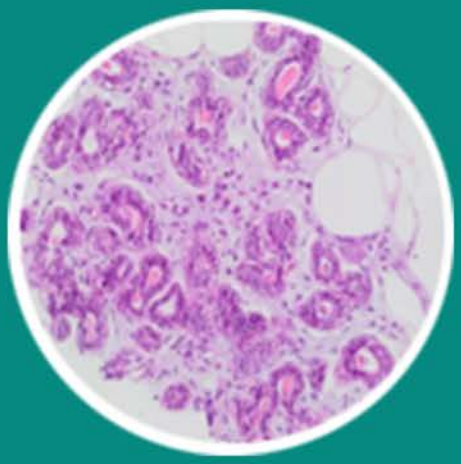
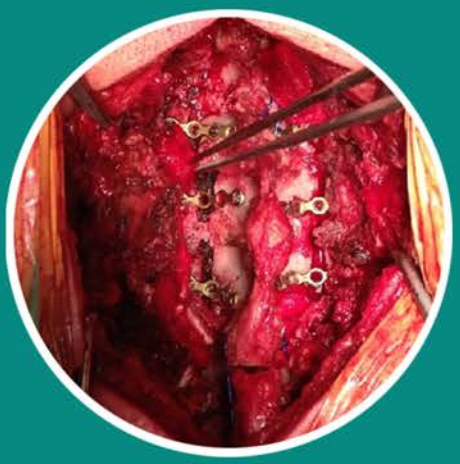
Volume 5 Issue 3 May 2019

e-ISSN: 2149-3189

The European Research Journal





The Association of Health Research & Strategy I www.dergipark.gov.tr/eurj

The European Research Journal

Aim and Scope

The European Research Journal (EuRJ) is an international, independent, double-blind peer reviewed, Open Access and online publishing journal, which aims to publish papers on all the related areas of basic and clinical medicine.

Editorial Board of the European Research Journal complies with the criteria of the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), and Committee on Publication Ethics (COPE).

The journal publishes a variety of manuscripts including original research, case reports, invited review articles, technical reports, how-to-do it, interesting images and letters to the editor. The European Research Journal has signed the declaration of the Budapest Open Access Initiative. All articles are detected for similarity or plagiarism. Publication language is English. The journal does not charge any article submission or processing charges.

EuRJ recommends that all of our authors obtain their own ORCID identifier which will be included on their article.

The journal is published bimonthly (January, March, May, July, September, and November).

Abstracting and Indexing

The journal is abstracted and indexed with the following: TR Index (ULAKBİM TR Dizin), Google Scholar, Index Copernicus (ICV 2017: 100), ProQuest Central, ROAD, EMBASE (Pending), SciLit, MIAR, J-Gate, SHERPA/RoMEO, BASE, EZB, CrossRef, JournalTOCs, WorldCat, TURK MEDLINE, Türkiye Atıf Dizini.

Publisher

The European Research Journal (EuRJ)
The Association of Health Research & Strategy
Kırcaali Mah. Fevziçakmak Cd. Göktaş İş Mrk. Kat:3 No:62/12
Osmangazi/BURSA-TURKEY
www.dergipark.gov.tr/eurj/

e-ISSN: 2149-3189

Editorial Board

INTERNATIONAL EDITORIAL BOARD MEMBERS

Table of Contents

Original Articles

Reviews

Case Report

The European Research Journal 2019;5(3):433-439 ORIGINAL ARTICLE

Effect of media content and media use habits on aggressive behaviors in the adolescents

Duygu Akçay[1], Bülent Devrim Akçay[2]

[1]*Public Health Nursing, National Defense Department, Ankara, Turkey*
[2]*Department of Mental Health and Disease, Gülhane Training and Research Hospital, Ankara, Turkey*

DOI: 10.18621/eurj.395892

ABSTRACT

Objective: This study aims to assess the effect of media content and media use habits on aggression in adolescents.

Methods: This descriptive study was conducted between December 28, 2015 and January 7, 2016. The study sample consisted of 406 (66% male, 44% female, mean age: 15.16 ± 1.56 years) students who were registered in two schools in the provincial center of Konya, Turkey during the 2015-2016 academic year.

Results: Surveyed aggression scores were higher in students who were frequently exposed to violent media ($p < 0.001$). The aggression scores were positively correlated with viewing television, DVDs, films/movies, playing computer/console games, using the Internet, listening to music, playing games on mobile phones, and total screen time and negatively correlated with participating in sports and reading newspapers and books.

Conclusion: Health professionals should provide parents, educators, and children with information and advice on the attentive use of media and the negative health effects related to its uncontrolled use.

Keywords: Adolescent, media, aggression, screen time, violent content

Received: February 16, 2018; Accepted: July 14, 2018; Published Online: September 4, 2018

Adolescents are surrounded by media products in both electronic (televisions, computers, electronic games, the Internet, mobile phones, and music players) and non-electronic (magazines, newspapers, and books) formats. The growing impact of electronic media products on adolescence, an important period in human development, has become of interest. Duringadolescence, new responsibilities arise that can lead to conflicts with authority and the need to form a personal identity. Adolescents sometimes seek to solve the conflicts they experience, both within themselves and with society, by resorting to violence. These violent acts often occur among adolescents, particularly at school [1-3]. Today, children spend a lot of time with media products and are exposed to scenes of violence in almost all type of media content [4]. The amount of time spent in front of the screen can be problematic, triggering a sedentary lifestyle as well as tyrannical and risky behaviors. Studies and literature on the subject have shown that exposure tomedia products with violent content and long periods spent engaged with these products increase the tendency toward aggression and/or aggressive behaviors [5-12].

Aggression is defined by psychologists as any behavior that is intended to harm another person. There are many forms of aggression. For example, verbal aggression usually involves saying hurtful things to avictim. Relational or indirect aggression refers to behavior that is intended to harm atargeted person, such as telling lies to get the person into trouble or to

Address for correspondence: *Duygu Akçay, PhD, Public Health Nursing, National Defense Department, Ankara, Turkey*
E-mail: dakcay2010@hotmail.com

e-ISSN: 2149-3189

harm his or her interpersonal relationships [13]. Even short-term media violence exposure increases the likelihood of physically and verbally aggressive behavior, aggressive thoughts, and aggressive emotions. Recent large-scale longitudinal studies have provided converging evidence linking frequent exposure to violent media in childhood with aggression later in life, including physical assaults and spousal abuse [5, 9, 13-16].

Adolescents who have access to an array of media products prefer to spend time with more than one media product simultaneously rather than focusing on a single media product. Consequently, it is necessary to explore the amount oftime spent using all media productsand theeffect on the adolescent user. This study assessed the effect of media content and media use habits on aggressive behaviors in adolescents.

Research Hypothesis

The following hypotheses have been evaluated in this study.

H0Violence involving media does not affect the aggressivebehaviors of adolescents.

H1 Violence involving media affects the aggressivebehaviors of adolescents.

METHODS

Study Design and Sample Population

A descriptive study assessing the effect of media use on aggression in adolescents was conducted between December 28, 2015 and January 7, 2016. The members of the study population (n = 1157) were registered at two schools in the provincial center of Konya during the 2015-2016 academic year. Data was collected from 418 students who voluntarily took part in the study. The evaluation excluded 12 students who filled out the form but who reported that they had been subjected to or had experienced violence. The 406 students (138 in elementary and 268 in high school) who were assessed in the study stated that they did not have any psychiatric or neurological diseases and that they had not been subjected to or experienced violence includingdomestic violence.

Data Collection Instruments

The study data was collected using an aggression inventory and a questionnaire that was developed by the investigators after a review of the relevant literature. After an introduction and explanation, the forms used to collect the data were administered to student groups of 15-20 adolescents. The students took approximately 20-25 minutes to complete the forms.

Study Questionnaire

The questionnaire was prepared by the investigators after a review of the relevant literature [2-5, 9, 17]. This questionnaire was used to collect information on the descriptive characteristics of the students and on media-related variables. The form included questions about the student's exposure to violent scenes in media and the extent to which their families set limits on mediaconsumption, as well as questions about the amount of time the studentsspent viewing TV, playing computer/video games, using the Internet, listening to music, playing games on mobile phones, participating in sports, and reading newspapers/books (both on weekdays and weekends).

Aggression Inventory

Developed by Tuzgöl [18] utilizing the aggression inventory of Kocatürk [19], the aggression scale used in this study consisted of 45 items for measuring behaviors involving expressed, hidden, physical, verbal, and indirect aggression (exemplified by behaviors like gossiping, spreading rumours, social exclusion etc.) in young people. The scale included 30 items related to aggressive behaviors and 15 items related to nonaggressive behaviors. The inventory used a Likert Scale answering system. For each item in the scale, study subjects were asked to select the choice that best suited them from the following options: (5) always, (4) often, (3) sometimes, (2) rarely, or (1) never. Since 13 scale items were negative statements, those items were scored in the reverse order. Potential aggression scale scores range from 45 to 225. The study reliability was confirmed by repeating the test and calculating the Pearson product-moment correlation coefficient (r = 0.85). The Cronbach reliability coefficient of the scale was found to be 0.71.

Ethical considerations

The study began after obtaining institutional permission from the National Education Directorate in Konya and ethical permission, numbered 2015/329 and dated December 22, 2015, from the ethics committee of Konya Selçuk University.

Statistical Analysis

Students' daily screen times were obtained by totaling the time spent viewing TV/DVDs/movies, playing computer/video games, using the Internet, and playing games on mobile phones. The mean daily media use time was calculated using the following formula: (weekday time × 5 + weekend time × 2)/7. The data obtained from the study was assessed using the SPSS version 15.00 program. Techniques for obtaining frequencies and percentages were used to analyze the demographic data and media use habits of the students, and the bivariate Pearson correlation and F tests (variance analysis) were used to test the correlation between the aggression scale and some of the surveyed variables. A value 0.05 was considered statistically significant.

Table 1. Descriptive characteristics of the study group (n = 406)

Gender	**n**	**%**
Female	138	34.0
Male	268	66.0
Family Structure		
Nuclear	353	86.9
Broad	42	10.3
Broken	11	2.7
Mother's Education		
Basic education	244	60.1
Secondary school	105	25.9
Undergraduate or higher	57	14.0
Father's Education		
Basic education	142	35.0
Secondary school	110	27.1
Undergraduate or higher	154	37.9
Family Income		
Low	30	7.3
Moderate	185	45.7
High	191	47.0
Total	406	100

Table 2. Variance analysis results of media parameters and aggression scores of the study group.

		n (%)	**Aggression Score (Mean/SD)**	**Significance**		
				F	***p** value*	**Difference**
Viewing violent programs involving yelling, weapons, quarrels, fights, wars, etc. in television and movies	Always	252 (62.1)	124.12 ± 22.37	18.752	**< 0.001**	1 and 2 1 and 3 2 and 3
	Sometimes	110 (27.1)	117.95 ± 19.00			
	Never	44 (10.8)	103.64 ± 16.95			
Viewing violent programs involving yelling, weapons, quarrels, fights, wars, etc. in social network sites	Always	208 (51.2)	126.15 ± 20.83	17.003	**< 0.001**	1 and 2 1 and 3
	Sometimes	69 (17.0)	113.04 ± 19.61			
	Never	129 (31.8)	114.51 ± 22.15			
Viewing violent programs involving yelling, weapons, quarrels, fights, wars, etc. in computer games	Always	241 (59.4)	125.64 ± 20.15	19.823	**< 0.001**	1 and 2 1 and 3
	Sometimes	46 (11.3	112.78 ± 21.01			
	Never	119 (29.3)	112.15 ± 22.39			
Listening to or viewing violence-involving or promoting songs or clips	Always	83 (20.4	139.73 ± 18.36	52.277	**< 0.001**	1 and 2 1 and 3
	Sometimes	62 (15.3)	116.90 ± 19.56			
	Never	261 (64.3)	114.81 ± 19.89			
Family forbidding the of viewing and playing of violent programs	Always	267 (65.8)	116.76 ± 21.38	10.273	**< 0.001**	1 and 2 1 and 3
	Sometimes	38 (9.4)	127.34 ± 20.76			
	Never	101 (24.8)	126.72 ± 21.65			

*One Way Variance Analysis (F Test)

Table 3. Distribution of mean media use, newspaper/book reading, and sports participation times of the study group and their aggression scores.

Mean Time (Days/Hours)/Score		Mean/SD
TV/DVD Film/Movie	Weekdays	2.04 ± 2.00
	Weekends	2.74 ± 2.30
	Daily Average	2.24 ± 1.93
Playing Computer/Console Games	Weekdays	1.22 ± 1.94
	Weekends	1.89 ± 2.72
	Daily Average	1.41 ± 2.02
Using the Internet	Weekdays	2.90 ± 2.88
	Weekends	3.76 ± 3.48
	Daily Average	3.15 ± 2.96
Listening to Music	Weekdays	2.26 ± 3.43
	Weekends	2.66 ± 4.01
	Daily Average	2.37 ± 3.46
Playing Games on Mobile Phones	Weekdays	0.83 ± 1.36
	Weekends	0.96 ± 1.55
	Daily Average	0.86 ± 1.32
Participating in Sports	Weekdays	0.74 ± 1.41
	Weekends	0.71 ± 1.53
	Daily Average	0.73 ± 1.31
Reading Newspapers/Books	Weekdays	0.69 ± 0.92
	Weekends	0.80 ± 1.06
	Daily Average	0.72 ± 0.89
Screen Time		7.66 ± 5.31
Aggression Score		120.23 ± 21.88

RESULTS

The descriptive characteristics of the study group are shown in Table 1. According to the analysis of variance, there was no relationship between parental education status, family structure, income and aggression scores.

The students who reported more exposure to violent television, social networking, computer games and music were found to have higher aggression scores than those who reported less exposure (Table 2). The mean media use, newspaper/book reading, and sports participation times of the study group areshown in Table 3.

The aggression scores were positively correlated with viewing television, playing computer/console games, using the Internet, listening to music, playing games on mobile phones, and the total time spent in front of the screen ($r = 0.126$, $p < 0.05$; $r = 0.233$, $p < 0.001$; $r = 0.472$, $p < 0.001$; $r = 0.291$, $p < 0.001$; $r = 0.300$, $p < 0.001$; $r = 0.472$, $p < 0.001$, respectively), and negatively correlated with participating in sports and reading newspapers/books ($r = -0.035$, $p > 0.05$; $r = -0.103$, $p < 0.001$) (Table 4).

DISCUSSION

In accordance with previous studies [20-24], we found no significant difference between parental education level, family income status, and aggression. In this study, it supports the findings of previous studies. The aggression scores of the students in this study who were exposed to violent media scenes were high (see Table 2). Previous studies have demonstrated a connection between media violence and aggressive behaviors exhibited in following years [7, 8, 12]. A study that took place in seven countries showed that exposure to violent screen media was positively associated with aggression [6]. In addition, a meta-analysis of 35 reports concluded that exposure to violent video games increased aggressive behaviors [25]. Huesmann [26] reported that exposure to electronic media violence increased the risk of aggressive behavior in both children and adults in the short term and in children in the longterm. Similar studies on Turkish students have found that playing violent video games increases aggressive, antisocial behavior [10] and is associated with youngsters resorting to violence more often in problem-solving situations [11]. Recent meta-analyses have shown that shortly after playing a violent video game, the aggressiveness of the player increases [5, 9]. The results of this study are similar to the results of other studies.

Table 4. Comparison of mean media use, newspaper/book reading, and sports participation times of the study group and their aggression scores.

Mean Time (Hours)	Aggression Score	
	r	*p* value
Viewing TV	0.126	**0.011**
Playing Computer Games	0.233	**< 0.001**
Using the Internet	0.472	**< 0.001**
Listening to Music	0.291	**< 0.001**
Playing Games on Mobile Phone	0.300	**< 0.001**
Total Screen Time	0.472	**< 0.001**
Participating in Sports	-0.035	0.479
Reading Newspapers/Books	-0.103	**0.039**

The content and age-based program rating system, also called smart signs, may provide guidance on adolescent protection from the contents of certain TV programs in Turkey. The adolescents in the study group should be provided with education and advice concerning the use of smart signs. Previous studies have shown that parents who set rules on media consumption and serve as positive role models can help to reduce the time adolescents spend in front of the screen [27-30]. Although parental supervision and the frequencyof family TV time decreases as children grow older, families should regulate the purpose and content of children's media use, restrict the amount ofuse, and provideexplanatory assistanceto children by using the media with them.

The mean total screen-viewing time of the participating adolescents in a day was 7.66 ± 5.31 hours (see Table 3). Several studies have assessed media screen time. In one study, participants spent 2.2 hours daily in front of a screen [31]. Another study found that adolescents spent a daily average of 193 minutes in front of ascreen [27]. Haines et al. [32] found that 33.7% of females and 43.9% of males spent two hours and more in front of a screen daily. Studies in China and Australia assessing screen time, which included TV/video viewing and computer use, showed that the mean daily viewing times were 1.4 hours [33] and 3.1 hours [34], respectively. The total screen time of the participating students in the current study was much higher than in these previous studies. This large amount of screen time indicates that the adolescents in this study chose to spend time with more than one media product simultaneously rather than focusing on a single media product.

Media is an indispensable part of adolescent life, and the negative health impacts of media overuse are inevitable. Experts stress that the screen time of children older than two years should be limited to at most two hours per day [35]. Consequently, the media viewing habits of the students in this study group need to change. Previous studies have found that interventions to reduce adolescent screen time can be effective [36-38]. It would be helpful to provide education on the conscientious use of media to the study group students, their families, and the school staff, and to sponsor an intervention program to limit screen time and media use.

The mean aggression score of the study group was 120.23 ± 21.88 (see Table 3). There was a positive correlation between the media time of the adolescents and their aggression scores (see Table 4). Studies have found that increased screen time during leisure periods is associated with violent, aggressive, and despotic behavior [39]. In a study by Iannotti et al. [40] on adolescents in two different countries, increased screen time was found to be positively correlated with several negative health indicators. The results of this study are similar to those of other studies. The negative correlation between the students' aggression scores and the level of participation in sports and the time spent reading newspapers/books should serve as guidance for parents and educators (see Table 4).

Proper intervention should include redirecting adolescents from spending time using media to participating in quality enriching activities such as sports and creative and social games. Consequently; H1 hypothesis has been accepted.

Limitations

The most important limitation of this study was the selection of a non-randomized study sample. Media use times were evaluated according to the statements of the adolescent study participants rather than more objective sources. To increase the generalization of the results, researchers should conduct randomized controlled experiments with a larger sample group. Previous randomized controlled studies have consistently shown that youngsters who were exposed to scenes with violent content have more aggressive behaviors, thoughts, or feelings in the later periods of their lives compared to those who were not. These previous studies can serve as a guide for researchers interested in the subject [5, 9, 14, 41].

CONCLUSION

Before aggressive behaviors manifest and become persistent, health professionals in collaboration with families should identify uncontrolled adolescent media use. Health professionals should plan and implement evidence-based interventions and early intervention programs targeting behavioral changes. Researchers who are interested in this subject should carry out randomized, controlled studies involving broad sample groups.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] Özgür G, Yörükoğlu G, Baysan Arabacı L. [High school student's perception of violence, level of tendency to violence and effective factors]. Psikiyatri Hemşireliği Dergisi 2011;2:53-60. [Article in Turkish]

[2] Gradisar M, Wolfson AR, Harvey AG, Hale L, Rosenberg R, Czeisler CA. The sleep and technology use of Americans: findings from the National Sleep Foundation's 2011 Sleep in America poll. J Clin Sleep Med 2013;9:1291.

[3] Cain N, Gradisar M. Electronic media use and sleep in school-aged children and adolescents: a review. Sleep Med 2010;11:735-42.

[4] Aydeniz H. Medyayı Kavramak. T.C. Aile ve Sosyal Politikalar Bakanlığı Aile ve Toplum Hizmetleri Genel Müdürlüğü Aile Eğitim Programı. Ankara: Afşaroğlu Matbaası; 2012.

[5] Anderson CA, Shibuya A, Ihori N, Swing EL, Bushman BJ, Sakamoto A, et. al. Violent video game effects on aggression, empathy, and prosocial behavior in Eastern and Western countries: a metaanalytic review. Psychol Bull 2010;136:151-73.

[6] Anderson CA, Suzuki K, Swing EL, Groves CL, Gentile DA, Prot S, et al. Media violence and other aggression risk factors in seven nations. Pers Soc Psychol B 2017;43:986-98.

[7] Coyne SM. Effects of viewing relational aggression on television on aggressive behavior in adolescents: a three-year longitudinal study. Dev Psychol 2016;52:284-95.

[8] Gentile DA, Coyne S, Walsh DA. Media violence, physical aggression, and relational aggression in school age children: a short term longitudinal study. Aggressive Behav 2011;37:193-206.

[9] Greitemeyer T, Mügge DO. Video games do affect social outcomes: a metaanalytic review of the effects of violent and prosocial video gameplay. Pers Soc Psychol B 2014;40:578-89.

[10] Kars G. Şiddet içerikli bilgisayar oyunlarının çocuklarda saldırganlığa etkisi. Yayınlanmamış Yüksek Lisans Tezi. Ankara: Ankara Üniversitesi; 2010.

[11] Kıran Ö. Şiddet içeren bilgisayar oyunlarının ortaöğretim gençliği üzerindeki etkileri (Samsun örneği). Yayınlanmamış Yüksek lisans Tezi. Samsun: Ondokuz Mayıs Üniversitesi; 2011.

[12] Krahé B, Möller I. Longitudinal effects of media violence on aggression and empathy among German adolescents. J Appl Dev Psychol 2010;31:401-9.

[13] Anderson CA, Berkowitz L, Donnerstein E, Huesmann LR, Johnson JD, Linz D, et al. The influence of media violence on youth. Psychol Sci Public Interest 2003;4:81-110.

[14] Anderson CA, Bushman BJ. Effects of violent video games on aggressive behavior, aggressive cognition, aggressive affect, physiological arousal, and prosocial behavior: a meta-analytic review of the scientific literature. Psychol Sci 2001;12:353-9.

[15] Huesmann LR, Moise JF, Podolski CL. The effects of media violence on the development of antisocial behavior. In: Handbook of antisocial behavior. Stoff DM, Breiling J, Maser JD.,eds., New York: John Wiley & Sons, 1997: pp. 181-93.

[16] Huesmann LR, Moise-Titus J, Podolski CL, Eron L. Longitudinal relations between children's exposure to TV violence and their aggressive and violent behavior in young adulthood: 1977-1992. Dev Psychol 2003;39:201-21.

