-foot level immediately distal to the anterior operating area; the other is placed at the achille insertion site at the posterior of calcaneus and the appropriate tension is adjusted (Figures 6, 7, 8). After the surgeon adjusts the distance between the ankle and his own abdomen and eliminates the margins of the bandage, the two remaining ends of the gauze roll are firmly tied behind the primary surgeon (Figure 9). Thus, the surgeon can visualize the ankle, whose arthroscopic view without distraction was as in Figure 10, as in Figure 11 by just using his waist, and obtain a clear image and operating area for himself. As seen in Figure 10 and 11 surgeons may easily perform controlled distraction by simple movement. Local ethics committee approved the study and informed consent was obtained from participant(s)

Figure 1: An approximately 3-meter-long bandage is folded in half

Figure 2: The bandage folded in half is crossed and using the other hand the bandage on the upper side is passed through the loop.

Figure 3: Passing the bandage on the upper side through the loop using the other hand

Figure 4: Passing the bandage through the loop

Figure 5: Two loops formed

Figure 6: Position to slip the 2 loops on the ankle

Figure 7: Lateral visualization of the ankle after slipping the 2 loops on the ankle and ensuring their tightness

Figure 8: Anterior visualization of the ankle after slipping the 2 loops on the ankle and ensuring their tightness

Figure 9: Tying the two free ends of the bandage behind the primary surgeon

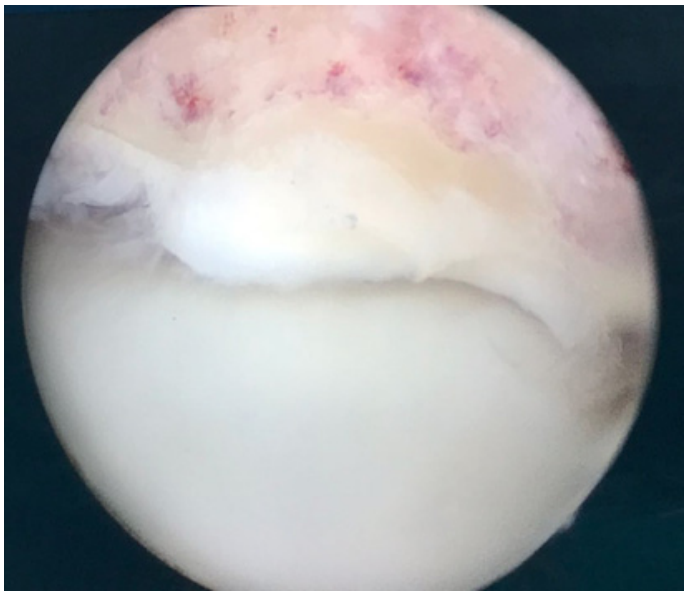

Figure 10: Arthroscopic image of the ankle with no distraction

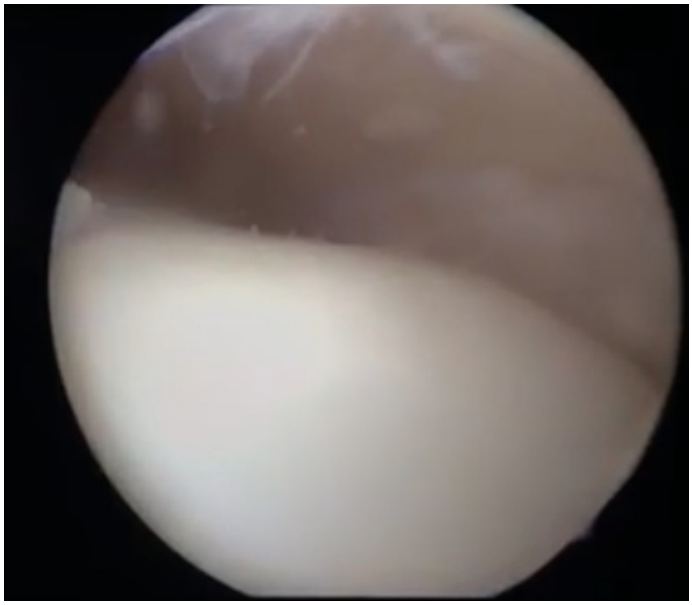

Figure 11: Arthroscopic image of the ankle after distraction

Discussion

Similar distraction methods have been described before. Some require orthopaedic traction tables and special traction materials. Due to problems in sterilization and the time required for their installation, these materials cause problems, such as prolonged preoperative preparation time. Another problem is that every hospital may not have the financial means to purchase these materials [5,7].