[17] Strasburger VC, Hogan MJ, Mulligan DA, Ameenuddin N, Christakis DA, Cross C. et al. Children, adolescents, and the

media. Pediatrics 2013;132:958-61.
[18] Tuzgöl M. [Examining aggressiveness levels o f high school students whose parents have different attitudes in terms of various variables]. Türk Psikolojik Danışma ve Rehberlik Dergisi 2016;2:39-48. [Article in Turkish]
[19] Kocatürk R. Saldırganlık güdüsünün spor ve eğitim alanında meslek seçimine etkisi. Yayınlanmamış Yüksek Lisans Tezi. Ankara: Ankara Üniversitesi; 1982.
[20] Kula E. Endüstri meslek lisesi öğrencilerinin umutsuzluk düzeyleri ve saldırganlık durumları arasındaki ilişkinin incelenmesi. Yayınlanmamış Yüksek Lisans Tezi. İstanbul: Yeditepe Üniversitesi; 2008.
[21] Göktaş E. Özel ve devlet liselerinde şiddete eğilim nedenleri ve şiddet etkenlerinin karşılaştırılması: Üsküdar örneği. Yayınlanmamış Doktora Tezi. İstanbul: İstanbul Teknik Üniversitesi; 2010.
[22] Nair, B. Ergenlerin saldırganlık davranışlarının bazı değişkenler açısından değerlendirilmesi. Yayınlanmamış Yüksek Lisans Tezi. Sivas: Cumhuriyet Üniversitesi; 2014.
[23] Yılmaz, İ. Endüstri meslek lisesi öğrencilerinin saldırganlık düzeylerinin çok boyutlu olarak incelenmesi. Yayınlanmamış Yüksek Lisans Tezi. İstanbul: Yeditepe Üniversitesi; 2008.
[24] Cengiz, S. Ergenlerde saldırganlık ve problem çözme. Yayınlanmamış Yüksek Lisans Tezi. Ankara: Gazi Üniversitesi; 2010.
[25] Hofferth SL. Home media and children's achievement and behavior. Child Dev 2010:81;1598-619.
[26] Huesmann LR. The impact of electronic media violence: Scientific theory and research. J Adolesc Health 2007;41(6 Suppl 1):S6-13.
[27] Bounova A, Michalopoulou M, Agelousis N, Kourtessis T, Gourgoulis V. The parental role in adolescent screen related sedentary behavior. Int J Adolesc Med Health 2016;30.
[28] Brindova D, Pavelka J, Ševčikova A, Žežula I, Van Dijk JP, Reijneveld SA, et al. How parents can affect excessive spending of time on screen-based activities. BMC Public Health 2014;14:1261.
[29] Carlson SA, Fulton JE, Lee SM, Foley JT, Heitzler C, Huhman M. Influence of limit-setting and participation in physical activity on youth screen time. Pediatrics 2010:126:e89-96.
[30] Schoeppe S, Rebar AL, Short CE, Alley S, Van Lippevelde W, Vandelanotte C. How is adults' screen time behaviour influencing their views on screen time restrictions for children? A cross-sectional study. BMC Public Health 2016;16:201.
[31] Nguyen PVN, Hong TK, Robert AR. Excessive screen viewing time by adolescents and body fatness in a developing country: Vietnam. Asian Pac J Clin Nutr 2016;25:174-83.
[32] Haines J, Rifas-Shiman SL, Horton NJ, Kleinman K, Bauer KW, Davison KK, et al. Family functioning and quality of parent-adolescent relationship: cross-sectional associations with adolescent weight-related behaviors and weight status. Int J Behav Nutr Phys Act 2016;13:68.
[33] Cui Z, Hardy LL, Dibley MJ, Bauman A. Temporal trends and recent correlates in sedentary behaviours in Chinese children. Int J Behav Nutr Phys Act 2011;8:93.
[34] Hardy LL, Dobbins TA, Denney-Wilson EA, Okely AD, Booth ML. Descriptive epidemiology of small screen recreation among Australian adolescents. J Paediatr Child Health 2006;42:709-14.
[35] Altenburg TM, Kist-van Holthe J, Chinapaw MJ. Effectiveness of intervention strategies exclusively targeting reductions in children's sedentary time: a systematic review of the literature. Int J Behav Nutr Phys Act 2016;13:65.
[36] Friedrich RR, Polet JP, Schuch I, Wagner MB. Effect of interventionprograms in schools to reduce screen time: a meta-analysis. J Pediatr 2014;90:232-41.
[37] Granger C. Effectiveness of ınterventions for reducing screen time in children: rapid review of the evidence 2012. Retrieved from https://www.peelregion.ca/health/library/pdf/screen-time-rapid-review.pdf on 07.07.2014.
[38] Busch V, Ananda Manders L, De Leeuw JR. Screen time associated with health behaviors and outcomes in adolescents. Am J Health Behav 2013;37:819-30.
[39] Kelishadi R, Qorbani M, Motlagh ME, Heshmat R, Ardalan G, Jari M. Relationship between leisure time screen activity and aggressive and violent behaviour in Iranian children and adolescents: the CASPIAN-IV Study. Paediatr Int Child Health 2015;35:305-11.
[40] Iannotti RJ, Kogan MD, Janssen I, Boyce WF. Patterns of adolescent physical activity, screen-based media use, and positive and negative health indicators in the US and Canada. J Adolescent Health 2009;44:493-9.
[41] Bushman BJ, Huesmann LR. Effects of televised violence on aggression. In: Handbook of children and the media. D. Singer D, Singer J. eds., Thous and Oaks, CA: Sage Publications. 2001: pp. 223-54.

The European Research Journal 2019;5(3):440-448 ORIGINAL ARTICLE

Physio-chemical investigation and analyses of contaminants in groundwater flow. Case study - Papalanto, Ifo local government area, South - Western Nigeria, Ogun State

Oluwaseun Deborah Olorode[1], Samuel Olaolu Adeneye[2], Aderonke Deborah Morakinyo[2], Opeyemi Aliu Oyeneyin[3], Michael Onoriode Akpochafor[2], Akintayo Daniel Omojola[2]

[1]Department of Physics, University of Lagos, Akoka, Yaba, Lagos State, Nigeria
[2]Department of Radiation Biology, Radiotherapy, Radiodiagnosis and Radiography, College of Medicine, Lagos University Teaching Hospital, Lagos, Nigeria
[3]Department of Oral and Maxillofacial studies, College of Medicine, Lagos University Teaching Hospital, Lagos, Nigeria

DOI: 10.18621/eurj.382807

ABSTRACT

Objectives: Groundwater is the primary source of drinking water for roughly, a third of the world's population, but highly vulnerable to pollution. A thorough research was carried out to investigate the extent of groundwater contamination on four active dumpsite and a control point at Papalanto, Abeokuta area, and South-Western Nigeria.

Methods: Domestic wells in the area facilitated the resources for water chemistry. A total of five groundwater samples were collected from wells located close to different dumpsite in the study area, to determine the extent of groundwater contamination. Physio-chemical analysis was carried out on the five water samples; the basic method adopted in the chemical analysis includes titrimetric method, atomic absorption spectroscopy and calometric method.

Results: The results showed that water quality parameter like temperature, pH, taste, odour, total solids, sulphate, copper, iron, zinc, cadmium and chromium are in appropriate standard prescribed by WHO and NSDWQ. Other physical parameters like color, turbidity, conductivity, total suspended solids, total dissolved solid, total hardness, total alkalinity, total acidity, calcium, magnesium, chloride, nitrite, manganese, lead, nickel, nitrate, have higher values than the authorized standard value, which directly or indirectly affect the water content found in the area for drinking purpose. These features could be attributed to the possible activities of contaminants facilitated by leachate plume from the dumpsite.

Conclusions: The study shows that the regolith aquifer in the area of study is highly vulnerable to pollution from the refuse dumps. From the geophysical and physio-chemical analysis carried out, the values of most parameters obtained in the water samples collected at locations close to the leachate have been confirmed to be higher than those collected at locations away from the leachate. Hence, the groundwater near the leachate is confirmed contaminated.

Keywords: Groundwater, contaminants, well, dumpsite, physio-chemical, pollution

Received: .January 23, 2018; Accepted: March 20, 2018; Published Online: June 17, 2018

Address for correspondence: *Samuel Olaolu Adeneye, MD., College of Medicine, Lagos University Teaching Hospital, Department of Radiation Biology, Radiotherapy, Radiodiagnosis and Radiography, Lagos, Nigeria*
E-mail: soadeneye@unilag.edu.ng, Tel: 0 803 5386915

e-ISSN: 2149-3189

Waste disposal is one of the major problems in developing countries world over. Waste is any substance, solution, mixture or article for which no direct use is envisaged but which is transported for reprocessing, dumping, elimination by incineration or other methods of disposal [1]. Wastes are produced frequently on daily basis as a result of human activities. Individual efforts to control/eradicate waste have led to the emergence of waste disposed irresponsibly in bushes, river body and road side without much concern to the regions beneath the surface of the earth, geology of the study area and their closeness to the living quarters. This action is detrimental to human health further escalating environmental health risk [2]. In residential quarters, poor settlement structure and lack of septic facilities for domestic and human waste removal are factors to be greatly concerned about. Presence of prominent dumpsite in residential quarters is a major source of environmental pollution, air infectious disease, soil pollution, leachate and contaminants migration to water table. Different environmental degradation, activities and inconsiderate exploitation of water channel can be said to be responsible for this menace [3]. In addition, waste if not properly disposed could lead to contamination of surface and groundwater in its immediate environment [4, 5]. Sometimes, during the peak of the raining season, the dumpsite is usually covered with flood. It is this contaminated liquid that spread through the soil and ground water system. This results in pollutant loads on the environment which depends on the quality and quantity of the water that percolates through the dumpsite and penetrates down to the ground water. Generally, leachate from dumpsite consists of different organism, microbes, chemicals and other harmful substance, this is because water in its natural state is not pure coupled with introduction of leachate plume from dumpsite, this pose great danger to the composition, constituent and relevance of water in that area [6].

In Papalanto area, which is a rural community in Nigeria, the primary source of drinking water is from hand dug well. This is due to lack of pipe borne water occasioned by lack of functional water treatment facilities. Hence, the community is exposed to polluted water for its domestic and agricultural purposes thereby increasing the risk of contracting water related health hazards [7]. Leachate plume and other pollutants pose a high risk to groundwater resource if not adequately managed. To overcome this, there is need to assess some of the important parameters of the leachate with a view to providing solution to water pollution occasioned by indiscriminate waste disposal. Consequently this study aims to examine the physio-chemical composition and level of contaminants in the water samples from hand dug wells in the study area while comparing the results obtained with the standards for drinking water of World Health Organization (WHO) and Nigerian Standard of Drinking Water Quality (NSDWQ).

Papalanto metropolis is a semi urban area in Ifo local government area, in Ogun state, South-Western Nigeria. Papalanto has a latitude of 6.8821, latitude (DMS) 6°52’56N and longitude of 3.1931, longitude (DMS) 3°11”35E, altitude (feet dimension) 236, altitude (meters dimension) 71 m above sea level [8]. The physiography of the study area is that of extensive lowland that is gently undulating with a gentle sloping dissected escarpment known as southern uplands [9], it lies in the tropical climate belt, where the climate condition is friendly, while the monthly temperature varies between 25°C and 30°C.

Papalanto is a major town situated along the Lagos-Abeokuta Road. It has an intersection with the Sagamu/Ilaro Road in the Ewekoro local government area of Ogun State. It stands as a vantage point for trade, transportation and communication. The construction of New Lagos-Abeokuta express road led to the migration of different tribes to Papalanto which brought about physical development to places like Ori-Ogbo, Araromi, Ajegunle, Fowowawo (now called Sawmill) and many other areas after places like Oju-Oja Isale Alfa, Alagbede compound, Ago-Ika and Ago-Ijaiye compound [10].

One of the major source of revenue was generated through sugar cane plantation and sale, which was very predominant in Papalanto till date. The area is characterized by different activities as a result of the cement factory, schools and other facilities located in the vicinity.

As a result of commercial activities in the area, huge masses of waste are generated and its management could be cumbersome despite the presence of few licensed refuse government agencies. In the area, refuse are mostly dumped on road side, farm lands, water bodies, bushes and roadside,

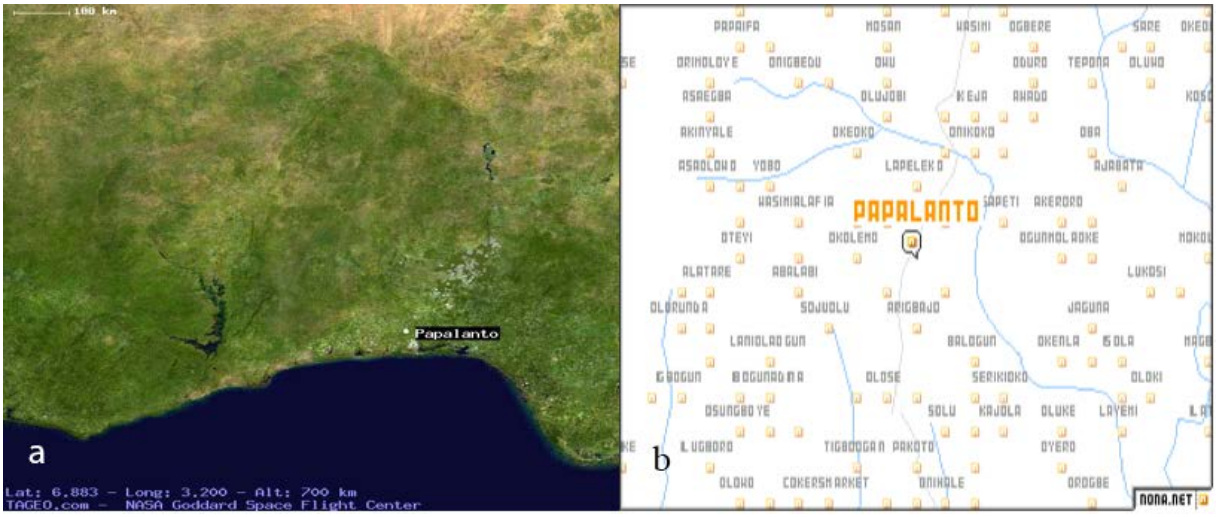


Figure 1. The research area for this study (a and b).

constituting serious environmental and health nuisance. The study area (Figures 1a and 1b) (Papalanto) belongs to the eastern part of Dahomey basin, extending from the Volta Delta (Southern Ghana) to the Western border of Niger Delta region in Nigeria [11]. However, the general succession of the rock unit is that of concealed rock which encompasses Abeokuta group, followed by Ewekoro, Akimbo, Oshosun, and Ilaro formations respectively. On the uppermost surface of Ilaro formation is the coastal plain sands. The Ewekoro formation is the local geology in the study area. It comprises of non-crystalline and highly non-fossiliferous limestone and thinly laminated fossile and probably non-fossiliferous shale [12].

This is necessitated by the influence of properties of underlying permeable strata on the subsurface movement of potentially polluting substances deposited on the ground surface.

The sediments here consist of diverse layer of sands and mud with a varying proportion of vegetal matter (from sugar cane plantation). Occasional beds of sandstone and sediments were clearly deposited under littoral and lagoonal conditions. Due to high amount of compost, animal/plant material waste, clay, manure and silt above the gruss zone, water residence times are high in this section. Accompanied by spacious reactions surface, there are the best conditions for water-rock interactions and hydro-chemical changes. Regarding the hydro-chemical situation, acidification process are other important factors. Groundwater recharge and storage is limited to the weathering zone and zonal soil. The good capabilities and the capacity in the covering layers are lowered in parts with local kaolinite bearing sections areas and muddy-loamy interculations. Areas of the highest total permeability were found in vicinity of faults system. In this part, there are possible electric contact between fissured aquifers and shallow pore aquifers.

METHODS

There are four active dumpsite and one control point in the study area. These dumpsites are located close to residential quarters and developing layout, such that waste disposal activity is still prominent in the areas till the date of collection of the samples (November 2013). The first dumpsite is located along the New Palace road, approximately 20 m to the west of Papalanto high school. It is delineated between latitude 4°52.36'N to 4°52.75'N and longitude 6°57.17'E to 6°57.43'E. The second sampling point is the control point, located at the backyard of Papalanto high school. The third dumpsite is located along Tipper /Ilaro road, the fourth dumpsite is located along Agbede /Ago-Ijaiye compound and the fifth dumpsite is located along Sawmill road.

2D Electrical resistivity method, (using the ABEM Terrameter system ES10-64C electrode selector) was used to investigate the subsurface potential of different dumpsites. A total of eight wells within the region were sampled, of which five wells where taken as case

study. Each water sample was collected in a chemically clean double sealed plastic bottle. Distilled water was first used to rinse the bottle to nullify pollution in any form [13]. The samples were collected in the afternoon and toward evening after the well have been put to use. The water samples were taken to the laboratory for physio-chemical investigation and analysis. The recommended standard put in place by NSDWQ and WHO were appropriately followed to investigate the water quality of the water samples from the study area.

Physical and chemical parameters that were tested for includes the followings: temperature, pH, colour, taste, odour, turbidity, conductivity, total solids, total suspended solids, total dissolved solid, total hardness, total alkalinity, total acidity, calcium, magnesium, chloride, nitrate, nitrite, sulphate, copper, manganese, zinc, lead, cadmium, nickel, and chromium. All the results obtained were compared with NSDWQ and WHO standards.The temperature value of the water samples were measured using a thermometer. The terrameter system electrodes were immersed in buffer 7 solution, the temperature was selected to 25°C. The display was set to read the correct value of buffer using buffer control knob. The electrode was rinsed using distilled water and Immersed in buffer 4 or 10 depending on the available buffer and given sufficient time to stabilize. Then reading was set using the slope control. The electrode was rinsed in deionized water and Immersed in an unknown solution. The electrode was allowed to stabilize for 2-3 minutes and the reading was taken. The electrode was rinsed with deionized/distilled water and blotted with clean tissue before immersing in another sample to avoid contamination. After the chemical analysis, the electrode was rinsed properly with de-ionized /distilled water and then immerse in buffer 4 (pH:4) for storage. (Visual comparison method) the water sample's color was observed by filling a matched Nessler tube to 50 ml mark with sample and comparing it with standard. Look vertically downward through the tubes towards a white or specular surface placed at such an angle that light is reflected upward through the column of the liquid. These procedure helps determines if turbidity is present and has not been removed, it is reported as `apparent color'. If color exceeds 70 units, the sample is diluted with distilled water in known proportions until the color is within the range of the standards. The pH of each sample was then measured. The water samples was taken into the mouth and tasted orally. The taste sampling is only carried out on samples that are safe for ingestion i.e. samples that do not contain bacteria, viruses, parasites and hazardous chemicals. The odour was determined orally by perceiving the water samples using the nose. Presence of odour signified negative inference and absence of odour signified positive interference. The turbidity was measured using turbidimeter, the samples were thoroughly shaked and observed until air bubbles disappeared, then the sample were poured into the turbidimeter tube and immersed in an ultrasonic bath for 1 to 2 seconds. This caused complete bubble release which shows the turbidity direct from instrument scale. The conductivity was measured using aconductimeter. It was switched on to stabilize for 15 minutes. The conductivity electrode was rinsed using the sample to be determined. The knob to conductivity menu (point) was turned up and the temperature was set to 25°C within an appropriate range. When the reading did not appear, the conductimeter was switched to the next lower range for greater sensitivity. The reading was taken and the electrode was mixed with distilled water. If the conductivity of the sample exceeds that of the instrument, known volume of the sample should be mixed accordingly to 100 ml with diluted/deionized water of little or no conductivity. For total solids (T.S)- the dish was cleaned heated between 103 to 105°C. It was stored and cooled in a desiccator until needed (the weight was measured immediately before use). About 100 ml of water sample was pipetted into the evaporating dish. The dish was evaporated to dryness on a steam bath. The water sample was stirred with a magnetic stirrer during transfer. Optionally, successive water sample portion was added to the same dish after evaporation. The evaporating sample was dried for at least 1 hour in an oven at 103 to 105°C. The dish was cooled in desiccator to balance temperature. The cycle of drying, cooling, desiccating and weighing was repeated until a constant weight is obtained. When evaporating in a drying oven, the temperature is usually lowered to approximately 2°C below boiling point to prevent splattering. Total suspended solid is obtained when the result of total solid is subtracted from dissolved solid (D.S), the output is suspended solid i.e. Suspended solid mg/l = T.S – D.S. Total

dissolved solids (TDS)-the conductimeter was switched on, the electrode was rinsed using the water sample to be determined, the knob was set to TDS menu and the temperature was set to 25°C, the value was displayed on the meter screen, the electrode was rinsed with distilled water. Total hardness-50 ml of water sample was pipetted into 250 ml conical flask. 1 ml or 25 drops of buffer 10 (ammonium chloride buffer) was added. 3 drops of Erichrome black T indicator was added and swirled to mix. The mixture was titrated using standardized E.D.T.A to blue end point. Total alkalinity-50 ml of the water sample was taken. 6 drops of phenolphthalein indicator + 6 drops of bromophenol blue was added. The mixture was titrated with 0.02 M hydrochloric acid to green end point, if phenolphthalein is added to the sample and pink color observed, it means there is carbonate in the sample. The mixture was titrated till the pink color turned to colorless and the titre value was noted before bromophenol blue indicator was added, to calculate the total alkalinity add the titre value of phenolphthalein and bromophenol blue indicator. Total acidity-50 ml of the water sample was added into 250 ml conical flask. Chlorine residue was removed by adding a drop of 0.1 M sodium thiosulfate. 6 drops of bromophenol blue indicator was added and swirled to mix thoroughly. The mixture was titrated with standardized 0.02 M sodium hydroxide until the color changes from yellow to purple green. Calcium-20 ml of the water sample was pipetted out, a pinch of ammonium purpurate was added, the burette was filled with EDTA. The mixture was titrated against EDTA solution. The titration was continued till the colour changes to purple. The calcium hardness was calculated., i.e. volume of EDTA × Normality × 50 × 1000/volume of sample taken. Dissolved oxygen-an oxygen bottle of known capacity was filled to overflow with water sample, avoiding the inclusion of air bubbles. 0.5 ml each of manganese II chloride solution and sodium hydroxide solution containing potassium iodide was added. The bottle was closed without any air bubble inclusion and shaked vigorously. After the precipitate had settled, the clear supernatant liquid was carefully decanted. The precipitate was dissolved in 2 ml conc. phosphoric acid. The liberated iodide was titrated against 0.01 M Na2S2O3 until colorless using starch solution as indicator (add towards the end of titration) the end color is pale yellow. Chloride-50 ml of the sample. 1 ml of potassium chromate was added and titrated with standardized 0.01 M silver nitrate to a red-pinkish yellow. If the conductivity of the sample is expected to be high, a measurement of 0.1 M standardized silver nitrate is used. Nitrite-two 25 ml flat bottom flask was used, one for sample, the other for blank. One of the 25 ml flask was filled with water sample and the other was filled with distilled water (the blank). 1 ml sulfanilamide reagent was added to each mixture. 1 ml naphthalene solution was also added to each mixture. The content was placed in the dark for 30 minutes. The absorbance was measured at 540 nm. Nitrate-10 ml of water sample was transferred into a large test tube. The test tube was placed in cold-water bath and 2 ml of sodium chloride solution was added. The content was mixed thoroughly by hand and 10 ml H2SO4 acid solution was added, Mixed by swirling and allowed to cool. 0.5 ml bruline sulfanilic acid reagent was added to the mixture. The tubes were swirled to mix thoroughly and the tubes were placed in a well-stirred boiling water bath that maintains a temperature of not less than 95°C. After exactly 20 mins, the sample was removed and immersed in a cool water bath and allowed to cool to room temperature. Absorbance was measured at 410 mn using distilled water treated in the manner as blank. Sulphate-100 ml of water sample was taken. Spatula level of barium chloride was added to the sample and allowed to stand for 5 minutes. The sulphate content was measured by using turbidimeter. The instrument was set using turbidimeter standard that has 10 NTU. When that was carried out, the turbidimeter was taken out of the sample. Zinc-50 ml of sample was acidified with few drops of 0.5 M hydrochloric acid, about 5 ml of sodium acetate solution was added to the solution to bring the pH to about 5.3 ml of sodium thiosulphate solution and 10 ml of dithizone solution was added and shaked thoroughly. The absorbance value is checked at 540 nm against a blank of distilled water treated in the way. Cadmium-50 ml or smaller volume of water was pipetted into glass beaker and heated for 10 minutes with 5 ml of 2 M hydrochloric acid (for turbid sample, filter). The mixture was cooled and 5 ml potassium tartrate solution was added. 1 drop of methyl orange indicator and 2 M NaOH, was added drop wise until color changes from red to yellowish orange. The solution was transferred to a 100 ml separating funnel.

Titrate with 5 ml NaOH-KCN solution (a), 2 ml hydroxyl ammonium chloride solution and 15 ml dithizone solution (a) in that order mixing thoroughly on each addition. The mixture was shaked for 1 minute and allowed the layers to separate. The solvent phase was transferred to a second 100 ml separating funnel containing 25 ml cold tartaric acid solution. 10 ml chloroform was pipetted into the first separating funnel. It was shaked again for 1 minute, allowed the chloroform to separate and transferred to the second separating funnel taking care that none of the strongly alkaline aqueous phase is entrained. The second separating funnel is shaked for 2 minutes. The chloroform phase is drained and discarded. 5 ml chloroform was added and shaked for 1 minute again and discarded.

RESULTS

The results of the physio-chemical analysis of the five water samples are shown in Table 1. The results showed that water quality parameter like temperature, pH, taste, odour, total solids, sulphate, copper, iron, zinc, cadmium and chromium are in appropriate standard prescribed by WHO and NSDWQ. Other physical parameters like color, turbidity, conductivity, total suspended solids, total dissolved solid, total hardness, total alkalinity, total acidity, calcium, magnesium, chloride, nitrite, manganese, lead, nickel, nitrate, have higher values than the authorized standard value, which directly or indirectly affect the water content found in the area for drinking purpose. These features could be attributed to the possible activities of contaminants

DISCUSSION

The conductivity of the study area falls within appropriate range (120-220 µs/cm) except for S3 and S5 (2270-2280 µs/cm) which are high and above WHO standard. The increased conductivity could be attributed to the geology of the area and migration of leachate plume. Proximity of the well to the dumpsite could also be responsible factor. This is in line with the findings of Oyelami *et al*. [4] .The study area (S3-Tipper/Ilaro road, S5-Sawmill road) has a history of swampy foundation. Over time, due to development and commercial activities in the area, the swampy area was filled with decomposed waste and clay sand materials. With consistent activity of land filling the area, the swampy water body combined with the decomposed waste material have sunk down to the ground at a depth of 4.0 metres. This results for the underlying presence of layers of leachate plume and chemical waste. It is a zone with extremely low resistivity, presence of decomposed contaminants prominent over past years. This fluid has delineated deep into the soil. Other reasons are due to the poor septic drainage system for domestic and human waste disposal. This contaminated fluid called effluent has percolated the region and also contributes to the level of contamination in the study area [14-17].

The well situated inside Papalanto high school has the highest color concentration (slightly turbid), while other locations has a clear colour of water (places like Palace road, Agbede Compound, Sawmill road and Papalanto/Ilaro road). Although water is naturally colorless, but the location of the well and soil composition of the study area brings about the change in color of the water. Other factor that could account for the turbid look of the water is the high level of limestone sediment, due to the local geology of the study area. This sediment consists of indissoluble inorganic mineral matter. These sediments are scattered unevenly all through the fluid content and this helps the particles to easily absorb light. This is the brain discovery behind the dusty or foggy turbid look of the well water in study area S2.

From the data in the Table 1, the highest concentration of total dissolved solid is 1140 mg/l at Sawmill road and the least value of 60 mg/l at Papalanto high school. This high value is due to leachate plume, chemical waste contaminants, decomposed landfill and soil content, found at the study area at sSwmill road. This area shows undissolved materials that are present in the groundwater.

From Table 1, the total suspended solid values ranges between 0.30 and 30 mg/l. Water samples from Palace road, Tipper/Ilaro road and Sawmill road have the highest values. This could be caused by the constituents of leachate plume accumulated over the years, other probable factors could be industrial/ chemical waste, sediments, silts and organic particles

Table 1. Physio-chemical analysis of water

S/N	PARAMETERS Physical, chemical & microbiological	RESULTS					NSDWQ
		S1	S2	S3	S4	S5	
1	**Temperature (°C)**	24.8	25.2	25.6	25.9	25.0	22-30
2	**PH**	6.74	6.93	7.64	7.68	7.28	6.8-8.5
3	**Colour**	Clear	Slightly turbid	Clear	Clear	Clear	Clear/Colorless
4	**Taste**	Unobj.	Unobj.	Unobj.	Unobj.	Unobj.	Unobj.
5	**Odour**	Unobj.	Unobj.	Unobj.	Unobj.	Unobj.	Unobj.
6	**Turbidity (NTU)**	2.09	15.7	1.31	5.21	0.78	5
7	**Conductivity - - S/cm)**	220	120	2270	220	2280	1,500
8	**Total solids (mg/l)**	120	60.30	1185	112	1170	1,200
9	**Total suspended solids (mg/l)**	10	0.30	50	2	30	-
10	**Total dissolved solids (mg/l)**	110	60	1135	110	1140	-
11	**Total hardness (mg/l)**	112.0	100.0	616.0	60.0	580.0	400
12	**Total alkalinity (mg/l)**	60	60	540	440	100	-
13	**Total acidity (mg/l)**	20	20	140	40	100	-
14	**Calcium (mg/l)**	44.89	40.08	246.89	24.01	232.46	50 (WHO)
15	**Magnesium (mg/l)**	16.31	14.56	85.32	8.74	84.45	50(WHO)
16	**BOD (mg/l)**						-
17	**Dissolved oxygen (mg/l)**						-
18	**Chloride (mg/l)**	56.72	70.90	340.32	212.7	368.68	250
19	**Nitrate (mg/l)**	19.00	24.66	20.00	29.00	70.00	50
20	**Nitrite (mg/l)**	1.8	1.95	2.0	1.99	2.51	-
21	**Sulphate (mg/)**	75.60	79.07	120.9	132.0	98.6	200
22	**Copper (mg/l)**	0.437	0.552	0.327	0.428	0.298	2
23	**Manganese (mg/l)**	0.932	0.732	0.559	0.687	0.429	0.5
24	**Iron (mg/l)**						0.3 (WHO)
25	**Zinc (mg/l)**	1.332	2.080	1.009	0.649	1.129	5 (WHO)
26	**Lead (mg/l)**	0.023	0.020	0.079	0.019	0.087	0.05
27	**Cadmium (mg/l)**	-0.034	-0.077	0.003	-0.132	0.001	0.003
28	**Nickel (mg/l)**	0.011	0.014	0.035	0.065	0.029	-
29	**Chromium (mg/l)**	0.021	0.029	0.027	0.031	0.053	0.05
30	**Total bacterial count (cfu/ml)**						-
31	**Total coliform (cfu/100ml)**						-
32	**Total fungi/yeast counts**						-

ND = Not detected, cfu = colony forming unit, WHO = World Health Organization, NSDWQ = Nigerian Standard for Drinking Water Quality, unobj. = unobjectionable

that are less than visible macroscopic view, that float in the water body of the area of study. The minimum values were recorded in Papalanto high school and Agbede compound.

The total hardness of water ranges from 60 to 616 mg/l, showing that areas like Tipper/Ilaro road (S3) and Sawmill road (S5) have very high hard water content (580-616 mg/l), which will make the water less consumable for human use. The hardness of water had being characterized by two major chemical elements namely calcium and magnesium. This is buttressed by the increased values (246.89 mg/l and 232.46 mg/l) of calcium for S3 and S5 respectively when compared to WHO and NSDWQ standards. Though calcium and magnesium are basically two components that the body needs for growth, development and regular metabolism. With a view into the study area, S3 (Tipper/Ilaro road) and S5 (Sawmill road) have the highest level of total water hardness which can also be confirmed by the result of the physio-chemical analysis. S3 (Tipper/Ilaro road) has a recorded data of 85.32 mg/l and S5 (Sawmill road) has a recorded data of 84.45 mg/l respectively of magnesium content. S3 and S5 also have calcium content recorded data of 246.89 mg/l and 232.46 mg/l, respectively. The two major chemical components that contribute to hardness of water (i.e. calcium and magnesium) are found dominant in S3 and S5 with high value against the NSWDQ and WHO standard. This could be a result of dissolution of divalent mineral substance, magnesium and calcium components bombarded in the area as a result of landfill and accumulated swamp leachate plume over a long period of time.

The study area shows a high level of alkalinity from the water samples. Ranging from 60-540 mg/l, S3 (Tipper Park) and S4 (Agbede compound) have the highest level of alkalinity, 540 mg/l and 440 mg/l, respectively. Alkalinity is associated with hardness in water, and the major compound which might account for this is calcium, carbon and oxygen components which are predominantly elements for limestone formation and calcite. The basic element in the study area is within 8.74 to 85.32 mg/l. The range of chloride deposit in the study area is within 56.72 to 368.68 mg/l. In the study area, the local geology comprises of non- crystalline and highly non-fossiliferous limestone and thinly laminated fissile and probably non-fossiliferous shale (these materials listed above are basically carbonate and calcium based compounds which are predominant in the study area [12, 18-21]. The predominant present of calcite, carbon and calcium component also facilitated the presence of a cement producing industry located in the environs of Papalanto. The sediments here consists of diverse layer of sands and mud with a varying proportion of vegetal matter (from sugar cane plantation). Occasional beds of sandstone and sediments were clearly deposited under littoral and lagoonal conditions. Accompanied by spacious reactions surface there are the best conditions for water-rock interactions and hydro-chemical changes. The generality/totality of this research study has vividly evaluated the physio-chemical measurable constituents of the research area. [19-25].

The following parameters have higher value which exceeds the recommended NSDQW and WHO standard. The physical parameters include nickel (S1-S5), lead (S3, S5), manganese (S1-S4), nitrite (S1-S5), nitrate (S5), chloride (S3, S5), magnesium (S3, S5), calcium (S3, S5), total acidity (S1-S5), total alkalinity (S1-S5), total hardness (S3,S5), total dissolved solid (S1-S5), total suspended solid (S1-S5), conductivity (S3-S5), and turbidity (S2).

CONCLUSION

With a comprehensive research carried out in the study area to investigate the extent of leachate contaminant in the water table, the water samples from different strategic areas of Papalanto have been assessed and the physio-chemical analysis carried out. Evidently, contaminants are characterized by high level of toxic, organic and inorganic waste materials. The water samples obtained from well situated in the area of the prominent dumpsite area are not terribly contaminated but certain physio-chemical parameters have exceeded the WHO and NSDWQ standard for quality drinking water. Thus physio-chemical analysis is a useful technique for monitoring groundwater contamination due to leachate at the refuse disposal sites.

Conflict of interest

The authors disclosed no conflict of interest during

the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] Brand EC. Hazardous waste management in the European Community. Implications of '1992' Sci Total Environ 1993;129:241-51.
[2] Cooke RU, Doornkamp JC. Geomorphology in Environmental Management: An Introduction. Oxford: University Press. 1st Ed. edition (October 24, 1974) Available at: https://www.amazon.com/Geomorphology-Environmental-Management-Introduction.
[3] Vijaya Sankar M, Abideen S, Babu Selvam M, Gunasekaran T, Hussain Syed Bava M. A comparative study of ground water by physiochemical parameter and water quality in the Lalgudi taluk of angari pancyayat of Tiruchirappalli district in Tamilnadu, India. Int J Sci Environ Technol 2014;3:348-56.
[4] Oyelami AC, Ojo AO, Aladejana JA, Agbede OO. Assessing the effect of a dumpsite on groundwater quality: a case study of Aduramigba Estate within Osogbo Metropolis. J Environ Earth Sci 2013;3:120-30.
[5] Vodela JK, Renden JA, Lenz SD, McElhenney WH, Kemppainen BW. Drinking water contaminants (arsenic, cadmium, lead, benzene, and trichloroethylene). 1. Interaction of contaminants with nutritional status on general performance and immune function in broiler chickens. Poult Sci 1997;76:1474-92.
[6] Mendie U. The Nature of Water. In: The Theory and Practice of Clean Water Production for Domestic and Industrial Use Lagos: Lacto-Medals publishers, 2005:pp.1-21.
[7] Ikem A, Osibanjo O, Sridhar MKC, Sobande A. Evaluation of groundwater quality characteristics near two waste sites in Ibadan and Lagos, Nigeria. Water Air Soil Poll 2002;140:307-33.
[8] Ushie F, Harry T, Affiah U. Reserve estimation from geoelectrical sounding of the Ewekoro Limestone at Papalanto, Ogun State, Nigeria. J Energy Technol Policy 2014;4:28-32.
[9] Jones HA, Hockey RD. The geology of parts of South-Western Nigeria. Geol Surv Nig Bull 1964;31:101.
[10] Owulakoda Blog. Authority Site of Owu People of the Yoruba Tribe, Nigeria. 2010.
[11] Ogbe FGA. Stratigraphy of strata exposed in the Ewekoro Quarry, SW Nigeria, in: Dessauvagie TFJ, Whiteman (eds.), African Geology, Press, Nigeria. 1972:pp. 305.
[12] Gbadebo AM, Amos AJ. Assessment of radionuclide pollutants in Bedrocks and soils from Ewekoro cement factory, Southwestern Nigeria. Asian J Appl Sci 2010;3:135-44.
[13] Alile OM, Oranusi S, Adetola OO, Airen JO. Subsurface geophysical investigation and physiochemical/microbial contaminant in Ota, Southwestern Nigeria. Geosciences 2012;2:179-84.
[14] Water conductivity, 2013, Lenntech-http://www.lenntech.com/applications/ultrapure/conductivity/water-conductivity.html. Retrieved 5 January 2017.
[15] Bengtsson L, Bendz D, Hogland W, Rosqvist H, Akesson M. Water balance for landfills of different age. J Hydrol 1994;158:203-17.
[16] pH in drinking water, Revised background document for development of WHO Guidelines for Drinking- water quality, WHO/SDE/WSH/07.01/1, World Health Organization, 2007.
[17] Ayuba KA, Abd Mnaf L, Sabrina AH, Nur Azim SW. Current status of municipal solid waste management in F.C.T Abuja. Res J Environ Earth Sci 2013;5:295-30.
[18] APEC Water Systems, 2000 - 2016, Reverse Osmosis System/Distiller method.
[19] Harter T. - EPA secondary drinking water guidelines. Ground water quality and ground pollution. Publication 8084. 2003.
[20] Blaurock- Bosch E. The Clinical effects of manganese (Mn). 2002. http://www.tldp.com/issue/180/Clinical%20Effects%20of%20Mn.html
[21] NSDQW, Nigerian Standard for Drinking Water Quality. Nigerian Industrial Standard NIS 554, Standard Organization of Nigeria, 2007:p. 30.
[22] Abd El-Salam MM, I Abu-Zuid G. Impact of landfill leachate on the groundwater quality: a case study in Egypt. J Adv Res 2015;6:579-86.
[23] Mann AG, Tam CC, Higgins CD, Rodrigues LC. The association between drinking water turbidity and gastro-intestinal illness: a systematic review. BMC Public Health 2007;7:256.
[24] Myre E, ShawR. The turbidity tube :simple and accurate measurement of turbidity in the field. Master's International Program, Michigan Technological University, 2006.
[25] World Health Organization (WHO). Guidelines for drinking water quality. 3rd ed. Vol. 1 Recommendations. WHO: Geneva, 2008.

The European Research Journal 2019;5(3):449-460 ORIGINAL ARTICLE

Incidences and reporting rates of incidental findings on lumbar, thoracic, and cervical spinal magnetic resonance images and extra-neuronal findings on brain magnetic resonance images

Volkan Kızılgöz[1], Hasan Aydın[2], Ali Kemal Sivrioğlu[3], Ümit Can Özcan[1], Utku Menderes[4], Sunay Sibel Karayol[1], Ahmet Erdem[1]

[1]Department of Radiology, Kafkas University School of Medicine, Kars, Turkey
[2]Department of Radiology, Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Ankara, Turkey
[3]Department of Radiology, Okmeydanı Training and Research Hospital, İstanbul, Turkey
[4]Department of Radiology, Eskişehir State Hospital, Eskişehir, Turkey

DOI: 10.18621/eurj.379704

ABSTRACT

Objective: This study aimed to evaluate the incidence rates, reporting rates, and the best imaging plane and sequence for incidental findings in patients undergoing spinal and brain magnetic resonance (MR) imaging.
Methods: Three experienced radiologists retrospectively re-evaluated the MR images of 1056 consecutive patients.
Results: The incidence rates for extraspinal incidental findings for the images of the lumbar, thoracic, and cervical spine, and extra-neuronal incidental findings on MR images of the brain were 35.47%, 32.25%, 29.16%, and 54.35%; respectively, with reporting rates of incidental findings for these examinations of 31.47%, 8.33%, 29.50%, and 59.62%; respectively. For all examination types, the T2-weighted sequence and the axial plain were the best to reveal the incidental findings of MR examinations, other than that of the cervical spine.
Conclusions: Incidental findings, which are commonly detected during routine spinal and brain MR evaluations, are occasionally omitted from formal radiological reports in daily practice. We strongly recommend checking the T2-weighted axial plane for MR imaging of the lumbar, thoracic spine and brain and taking a second look at the T2-weighted sagittal plane MR images of the cervical spine during radiological evaluations.

Keywords: Incidental findings, magnetic resonance imaging, spine, brain, report

Received: January 16, 2018; Accepted: May 14, 2018; Published Online: August 30, 2018

Magnetic resonance imaging (MRI) of the lumbar, thoracic, and cervical spine, as well as the brain is a routine procedure in radiological examinations. The majority of focused diagnostic issues associated with back pain, neck pain, and positive physical examination results indicating radiculopathy include disc hernias, spinal lesions, and degenerative changes of the vertebral column. Brain MRI is useful to diagnose the possible causes of headache, dizziness, cognitive function disorders, demyelinating disorders, vascular malformations, and aberrant physical examination results due to stroke, infection, trauma, and tumor formation. A physical examination is crucial to evaluate patient complaints and is very important to

Address for correspondence: *Volkan Kızılgöz, MD., Kafkas University School of Medicine, Department of Radiology, Mimar Kars, Turkey*
E-mail: volkankizilgoz@gmail.com

e-ISSN: 2149-3189

determine whether MRI would be beneficial to arrive at a diagnosis. Incidental findings are defined as previously undiagnosed and unintentionally encountered medical conditions that are unrelated to the current medical condition for which tests are being performed or the patient is being treated. These findings range from abnormalities of potential clinical disorders relevant to the main underlying pathology or accidentally discovered problems that are unrelated to the main purpose of the MR examination. This study investigated the incidence rates and reporting rates, as well as the best imaging MR plane and sequence in order to reveal incidental findings on spinal and brain MR images.

METHODS

The protocol of this retrospective study was approved by a local Ethics Committee. Due to the methodology and design of the study, the requirement for informed consent was waived. Lumbar, thoracic, and cervical spinal MR images, and brain MR images of 1056 consecutive patients [489 (46.30%) males and 567 (53.69%) females; mean age, 50.11 years; age range, 4-96 years] from examinations conducted between June 1 and September 30, 2016 were retrieved from the picture archive and communication system (PACS) (MediPlus PACS; Turmap Information Technologies, Ankara, Turkey) of our hospital and were reinterpreted for the occurrence of incidental findings.

Interpretation

MR images of each patient were separately reinterpreted by three radiologists (a musculoskeletal radiologist with 11 years of experience and two neuroradiologists with 14 and 15 years of experience), and incidental findings were ascertained by the consensus of at least two of the interpreters. Medical conditions that were visible on MR images, but were unrelated to the current clinical information or prediagnosis of the patient's condition for which medical tests had been performed or had been treated were accepted as incidental findings. The incidental findings comprised lesions, anatomical variants, and anomalies. After the MRI evaluation, the prediagnostic information given by the clinician and the incidental findings of the patients were determined and former radiology reports were reviewed to determine whether the incidental finding had been noticed. Additionally, the best MRI sequence and plane that revealed the incidental findings were determined by the consensus of at least two of the three reviewers. The MRI sequence that best depicted lesion contours and revealed a visual contrast of the lesion was accepted as the best sequence. The MRI plane in which the anomaly and anatomical variance of the lesion were entirely or almost entirely visible and the one that indicated the specific morphology or radiological appearance of the incidental findings better was accepted as the best plane. Scout images were also examined in addition to other routine sequences. Incidence rates were calculated as the ratio of the number of patients to all examined patients. Extraspinal and extraneuronal findings were classified by organ or system, and the incidence rate of each finding was calculated separately. Hemangiomas, vertebral anomalies, and fractures were not considered as incidental findings in this study because these conditions are commonly located very near to discs and are easily noticed in daily clinical practice. For brain MRI, 24 mild nasal septal deviations and spur formations, which caused obvious blockage of air flow in the nasal passage, were excluded from analysis. Among the patients with MRI of the cervical spine, four were excluded from the study due to the presence of primary malignancies involving larger lymphadenopathies than those mentioned in the corresponding clinical report.

MR Imaging

A Magnetom Essenza 1.5T MRI system (Siemens Healthcare GmbH, Erlangen, Germany) was used to obtain all images. Cervical, thoracic, and lumbar spinal examinations were performed using an 8-channel spinal coil, and brain MR examinations were performed using an 8-channel head coil. The routine cervical spinal MR protocol included sagittal T1-weighted, sagittal T2-weighted, and axial T2-weighted sequences. The thoracic spinal MR protocol included sagittal T1-weighted, sagittal T2-weighted, and axial

T2-weighted sequences. The lumbar spinal MR protocol included sagittal T1-weighted, sagittal T2-weighted, and axial T2-weighted sequences. Brain MR images included axial T1-weighted, axial T2-weighted, axial fluid attenuation inversion recovery (FLAIR), sagittal FLAIR, and coronal T2-weighted sequences. The scout images for cervical, thoracic, lumbar spinal MRI and brain MRI were also obtained before the routine imaging sequences. The axial section images were taken between the L1 and S1 vertebrae for lumbar MR imaging, between the T1 and T12 vertebrae for thoracic imaging, and between the C2 and C7 vertebrae for cervical imaging. The pre-saturation band was only applied in sagittal series for spinal imaging.

Statistical Analysis

The frequencies of incidental findings, the organ or system which the incidental was located, reporting rates, best imaging plane and best MRI sequences to visualize the incidental finding were expressed as the number of cases and correspondent percentages.

RESULTS

Lumbar Spinal MRI

The mean age of patients with incidental findings on MR imaging of the lumbar spinal (n = 210) was 51.63 (range, 15-85) years. Of these 210 patients, 87 (41.42%) were males and 123 (58.57%) were females.

Incidental findings were observed on 35.47% of the MR images of the lumbar spinal (Table 1) with renal cyst formation being the most common (43.42% of all incidental findings) and 64 (58.7%) of all 109 patients with this incidental finding were not reported in routine practice (reporting rate of 41.28%).

Of all incidental findings on lumbar spinal MR images, the kidney was the most commonly affected organ with findings of extra spinal involvement (64.94%). The incidences of renal stones, renal atrophies, an extra renal pelvis, left accessory renal arteries, and solitary kidneys were most commonly overlooked in the radiology reports. Hepatomegaly, splenomegaly, choledochal ecstasies, Nabothian cysts, and paraaortic lymphadenopathy were also commonly missed. For lumbar MRI examinations, hepatomegaly was only discerned on scout images. Localizer views were also the best sequence to reveal splenomegaly and prostate enlargement. All cases of horseshoe kidney, renal sinus lipomatosis, renal mass, focal renal caliectasis, diverticulosis of the colon, paravertebral soft tissue abscess, and ovarian mass were appropriately cited in the radiology reports.

The reporting rate of incidental findings on lumbar spinal MR images was 31.47%. The best sequence to detect incidental findings on these images was the T2-weighted sequence (78.08%) and axial planes (70.11%) were better than sagittal views (Table 2) (Figures 1, 2, 3, and 4).

Thoracic Spinal MRI

The mean age of patients with incidental findings on spinal MR images of the thoracic region (n = 10) was 32.40 (range, 4-83) years and half of these patients were male. The incidence rate for this examination was 32.25% (Table 1). The incidental findings were mostly related to the lungs and pleura (50%). Pleural effusion was the most common incidental finding with an incidence rate of 25% and

Table 1. Incidence rates of each MRI examination included in this study

Examination	Number of patients	Number of incidental findings	Number of patients with incidental findings	Incidence rate (%)
Lumbar MRI	592	251	210	35.47
Thoracic MRI	31	12	10	32.25
Cervical MRI	192	61	56	29.16
Brain MRI	241	162	131	54.35
TOTAL	1056	486	407	38.54

Table 2. Incidental extraspinal findings of lumbar spine MR imaging

Incidental finding	Related organ/system	Number (%)	Incidence Rate (%)	Reported	Unreported	Reporting rate (%)	Best sequence*	Best imaging plane*
Cyst	Kidney	109 (43.42)	18.41	45	64	41.28	T2 (81 of 109)	AX (96 of 109)
Retroaortic left renal vein	Kidney	24 (9.56)	4.05	1	23	4.16	T2 (24 of 24)	AX (24 of 24)
Stones	Kidney	2 (0.79)	0.33	0	2	0	T2 (2 of 2)	AX (2 of 2)
Atrophy	Kidney	2 (0.79)	0.33	0	2	0	T2 (2 of 2)	AX (2 of 2)
Horseshoe kidney	Kidney	1 (0.39)	0.16	1	0	100	T2 (1 of 1)	AX (1 of 1)
Left accessory renal artery	Kidney	2 (0.79)	0.33	0	2	0	T2 (2 of 2)	AX (2 of 2)
Renal sinus lipomatosis	Kidney	1 (0.39)	0.16	1	0	100	T2 (1 of 1)	AX (1 of 1)
Extrarenal pelvis	Kidney	6 (2.39)	1.01	0	6	0	T2 (4 of 6)	AX (4 of 6)
Hydronephrosis	Kidney	8 (3.18)	1.35	5	3	62.50	T2 (8 of 8)	AX (8 of 8)
Renal malrotation	Kidney	4 (1.58)	0.67	0	4	0	T2 (4 of 4)	AX (4 of 4)
Renal mass	Kidney	1 (0.39)	0.16	1	0	100	T2 (1 of 1)	AX (1 of 1)
Focal renal caliectasis	Kidney	1 (0.39)	0.16	1	0	100	T2 (1 of 1)	AX (1 of 1)
Solitary kidney	Kidney	2 (0.79)	0.33	0	2	0	T2/SC (1 of 2)	AX/COR (1 of 2)
Gallbladder stone	Gallbladder	4 (1.59)	0.67	2	2	50	T2 (4 of 4)	AX (3 of 4)
Hepatomegaly	Liver	4 (1.59)	0.67	0	4	0	SC (4 of 4)	COR (4 of 4)
Hepatic cyst	Liver	3 (1.19)	0.50	1	2	33.33	SC (2 of 3)	COR (2 of 3)
Hepatic mass	Liver	2 (0.79)	0.33	2	0	100	T2 (2 of 2)	AX (2 of 2)
Splenomegaly	Spleen	1 (0.39)	0.16	0	1	0	SC (1 of 1)	COR (1 of 1)
Choledochal ectasia	Biliary system	2 (0.79)	0.33	0	2	0	T2 (2 of 2)	AX (2 of 2)
Wall thickening	Bladder	8 (3.18)	1.35	1	7	12.50	T2 (7 of 8)	AX (6 of 8)
Nabothian cyst	Cervix	3 (1.19)	0.50	0	3	0	T2 (2 of 3)	SAG (3 of 3)
Myoma	Uterus	10 (3.98)	1.68	2	8	20	T2 (10 of 10)	SAG (9 of 10)
Retroverted Uterus	Uterus	22 (8.76)	3.71	2	20	9.09	T2 (15 of 22)	SAG (21 of 22)
Diverticulosis	Colon	1 (0.39)	0.16	1	0	100	T2 (1 of 1)	AX (1 of 1)
Paraaortic lymphadenopathy	Lymphatic system	1 (0.39)	0.16	0	1	0	T2 (1 of 1)	AX (1 of 1)
Pelvic free fluid	Pelvic cavity	4 (1.59)	0.67	2	2	50	T2 (4 of 4)	SAG (3 of 4)
Cyst	Ovaries	20 (7.97)	3.37	9	11	45	T2 (15 of 20)	AX (13 of 20)
Ovarian mass	Ovaries	1 (0.39)	0.16	1	0	100	T2 (1 of 1)	AX (1 of 1)
Enlarged prostate	Prostate	2 (0.79)	0.33	1	1	50	SC (2 of 2)	SAG (2 of 2)
TOTAL	**Kidney# (64.94%)**	**251 (100)**	**35.47**	**79**	**172**	**31.47**	**T2# (78.08%)**	**AX# (70.11%)**