Ankle distraction with bandage technique previously described by Yates CK and Grana WA but they applied using a different tying technique from ours [8]. The direction of traction is also different from ours and we can say that the traction direction in our method is the best technical modification. The method we

described is very easy to use, and it is very suitable for traction considering the structure of the ankle. The bandage technique described by Takao et al in 1999 has some disadvantages such as loss of traction force when the bandage is wet [4].

The non-invasive distraction method we described does not require calcaneal or tibial pin for distraction. At the same time, its installation is simple; and it is an easy to obtain and cost-effective method. In our series it was always possible to perform the operation in all cases without the requirement of invasive distraction method.

Conclusion

With this method, the surgeon can easily perform distraction by using only his waist and depending on the procedure and the location of the lesion surgeon can adjust the tightness and degree of the traction. If traction is not required, the surgeon does not need to dismount the traction table or remove the bandage. With this method, the surgeon can stop the distraction simply by relaxing his waist. As can be seen in Figure 11, the operation area is very wide and if needed more working area can be obtained in the talus dom or even on the posterior aspect of the talus.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

References

1. Zengerink M, van Dijk CN. Complications in ankle arthroscopy. Knee Surgery, Sports Traumatology, Arthroscopy 2012; 20: 1420-31.
2. Aydin AT, Ozcanli H, Soyuncu Y, Dabak TK. A new noninvasive controlled intra-articular ankle distraction technique on a cadaver model. Arthroscopy. 2006, 22:905e1–905e3
3. Cameron SE. Noninvasive distraction for ankle arthroscopy. Arthroscopy 1997; 13: 366–69.
4. Takao M, Ochi M, Shu N et al. Bandage distraction technique for ankle arthroscopy. Foot & ankle international 1999; 20: 389-91.
5. Boutefnouchet T, Laios T, Baksheysh P, Ali AS. An Effective Non-Invasive Joint Distraction Technique for Ankle Arthroscopy. J Orthopedics Rheumatol 2016; 3: 2.
6. Beals TC, Junko JT, Amendola A, Nickisch F, Saltzman CL. Minimally invasive distraction technique for prone posterior ankle and subtalar arthroscopy. Foot & ankle international 2010; 31: 316-19.
7. Hedley D, Geary NPJ, Meda P. Ankle arthroscopy: a new technique for non-invasive ankle distraction. Foot and ankle surgery 2001; 7: 137-39.
8. Yates CK, Grana WA. A simple distraction technique for ankle arthroscopy. Arthroscopy: The Journal of Arthroscopic & Related Surgery, 1988; 4: 103-5.

TURKISH JOURNAL of CLINICS and LABORATORY

Türk Klinik ve Laboratuvar Dergisi

Turkish Journal of Clinics and Laboratory - Türk Klinik ve Laboratuvar Dergisi

Tıp dergilerine gönderilecek makalelerin standart gereksinmeleri ile ilgili tüm bilgileri www.icmje.org internet adresinde bulabilirsiniz

Amaç ve kapsam: "Turkish Journal of Clinics and Laboratory", hakemli, açık erişimli ve periyodik olarak çıkan, DNT Ortadoğu Yayıncılık A.Ş. ye ait bir dergidir. Hedefimiz uluslararası bir tabanda hastalıkların teşhis ve tedavisinde yenilikler içeren yüksek kalitede bilimsel makaleler yayınlamaktır. Yılda dört kez çıkan bir bilimsel bir tıp dergisidir. Hakemli bir dergi olarak gelen yazılar konsültanlar tarafından, öncelikle, biyomedikal makalelere ait Uluslararası Tıp Dergileri Editörleri Komitesi (www.icmje.org adresinden ulaşılabilir) tarafından tanımlanan standart gereksinimler ile ilgili ortak kurallara uygunluğu açısından değerlendirilir. Tıbbın her dalı ile ilgili retrospektif/prospektif klinik ve laboratuar çalışmalar, ilginç olgu sunumları, davet üzerine yazılan derlemeler, editöre mektuplar, orijinal görüntüler, kısa raporlar ve cerrahi teknik yazılarıları yayımlayan bilimsel, uluslar arası hakemli bir dergidir. Başka bir dergide yayımlanmış veya değerlendirilmek üzere gönderilmiş yazılar veya dergi kurallarına göre hazırlanmamış yazılar değerlendirme için kabul edilmez.