*Indicates the MR sequence and imaging plane that best depicts the incidental finding. Numbers in parenthesis (… of …) indicate the frequencies of certain incidental finding revealed by the best sequence or best plane among all MR sequences or planes. **#Indicates the organ/system, best sequence, or the best imaging plane which the incidental findings of lumbar spine MR imaging is mostly seen.**

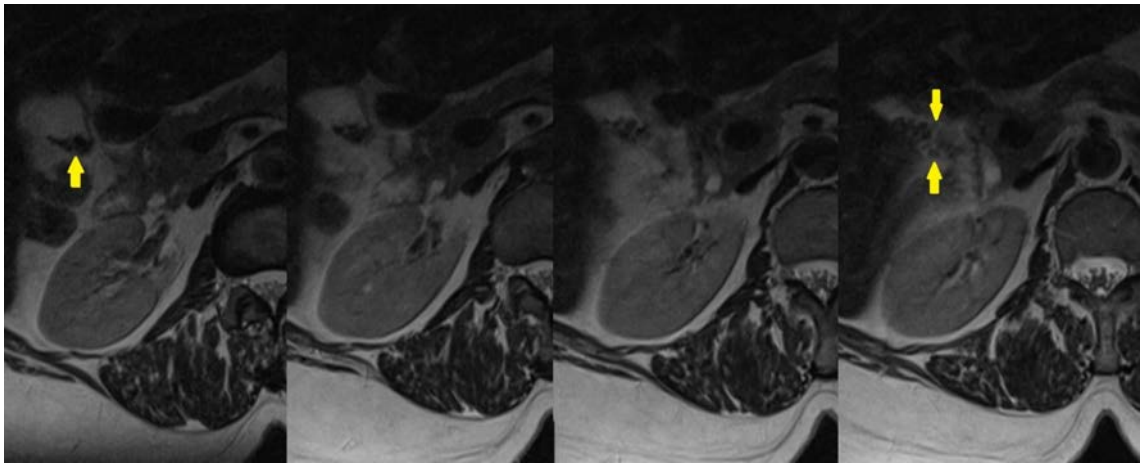


Figure 1. Lumbar spinal MR images of a 61-year-old female. Consecutive axial T2-weighted images of the patient indicate incidental gallbladder stones (yellow arrows). The diagnosis was confirmed by ultrasonography

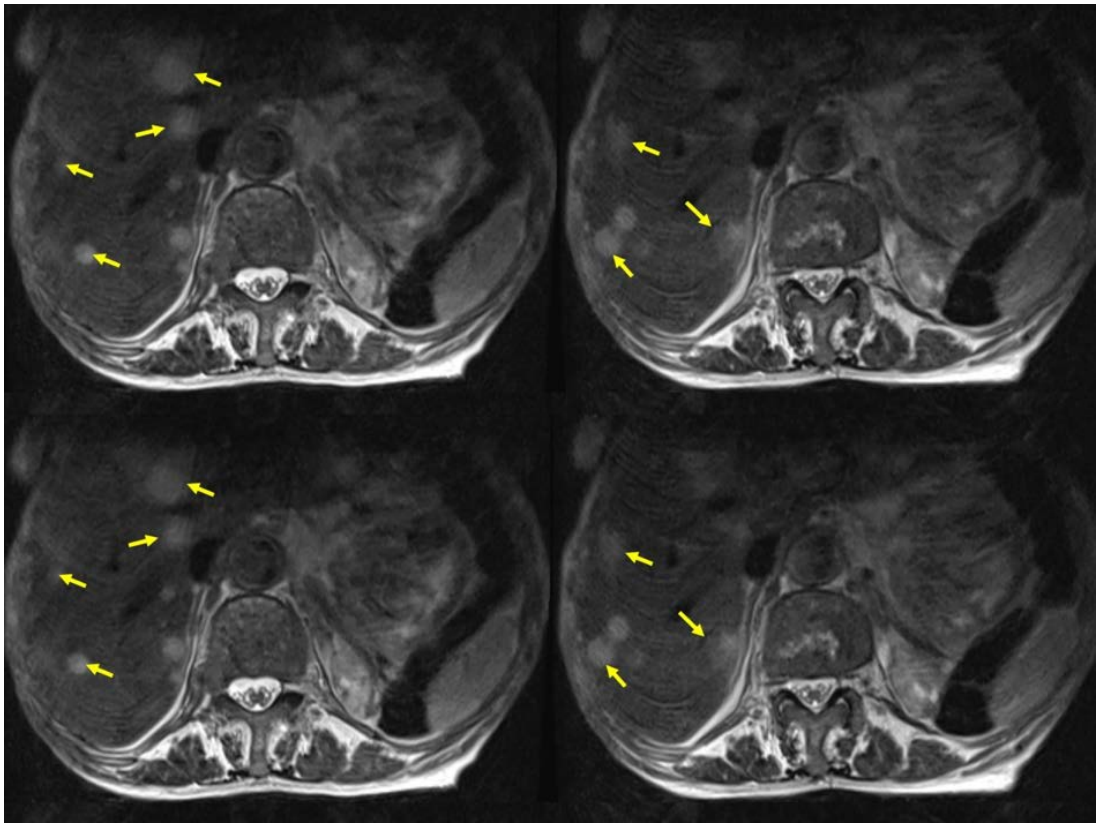


Figure 2. Lumbar spinal MR images of a 73-year-old female. Consecutive axial T2-weighted images of the patient revealed multiple hepatic masses (some of them were indicated with yellow arrows). Further medical investigations confirmed metastasis of lung cancer.

a reporting rate of 33.33%. For all patients with incidental findings on thoracic spinal MR images, the reporting rate was 8.33% and the best sequence and best plane to indicate these findings were T2-weighted (100%) and sagittal images (83.33%), respectively (Table 3) (Figure 5).

MR Images of the Cervical Spine

Incidental findings on cervical spinal MR images were detected for 56 patients [25 (44.64%) males and 31 (55.35%) females; mean age, 44.41 years; age range, 4-82 years]. The incidence rate for this examination was 29.16% (Table 1). Mucosal

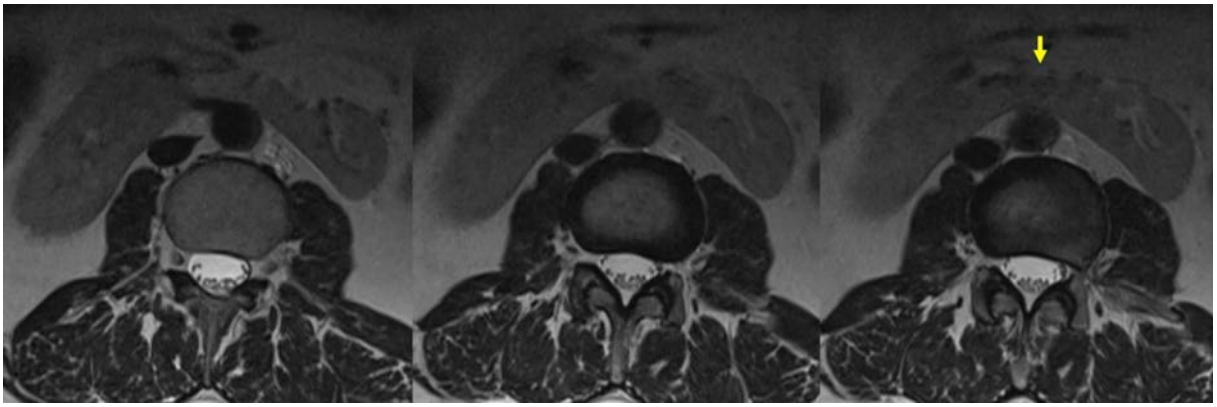


Figure 3. Consecutive T2-weighted images of lumbar spinal MR examination of 51-year-old male showing two kidneys with fusion of the lower poles (yellow arrow), consistent with horseshoe kidneys.

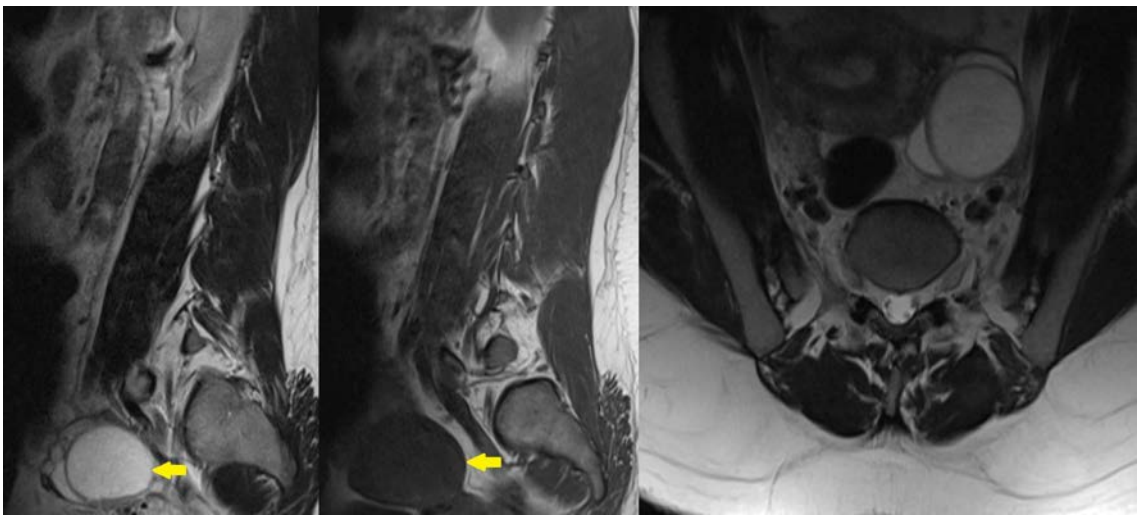


Figure 4. Sagittal T2-weighted, sagittal T1-weighted, and axial T2-weighted MR images of a 31-year-old female. Left ovarian cysts were noticed on images of the lumbar spine (yellow arrows)

thickening (34.42% of all incidental findings for this examination) was the most common incidental finding with a reporting rate of 14.28%. The overall the reporting rate was 29.5%, and the best sequence and the best plane to discriminate incidental findings on MR images of the cervical spine were the T2-weighted sequence (100%) and the sagittal view (93.44%), respectively. However, the axial plane was best suited to identify cervical lymphadenopathies (Table 4) (Figures 6 and 7).

Brain MRI

Incidental findings on brain MR images (n = 131) were identified in 131 patients [67 (51.14%) males and 64 (48.85%) females; mean age, 47.48 years; age range 6–93 years] demonstrating an incidence rate of 54.35% (Table 1). The paranasal sinuses were the most common site of the incidental findings. Mucosal thickening, retention cyst formation, and decreased pneumatization of mastoid air cells were the most common entities discerned asincidental findings. One patient with mucosal thickening of the nasopharynx, two with phthisis bulbi, one with scalp hematoma, one with a parotid lesion, and two with nasal septal deviation were noted with a reporting rate of 100%. Two instances of antrochoanal polyp formation were overlooked. T2-weighted images (98.13%) and axial planes (59.62%) were the best imaging approaches to

Table 3. Incidental extraspinal findings of thoracic spine MR imaging

Incidental finding	Related organ/system	Number (%)	Incidence Rate (%)	Reported	Unreported	Reporting rate (%)	Best sequence*	Best imaging plane*
Azygos lobe	Lung	1 (8.33)	3.22	0	1	0	T2 (1 of 1)	AX (1 of 1)
Decreased pneumatization	Lung	2 (16.66)	6.45	0	2	0	T2 (2 of 2)	AX (2 of 2)
Pleural effusion	Pleura	3 (25)	9.67	1	2	33.33	T2 (3 of 3)	AX (3 of 3)
Abdominal aorta aneurysm	Abdominal aorta	1 (8.33)	3.22	0	1	0	T2 (1 of 1)	AX (1 of 1)
Subcutaneous lipoma	Subcutaneous fat tissue	1 (8.33)	3.22	0	1	0	T2 (1 of 1)	SAG (1 of 1)
Paraaortic lymphadenopathy	Lymphatic system	1 (8.33)	3.22	0	1	0	T2 (1 of 1)	SAG (1 of 1)
Paravertebral soft tissue edema	Paravertebral soft tissue	1 (8.33)	3.22	0	1	0	T2 (1 of 1)	AX (1 of 1)
Hepatic mass	Liver	2 (16.66)	6.45	0	2	0	T2 (2 of 2)	AX (2 of 2)
TOTAL	**Lung and pleura# (50%)**	**12 (100)**	**32.25**	**1**	**11**	**8.33**	**T2# (100%)**	**AX# (83.33%)**

*Indicates the MR sequence and imaging plane that best depicts the incidental finding. Numbers in parenthesis (… of …) indicate the frequencies of certain incidental finding revealed by the best sequence or best plane among all MR sequences or planes. **#Indicates the organ/system, best sequence, or the best imaging plane which the incidental findings of lumbar spine MR imaging is mostly seen.**

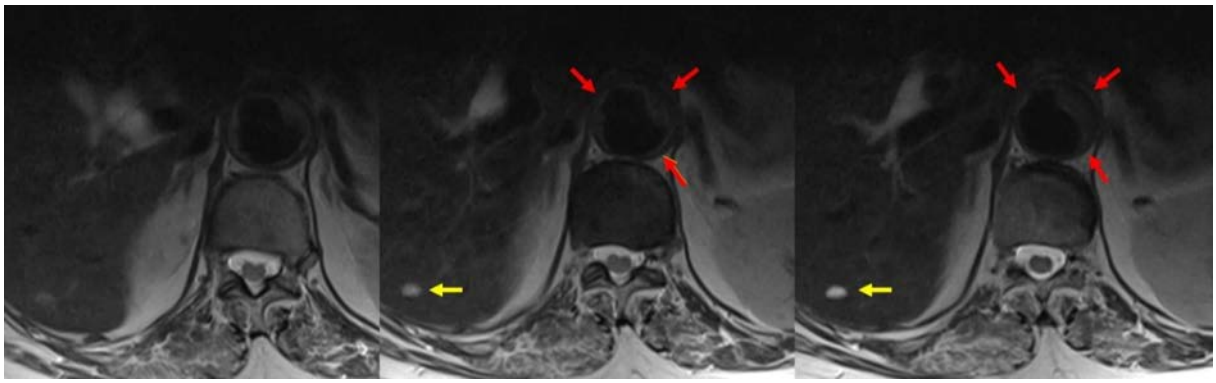


Figure 5. Thoracic axial MR images of an 84-year-old female. Thrombosed abdominal aorta aneurysm (red arrows) and a hepatic cyst (yellow arrows) were detected incidentally on T2-weighted images.

Table 4. Incidental extraspinal findings of cervical spine MR imaging

Incidental finding	Related organ/system	Number (%)	Incidence Rate (%)	Reported	Unreported	Reporting rate (%)	Best sequence*	Best imaging plane*
Mucosal thickening	Nasopharynx	5 (8.19)	2.60	0	5	0	T2 (5 of 5)	SAG (5 of 5)
Thornwaldt cyst	Nasopharynx	2 (3.27)	1.04	1	1	50	T2 (2 of 2)	SAG (2 of 2)
Mucosal thickening	Paranasal sinuses	21 (34.42)	10.93	3	18	14.28	T2 (21 of 21)	SAG (21 of 21)
Retention cyst	Paranasal sinuses	14 (22.95)	7.29	6	8	42.85	T2 (14 of 14)	SAG (14 of 14)
Cervical lymphadenopathy	Lymphatic system	3 (4.91)	1.56	0	3	0	T2 (3 of 3)	AX (3 of 3)
Thyroglossal duct cyst	Thyroid	1 (1.63)	0.52	1	0	100	T2 (1 of 1)	SAG (1 of 1)
Thyroid hypertrophy	Thyroid	4 (6.55)	2.08	2	2	50	T2 (4 of 4)	SAG (4 of 4)
Thyroid nodule	Thyroid	11 (18.03)	6.72	5	6	45.45	T2 (11 of 11)	SAG (10 of 11)
TOTAL	**Paranasal sinuses# (34.42%)**	**61 (100)**	**29.16**	**18**	**43**	**29.50**	**T2# (100%)**	**SAG# (93.44%)**

*Indicates the MR sequence and imaging plane that best depicts the incidental finding. Numbers in parenthesis (… of …) indicate the frequencies of certain incidental finding revealed by the best sequence or best plane among all MR sequences or planes**. #Indicates the organ/system, best sequence, or the best imaging plane which the incidental findings of lumbar spine MR imaging is mostly seen.**

Table 5. Incidental extraneuronal findings on brain MR imaging.

Incidental finding	Related organ/system	Number (%)	Incidence Rate (%)	Reported	Unreported	Reporting rate (%)	Best sequence*	Best imaging plane*
Mucosal thickening	Paranasal sinuses	78 (48.44)	32.36	42	36	53.84	T2 (78 of 78)	AX (64 of 78)
Retention cyst	Paranasal sinuses	28 (17.39)	11.61	25	3	89.28	T2 (28 of 28)	COR/AX (14 of 28)
Decreased pneumatization	Mastoid cells	22 (13.66)	9.12	11	11	50	T2 (22 of 22)	COR (21 of 22)
Mucosal thickening	Nasopharynx	1 (0.62)	0.41	1	0	100	FL (1 of 1)	SAG (1 of 1)
Concha hypertrophy	Nasal cavity	10 (6.21)	4.14	4	6	40	T2 (10 of 10)	COR (9 of 10)
Antrochoanal polyp	Paranasal sinuses-nasopharynx	2 (1.24)	0.82	0	2	0	T2 (2 of 2)	AX (2 of 2)
Intraorbital hemorrhage	Orbit	3 (1.86)	1.24	2	1	66.66	T2 (2 of 3)	AX (3 of 3)
Phthisis bulbi	Orbit	2 (1.24)	0.82	2	0	100	T2 (2 of 2)	AX (2 of 2)
Intraocular lens (implants)	Orbit	8 (4.96)	3.31	3	5	37.50	T2 (8 of 8)	AX (8 of 8)
Scalp lesion	Scalp	3 (1.86)	1.24	2	1	66.66	T2 (3 of 3)	COR (2 of 3)
Scalp hematoma	Scalp	1 (0.62)	0.41	1	0	100	FL (1 of 1)	AX (1 of 1)
Parotid lesion	Parotid gland	1 (0.62)	0.41	1	0	100	T2 (1 of 1)	AX (1 of 1)
Septal deviation	Nasal septum	2 (1.24)	0.82	2	0	100	T2 (2 of 2)	COR/AX (1 of 2)
TOTAL	**Paranasal sinuses# (67.08%)**	**161 (100)**	**54.35**	**96**	**65**	**59.62**	**T2# (98.13%)**	**AX# (59.62%)**

*Indicates the MR sequence and imaging plane that best depicts the incidental finding. Numbers in parenthesis (… of …) indicate the frequencies of certain incidental finding revealed by the best sequence or best plane among all MR sequences or planes**. #Indicates the organ/system, best sequence, or the best imaging plane which the incidental findings of lumbar spine MR imaging is mostly seen.**

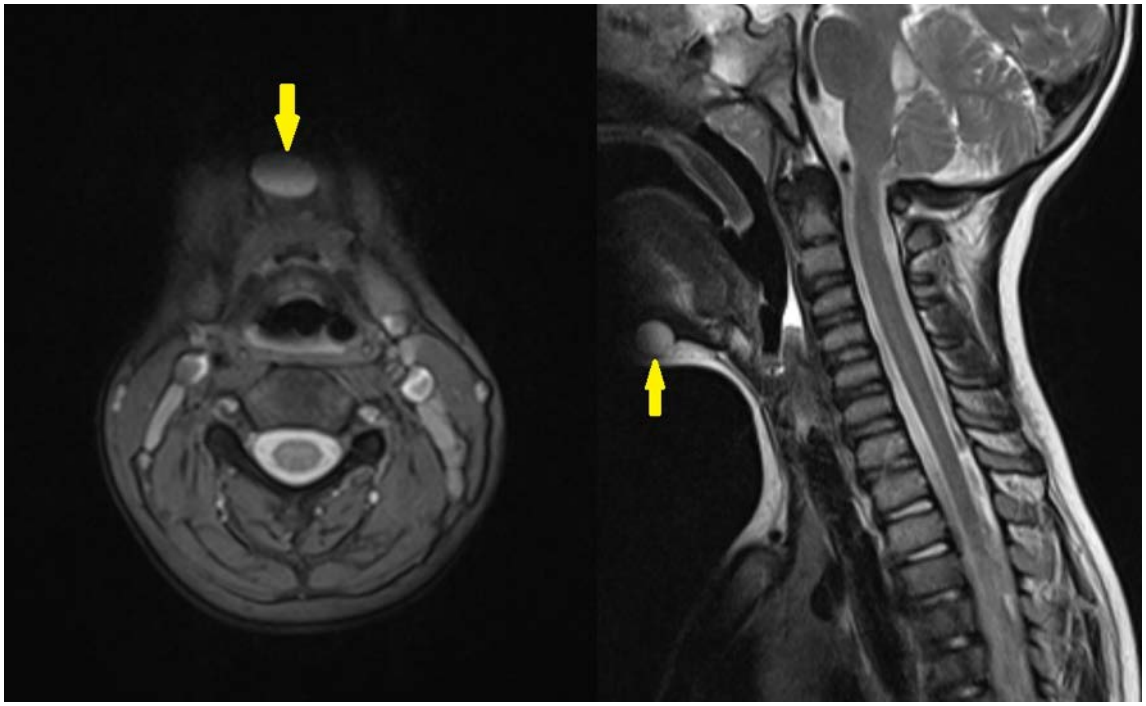


Figure 6. Axial and sagittal plane MR images of the cervical spine of a 4-year-old male revealed a hyperintense lesion with smooth contours (yellow arrows). Surgery confirmed that this lesion was consistent with a thyroglossal cyst.

discern incidental findings on brain MR images (Table 5) (Figure 8).

For all MRI examinations

Regarding 407 patients with incidental findings in this study [184 (45.20%) males and 223 (54.79%) females; mean age, 48.71 years; age range, 4-93 years], the incidence rate was 38.54% (Table 1) and the reporting rate was 39.91%. Overall, according to the interpreters, T2-weighted images were the best sequence (87.86%) and the axial view was the best plane (58.64%) to reveal the incidental findings.

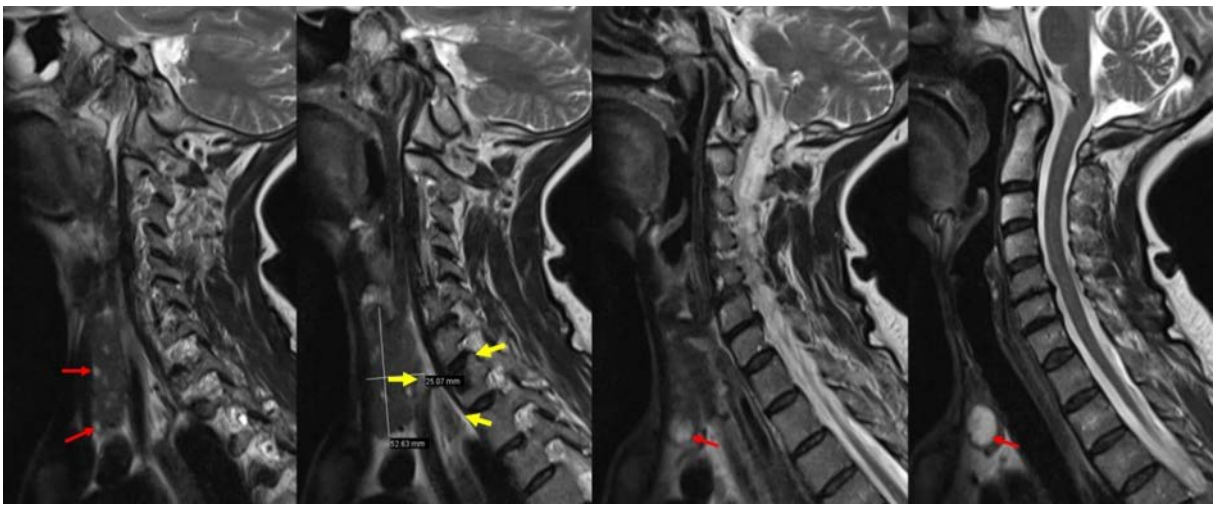


Figure 7. Consecutive sagittal T2-weighted MR images of a 65-year-old female. Thyroid hypertrophy (yellow arrows) and multiple nodule formations (some of them were indicated with red arrows

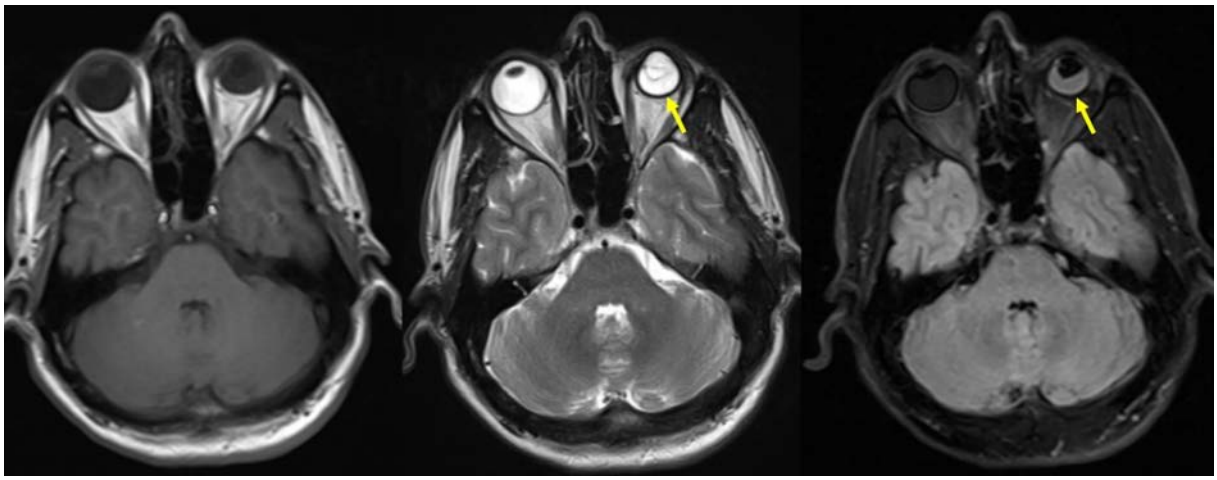


Figure 8. Axial T1-weighted, T2-weighted and FLAIR sequences of the brain MR images of a 36-year-old male. The left ocular bulbus (yellow arrow) was smaller than the normal right eye with signal alterations possibly indicating intraocular hemorrhage. Patient's file confirmed that a history of trauma to the left eye before the examination. No further information about the orbit was provided by the clinician.

DISCUSSION

In this study, the highest rate of incidental findings occurred with brain MR images, the lowest reporting rate was observed for images of the thoracic spine, the T2-weighted sequence was the best imaging sequence, and the axial plane was the most useful imaging plane to identify incidental findings with regard to percentage.

An abundance of data can be derived from MR images about the region of interest, besides the focusing point and parameters, which is a very important aspect of interpretation of MR images for the radiologist. An incidental lesion might be an explanatory cause of the major problem of the patient or could be the first obvious manifestation or a proof of an important disease that is otherwise non-symptomatic.

The medicolegal aspects of incidental lesions are of great importance to the radiologist. Magnavita *et al*. [1] and Fileni *et al*. [2] noted that diagnostic error is often the basis of lawsuitsagainst radiologists. Moreover, the authors previously reported possible causes of perception errors resulting in the failure to detect an abnormality on a radiological examination.

In a retrospective review of 1517 lumbar CT examinations conducted in 1986, Frager *et al*. [3] reported that extra spinal pathologies were overlooked in 22 (1.45%) cases with uterine leiomyoma and abdominal aorta aneurysm being the most common incidental lesions. Lee *et al*. [4] reported an incidence rate of extra spinal findings among 400 lumbar spine CT examinations of 40.5% with the gastrointestinal system (71 patients) and genitourinary system (50 patients) being the most common systems with incidental lesions. Park *et al*. [5] evaluated the frequency and types of incidental findings on MR images of the lumbar spine and reported incidental findings in 107 (8.4%) of 1268 patients.

In the present study, the incidence rates as well as the reporting rates were evaluated. Tuncel *et al*. [6] reinterpreted 1278 lumbar MR images and described incidental findings in 253 cases with a reporting rate of overall incidental findings of 28%, which was in accordance with the reporting rate of 31.74% in the present study. Similar to this study, the kidney was the most common location (37.15%) and renal cysts were the most common incidentally discovered lesions. Myoma was the most common uterine incidental lesion (15.81%) as well as in our study. A study by Tuncel *et al*. [6] reported incidental findings of retroaortic renal vein variations in 52 (20.5%) of 253 patients with an incidence rate of 4%. In the present study, anatomic variances occurred as incidental findings in 24 patients with an incidence rate of 4.05%, nearly the same as that reported previously.
The main purpose of thoracic spinal MR imaging is to evaluate the intervertebral discs and spine, as well the large thoracic space around the region of interest to enable observation of the intrathoracic area, especially

the lungs and pleura. Respiratory and cardiovascular motions cause low spatial resolution and a low signal to noise ratio of the lung parenchyma, thus spinal MR imaging is not sufficient to characterize a lung lesion. However, the signal loss due to thepresence of air in the lungs also creates contrast; therefore, MR images may be suitable to reveal prominent lesions. Even a huge space occupied by lesions or large areas of air loss can be overlooked during spinal evaluations if the radiologist solely focuses on the main parameters of thoracic spinal MR imaging. Kamath *et al*. [7] reported that solitary pulmonary nodules, pleural effusions, interstitial fibrosis of the lungs, and pneumonia were frequent incidental findings on thoracic images. In the present study, the lungs and pleura were the most common sites of incidental findings while the most common finding was pleural effusion.

Most similar studies on incidental findings in cervical imaging methods have focused on thyroid nodules. For example, Grady *et al*. [8] reported a highly variable size of thyroid nodules ranging from 10 to 19 mm in diameter, and only 73% of patients with incidental thyroid nodules of ≥ 20 mm in diameter were mentioned in the "Impression" section of the radiology report. In a retrospective study of 61 patients who underwent both spinal MRI and thyroid ultrasonography, Cho *et al*. [9] reported that very few thyroid nodules less than 1 cm in size and only one-third of those larger than 1 cm were detected by MRI, thus the authors recommended sonography for detection of thyroid nodules that are not readily recognized on MR images. Mancuso [10] commented that "the younger the patient, the higher the risk of malignancy" in regards to an individual thyroid nodule and suggested baseline ultrasonography to evaluate incidental nodules. Kamath *et al*. [7] reported meningioma, thyroid and salivary gland lesions, and nasopharyngeal tumors as the most frequent incidental findings encountered during cervical spinal MRI evaluation. In the present study, the paranasal sinuses were the most common site of incidental findings with an incidence rate of 10.93%, whereas the incidence rate of thyroid nodules was 5.72% with no instance of a meningioma or nasopharyngeal tumor as an incidental lesion.

Katzman *et al*. [11] studied brain MRI scans of 1000 volunteers who participated as control subjects for various research protocols and found that 18% of all volunteers had incidental abnormal findings, which included 132 volunteers with sinusitis; this was the most common incidental finding. In a study of images of 2000 people from a population based on the Rotterdam Study, Vernooij *et al*. [12] reported that the most frequent finding was brain infarct, followed by cerebral aneurysm and benign primary tumors. A systematic review and meta-analysis of 16 studies of incidental findings of brain MRI of 19559 patients conducted by Morris *et al*. [13] in 2009 reported that the crude prevalence of incidental findings on brain MRI was 2.7%, or in other words, one incidental finding for every 37 neurologically asymptomatic subjects scanned. The prevalence of incidental neoplastic brain findings was 0.70% in a meta-analysis of 16 studies and 2.0% (range, 1.1%-3.1%)in a review of 15 studies that excluded white matter hyperintensities, silent infarcts, and microbleeds. In the present study, besides the most common lesions of mucosal thickening, retention cysts of the paranasal sinuses, and decreased pneumatization of mastoid cells, other lesions of the scalp, parotid gland, and orbitwere also observed.

To the best of our knowledge, there is limited information in the literature regarding optimal sequences and plains to reveal incidental findings on MR images. In this study, the T2-weighted sequence was the most useful for all examination types while the axial plain was best for the lumbar and thoracic spine as well as the brain. Moreover, the sagittal plain was best for MR imaging of the cervical spine to reveal incidental findings.

As an alternative aspect to this discussion, other reports have implied that reporting incidental findings may not always be beneficial to the patient. For example, Westbrook *et al*. [14] claimed that, although incidental lesions are indeed serendipitous and subsequent treatment reduces morbidity and mortality, a number of patients may undergo extensive diagnostic examinationswhich may lead to no improvement in health. The authors agree that some patients are in fact harmed by such examinations because of various reasons, such as cumulative radiation exposure resulting from serial scans, as well as unnecessary anxiety and distress.

Limitations

Although it is a rather difficult and subjective approach to determine the best sequence and imaging plain for this purpose, the aim of this study was to ascertain the importance of specific imaging sequences and the best planes for the evaluation process, especially to avoid underestimation or overlooking of the so-called "incidental" findings. Even though interpretations were made by the consensus of at least two experienced radiologists, this situation may have been a limitation to this study. The FOV for the specific areas of each MRI examination might have limited the exact visualization of other incidental findings. The interpreters were not able to identify some vague MRI signals in the marginal parts of the frames or the first or last cross-sectional views, which may represent the edge of another incidental finding or an artifact of no significance. Only the MRI signals that clearly and undoubtedly indicated the lesion, anomaly, or anatomical variance were accepted as an incidental finding by the reviewers, which may have been another limitation to the detection of incidental findings. Moreover, although the MR images were evaluated by three experienced radiologists, human errors may have occurred, thus the results may not perfectly represent the rates of incidental findings. Lastly, some important parameters (such as reporting rates, best plane, and sequence.) were statistically compared for each MRI examination, but the total number of patients who underwent thoracic spinal MRI was not sufficient for comparisons.

CONCLUSION

In conclusion, incidental findings are commonly detected during routine spinal and brain MRI interpretations. However, these findings may not have clinical importance and are occasionally omitted from formal radiological reports in daily practice. We strongly recommend checking the T2-weighted axial plane for MR imaging of the lumbar, thoracic, and cervical spine, and brain, and taking a second look at the T2-weighted sagittal plane MR images of the cervical spine during radiological evaluations.

Author Contributions

Guarantor of integrity of entire study: VK; Study concepts: VK, UM; Study design: VK, HA, ÜCÖ, SSK;Data acquisition: VK, ÜCÖ; Data analysis: VK, ÜCÖ, AKS, HA; Interpretation: VK, ÜCÖ, SSK; Literature research: VK, AKS, HA; Manuscript drafting: VK, UM, AKS, HA; Manuscript editing: VK, UM, ÜCÖ, SSK, AKS, HA, AE.

Ethics

This study has been approved by ethics committee.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

Acknowledgements

We thank to our resident, Dr. Hanife Özgen, to assist in data entry of patients' findings and we thank to our radiology technicians, Mr. Sercan Demiral and Mr. Tayfun Tayfun for their assistance in handling of the MRI procedures.

REFERENCES

[1] Magnavita N, Magnavita G, Fileni A, Bergamaschi A. Ethical problems in radiology: medical error and disclosure. Radiol Med 2009;114:1345-55.

[2] Fileni A, Magnavita N. A 12-year follow-up study of malpractice claims against radiologists in Italy. Radiol Med 2006;111:1009-22.

[3] Frager DH, Elkin CM, Kansler F, Mendelsohn SL, Leeds NE. Extraspinal abnormalities identified on lumbar spine CT. Neuroradiology 1986;28:58-60.

[4] Lee SY, Landis MS, Ross IG, Goela A, Leung AE. Extraspinal findings at lumbar spine CT examinations: prevalence and clinical importance. Radiology 2012;263:502-9.

[5] Park HJ, Jeon YH, Rho MH, Lee EJ, Park NH, Park SI, et al. Incidental findings of the lumbar spine at MRI during herniated intervertebral disk disease evaluation. Am J Roentgenol 2011;196:1151-5.

[6] Tuncel SA, Çağlı B, Tekataş A, Kırıcı MY, Ünlü E, Gençhellaç H. Extraspinal incidental findings on routine MRI of lumbar spine: prevalence and reporting rates in 1278 patients. Korean J Radiol 2015;16:866-73.

[7] Kamath S, Jain N, Goyal N, Mansour R, Mukherjee K. Incidental findings on MRI of the spine. Clin Radiol

2009;64:353-61.
[8] Grady AT, Sosa JA, Tanpitukpongse TP, Choudhury KR, Gupta RT, Hoang JK. Radiology reports for incidental thyroid nodules on CT and MRI: high variability across subspecialties. Am J Neuroradiol 2015;36:397-402.
[9] Cho HW, Park JO, Lee YH, Chung SY, Suh JS. Should we recommend ultrasonography for an incidental thyroid nodule on additional cervicothoracic sagittal T2-weighted image of lumbar spine MRI? Investig Magn Reson Imaging 2015;19:224-30.
[10] Mancuso AA. Another pesky incidental thyroid nodule! Am J Neuroradiol 2005;26:2444-5.
[11] Katzman GI, Dagher AP, Patronas NJ. Incidental findings on brain magnetic resonance imaging from 1000 asymptomatic volunteers. JAMA 1999;282:36-9.
[12] Vernooij MW, Ikram MA, Tanghe HL, Vincent AJPE, Hofman A, Krestin GP, et al. Incidental findings on brain MRI in the general population. New Engl J Med 2007;357:1821-8.
[13] Morris Z, Whiteley WN, Longstreth WT Jr, Weber F, Lee YC, Tsushima Y, et al. Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis. BMJ 2009;339:b3016.
[14] Westbrook JI, Braithwaite J, McIntosh JH. The outcomes for patients with incidental lesions: serendipitous or iatrogenic? Am J Roentgenol 1998;171:1193-6.

The European Research Journal 2019;5(3):461-466 ORIGINAL ARTICLE

Effect of low-dose dopamine on depression score in patients with heart failure

Tarık Kıvrak

Department of Cardiology, Fırat University School of Medicine, Elazığ, Turkey

DOI: 10.18621/eurj.376910

ABSTRACT

Objectives: This study aimed to assess the effects of low-dose dopamine on patients with depression in the intensive coronary unit.

Methods: Relatives of 43 ICU patients enrolled in the study. Sociodemographic characteristics of patients and their families recorded. Patients evaluated basal echocardiographic and biochemical values measured in the patient group. The Beck Anxiety and Depression Scale was used to assess anxiety and depression. The assessment performed by Beck scale at the 1st and 24th hour.

Results: The final study population consisted of 42 patients hospitalized with heart failure. Mean patient age was 67.5 ± 12.6 years. Average EF was 23.5% ± 8.7% and mean ProBNP was 6343.76 pg/mL in our study population. Changes of before and after dopamine treatment in depression score of heart failure patients was showed significantly (before value: 18.95 ± 9.89; after value: 17.29 ± 10.30, $p < 0.001$) however systolic and diastolic pressure difference was not significant.

Conclusion: Depression increased mortality and hospitalization in patients with heart failure. Therefore, it is an essential trial because of low-dose dopamine improve depression score in intensive care patients. However, prospective studies were needed to assess the long-term efficacy of dopamine.

Keywords: low dose dopamine, depression, Beck depression-anxiety scale, heart failure

Received: January 10, 2018; Accepted: June 1, 2018; Published Online: June 6, 2018

Symptoms of depression are common morbidity, affecting roughly 40% of patients with heart failure (HF) and are related to a reduced living standard [1-3]. Symptoms of depression have negative impacts not only on daily social and domestic activities but also on hospitalizations and mortality rates in HF patients [4]. Depressive symptoms contain depressed mood, guilt, hopelessness, low self-esteem, fatigue, sleep disturbances, appetite change, and inability to concentrate [5]. They measure by self-report instruments for these symptoms are subjective(for example Beck depression-anxiety scale) [6]. Previous studies have ensured evidence about the epidemiology factors, and results of depressive symptoms in patients with HF [5, 7]. However, our understanding of the patients with HF in the hospital and how to treat is not clear.

Dopamine and other inotropes have been in use for many years for the treatment of patients with acute decompensated systolic heart failure, known as heart failure with reduced left ventricular ejection fraction (HFrEF) too. Inotropic agents improve the contractility of the myocardium but can impress the peripheral vascular resistance and heart rate too.The

Address for correspondence: *Tarık Kıvrak, MD., Fırat University School of Medicine, Department of Cardiology, Elazığ, Turkey*
E-mail: tarikkivrak@gmail.com

e-ISSN: 2149-3189

most prevalent use of inotropes is amongst hospitalized patients with HFwith signs of end-organ dysfunction because of low cardiac output. Inotropic drugs can be used in patients with advanced systolic heart failure awaiting heart transplant to resume hemodynamic stability, or as a bridge to a decision. Dopamine is primarily an inotropic agent that has additive effect on renal blood flow(1 to 5 mcg/kg/min), additive effect on cardiac output and contractility(5 to 10 mcg/kg/min) and Alfa adrenergic effect(> 10 mcg/kg/min). This study aimed to determine the effect of renal dose dopamine on depression in HF patients using Beck Depression scale. We know that dysfunction of dopaminergic system is related to depression; however, dopamine cannot pass through the blood-brain barrier.

METHODS

Patients with a history of chronic HF-based on left ventricular systolic dysfunction with moderate to severe HF symptoms (class III or IV) included in the study. All patients were undergoing standard therapy for HF. Inclusion in the study required the simultaneous presence of the following criteria: Age > 18 years, history of HF, deterioration of HF symptoms of recent onset (< 6 hours), namely, dyspnea at rest, orthopnea, and paroxysmal nocturnal dyspnea, accompanied by signs of congestion (third heart sound, jugular venous distension, pulmonary rales) on physical examination, levels of serum B-type natriuretic peptide (BNP) > 400 pg/mL or N-terminal proBNP > 1,500 pg/ml .Patients excluded from the study if they had: Acute de novo HF, severe renal failure (admission serum creatinine > 215 mmol/L [2.5 mg/dL] or estimated GFR < 30 mL, 1.73 m2), admission systolic blood pressure < 90 mm Hg, severe valvular disease, known adverse reactions to furosemide or dopamine, HF secondary to congenital heart disease, a scheduled procedure with a need for IV contrast dye in the present hospitalization, a scheduled cardiac surgery within 2 months. The total number of patients was 50. However, 42 patients fulfilled all inclusion criteria and enrolled in the study. Before enrollment, each of the patients gave informed consent according to the local institutional ethical guidelines. On the patient's arrival at the emergency department, hemodynamic parameters (systemic systolic and diastolic blood pressure, heart rate, and

Table 1. Demographic characteristics of patients

Characteristics	HF patients (n=43)
Age (years)	67.5 ± 12.6
Sex (male)	34 (80%)
CAD	30 (70%)
DM	12 (28%)
HT	26 (60%)
HL	18 (42%)
EF (%)	23.5 ± 8.7
LVEDD (mm)	62.0 ± 6.2
LVESD (mm)	53.0 ± 9.9
LAA (cm²)	28.6±4.5
RAA (cm²)	27.9±2.9
Systolic/diastolic blood pressure (mmHg)	115/70
Total diuretic dose (mg)	151.43 ± 33.97

Data are presented as mean ± standard deviation or number (%) of the patient. CAD = coronary artery disease, DM = diabetes mellitus, HT = hypertension, EF = ejection fraction, LVEDD = left ventricle end-diastolic diameter, LVESD = left ventricle end systolic diameter, LAA = left atrial area, RAA = right atrial area, HF = heart failure

Table 2. Laboratory findings of patients

Parameters	Minimum	Maximum	Mean value	SD
Hb (g/dL)	8.20	14.80	12.5	1.55
BUN (mg/dL)	12.10	41.10	22.6	7.50331
Cr (mg/dL)	0.58	1.71	1.05	0.29383
Na (mEq/L)	128.00	143.00	137.71	3.67115
K (mEq/L)	3.50	5.19	4.33	0.45277
ProBNP (pg/mL)	908	21000	6343.76	5580.909
CRP (mg/dL)	0.01	5.09	1.10	1.10181
Uric acid (mg/dL)	4.00	9.90	6.61	1.74783
Ferritin (ng/mL)	11	179	69.33	46.156
Troponin I (ng/mL)	0.01	0.21	0.0233	0.04309

Hb = hemoglobin, BUN = blood urea nitrogen, Cr = creatinine, Na = sodium, K = potassium, CRP = C-reactive protein

respiratory rate) measured, intravenous access established, venous samples took for blood gas, electrolyte, and cardiac enzyme estimations and baseline clinical, echocardiographic parameters assessed. The initial therapeutic approach consisted of IV furosemide infusion for all patients and a continuous IV infusion of 3 mcg/kg/min dopamine.

Statistical Analysis

Continuous variables are expressed as mean ± 1 SD, and categoric variables are expressed as proportions. Study group characteristics compared with the Mann-Whitney test (continuous variables) and the Fisher exact test (categoric variables). Repeated values evaluated with the nonparametric Wilcoxon signed rank test. Statistical significance set at a P-value of < 0.05. All statistical analyses were performed using SPSS version 17.0 for Windows (SPSS, Chicago, IL).

RESULTS

The final study population consisted of 42 patients hospitalized with heart failure. We assessed patient characteristics. Mean patient age was 67.5 ± 12.6 years. The most common comorbidities included hypertension (n = 26), coronary atherosclerosis (n = 30), disorders of lipid metabolism (n = 18), and diabetes without complications (n = 12).The demographic characteristics and baseline laboratory findings of the study population presented in Tables 1 and 2. Admission systolic and diastolic blood pressure was 115/70 mmHg. Total diuretic dose was 151.43 ± 33.97 mg. Average EF was 23.5% ± 8.7% and mean ProBNP was 6343.76 pg/mL in our study population. Current medications for heart failure patients presented in Table 3. Changes in depression score of HF patients before and after dopamine treatment was showed significantly (before value: 18.95 ± 9.89; after

Table 3. Current medications for heart failure patients

Group of drugs	Data n (%
Diuretics	40 (71.4)
Furosemide	30 (71.4)
Spironolactone	16 (38.1)
Spiranolacton+Hydrochlorotiazid	4 (9.5)
ASA+Klopidogrel	24 (57.1)
Statin	8 (19)
ACEI	6 (14.3)
ARB	10 (23.8)
Beta-blocker	16 (38.1)
Digoxin	6 (14.3)
Nitrates	8 (19)
Warfarin	2 (4.8)
Ivabradine	4 (9.5)
Trimetazidine	12 (28.6)

ASA = acetylsalicylic acid, ACEI = angiotensin converting enzyme inhibitors, ARB = angiotensin receptor blockers

Table 4. Changes in parameters of HF patients before and after dopamine treatment

	Before	After	*P* value
Depression score	18.95 ± 9.89	17.29 ± 10.30	**< 0.001***
Systolic blood pressure (mmHg)	115 ± 20	117 ± 17	0.342
Diastolic blood pressure (mmHg)	70 ± 11	69 ± 10	0.279

Table 5. Comparison of parameters in groups that decreased and not changed depression score

Parameters	Decreased group (n = 32) Mean rank	Not changed group (n = 10) Mean rank	*p* value
Ages	22.63	17.90	0.286
ProBNP	23.00	16.70	0.156
BUN	18.75	30.30	**0.009**
Cr	20.31	25.30	0.261
NA	21.50	21.50	1.000
K	21.25	22.30	0.813
Hb	21.06	22.90	0.678
EF	18.88	29.90	**0.010***
LVEDD	18.88	29.90	0.311
LVESD	22.81	17.30	0.213
RAA	19.19	28.90	**0.027**
LAA	19.38	28.30	**0.043**
Total diuretic dose	21.81	20.50	0.758
SBP	19.31	28.50	**0.032**
DBP	19.69	27.30	0.071

EF = ejection fraction, LVEDD = left ventricle end-diastolic diameter, LVESD = left ventricle end-systolic diameter, LAA = left the atrial area, RAA = right atrial area, Hb = hemoglobin, BUN = blood urea nitrogen, Cr = creatinine, Na = sodium, K = potassium, CRP = C-reactive protein, SBP = systolic blood pressure, DBP = diastolic blood pressure

value: 17.29 ± 10.30, $p < 0.001$) however systolic and diastolic pressure was not significant (Table 4). Comparison of parameters in groups that decreased and not changed depression score presented in Table 5.