On-line makale gönderimi: Tüm yazışmalar ve yazı gönderimleri dergipark üzerinden http://dergipark.gov.tr/tjcl yapılmalıdır. Yazı gönderimi için detaylı bilgi bu internet adresinden edinilebilir. Gönderilen her yazı için özel bir numara verilecek ve yazının alındığı e-posta yolu ile teyid edilecektir. Makalelerin "full-text" pdf formuna http://dergipark.gov.tr/tjcl linkinden ulaşılabilir.

Açık erişim politikası: Turkish Journal of Clinics and Laboratory açık erişimi olan bir dergidir. Kullanıcı lar yazıların tam metnine ulaşabilir, kaynak gösterilerek tüm makaleler bilimsel çalışmalarda kullanılabilir.

Aşağıdaki rehber dergiye gönderilen makalelerde aranan standartları göstermektedir. Bu uluslararası format, makale değerlendirme ve basım aşamalarının hızla yapılmasını sağlayacaktır.

Yazarlara Bilgi: Yazıların tüm bilimsel sorumluluğunu yazar(lar)a aittir. Editör, yardımcı editör ve yayıncı dergide yayınlanan yazılar için herhangi bir sorumluluk kabul etmez.

Dergi adının kısaltması: Turk J Clin Lab

Yazışma adresi: Yazılar e-mail yoluyla sorumlu yazar tarafından, Dergipark ta yer alan Turkish Journal of Clinics and Laboratory linkine girip kayıt olduktan sonra gönderilmelidir.

Makale dili: Makale dili Türkçe ve İngilizcedir. İngilizce makaleler gönderilmeden önce profesyonel bir dil uzmanı tarafından kontrol edilmelidir. Yazıdaki yazım ve gramer hataları içerik değişmeyecek şekilde İngilizce dil danışmanı tarafından düzeltilebilir. Türkçe yazılan yazılarda düzgün bir Türkçe kullanımı önemlidir. Bu amaçla, Türk Dil Kurumu Sözlük ve Yazım Kılavuzu yazım dilinde esas alınmalıdır.

Makalenin başka bir yerde yayımlanmamıştır ibaresi: Her yazar makalenin bir bölümünün veya tamamının başka bir yerde yayımlanmadığını ve aynı anda bir diğer dergide değerlendirilme sürecinde olmadığını, editöre sunum sayfasında belirtmelidirler. 400 kelimeden az özetler kapsam dışıdır. Kongrelerde sunulan sözlü veya poster bildirilerin, başlık sayfasında kongre adı, yer ve tarih verilerek belirtilmesi gereklidir. Dergide yayımlanan yazıların her türlü sorumluluğu (etik, bilimsel, yasal, vb.) yazarlara aittir.

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Basıma kabul edilmesi: Editör ve hakemlerin uygunluk vermesi sonrası makalenin gönderim tarihi esas alınarak basım sırasına alınır. Her yazı için bir doi numarası alınır.

Yayın hakları devri: http:/www.dergipark.ulakbim.gov.tr/tjclinlab adresi üzerinden online olarak gönderilmelidir. 1976 Copyright Act'e göre, yayımlanmak üzere kabul edilen yazıların her türlü yayın hakkı yayıncıya aittir.

Makale genel yazım kuralları: Yazılar Microsoft Word programı (7.0 ve üst versiyon) ile çift satır aralıklı ve 12 punto olarak, her sayfanın iki yanında ve alt ve üst kısmında 2,5 cm boşluk bırakılarak yazılmalıdır. Yazı stili Times New roman olmalıdır. "System International" (SI) unitler kullanılmalıdır. Şekil tablo ve grafikler metin içinde refere edilmelidir. Kısaltmalar, kelimenin ilk geçtiği yerde parantez içinde verilmelidir. Türkçe makalelerde %50 bitişik yazılmalı, aynı şekilde İngilizcelerde de 50% bitişik olmalıdır. Türkçede ondalık sayılarda virgül kullanılmalı (55,78) İngilizce yazılarda nokta (55.78) kullanılmalıdır. Derleme 4000, orijinal çalışma 2500, olgu sunumu 1200, editöre mektup 500 kelimeyi geçmemelidir. Özet sayfasından sonraki sayfalar numaralandırılmalıdır.