DISCUSSION

The results showed that low-dose dopamine associated with a significant reduction in depressive symptoms, and its anti-depressive effect influenced by EF and systolic blood pressure [8]. To our knowledge, this is the first trials to evaluate the effects of low-dose dopamine on symptoms of depression in HF patients in the hospital. Depression has been shown to be a risk factor for poor outcomes amongst heart disease patients. In a study of 1300 patients, 10.0% had a depression diagnosis in patients with cardiovascular disease [9]. Another study showed that enhanced depressive symptoms estimated long-term mortality in patients with heart failure [10]. In another famous trial, depression was found to be a powerful predictor of repeated hospitalizations for HF [11]. In the trial, depressed patients, by comparison, nondepressed, were hospitalized for HF 1.45 times more often, suggesting screening for depression early in the course of HF management. Patients with HF and depressive

symptoms commonly suffer from more reduced quality of life, declining functional status, more significant symptom burden, poorer adherence, more frequent rehospitalizations, and worse survival [12-14].

The effect of dopamine on depression is not known in heart failure patients. Dopamine is a catecholamine, and its effects are dose-dependent in patients with cardiogenic shock. At low doses (< 3 μg/kg/min), dopamine causes vasodilation in the body vasculature including the coronary and renal arteries [15]. Low-dose dopamine (< 5 μg/kg/min), widely combined with furosemide, is increased renal vasodilatation and blood flow, reduce the effects of norepinephrine and aldosterone, and promote natriuresis via effects on dopamine-1 and two receptors [16]. A critical study concluded that low-dose dopamine could worsen renal perfusion in patients with acute renal failure, supporting a trend to desert the routine use of low-dose dopamine in critically ill patients [17]. However, other studies challenge this conclusion. The Dopamine in Acute Decompensated Heart Failure (DADHF) Trial found that the combination of low-dose furosemide and low-dose dopamine is equally effective as high dose furosemide and associate with improved renal function and potassium homeostasis, as well [18].

Entry of dopamine into the brain is regulated by endothelial cells at the blood-brain barrier. Moreover, vascular smooth muscle contraction is controlled to a substantial degree by dopamine D1 receptors [19]. At dopamine treatment doses, dopamine binding to vasculature receptors is likely to result in vasodilation and local blood flow increases [20]. Thus, it is tempting to speculate that dopamine treatment leads to the development of microvascular changes such as angiogenesis, which under particular circumstances, can enhance the transport of the drug across the blood-brain barrier. Indeed, the autoradiographic data suggest that enhanced blood-brain barrier permeability, as well as concomitant increases in local cerebral blood flow, are dopamine-dependent phenomena that are not present in the off-state. We think that antidepressive effect can originate from these physiologic alterations. Physiological effects may be substantial mechanism into the explanation of antidepressive effect, in that depression has been linked to raised sympathetic activity, hypercoagulability, enhanced inflammation, endothelial dysfunction, and decreased heart rate variability, each of which has been associated with adverse clinical outcomes in patients with HF [21]. Additionally, all of the above factors may be improved significantly by the antidepressant effect of dopamine.

Limitations

Our trial has some limitations. Firstly, the patient population should be increased. An imaging method can be used to evaluate brain blood flow.

CONCLUSION

Low-dose dopamine treatment was associated with a demonstrable benefit in the symptoms of depression in clinically unstable HF patients. Large-scale, high-quality RCTs are needed to verify the benefits of exercise training in those populations. The evidence confirmed here should encourage physicians to recommend low-dose dopamine as a clinically substantial way to diminish the symptoms of depression in patients with HF.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] Rutledge T, Reis VA, Linke SE, Greenberg BH, Mills PJ. Depression in heart failure a meta-analytic review of prevalence, intervention effects, and associations with clinical outcomes. J Am Coll Cardiol 2006;48:1527-37.

[2] Sherwood A, Blumenthal JA, Hinderliter AL, Koch GG, Adams KF Jr, Dupree CS, et al. Worsening depressive symptoms are associated with adverse clinical outcomes in patients with heart failure. J Am Coll Cardiol 20 11;57:418-23.

[3] Lehman-Leegte I, van Veldhuisen DJ, Hillege HL, Moser D, Sanderman R, Jaarsma T. Depressive symptoms and outcomes in patients with heart failure: data from the COACH study. Eur J Heart Fail 2009;11:1202-7.

[4] Moraska AR, Chamberlain AM, Shah ND, Vickers KS, Rummans TA, Dunlay SM, et al. Depression, healthcare utilization, and death in heart failure: a community study. Circ Heart Fail 20 13;6:387-94.

[5] Gnanasekaran G. Epidemiology of depression in heart failure. Heart

Fail Clin 2011;7:1-10.
[6] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Washington, DC: American Psychiatric Association; 1994.
[7] Allman E, Berry D, Nasir L. Depression and coping in heart failure patients: a review of the literature. J Cardiovasc Nurs 2009;24:106-17.
[8] Pitt B, Deldin PJ. Depression and cardiovascular disease: have a happy day e just smile! Eur Heart J 2010;31:1036-7.
[9] May HT, Horne BD, Carlquist JF, Sheng X, Joy E, Catinella AP. Depression after coronary artery disease is associated with heart failure. J Am Coll Cardiol 2009;53:1440-7.
[10] Frasure-Smith N, Lespérance F, Habra M, Talajic M, Khairy P, Dorian P, et al. Elevated depression symptoms predict long-term cardiovascular mortality in patients with atrial fibrillation and heart failure. Circulation 2009;120:134-40.
[11] Johnson TJ, Basu S, Pisani BA, Avery EF, Mendez JC, Calvin JE Jr, et al. Depression predicts repeated heart failure hospitalizations. J Card Fail 2012;18:246-52.
[12] Newhouse A, Jiang W. Heart failure, and depression. Heart Fail Clin 2014;10:295-304.
[13] Sullivan M, Levy WC, Russo JE, Spertus JA. Depression and health status in patients with advanced heart failure: a prospective study in tertiary care. J Card Fail 2004;10:390-6.
[14] Sullivan M, Simon G, Spertus J, Russo J. Depression-related costs in heart failure care. Arch Intern Med 2002;162:1860-6.
[15] Cuffe MS, Califf RM, Adams KF Jr, Benza R, Bourge R, Colucci WS, et al; Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF) Investigators. Short-term intravenous milrinone for acute exacerbation of chronic heart failure: a randomized controlled trial. JAMA 2002;287:1541-7.
[16] Teerlink JR, Clarke CP, Saikali KG, Lee JH, Chen MM, Escandon RD, et al. Dose-dependent augmentation of systolic cardiac function with the selective cardiac myosin activator, omecamtiv mecarbil: a first-in-man study. Lancet 2011;378:667-75.
[17] Gheorghiade M, St Clair J, St Clair C, Beller GA. Hemodynamic effects of intravenous digoxin in patients with severe heart failure initially treated with diuretics and vasodilators. J Am Coll Cardiol 1987;9:849-57.
[18] Gheorghiade M, Braunwald E. Reconsidering the role of digoxin in the management of acute heart failure syndromes. JAMA 2009;302:2146-7.
[19] Sherwood A, Blumenthal JA, Trivedi R, Johnson KS, O'Connor CM, Adams KF Jr, et al. Relationship of depression to death or hospitalization in patients with heart failure. Arch Intern Med 2007;167:367-73.
[20] Krimer LS, Muly EC 3rd, Williams GV, Goldman-Rakic PS. Dopaminergic regulation of cerebral cortical microcirculation. Nat Neurosci 1998;1:286-9.
[21] Iadecola C. Neurogenic control of the cerebral microcirculation: is dopamine minding the store? Nat Neurosci 1998;1:263-5.

The European Research Journal 2019;5(3):467-472 ORIGINAL ARTICLE

Obesity frequency and related risk factors in primary school children

Cüneyt Ardıç, Esma Omar

Department of Family Medicine, Recep Tayyip Erdoğan University School of Medicine, Rize, Turkey

DOI: 10.18621/eurj.395207

ABSTRACT

Objectives: The aim of this study was to determine the obesity and overweight situations and related factors among the children between the ages of 6-11 studying in Rize, Turkey.

Methods: The study included 180 pediatric patients (86 girls and 94 boys) applying to our policlinic, who born between 2006 and 2010. The age, height, weight and gender of children and their parents, physical activity status of children, frequency of convenience goods consumption, education and income status of parents and duration of children spent on television were evaluated. Body mass indexes of participants were measured and compared with their socio-demographic characteristics.

Results: Obesity was found in 12.2% and overweight was found in 15% of all students participating the study. While a relation was found between being obese or overweight with gender, body mass index of parents, staying more than 2 hours a day in front of television, fast-food consumption and low physicial activity; no relation could be found between the educational status of parents, time of starting supplementary food during infancy and and the duration of total breastfeeding.

Conclusions: The increase in frequency of childhood obesity has been particularly important for identifying risk factors associated with obesity and competing with these factors in the early period. Family physicians, the first contact points of the patients, are the most important part of the health system in preventing childhood obesity. A higher prevalence of childhood obesity than other studies in the literature may indicate that obesity will become an increasingly common problem.

Keywords: .Obesity, pediatric, body mass index

Received: February 15, 2018; Accepted: June 5, 2018; Published Online: June 14, 2018

The World Health Organization (WHO) has characterized obesity as a global epidemic [1]. WHO now estimates that 42 million children under the age of 5 are obese [2]. Obesity is the result of complex interaction of cultural, social, genetic, physiological, behavioral and psychological factors [3].

Childhood obesity is a health problem that should be taken into consideration due to its progression as adult obesity, serious increase of morbidity and mortality, and most importantly, and being mostly preventable [4, 5]. It is known that the onset of obesity in the majority of adults extends to childhood [6, 7]. Both genetic and environmental factors such as inheritance, gender, ethnicity, sedentary lifestyle and low physical activity are responsible for obesity [8-

Address for correspondence: *Cüneyt Ardıç, MD., Recep Tayyip Erdoğan University School of Medicine, Department of Family Medicine, Rize, Turkey*
E-mail: drcuneytardic@hotmail.com

e-ISSN: 2149-3189

11].

Overweight and obesity in childhood can affect by genetic factors, environmental factors and psychological factors. The overweight or genetic predisposition of parents increases the likelihood that the child is obese [12]. Sedentary lifestyle including watching television, spending long time with computer and mobile phone, lack of time for physicial activities and games, and consumption of fast food, sugary and fatty food and beverages play an important role in obesity. In addition, problems of the children with their parents and friends, failures in their lessons and other psychological problems during puberty also affect the development of obesity [13, 14].

With this study, it was aimed to determine the level of excess weight and obesity prevalence in primary school students in Rize city center and to determine some factors that may affect this situation.

METHODS

Study Group

The study is an epidemiological study aimed at finding cross-sectional prevalence. A total of 180 pediatric patients at primary school born between 2006 and 2010 were included applying to the Family Medicine policlinic of Recep Tayyip Erdoğan University. The questionnaires given to the study groups were requested to be completed by their parents.

Measurements

Height measurement was made using a measuring tape mounted on wall. The students were made to take their shoes out and their height was measured from the head to the base in a position where the feet were ready to touch each other, back of the head, hip and heels were touching to a flat wall. The weight was removed by removing students' heavy clothes and feet. Portable bench scale sensitive to 100 grams was used. The weight recorded in kilograms was divided by the square of height (in meters) to calculate body mass index of the students. Body mass index (BMI) values were compared with the reference range of National Center of Health Statistics (NCHS), over the 85th percentile was regarded as overweight and over the 95th percentile was regarded as obesity.

Collecting data

Questionnaires were filled with students and their parents by talking face to face. Information on students' daytime activity or eating habits was recorded according to their parents' views.

The study was conducted in accordance with the Helsinki Declaration principles. Institutional ethical committee approval was obtained. Verbal approval was obtained from the students and their parents before questionnaire forms were applied.

Statistical Analysis

SPSS (Statistical Package for Social Sciences) for Windows 20.0 program was used for statistical analysis during the evaluation of findings obtained by the study. Besides descriptive statistical methods (mean, median, standard deviation) while evaluating study data, student t test was used for comparison of parameters with normal distribution and Mann-Whitney U test was used for comparison of parameters without normal distribution. Pearson's correlation was used to investigate the correlations between variables. Statistical significance was defined as a level of 5% ($p < 0.05$).

RESULTS

Having analyzed BMI values using reference table of the World Health Organization, obesity was found in 12.2% and overweight was found in 15% of all students participating in the study. The proportion of obese girl students was 10.4% and obese boy students was 13.8%. Prevalence of overweight was 12.79% in girls and 17.02% in boys. The prevalence of obesity and overweight in boy students was significantly higher than that of girl students (Table 1).

Table 1. Percentage of BMI by sex

BMI (%)	Girl	Boy
< 5	4 (4.65%)	3 (3.19%)
5-84	62 (72.09%)	62 (65.95%)
85-94	11 (12.79%)	16 (17.02%)
≥ 95	9 (10.4%)	13 (13.8%)
Total	86 (100%)	94 (100%)

Data are shown as number (%). BMI = body mass index

Table 2. Sociodemographic characteristics of obese or overweight children and normal or thin children

Characteristics		Normal or thin children	Obese or overweight children	*p* value
Gender	Boy	65 (49.6%)	32 (65.3%)	**0.023**
	Girl	66 (50.4%)	17 (34.7%)	
Educational status of mother	Primary-secondary	95 (72.5%)	37 (75.5%)	0.698
	High school-university	36 (27.5%)	12 (24.5%)	
Educational status of father	Primary-secondary	71 (54.2%)	30 (61.2%)	0.712
	High school-university	60 (45.8%)	19 (38.8%)	
Time spent for watching tv	More than 2 hours a day	54 (41.2%)	32 (65.3%)	**0.022**
	Less than 2 hours a fay	77 (58.8%)	17 (34.7%)	
Consumption of convenience food	Twice or more in a week	43 (32.8%)	36 (73.4%)	**0.015**
	Less than twice in a week	88 (67.2%)	13 (26.6%)	
Start of supplementary food	After 6 months	62 (47.3%)	26 (53.1%)	0.778
	Before 6 months	69 (52.7%)	23 (46.9%)	
How many days does s/he exercise regularly	2 days or more	89 (67.3%)	13 (26.6%)	0.041
	Less than 2 days	42 (32.7%)	36 (73.4%)	

Data are shown as number (%).

Of the 180 children included in the study, 47.7% (n = 86) were girls and 52.3% (n = 94) were boys. Students were in the age range of 6-11 and the average age was 10.82 ± 2.49. Fifty-six point one percent of the fathers were graduate of primary school, 22% were graduate of high school and 21.9% were university graduates. Seventy-three point three percent of the fathers were graduate of primary school, 15% were graduate of high school and 11.7% were university graduates. Students had 2.01 brothers or sisters at average, total 4.9 people were living at home, watching television for 2.2 hours at average; 72% of

Table 3. Distribution of parents according to BMI averages

	Obese or overweight n = 49	Non-obese n = 131	t	*p* value
Mother BMI (kg/m²)	28.36 ± 4.29	26.94 ± 4.24	2.66	**< 0.01**
Father BMI (kg/m²)	28.02 ± 5.11	25.89 ± 3.39	3.57	**< 0.001**

Data are shown as mean±standard deviation. BMI = body mass index

which had breastfed more than 18 months and 78% started supplementary food after the 6th month.

The relation of sociodemographic and socioeconomic variables with obesity and overweight was investigated. There was no relationship between parents' educational level and obesity and overweight. ($p > 0.05$) The percentage of obese or overweight children who spent more than 2 hours per day on television was 65.3%, while this rate was 34.7% in those with normal or less weight. Significant relationship was found between TV watching time and obesity. ($p < 0.05$) (Table 2).

While there was no significant difference between obese and overweight persons and non-obese persons in terms of delivery weight and time to start supplementary food, obesity was more prevalent among the ones who consume more convenience food ($p < 0.05$).

BMI of both mothers and fathers of the overweight and obese students were significantly higher than parents of the students with normal weight (Table 3).

DISCUSSION

Retrospective studies have shown that adult obesity started in childhood or adolescence in proportion of 1/3. Obesity problem in children should be emphasized. Studies indicated that problem will become serious in the near future if necessary measurements are not taken [15].

Childhood obesity has been increasing at an alarming rate for the last ten years. WHO estimates that 42 million children under the age of 5 are currently obese [16]. Although there is information that obesity is the problem of developed countries until today, there has been an increase in developing countries in recent years [17]. In our country, “Turkey Healthy Nutrition and Active Life Program" which was prepared with the participation of Ministry of Health and various stakeholders and published in 2010 and put into practise in various factors is a program to prevent obesity in Turkey [18]. In comparison with other studies conducted in Turkey, we found a higher prevalence of obesity in our study. For example, in a study conducted in Muğla, of the total 4260 (2040 girls, 2220 boys) of 6-15 year old, 7.6% of the girls and 9.1% of the boys were found to be obese or overweight [19]. In our study, we found the prevalence of excess weight in the primary school students to be 15% and the obesity rate to be 12.2%. This situation can be explained by the fact that parents of the children included in the study have more weights than the normal population and the obesity frequency increases day by day. We found that overweight and obesity rates were 37.3% and 23.8%, respectively. In the overall health research carried out in Turkey in 2014, overweight rate was found to be 33.7% and obesity rate was 19.9% [20]. Parental obesity is seen as one of the most important risk factors for childhood obesity. Children whose parents are obese are 2.5 times more likely to be obese than those who are thinner [21].

In order to prevent obesity, it is important that children do not spend more than 2 hours per day in front of television and computer in the direction of recommendation stated in the study by Metinoğlu *et al*. [22] and by the American Academy [23-25]. It is stated in the studies that obesity risk increases in the children who watch TV for a long time [23-25]. It is associated with being completely passive-inactive, watching food-related advertisements and increase of energy intake accordingly while watching television [26-29]. In this study, the duration of television watching in the obese group was longer than the control group and was identified as a risk factor increasing the obesity, in accordance with the literature.

In a study carried out in Mexico, it was found that every one hour of moderate physical activity per day reduced the risk of obesity in children by 10% [30]. Increasing rates of obesity in children with low activity are also shown in various studies [31, 32]. We also found in our study that obesity prevalence in children who regularly exercise for at least 2 days a week was significantly less than those who do not exercise ($p <0.05$).

Eating fastly and chewing less thereby are indicated as another factor facilitating the development of obesity [33]. Fast-food style eating habits is the most important factor. In our study, obesity prevalence was significantly higher in the children of families who responded to the question ‘does your child prefer fast food?’ as at least twice a week and more.

Limitations

There are some limitations in our study. Firstly, since there is usually only one parent with children who are admitted to polyclinics, the measurement of height and weight of the other parent could not be made and their statement was accepted. Moreover, parents who have been informed about the study beforehand might have responsed to the questions unfairly.

CONCLUSION

In the light of these results, it can be indicated that primary school children whose parents have obesity, who have less physical activity and serious fast-food eating habits face the risk of obesity. In the fight against obesity, which has become an important issue of the preventive medicine in particular, it is important that lifestyle changes are adopted as the main subject of primary protection before diseases come out and since from the childhood.

It is also a positive step to address obesity as a priority issue and to take measurements for preventing childhood obesity in particular in order to prevent adult obesity and many chronic diseases within the scope of the national health policy.

Authorship declaration

All authors listed meet the authorship criteria according to the latest guidelines of the International Committee of Medical Journal Editors, and all authors are in agreement with the manuscript.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] WHO: Obesity Preventing And Managing The Global Epidemic. Report of a WHO Concultation. WHO Technical Report Series 894. Geneva: World Health Organization, 2000.
[2] World Health Organization. World health statistics 2015. World Health Organization, 2015.
[3] Williams EP, Mesidor M, Winters K, Dubbert PM, Wyatt SB. Overweight and obesity: prevalence, consequences, and causes of a growing public health problem. Curr Obes Rep 2015;4,:363-70.
[4] Eke, Petronilla. Evaluating the impact of evidence-based weight reduction program among the obese at a medical facility in North Central United States. Diss. Walden University, 2017.
[5] Misra A, Khurana L. Obesity and the metabolic syndrome in developing countries. J Clin Endocrinol Metab 2008:93(11 Suppl 1):S9-30.
[6] Pulkki-Råback L, Elovainio M, Kivimäki M, Raitakari OT, Keltikangas-Järvinen L. Temperament in childhood predicts body mass in adulthood: the Cardiovascular Risk in Young Finns Study. Health Psychol 2005;24:307-15.
[7] Zitsman, JL, Inge TH, Reichard KW, Browne AF, Harmon CM, Michalsky MP. Pediatric and adolescent obesity: management, options for surgery, and outcomes. J Pediatr Surg 2014;49:491-4.
[8] Taveras EM, Gillman MW, Kleinman KP, Rich-Edwards JW, Rifas-Shiman SL. Reducing racial/ethnic disparities in childhood obesity: the role of early life risk factors. JAMA Pediatr 2013;167:731-8.
[9] Liu JH, Jones SJ, Sun H, Probst JC, Merchant AT, Cavicchia P. Diet, physical activity, and sedentary behaviors as risk factors for childhood obesity: an urban and rural comparison. Child Obes 2012;8:440-8.
[10] Güven A, Odaci H, Ozgen IT, Bek Y. Effects of individual factors on adolescent obesity: study in Turkey. Pediatr Int 2008;50:356-62.
[11] Kelishadi R, Poursafa P. A review on the genetic, environmental, and lifestyle aspects of the early-life origins of cardiovascular disease. Curr Probl Pediatr Adolesc Health Care 2014;44:54-72.
[12] Vicente-Rodríguez G, Rey-López JP, Martín-Matillas M, Moreno LA, Wärnberg J, Redondo C, et al. Television watching, videogames, and excess of body fat in Spanish adolescents: the AVENA study. Nutrition 2008;24:654-62.
[13] Larsen L, Mandleco B, Williams M, Tiedeman M. Childhood obesity: prevention practices of nurse practitioners. J Am Acad Nurse Pract 2006;18:70-9.
[14] Giammattei J, Blix G, Marshak HH, Wollitzer AO, Pettitt DJ. Television watching and soft drink consumption: associations with obesity in 11- to 13-year-old schoolchildren. Arch Pediatr Adolesc Med 2003;157:882-6.
[15] Spear BA, Barlow SE, Ervin C, Ludwig DS, Saelens BE, Schetzina KE, Taveras EM. Recommendations for treatment of child and adolescent overweight and obesity. Pediatrics 2007;120(Supplement 4):254-88.
[16] World Health Organization. Obesity and overweight. http://www.who.int/mediacentre/factsheets/fs311/en/.
[17] Delpeuch F, Maire B. Obesity and developing countries of the South. Med Trop l997;57:380-8.
[18] T.C. Sağlık Bakanlığı, Türkiye sağlıklı beslenme ve hareketli hayat programı [2010-2014], Ankara. www.beslenme. saglik.gov.tr
[19] Weker H, Baranska M. Models of safe nutrition of children and adolescents as a basis for prevention of obesity. Med Wieku Rozwoj 2011;15:288-97.
[20] TÜİK, Türkiye Sağlık Araştırması, 2014.
[21] Bice H. Potansiyel bir sağlık sorunu: çocukluk döneminde obezite. Türkiye Klinikleri J Med Sci 1989; 9:117-23.
[22] Metinoğlu İ, Pekol S, Metinoğlu Y. [Factors affecting the prevalence of obesity in students between the ages of 10-12 in Kastamonu]. . Acıbadem Üniversitesi Sağlık Bilimleri Dergisi 2012;3:117-23. [Article in Turkish]
[23] Andersen RE, Crespo CJ, Bartlett SJ, Cheskin LJ, Pratt M. Relationship of physical activity and television watching with body weight and level of fatness among children: results from the Third National Health and Nutrition Examination Survey. JAMA l998;279:938-42.

[24] Andersen RE. The spread of the childhood obesity epidemic. CMAJ 2000;l63:l46l-2.
[25] The Parliamentary Office of Science and Technology, Childhood obesity. Postnote September 2003 Number 205. www.parliament.uk/post.
[26] Epstein LH, Paluch RA, Consalvi A, RiordanK, Scholl T. Effects of manipulating sedentary behavior on physical activity and food intake. J Pediatr 2002;140:334-9.
[27] Kotz K, Story M. Food advertisements during children's Saturday morning television programming: are they consistent with dietary recommendations? J Am Diet Assoc l994;64:l296-l300.
[28] Robinson TN. Does television cause childhood obesity? JAMA l998;279:959-60.
[29] Saelens BE, Daniels SR. Childhood obesity: causes and therapies. Curr Opin Endocrinol Diabetes Obes 2003;l0:3-8.
[30] Para-Cabrera S. Association of obesity with physical activity, television programs and other forms of video viewing among children in Mexico City. Int J Obesity 1999;23:845-54.
[31] Amigo H, Bustos P, Erazo M, Cumsille P, Silva C. Determinant factors of excess of weight in school children: a multilevel study. Rev Med Chil 2007;135:1510-8.
[32] Wang Y, Liang H, Tussing L, Braunschweig C, Caballero B, Flay B. Obesity and related risk factors among low socio-economic status minority students in Chicago. Public Health Nutr 2007;10:927-38.
[33] Cinaz P, Bideci A. Obezite. İçinde: Günöz H, Öcal G, Yordam N, Kurtoğlu S. Pediatrik Endokrinoloji. Ankara. Kalkan Matbaacılık 2003; 487-505.