Yazının bölümleri

1. Sunum sayfası: Yazının Turkish Journal of Clinics and Laboratory 'de yayınlanmak üzere değerlendirilmesi isteğinin belirtildiği, makalenin sorumlu yazarı tarafından dergi editörüne hitaben gönderdiği yazıdır. Bu kısımda makalenin bir bölümünün veya tamamının başka bir yerde yayımlanmadığını ve aynı anda bir diğer dergide değerlendirilme sürecinde olmadığını, maddi destek ve çıkar ilişkisi durumu belirtmelidir.

2. Başlık sayfası: Sayfa başında gönderilen makalenin kategorisi belirtilmedir (Klinik analiz, orijinal çalışma, deneysel çalışma, olgu sunumu vs).

Başlık: Kısa ve net bir başlık olmalıdır. Kısaltma içermemelidir. Türkçe ve İngilizce yazılmalı ve kısa başlık (runing title) Türkçe ve İngilizce olarak eklenmelidir. Tüm yazarların ad ve soyadları yazıldıktan sonra üst simge ile 1'den itibaren numaralandırılıp, unvanları, çalıştıkları kurum, klinik ve şehir yazar isimleri altına eklenmelidir.

Bu sayfada "sorumlu yazar" belirtilmeli isim, açık adres, telefon ve e-posta bilgileri eklenmelidir.

Kongrelerde sunulan sözlü veya poster bildirilerin, başlık sayfasında kongre adı, yer ve tarih verilerek belirtilmesi gereklidir.

3. Makale dosyası: (Yazar ve kurum isimleri bulunmamalıdır)

Başlık: Kısa ve net bir başlık olmalıdır. Kısaltma içermemelidir. Türkçe ve İngilizce yazılmalı ve kısa başlık (runing title) Türkçe ve İngilizce olarak eklenmelidir.

Özet: Türkçe ve İngilizce yazılmalıdır. Orijinal çalışmalarda özetler, Amaç (Aim), Gereç ve Yöntemler (Material and Methods), Bulgular (Results) ve Sonuçlar (Conclusion) bölümlerine ayrılmalı ve 250 sözcüğü geçmemelidir. Olgu sunumları ve benzerlerinde özetler, kısa ve tek paragraflık olmalıdır (150 kelime), Derlemelerde 300 kelimeyi geçmemelidir.

Anahtar kelimeler: Türkçe ve İngilizce özetlerin sonlarında bulunmalıdır. En az 3 en fazla 6 adet yazılmalıdır. Kelimeler birbirlerinden noktalı virgül ile ayrılmalıdır. İngilizce anahtar kelimeler "Medical Subject Headings (MESH)" e uygun olarak verilmelidir. (www.nlm.nih.gov/mesh/MBrowser.html). Türkçe anahtar kelimeler "Türkiye Bilim Terimleri' ne uygun olarak verilmelidir (www.bilimterimleri.com). Bulunamaması durumunda birebir Türkçe tercümesi verilmelidir.

Metin bölümleri: Orijinal makaleler; Giriş, Gereç ve Yöntemler, Bulgular, Tartışma olarak düzenlenmelidir. Olgu sunumları; Giriş, Olgu sunumu, Tartışma olarak düzenlenmelidir. Şekil, fotoğraf, tablo ve grafiklerin metin içinde geçtiği yerler ilgili cümlenin sonunda belirtilmeli metin içine yerleştirilmemelidir. Kullanılan kısaltmalar altındaki açıklamada belirtilmelidir. Daha önce basılmış şekil, resim, tablo ve grafik kullanılmış ise yazılı izin alınmalıdır ve bu izin açıklama olarak şekil, resim, tablo ve grafik açıklamasında belirtilmelidir. Tablolar metin sonuna eklenmelidir. Resimler/fotoğraf kalitesi en az 300dpi olmalıdır.

Etik kurallar: Klinik araştırmaların protokolü etik komitesi tarafından onaylanmış olmalıdır. İnsanlar üzerinde yapılan tüm çalışmalarda, "Yöntem ve Gereçler" bölümünde çalışmanın ilgili komite tarafından onaylandığı veya çalışmanın Helsinki İlkeler Deklerasyonuna (www.wma.net/e/policy/b3.htm) uyularak gerçekleştirildiğine dair bir cümle yer almalıdır. Çalışmaya dahil edilen tüm insanların bilgilendirilmiş onam formunu imzaladığı metin içinde belirtilmelidir. Turkish Journal of Clinics and Laboratory gönderilen yazıların Helsinki Deklarasyonuna uygun olarak yapıldığını, kurumsal etik ve yasal izinlerin alındığını varsayacak ve bu konuda sorumluluk kabul etmeyecektir.