The European Research Journal 2019;5(3):473-478 ORIGINAL ARTICLE

Comparison of femoral block and adductor canal block in the postoperative analgesia of patients undergoing arthroscopic knee surgery

Evrim Kucur Tülübaş[1], İpek Bostancı[1], Gökhan Sertçakacılar[1], Yaser Pektaş[1], Erdem Edipoğlu[2]

[1]Department of Anesthesiology and Critical Care Medicine, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkey
[2]Department of Orthopedic Surgery, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkey

DOI: 10.18621/eurj.390275

ABSTRACT

Objectives: The aim of the study was to compare adductor canal block and femoral nerve block in the postoperative analgesia of patients undergoing elective arthroscopic knee surgery with respect to opioid use and Visual Analogue Scale (VAS), which is a unidimensional measurement of pain intensity.

Methods: The study was designed and conducted prospectively between April 2016 and November 2016 in a tertiary care hospital but the results were evaluated retrospectively. Prior to the induction of general anesthesia for knee surgery, (the first) 20 consecutive patients underwent femoral nerve block, and (the second) 20 consecutive patients received adductor canal block. Patients receiving adductor canal block for analgesia were referred to as Group A and patients receiving femoral nerve block for analgesia were defined as Group F. Pain was evaluated using the VAS score.The results were compared statistically.

Results: Both the femoral nerve block and adductor canal block groups showed similar results in terms of VAS and opioid use ($p < 0.05$).

Conclusion: In the postoperative analgesia of patients undergoing elective arthroscopic knee surgery, no difference was found between adductor canal block and femoral nerve block in terms of opioid use and VAS scores.

Keywords: adductor canal block, femoral nerve block, visual analogue scale

Received: February 5, 2018; Accepted: March 8, 2018; Published Online: June 10, 2018

Knee arthroscopy is a frequent procedure in orthopedic surgery. Providing effective analgesia after such a procedure is crucial to facilitate early rehabilitation and to reduce the duration of hospitalization [1]. There are several methods to provide analgesia in the postoperative period. Among these methods, peripheral nerve blocks are increasingly being used It has been reported that peripheral nerve blocks cause fewer systemic side effects [1, 2].

The femoral nerve block has been shown to be superior to intra-articular local anesthesia in the postoperative analgesia of patients undergoing knee surgery [3, 4). However, reduced quadriceps muscle strength as a result of motor blockade and the consequent increase in the risk of falls may limit the value of this procedure, especially in minor surgeries [3, 5]. On the other hand, adductor canal block has

Address for correspondence: *Evrim Kucur Tülübaş1, MD., Bakırköy Dr. Sadi Konuk Training and Research Hospital, Department of Anesthesiology and Critical Care Medicine, Zuhuratbaba, Tevfik Sağlam Cad. No:11, 34147 Bakırköy, İstanbul, Turkey*
E-mail: evrim.kucurtulubas@saglik.gov.tr

e-ISSN: 2149-3189

been reported to preserve quadriceps muscle strength better than femoral nerve block [6, 7].

Our aim in this study was to compare adductor canal block and femoral nerve block in the postoperative analgesia of patients undergoing elective arthroscopic knee surgery with respect to opioid use and Visual Analogue Scale (VAS), which is a unidimensional measurement of pain intensity.

METHODS

The study was designed and conducted retrospectively between April 2016 and November 2016 in a tertiary care hospital. Ethical committee approval was obtained before the study, and informed patient consent was taken from all patients. Prior to the induction of general anesthesia for knee surgery, (the first) 20 consecutive patients underwent femoral nerve block, and (the second) 20 consecutive patients received adductor canal block as a complement to a standardized analgesic regimen. Patients between 20 and 60 years of age, who had an ASA score of I-III and who underwent elective surgery were included in the study. Patients with neurological or psychiatric pathologies and patients with BMI > 40 were excluded from the study. Exclusion criteria also included contraindications to peripheral nerve blockade such as infection, bleeding disorders and allergy to the drugs used in thestudy.

Patients receiving adductor canal block for analgesia were referred to as Group A and patients receiving femoral nerve block for analgesia were defined as Group F. Nerve blocks were performed under aseptic conditions using an ultrasound device equipped with a high frequency linear probe (LOGIQE GE Healthcare ultrasound machine, GE Medical Systems, Phoenix - USA).

For femoral nerve block, the femoral artery was located using the in-plane technique, under aseptic conditions. Then, the femoral nerve immediately lateral to the femoral artery was identified and 30 mL of 0.25% bupivacaine was injected around the nerve. For adductor canal block, the probe was placed on the medial part of the mid-thigh, halfway between the anterior spina iliaca superior and the patella. The superficial femoral artery and vein were identified under the sartorius muscle. Using an in-plane technique, the needle was advanced towards the saphenous nerve, which was visualized as a hyperechoic structure located immediately lateral to the superficial femoral artery, and 10 mL 0.25% bupivacaine was injected around the nerve.

After administration of the block, general anesthesia was induced with 2 mg/kg propofol, 2 mg midazolam, 2 µg/kg fentanyl and 0.6 mg/kg rocuronium. During the operation, anesthesia was maintained in all patients with 2% sevoflurane. Adductor canal block and femoral nerve block are used routinely in our clinic.

Postoperative analgesia was provided by peripheral nerve blocks and a standardized analgesic regimen. As routine postoperative analgesia, the patients were given 50 mg iv tramadol and 20 mg/kg acetaminophen every 12 hours. If insufficient, 2 mg morphine was administered as supplementary analgesia. Additional doses of morphine were recorded.

Pain was evaluated using the VAS score. We routinely use this score in our clinic. Patients were asked to rate their pain on a scale of 0-10, with 0 representing "no pain" and 10 representing "worst possible pain". The hemodynamic data were also recorded alongside VAS at the 1st, 6th, 12th, 18th and 24th hours after surgery. The patients were discharged after 24 hours.

Statistical Analysis

Statistical analyses were performed using SPSS version 20 (SPSS Inc., Chicago, Illinois) program. The descriptive data (average, standard deviation, median, frequency, and ratio) and the quantitative data with non-normal distribution were analyzed using the Mann Whitney U test. The Student's t test was used for data with normal distribution. All statistical analyses were performed at a 95% confidence interval. A p-value < 0.05 was considered significant.

RESULTS

The demographic data of the patients are presented in Table 1. There was no demographic difference between the two groups ($p < 0.05$).

During the 24-hour postoperative follow-up, the mean arterial pressure and heart rate were monitored

Table 1. Demographic data

	Group F (n = 20)	Group A (n = 20)	*p* value
Age (year)	40.41 ± 15.31	33.42 ± 12.21	0.183
ASA	2.30 ± 1.65	1.57±0.64	0.129
Duration of surgery (min)	87.14 ± 51.65	99.50 ± 36.70	0.524
Duration of anesthesia (min)	10.81 ± 4.90	12.28 ± 4.17	0.373
Gender (male)	16 (80%)	14 (70%)	0.478

Data are shown as mean±standard deviation or number (%). ASA = American Society of Anaesthesiologists, Group A = patients receiving adductor canal block for analgesia, Group F = patients receiving femoral nerve block for analgesia

and recorded (Table 2), but no statistically significant difference was observed between the groups ($p < 0.05$).

The data on analgesia are presented in Table 3. The VAS scores were recorded at 1, 6, 12, 18, and 24 hours postoperatively. No difference was observed between the two groups in terms of VAS scores ($p < 0.05$). There was no statistically significant difference between the groups in terms of morphine consumption. Both the femoral nerve block and adductor canal block groups showed similar results in terms of VAS scores and opioid consumption.

None of the patients in the two groups experienced any complications of nerve damage due to regional block. Two of the patients in Group A, and one patient in Group F had postoperative nausea and vomiting. These patients received granisetron as antiemetic treatment.

DISCUSSION

In this study, no difference was observed between adductor canal block and femoral nerve block in terms of VAS and opioid consumption in the postoperative analgesia of patients undergoing knee arthroscopy. Our findings are in accordance with theliterature.

It is important to ensure early mobilization and efficient rehabilitation after arthroscopic knee surgery. Uncontrolled pain may hinder mobilization and consequently prolong the rehabilitation period [8]. Previous studies have shown that effective pain control results in better outcomes and decreases the duration of hospitalization [3, 8-10].

Femoral nerve block has been reported to be nearly as effective as epidural block, with fewer opioid-related side effects [8, 11, 12]. In terms of

Table 2. Postoperative hemodynamic data

	Group F (n = 20)	Group A (n = 20)	*p* value
MAP 1st hour (mmHg)	88.38 ± 8.62	87.26 ± 10.84	0.759
MAP 12th hour (mmHg)	85.60 ± 4.64	88.00 ± 5.52	0.163
MAP 24th hour (mmHg)	83.48 ± 6.35	88.92 ± 9.06	0.113
HR 1st hour (beat/min)	71.93 ± 8.91	78.00 ± 8.83	0.061
HR 12th hour (beat/min)	76.15 ± 8.51	76.32 ± 4.67	0.941
HR 24th hour (beat/min)	77.86 ± 6.76	75.31 ± 4.88	0.343

MAP = mean arterial pressure, HR = heart rate, Group A = patients receiving adductor canal block for analgesia, Group F = patients receiving femoral nerve block for analgesia

Table 3. Data on analgesia

	Group F (n = 20)	Group A (n = 20)	*p* value
VAS 1st hour	2.07 ± 2.40	1.50 ± 1.97	0.463*
VAS 6th hour	3.47 ± 2.19	4.24 ± 2.19	0.306*
VAS 12th hour	4.65 ± 2.00	4.22 ± 2.04	0.520*
VAS 18th hour	4.33 ± 2.16	4.73 ± 2.63	0.653*
VAS 24th hour	3.40 ± 2.01	4.50 ± 1.78	0.189*
Total Opioid Consumption 1st hour	2.10 ± 0.14	2.23 ± 0.32	0.574**
Total Opioid Consumption 6th hour	4.10 ± 1.04	3.70 ± 1.22	0.613**
Total Opioid Consumption 12th hour	6.38 ± 3.26	8.25 ± 3.35	0.376**
Total Opioid Consumption 18th hour	12.10 ± 4.76	12.55 ± 5.51	0.898**
Total Opioid Consumption 24th hour	18.57 ± 8.86	16.52 ± 6.98	0.728**

*The Student's t test, **Mann Whitney U. VAS = Visual Analogue Scale, Opioid = amount of morphine used (mg), Group A = patients receiving adductor canal block for analgesia, Group F = patients receiving femoral nerve block for analgesia

showing the efficacy of femoral nerve block, the results of our study comply with a recent study by Moura *et al*. [1], who have stated that femoral nerve block applied under ultrasonography guidance provides longer postoperative analgesia in patients undergoing knee surgery, in correlation to the bupivacaine concentration used.

In a recently conducted randomized controlled trial, adductor canal block was compared to placebo in a series of 50 arthroscopic knee surgery patients, and adductor canal block was found to be an effective method for analgesia following knee arthroscopy [14]. These results are in accordance with our study in terms of showing the effectiveness of adductor canal block. In another study comparing adductor canal block to placebo in patients undergoing arthroscopic medial meniscectomy, the Numerical Rating Scale (NRS) was used to score the pain, and significantly better results were observed in the adductor canal block group [3]. We have not found a significant difference between the two groups seems to support the previous literature suggesting that both methods have similar efficacies. There are studies in literature stating that femoral nerve block and adductor canal block both yieldexcellent results according to scoring systems based onpatient-satisfaction.

Kim *et al*. [13] have conducted a study similar to the present study, in which they compared femoral nerve block with adductor canal block in 93 patients, and they found no difference between the two groups in terms of opioid consumption. Jaeger *et al*. [7] have compared adductor canal block and femoral nerve block in patients undergoing knee arthroplasty. In their 54 patient series, both groups were shown to be similar in terms of opioid consumption [7]. Similarly, in a series of 100 patients undergoing anterior ligament repair, adductor canal block and femoral nerve block were found to be equal in terms of cumulative oral morphine consumption [15]. In the same way as our subjects, Dong *et al*. [16] reported that adductor canal block (ACB) shows no superiority than femoral nerve block (FNB) group regarding muscle strength and pain control. However, Li *et al*. [17] demonstrated that ACB preserved greater quadriceps strength more than FNB with similar pain control. Likewise again, the VAS pain scores were relatively lower in the two

groups compared with baseline, no significant difference was observed in pain relief at any follow-up time between the groups, suggesting both ACB and FNB provided better analgesia without any statistical significance in the last meta analyze [18].

Limitations

Our study has some limitations. Firstly, the data were gathered retrospectively and consecutively. The lack of randomization may lower the value of this study. However, the results were in accordance with the literature. Another limitation in this study is the lack of an objective assessment of the motor blockade in the quadriceps muscle. Thus, this study is unable to contribute to the literature in terms of early patient mobilization.

CONCLUSION

In conclusion, no difference was found between adductor canal block and femoral nerve block in the postoperative analgesia of patients undergoing elective arthroscopic knee surgery with respect to opioid use and VAS, which is a unidimensional measurement of pain intensity.

Authorship declaration

EKT conceived, designed and did statistical analysis & editing of manuscript; EKT, IB, GS, YP & EE did data collection and manuscript writing; and EKT did review and final approval of manuscript.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] Moura EC, de Oliveira Honda CA, Bringel RC, Leal Pda C, FilhoGde J, Sakata RK. Minimum effective concentration of bupivacaine in ultrasound-guided femoral nerve block after arthroscopic knee meniscectomy: a randomized, double-blind, controlled trial. Pain Physician 2016;19:E79-86.

[2] Tantry TP, Muralishankar BG, Hukkery R. Use of a single injection femoral nerve block in the patients of total knee replacement with concomitant epidural analgesia. J Clin Diagn Res 2012;6:1744-48.

[3] Hanson NA, Derby RE, Auyong DB, Salinas FV, Delucca C, Nagy R, et al. Ultrasound-guided adductor canal block for arthroscopic medial meniscectomy: a randomized, double-blind trial. Can J Anaesth 2013;60:874-80.

[4] Iskandar H, Benard A, Ruel-Raymond J, Cochard G, Manaud B. Femoral block provides superior analgesia compared with intraarticular ropivacaine after anterior cruciate ligament reconstruction. Reg Anesth Pain Med 2003;28:29-32.

[5] Muraskin SI, Conrad B, Zheng N, Morey TE, Enneking FK. Falls associated with lower-extremity-nerve blocks: a pilot investigation of mechanisms. Reg Anesth Pain Med 2007;32:67-72.

[6] Grevstad U, Mathiesen O, Lind T, Dahl JB. Effect of adductor canal block on pain in patients with severe pain after total knee arthroplasty: a randomized study with individual patient analysis. Br J Anaesth 2014;112:912-9.

[7] Jæger P, Nielsen ZJ, Henningsen MH, Hilsted KL, Mathiesen O, Dahl JB. Adductorcanal block versus femoral nerve block and quadriceps strength: a randomized, double-blind, placebo-controlled, crossover study in healthy volunteers. Anesthesiology 2013;118:409-15.

[8] Elazab A, Al-zahrani A, Radwan-M, Salama A, Abd-elhady A. Evaluation of the adductor canal block for postoperative pain control and early functional recovery in arthroscopic knee surgery: a systematic review and meta-analysis of randomized trials. Orthop Rheumatol Open Access J 2015;1:555570.

[9] Lundblad M, Forssblad M, Eksborg S, Lönnqvist PA. Ultrasound-guided infrapatellar nerve block for anterior cruciate ligament repair: a prospective, randomised, double- blind, placebo controlled clinical trial. Eur J Anaesthesiol 2011;28:511-8.

[10] Hsu LP, Oh S, Nuber GW, Doty R Jr, Kendall MC, Gryzlo S, Nader A. Nerve block of the infrapatellar branch of the saphenous nerve in knee arthroscopy: a prospective, double-blinded, randomized, placebo controlled trial. J Bone Joint Surg Am 2013;95:1465-72.

[11] Paul JE, Arya A, Hurlburt L, Cheng J, Thabane L, Tidy A, et al. Femoral nerve block improves analgesia outcomes after total knee arthroplasty: a meta-analysis of randomized controlled trials. Anesthesiology 2010;113:1144-62.

[12] Fowler SJ, Symons J, Sabato S, Myles PS. Epidural analgesia compared with peripheral nerve blockade after major knee surgery: a systematic review and meta- analysis of randomized trials. Br J Anaesth 2008;100:154-64.

[13] Kim DH, Lin Y, Goytizolo EA, Kahn RL, Maalouf DB, Manohar A, et al. Adductor canal block versus femoral nerve block for total knee arthroplasty: a prospective, randomized, controlled trial. Anesthesiology 2014;120:540-50.

[14] Espelund M1, Grevstad U, Jaeger P, Hölmich P, KjeldsenL, Mathiesen O, et al. Adductor canal blockade for moderate to severe pain after arthroscopic knee surgery: a randomized controlled trial. Acta Anaesthesiol Scand 2014;58:1220-7.

[15] Abdallah FW, Whelan DB, Chan VW, Prasad GA, Endersby RV, Theodoropolous J, et al. Adductor canal block provides noninferior analgesia, and superior quadriceps strength compared with femoral nerve block in anterior cruciate ligament reconstruction. Anesthesiology 2016;124:1053-64.

[16] Dong CC, Dong SL, He FC. Comparison of adductor canal block and femoral nerve block for postoperative pain in total knee arthroplasty: a systematic review and meta-analysis. Medicine (Baltimore) 2016;95:e2983.

[17] Li D, Ma GG. Analgesic efficacy and quadriceps strength of adductor canal block versus femoral nerve block following total knee

arthroplasty. Knee Surg Sports Traumatol Arthrosc 2016;24:2614-9.
[18] Xing Q, Dai W, Zhao D, Wu J, Huang C, Zhao Y. Adductor canal block with local infiltrative analgesia compared with local infiltrate analgesia for pain control after total knee arthroplasty: a meta-analysis of randomized controlled trials. Medicine (Baltimore) 2017;96:e8103.

The European Research Journal 2019;5(3):479-483 ORIGINAL ARTICLE

How does occupational radiation exposure affect corneal endothelial cell density?

Mehmet Erol Can

Department of Ophthalmology, University of Health Sciences, Bursa Yüksek Ihtisas Traning and Research Hospital, Bursa, Turkey

DOI: 10.18621/eurj.509803

ABSTRACT

Objectives: To evalute the corneal endothelium ofradiology technicians.

Methods: The study included 35 radiology technicians (study group), and 34 healthy individuals as the control group. Central corneal thickness (CCT), Endothelial cell density (ECD), the coefficient of variation (CoV), and the percentage of hexagonal cells (Hexa) were measured using specular microscopy (Konan Medical Inc., Nishinomiya, Japan).

Results: The mean age of the study participants was 35.82 ± 9.34 years in the study group, and 37.82 ± 8.40 years in the control group (p = 0.332). The mean ECD was 2740.63 ± 249.92 cells/mm2 in the study group, and 2828.70 ± 287.40 in the control group (p > 0.05). The mean CoV was 44.34 ± 6.78 % in the study group, and 44.24 ± 4.99 % in the control group (p > 0.05). Hexa was determined as 44.97 ± 7.98% in the study group, and 45.97 ± 7.06% in the control group (p > 0.05). The mean CCT was 511.50 ± 42.52 in the study group, and 514.18 ± 43.55 in the control group (p > 0.05). The mean ECD, CoV, Hexa, and CCTvalues were not statistically significant (p > 0.05).

Conclusion: This study revealed that endothelial cell density, the coefficient of variation, and percentage of hexagonal cells (Hexa) were not statistically different between the radiology technicians and control group. Nevertheless, there is a need for more comprehensive, controlled studies with larger samples.

Keywords: Radiology technicians, endothelial cell density, specular microscope, occupational radiation

Received: January 8, 2019; Accepted: February 19, 2019; Published Online: February 22, 2019

Radiation can be defined as the movement of energythrough space [1]. Visible light, X-rays, gamma-rays, microwaves and radio waves are forms of radiation [1]. X-rays are a type of ionizing radiation which includes two sources; natural background radiation and medical exposure. The Sun (cosmic radiation), the Earth (mostly Radon gas) and from naturally radioactive substances in our body are natural background radiations [2]. Plain films, fluoroscopy and computed tomography are medical exposure radiations [3]. X-rays cross over the body and generate an image on film based on how many X-rays are absorbed and how many pass through [4]. However, X-rays passing through the body can damage the DNA, especially in radiation-sensitive tissues and organs. Lymphoid organs, bone marrow, blood, testes, ovaries, intestines, skin and other organs with epithelial cell lining (cornea, oral cavity, esophagus, rectum, bladder, vagina, uterine cervix, ureters, optic lens, stomach, growing cartilage, fine vasculature, and growing bone

Address for correspondence: *Mehmet Erol Can, MD., University of Health Sciences, Bursa Yüksek Ihtisas Traning and Research Hospital, Mimar Sinan Mahallesi Emniyet Caddesi Polis Okulu Karşısı, Yıldırım, Bursa, Turkey*
E-mail: drm.erolcan@gmail.com, Fax: 0090 0224 295 50 00

e-ISSN: 2149-3189

are radiosensitivity tissues and organs. Mature cartilage or bones, salivary glands, respiratory organs, kidneys, liver, pancreas, thyroid, adrenal and pituitary glands, muscle, brain, and the spinal cord are low radiosensitivity tissues and organs [5].

The cornea is avascular, transparent tissue which is located at the most anterior aspect of the eye [6]. The cornea has 6 layers; corneal epithelium, Bowman's layer, the corneal stroma, Descemet's membrane, Dua layer, and corneal endothelial cells [6, 7]. The corneal epithelium acts as a natural barrier against radiation [8], and although the cornea blocks Ultraviolet C and B, Ultraviolet A can penetrate full thickness cornea [8]. In the electromagnetic spectrum, x-rays are very high frequency waves and carrying higher energy than ultraviolet rays, and therefore, X-rays can cause more cell damage than ultraviolet rays [1].

Corneal specular microscopy is a non-invasive technique used in morphological analysis of the corneal endothelial cell layer [9]. The corneal endothelial cell provides corneal clarity by regulating corneal hydration [10]. Unlike the corneal epithelium, cells have to migrate and change shape to fill endothelial defects, and corneal endothelial cells do not proliferate [10], but decrease with aging.

The main aim of this study was to investigate whether there were any changes in corneal endothelial cell parameters in radiology technicians compared with healthy subjects not exposed to occupational radiation.

METHODS

Study Subjects

This prospective, cross-sectional study investigated 35 radiology technicians and 34 healthy individualsas the control group. The study was performed in accordance with the Declaration of Helsinki. Approval for this human study was granted by the Local Ethics Committee of Bursa Yuksek Ihtisas Training and Research Hospital. All adult participants provided written informed consent to participate in the study.

Examination Protocol and Study Measurements

Each participant underwent a complete ophthalmological assessment, including best-corrected visual acuity (BCVA), slit-lamp biomicroscopy, and intra-ocular pressure (IOP).

Specular microscopy (Konan Medical Inc., Nishinomiya, Japan) was used to measure the corneal endothelial cells. Central corneal thickness (CCT), endothelial cell density (ECD), the coefficient of variation (CoV), and percentage of hexagonal cells (Hexa) were measured using specular microscopy. The right eye of each participant was used for analysis. All measurements were taken by an experienced clinician (M.E.C.).

Exclusion Criteria

Ophthalmic exclusion criteria included patients with any history of orbital disease, a best corrected visual acuity (BCVA) worse than 20/20, a refractive error less than -4 diopters (D) or more than +2 D, intraocular pressure (IOP) readings > 21 mm Hg, a history of uveitis, retinal disease, corneal disease, corneal or intraocular surgery, pregnancy, or any associated systemic disorders that might affect the eyes (e.g., uncontrolled diabetes, hypertension, or connective tissue diseases).

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences software version 20.0 (SPSS Inc., Chicago, IL, USA). Ocular parameter measurements of the right eyes were used for the analyses. For the continuous variables, the data were tested for normality using the Kolmogorov–Smirnov test. The Chi-square test was used to define variations in categorical variables. The Independent t test was used to assess differences in scale variables and Pearson correlation analysis to evaluate correlations between each pair of measurements. All the results were stated as mean ± standard deviation(SD). A value of $p < 0.05$ was considered statistically significant.