Çalışmada "Hayvan" öğesi kullanılmış ise yazarlar, makalenin Gereç ve Yöntemler bölümünde Guide for the Care and Use of Laboratory Animals (www.nap.edu/catalog/5140.html) prensipleri doğrultusunda çalışmalarında hayvan haklarını koruduklarını ve kurumlarının etik kurullarından onay aldıklarını belirtmek zorundadır.

Teşekkür yazısı: Varsa kaynaklardan sonra yazılmalıdır.

Maddi destek ve çıkar ilişkisi: Makale sonunda varsa çalışmayı maddi olarak destekleyen kişi ve kuruluşlar ve varsa bu kuruluşların yazarlarla olan çıkar ilişkileri belirtilmelidir. (Olmaması durumu da "Çalışmayı maddi olarak destekleyen kişi/kuruluş yoktur ve yazarların herhangi bir çıkar dayalı ilişkisi yoktur" şeklinde yazılmalıdır.

Kaynaklar: Kaynaklar makalede geliş sırasına göre yazılmalıdır. Kaynaktaki yazar sayısı 6 veya daha az ise tüm yazarlar belirtilmeli, 7 veya daha fazla ise ilk 3 isim yazılıp ve ark. ("et al") eklenmelidir. Kaynak yazımı için kullanılan format Index Medicus'ta belirtilen şekilde olmalıdır (www.icmje.org). Kaynak listesinde yalnızca yayınlanmış ya da yayınlanması kabul edilmiş veya DOI numarası almış çalışmalar yer almalıdır. Dergi kısaltmaları "Cumulated Index Medicus" ta kullanılan stile uymalıdır. Kaynak sayısının araştırmalarda 25 ve derlemelerde 60, olgu sunumlarında 10, editöre mektupta 5 ile sınırlandırılmasına özen gösterilmelidir. Kaynaklar metinde cümle sonunda nokta işaretinden hemen önce köşeli parantez kullanılarak belirtilmelidir. Örneğin [4,5]. Kaynakların doğruluğundan yazar(lar) sorumludur. Yerli ve yabancı kaynakların sentezine önem verilmelidir.

Şekil ve tablo başlıkları: Başlıklar kaynaklardan sonra yazılmalıdır.

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Kaynak Yazım Örnekleri

Dergilerden yapılan alıntı;

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Kitaptan yapılan alıntı;

Tos M. Cartilage tympanoplasty. 1st ed. Stuttgart-New York: Georg Thieme Verlag; 2009.

Tek yazar ve editörü olan kitaptan alıntı;

Neinstein LS. The office visit, interview techniques, and recommendations to parents. In: Neinstein LS (ed). Adolescent Health Care. A practical guide. 3rd ed. Baltimore: Williams&Wilkins; 1996: 46-60.

Çoklu yazar ve editörü olan kitaptan alıntı;

Schulz JE, Parran T Jr: Principles of identification and intervention. In:Principles of Addicton Medicine, Graham AW. Shultz TK (eds). American Society of Addiction Medicine, 3rd ed. Baltimore: Williams&Wilkins; 1998:1-10.

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Diener HC, Wilkinson M (editors). Drug-induced headache. In: Headache. First ed., New York: Springer-Verlag;1988:45-67.

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Kılıç C. General Health Survey: A Study of Reliability and Validity. phD Thesis, Hacettepe University Faculty of Medicine, Department of Psychiatrics, Ankara; 1992.

Bir internet sitesinden alıntı;

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DOI numarası vermek;

Joos S, Musselmann B, Szecsenyi J. Integration of Complementary and Alternative Medicine into Family Practice in Germany: Result of National Survey. Evid Based Complement Alternat Med 2011 (doi: 10.1093/ecam/nep019).

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b. Makalenin taslağının hazırlanması veya bilimsel içeriğinin gözden geçirilmesi

c. Makalenin basılmaya hazır son halinin onaylanması.

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3. Makalenin metin sayfası (Makale başlığı/kısa başlık Türkçe ve İngilizce, Özet/anahtar kelimeler, Summary/keywords, makale metni, kaynaklar, tablo ve şekil başlıkları, tablolar, şekiller)

4. Tablo ve grafikler metin içinde olmalıdır.

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