RESULTS

Demographic Characteristics

The study group comprised 16 (46%) females and 19 (54%) males, and the control group comprised 22 (65%) females and 12 (35%) males ($p = 0.148$). The mean age was 35.82 ± 9.34 years (range, 22-53 years)

Table 1. Patient demographics and characteristics of each group

	Study group (n = 35)	Control group (n = 34)	*p* value[a]
Age (years)			
Mean ± SD	35.82 ± 9.34	37.82 ± 8.40	0.148
Range	22-53	21-56	
Sex			
Female	16 (46%)	22 (65%)	0.332[b]
Male	19 (54%)	12 (35%)	
Working in radiology (years)			
Mean ± SD	12.56 ± 7.85	NA	
Range	4-24	NA	

NA: Not applicable SD: Standard deviation, [a] Independent Samples t test, [b] Chi-square test.

in the study group and 37.82 ± 8.40 years (range, 21-56 years) in the control group ($p = 0.332$).

The mean values of age, age gender distribution, and working in radiology (years) in the study group and the control group are summarized in Table 1.

Results of Corneal Specular Microscopy

The mean ECD was 2740.63 ± 249.92 in the study group, and 2826.70 ± 287.40 in the control group ($p > 0.05$). The mean CoV was 44.34 ± 6.78 in the study group, and 44.24 ± 4.99 in the control group ($p > 0.05$). The mean Hexa was 44.97 ± 7.98 in the study group, and 45.97 ± 7.06 in the control group ($p > 0.05$). The mean CCT was 511.40 ± 42.52in the study group, and 514.18 ± 43.55 in the control group ($p > 0.05$). The corneal specular microscopy measurements of both the control and study groups are summarized in Table 2. The ECD, CoV, Hexa, and CCT values were not correlated with the time working in radiology (years) in the study group ($p > 0.05$).

DISCUSSION

In this study, the corneal cell features of the eye were evaluated in radiology technicians. The results demonstrated no difference between radiology technicians and the healthy control group in respect of ECD, CoV, Hexa, and CCT values.

X-rays are a type of radiation with shorter wavelengths, higher frequency and energy in the electromagnetic spectrum [1]. X-ray helps to create images of the inside of the body. This image is formed according to different amounts of radiation from different tissue. Hard tissues absorb x-rays the most, so appear white. Soft tissues absorb less, and appear gray or black. X-rays can damage the DNA either directly or through the production of free radicals, and this can ultimately cause cancer. This side-effect of DNA damage is seen in radiosensitive cells in particular [5]. Radiosensitivity is related to the susceptibility of cells. The corneal epithelium and lens

Table 2. Comparison of the corneal specular microscopy measurements in the study and control groups

	Study group	Control group	*p* value[a]
ECD	2740.63 ± 249.92	2826.70 ± 287.40	0.191
CoV	44.34 ± 6.78	44.24 ± 4.99	0.945
Hexa	44.97 ± 7.98	45.97 ± 7.06	0.588
CCT	511.40 ± 42.52	514.18 ± 43.55	0.791

Data are shown as mean±standard deviation. [a]The Independent t test, ECD = Endothelial cell density, CoV = Coefficient of variation, Hexa = percentage of hexagonal cells, CCT = Central corneal thickness

epithelium in the eye are more radiosensivite than other parts of the eye. Chalupecky first described the effects of ionizing radiation on the eye [11], while Birch-Hirschpeld identified the first case of radiation cataract [12] and Rohrschneider described the radiosensitivity of ocular parts, with the lens determined as the most sensitive tissue [13]. The conjunctiva, cornea, uvea, retina, and the sclera are less sensitive than the lens [14].

Damage to the conjunctiva, cornea, lens, ocular adnexa and retina has been reported in literature. The lens is an avascular structure located in the anterior segment of the eye, which is one of the most radiosensitive tissues in the human body. As a result of ionising radiation, the lens epithelium is damaged, resulting in abnormal lens fibres, followed by loss of transparency and ultimately a cataract is formed. Cataracts are a most frequently reported finding in literature whicch can develop in one or both eyes. Common symptoms are blurred vision, dull colors, glare, double vision, and changes in prescription eye wear. Cataract formation is not related to high dosage X-rays but is correlated to deterministic radiation-induced effects [15].

The cornea is the anterior transparent segment of the eye, which allows the transmission of light to the lens. The cornea and lens provide the refracting power of the eye and if they are damaged for any reason, vision defects will occur. The corneal epithelium is more radiosensitive than other parts of the cornea. The cornea blocks a significant proportion of ultraviolet radiation (UVR) with the corneal epithelium absorbing 96% of UVB but only 4% of UVA [8]. UVR causes corneal epithelium diseases such as pterygium, photokeratitis, climatic droplet keratopathy and ocular surface squamous neoplasia [8]. UVR can also cause corneal endothelial changes, cataract and retinal degeneration [16]. UVR has longer wavelengths, lower frequency and energy in the electromagnetic spectrum than X-rays, which are more harmful than UVR.

Another condition associated with ionizing radiation is radiation retinopathy, which can develop during radiotherapy. The X-rays affect the endothelial cells and capillary-like network formation in the retinal vessels. The pathogenesis of radiation retinopathy is related to the total radiation dosage, fraction size, concomitant chemotherapy, and pre-existing vascular disorders. These processes are associated with progressive time and dose-dependent reactions. The clinical presentation of radiation retinopathy includesmicroaneurysms, cotton wool spots, capillary dilation, telangectasia, capillary closure, retinal oedema, optic disc neovascularization, vitreous haemorrhage, and retinal detachment [17].

To the best of our knowledge, there have been noprevious studiesof corneal endothelial cell damage from X-rays. Therefore, this study is the first to describe an association between corneal endothelial cell morphology and occupational radiation exposure. According to the results, corneal endothelial cell morphology is not changed in radiology technicians.

In human body rapidly dividing, undifferentiated cells of tissues that are most susceptible to radiation effects. Corneal endothelial cells are not proliferating. This could be one reason for why corneal endothelial cells numbers and morphology are not diffirent in radiology technicians. However, the ECD was found to be lower in the radiology technicians than in the control group but not to a statistically significant level ($p = 0.191$). The CoV, Hexa, and CCT values were not statistically significant ($p > 0.05$). Fish *et al*. [18] studied the relationships of ocular pathology ininterventional pain physicians and reported that cataract formation was related to radiation-induced effects.

Chodick *et al*. [19] investigated the association between cataract and exposure to low doses of ionizing radiation in radiology technicians. That prospective cohort study was conducted over 20 years with 66,379 participants and as a result of the study, 2,382 cataracts and 647 cataract surgeries were reported.

To the best of our knowledge, this is the first study in literature to have examined corneal endothelial cell morphology in radiation technicians.

As there is a risk that other ocular pathologies are related tooccupational radiation exposure, further investigativestudies are required to define these. It can be strongly recommended that all personnel exposed to occupational radiation have routine eye examinations. Further research with greater patient numbers is required to further understand the association between corneal endothelial morphology and occupational radiation exposure.

CONCLUSION

The results of this study showed that corneal endothelial morphology was not changed in the radiology technicians. There is a need for further studies to demonstrate corneal effects associated with X-rays.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] Manickavasagan A, Jayasuriya H. Imaging with Electromagnetic Spectrum: Applications in Food and Agriculture.Springer Berlin Heidelberg; 2014.
[2] Ramachandran T V. Background radiation, people and the environment. Int J Radiat Res2011;9:63-76.
[3] Mazrani W, McHugh K, Marsden PJ. The radiation burden of radiological investigations. Arch Dis Child 2007;92:1127-31.
[4] Reed AB. The history of radiation use in medicine. J Vasc Surg 2011;53:3-5.
[5] Rubin P, Casarett GW. Clinical radiation pathology as applied to curative radiotherapy. Cancer1968;22:767-78.
[6] DelMonte DW, Kim T. Anatomy and physiology of the cornea. J Cataract Refract Surg2011;37:588-98.
[7] Dua HS, Said DG. Clinical evidence of the pre-Descemets layer (Dua's layer) in corneal pathology. Eye (Lond) 2016;30:1144-5.
[8] Delic NC, Lyons JG, Di Girolamo N, Halliday GM. Damaging Effects of Ultraviolet Radiation on the Cornea. Photochem Photobiol 2017;93:920-9.
[9] McCarey BE, Edelhauser HF, Lynn MJ. Review of corneal endothelial specular microscopy for FDA clinical trials of refractive procedures, surgical devices, and new intraocular drugs and solutions. Cornea 2008;27:1-16.
[10] Bourne WM. Biology of the corneal endothelium in health and disease. Eye 2003;17:912-8.
[11] Chalupecky H. Ueber die Wirkung der Rontgenstrahlen auf das Auge und die Haut. Zentralbl F Prakt Augenh 1897;21:886.
[12] Von Gassmann H, wurden nach Einwirkung F. Zur Wirkung der Röntgenstrahlen auf das menschliche Auge. Klin Monbl Augenheilkd. Verlag von Ferdinand Enke; 1908;46:129.
[13] Rohrschneider W. Experimentelle Untersuchungen über die Veränderungen normaler Augengewebe nach Röntgenbestrahlung. Albr von Graefes Arch für Ophthalmol 1929;122:282-98.
[14] Alberti WE, Richard G, Sagerman RH, editors. Age-Related Macular Degeneration Berlin, Heidelberg: Springer Berlin Heidelberg; 2001.
[15] The 2007 Recommendations of the International Commission on Radiological Protection. ICRP publication 103. Ann ICRP 2007;37:1-332.
[16] Van Kuijk FJ. Effects of ultraviolet light on the eye: role of protective glasses. Environ Health Perspect 1991;96:177-84.
[17] Gupta A, Dhawahir-Scala F, Smith A, Young L, Charles S. Radiation retinopathy: case report and review. BMC Ophthalmol 2007;7:6.
[18] Fish DE, Kim A, Ornelas C, Song S, Pangarkar S. The risk of radiation exposure to the eyes of the interventional pain physician. Radiol Res Pract 2011;2011:609537.
[19] Chodick G, Bekiroglu N, Hauptmann M, Alexander BH, Freedman DM, Doody MM, et al. Risk of cataract after exposure to low doses of ionizing radiation: a 20-year prospective cohort study among US radiologic technologists. Am J Epidemiol 2008;168:620-31.

The European Research Journal 2019;5(3):484-489 ORIGINAL ARTICLE

An evaluation of eating attitudes in patients with migraine and tension type headache

Yılmaz İnanç[1], Fatma Özlem Orhan[2], Ayşegül Erdoğan[3], Mustafa Gökçe[1], Yusuf İnanç[4], Erdem Özyurt[5]

[1]Department of Neurology, Kahramanmaraş Sütçü İmam University School of Medicine, Kahramanmaraş, Turkey
[2]Department of Psychiatry, Kahramanmaraş Sütçü İmam University School of Medicine, Kahramanmaraş, Turkey
[3]Department of Public Health, Kahramanmaraş Sütçü İmam University School of Medicine, Kahramanmaraş, Turkey
[4]Department of Neurology, Gaziantep University School of Medicine, Gaziantep, Turkey
[5]Department of Neurology, Mardin State Hospital, Mardin, Turkey

DOI: 10.18621/eurj.396989

ABSTRACT

Objective: The aim of the study was to examine eating attitudes in patients with migraine and tension type headache.

Methods: The study included 89 patients diagnosed with migraine according to the International Headache Society (IHS) 2004 criteria, 87 patients with tension type headache and 89 healthy volunteers matched in terms of age, gender and education level. A detailed neurological examination was made of all the participants and the Eating Attitudes Test (EAT), the Beck Anxiety Inventory (BAI) and the Beck Depression Inventory (BDI) were applied.

Results: In the comparisons of the EAT points, 23 of the tension type headache group and 18 of the migraine group were in the EAT ≥ 30 group, which was a statistically significantly higher rate compared to the control group ($p = 0.099$). The mean BDI points and the mean BAI points of both the migraine and the tension type headache groups were statistically significantly higher than those of the control group ($p = 0.001$ and $p = 0.002$, respectively).

Conclusions: The results showed impairment in the eating attitudes of patients with migraine and tension type headache compared to the control group. When it is considered that some foodstuffs trigger headaches, eating disorders or impaired attitudes to eating become important.

Keywords: migraine, tension type headache, eating attitude

Received: February 20, 2018; Accepted: July 25, 2018; Published Online: August 16, 2018

Headache is encountered extremely often in neurology practice. This is a significant health problem that causes a loss of workforce leading to personal, societal and economic losses and has a negative effect on an individual's quality of life [1]. The World Health Organisation (WHO) counts migraine as one of the diseases that creates the most limitation [2]. Migraine and tension type headache (TTH) are the two most often seen clinical tables in headaches [3, 4]. Eating disorders (eg, anorexia nervosa, bulimia nervosa) have both physical and psychological components and are seen particularly in young females.

Address for correspondence: *Yılmaz İnanç, MD., Assistant Professor, Kahramanmaraş Sütçü İmam University School of Medicine, Department of Neurology, Kahramanmaraş, Turkey*
E-mail: selmakulekci@yahoo.com.tr

e-ISSN: 2149-3189

Psychological and biological factors have been held responsible in the pathophysiology of eating disorders. Psychological factors include states such as depression, anxiety, obsessive symptoms and low self-esteem, while biological factors are serotonin, norepinephrine and dopamine metabolism disorders. However, the pathophysiology has not been fully clarified [5, 6]. The common pathways of eating disorders and migraine are that they are both seen more often in females, there is a high rate of psychiatric comorbidity and there are changes in serotonin metabolism in both diseases.

The aim of this study was to examine the attitudes to eating of patients with migraine and tension type headache.

METHODS

The study included 89 patients who presented with the complaint of headache at the Neurology Polyclinic of Kahramanmaraş Sütçü Imam University Medical Faculty Hospital between February and August 2016 and were diagnosed with migraine by a neurology specialist according to the International Headache Society (IHS) 2004 criteria, 87 patients with tension type headache and 89 healthy volunteers matched in terms of age, gender and education level. Approval for the study was granted by the Ethics Committee of Kahramanmaraş Sütçü Imam University. Informed consent was obtained from all the study participants.

Inclusion criteria were that participation was voluntary, the patients were literate, aged 18-45 years, not taking any regular medication, and that those in the migraine group had no disease other than migraine and those in the control group were healthy. The sociodemographic data of the participants were recorded. Height and weight were measured and the Body Mass Index (BMI) was calculated. According to the BMI values, 3 groups were formed of < 18.49 low BMI, 18.5-24.9 normal BMI and ≥ 25 high BMI. In the migraine group, the duration of the disease, duration of attacks and frequency of attacks were evaluated. A detailed neurological examination was made of all the participants. The Eating Attitudes Test (EAT), the Beck Anxiety Inventory (BAI) and the Beck Depression Inventory (BDI) were applied. The patients were grouped according to the EAT points as EAT <30 and EAT ≥ 30 and according to the BDI points as BDI <17 and BDI ≥ 17.

The Eating Attitudes Test (EAT)

The Eating Attitudes Test used in this study is a self-reporting scale comprising 40 items with 6 Likert-type responses. It was developed by Garner and Garfinkel in 1979 for screening purposes to objectively measure symptoms of anorexia nervosa, and can be applied to individuals over the age of 11 years. Just as it measures the attitudes and behaviour towards food of anorexia nervosa patients it can also identifty potential disorders in eating behaviour of normal individuals. The validity and reliability studies of this scale for use in Turkey were conducted by Savasir and Erol. Points over the accepted cutoff of 30 are accepted as an eating disorder [7, 8].

Beck Depression Inventory (BDI)

This is a self-evaluation form of 21 items scored from 0-3 as Likert-type responses. The scale was developed by Beck and aims to measure the severity of symptoms related to depression in cognitive, emotional, motivational and physical dimensions and takes the mental state of the previous week into consideration. The total points indicate the severity of depression, with a maximum of 63 points and a cutoff of 17 points, as defined by Hisli in validity and reliability studies for Turkey [9, 10].

Beck Anxiety Inventory (BAI)

This self-reporting scale measures the extent of anxiety symptoms experienced by the individual. The scale consists of 21 items scored from 0-3 and the total points indicate the severity of anxiety experienced. Validity and reliability studies for Turkey were conducted by Ulusoy *et al* and 17 points are accepted as the cutoff point [11, 12].

Statistical analysis

Analyses of the data obtained were made using SPSS soft ware (Statistical Package for the Social Sciences). Descriptive statistics were reported as mean ± standard deviation, number and percentage. The Chi-square test was applied to categorical data, and in the comparison of mean points, the Kruskal Wallis test was used. A value of $p < 0.05$ was accepted as statistically significant.

RESULTS

A total of 265 participants were evaluated in the study, as 89 in the migraine group, 87 in the TTH group and 89 in the control group. The mean age was mean 34.21 ± 9.07 years in the migraine group, 35.79 ± 9.05 years in the TTH group and 32.82 ± 9.28 years in the control group. No statistically significant difference was determined between the groups in respect of age or gender ($p > 0.05$). The sociodemographic data of the migraine, TTH and the control groups and the clinical data of the migraine and TTH groups are shown in Table 1.

In the migraine group, the duration of the complaint of headache was 5.09 ± 3.14 years, the frequency of attacks was 4.16 ± 1.87 per month and the mean duration of attacks was 19.65 ± 15.77 hours. In men, the duration of complaint of headache was 5.62 ± 3.11 years, the attack frequency was 2.87 ± 1.45 attacks/month and the duration of attack was 13.62 ± 15.24 hours. In women, the duration of complaint of headache was 5.11 ± 3,18 years, the attack frequency was 4.39 ± 1.87 attacks/ month and the duration of attack was 20.87 ± 14.46 hours.

In the comparisons of the EAT points, 23 of the TTH group and 18 of the migraine group were in the EAT ≥ 30 group, which was a statistically significantly higher rate compared to the control group ($p = 0.099$). The mean BDI points and the mean BAI points of both the migraine and the TTH groups were statistically significantly higher than those of the control group ($p = 0.001$ and $p = 0.002$, respectively) (Table 2).

When the groups were evaluated in respect of those with BMI ≥ 25, 59 of the migraine group, 55 of the TTH group and 44 of the control group were determined with high BMI. The number of patients in the migraine and TTH groups with high BMI was determined to be statistically significantly higher than the control group ($p = 0.048$) (Table 2).

The mean EAT points, mean BDI points, mean BAI points and mean BMI values of the migraine group and the TTH group were determined to be

Table 1. Sociodemographic characteristics of the migraine, TTH and control groups

	Migraine (n = 89)	Tension type headache (n = 87)	Control (n = 89)
Age (years)	34.21 ± 9.07	35.79 ± 9.05	32.82 ± 9.28
Gender			
Female	81 (91.0%)	73 (83.9%)	78 (87.6%)
Male	8 (9.0%)	14 (16.1%)	11 (12.4%)
Marital status			
Married	75 (84.3%)	57 (82.6%)	55 (61.8%)
Single /widowed/divorced	14 (15.7%)	12 (17.4%)	34 (38.2%)
Level of education			
Primary school or lower	48 (53.9%)	55 (63.2%)	15 (19.1%)
Middle school-High school	28 (31.5%)	19 (21.8%)	23 (25.8%)
Further education	13 (14.6%)	13 (14.9%)	49 (55.1%)
Place of residence			
City centre	60 (69.0%)	57 (67.1%)	74 (83.1%)
Regional town/village	27 (31.0%)	28 (32.9%)	15 (16.9%)
Employment status			
Employed	29 (32.6%)	27 (31.0%)	63 (70.8%)
Unemployed	60 (67.4%)	60 (69.0%)	29 (29.2%)
Economic status			
Poor	12 (13.6%)	10 (11.6%)	11 (12.4%)
Average	71 (80.7%)	73 (84.9%)	72 (80.9%)
Good	5 (5.7%)	3 (3.5%)	6 (6.7%)

Data are shown as mean ± standard deviation or number (%).

Table 2. Comparisons of the groups

	Migraine (n = 89)	Tension type headache (n = 87)	Control (n = 89)	*p** value
EAT ≥ 30	18 (20.2%)	23 (26.4%)	12 (13.5%)	0.099
BDI ≥ 17	34 (38.2%)	29 (33.3%)	10 (11.2%)	**0.001**
BAI ≥ 17	42 (47.2%)	38 (43.7%)	21 (23.6%)	**0.002**
BMI ≥ 25	59 (66.3%)	55 (63.2%)	44 (49.4%)	**0.048**

Data are shown as mean ± standard deviation or number (%). EAT = Eating Attitudes Test, BDI = Beck Depression Inventory, BAI = Beck Anxiety Inventory, BMI = Body Mass Index, *Kruskal Wallis test

Table 3. Comparisons of the groups

Tests	Migraine (n = 89)	Tension type headache (n = 87)	Control (n = 89)	*p** value
EAT	21.73 ± 10.56	24.61 ± 17.21	16.21 ± 12.27	**0.001**
BDI	15.51 ± 10.18	13.45 ± 8.28	8.85 ± 8.58	**0.001**
BAI	16.99 ± 12.61	17.08 ± 12.36	10.10 ± 7.61	**0.001**
BM	27.92 ± 6.45	27.74 ± 4.82	25.48 ± 4.05	**0.014**

Data are shown as mean ± standard deviation. EAT = Eating Attitudes Test, BDI = Beck Depression Inventory, BAI = Beck Anxiety Inventory, BMI = Body Mass Index, *Kruskal Wallis test

statistically significantly higher than those of the control group (Table 3). The highest mean EAT points and mean BDI points were determined in the migraine group. The highest mean BAI points were determined in the TTH group. The mean BMI values of the migraine and TTH groups were close to each other and were higher than those of the control group (Table 3).

DISCUSSION

Headache should be addressed not only in limiting the individual's social activities and work life, but also in terms of the multidimensional burden brought about by the collection of health expenditures, such as increasing drug consumption and many hospital applications and examining behaviors. Headache is the "primary headache" when an organic cause can not be determined; secondary headache "if it is associated with an organic pathology such as trauma, infection, or tumor. Approximately 90% of the headache is the primary headache, migraine and tension type headache are the two most common types of headache.

Migraine, and tension type headache, which is the second most common type of primary headaches, are a neurological disease characterised by moderate or severe recurrent attacks of headache accompanied by various combinations of neurological, gastrointestinal and autonomous symptoms. TTH can last from 30 minutes to 7 days and is a headache type that can become chronic with continuous pain. According to epidemiological studies in Turkey, the prevalence of TTH is 31.7% and migraine has been reported as 16.4% [13, 14].

Although primary headache is considered as a neurological pathology, it is frequently observed in the literature with psychiatric disorders such as anxiety and depression attention. Migraine is related to several psychiatric disorders such as major depression, bipolar disorder and anxiety disorder. In a study conducted in the United States of America, depressive disorder is three times more common in migraineurs than in the general population, and this rate is even greater in patients with GTBA or overuse [15]. Studies have revealed that there could be a relationship between migraine and eating disorders and it has been

suggested that there is a common biological predisposition [16, 17].

In the current study, an impaired eating attitude was determined in 34% of the migraine patients and in 43.4% of the TTH patients. These findings were determined to be higher than those of the control group but no statistically significant difference was determined between the groups. However, the mean EAT points of the migraine and TTH groups were found to be statistically significantly higher than those of the control group. To the best of our knowledge, this is the first study to have evaluated eating attitudes and eating disorders in patients with migraine and TTH. Demirci *et al*. [18] reported that the EAT points were significantly higher in a group of 59 migraine patients compared to a control group, and in the evaluation according to the EAT cutoff points, eating disorders were determined more in the migraine patients.

In a study of 34 migraine patients by Brewerton and George [19], 88% were determined with dieting behaviour, 59% with overeating and 26% with self-induced vomiting. In both studies, it was suggested that serotonin dysfunction could be a common pathophysiology of both diseases. Serotonin is a neuropeptide that controls energy intake by providing a sense of satiety. Although serotonin shows transient elevations during migraine attacks, migraines are low in the interictal period. This may lead to an increase in eating impulse and development of obesity in migraineurs [20].

When the groups in the current study were evaluated in respect of those with BMI ≥ 25, the number of those in the migraine and TTH groups with BMI ≥ 25 was found to be statistically significantly higher than those in the control group (p=0.048). In patients with chronic migraine, impaired insulin resistance, hypertension, diabetes, high cholesterol and obesity have been reported to be widely seen [21, 22].

In recent years, it has been thought that some orexigenic and anorexigenic peptides expressed from the hypothalamus related to appetite metabolism could have a role in the pathogenesis of migraine and obesity. Just as increased appetite, hypothalamic stimulants such as mood and sleep problems and postdromal symptoms seen in migraine have been associated with this state, it has also been reported that it could cause hyperphagia of the hypothalamus membrane and an increase in body weight in migraine [23]. The induction of migraine trigeminal ganglion nociceptors causes the release of proinflammatory substances such as CGRP and substance P. CGRP levels are also high in obese patients and are increasing with fat intake. Substance P is present in adipocytes and leads to fat deposition and proinflammatory environment [24]. It has been shown that there could be psychological factors such as accompanying anxiety, depression, obsessive-compulsive disorder and body dysmorphia disorders in the pathophysiology of eating disorders seen in migraine patients [25, 26].

In the multicentre HADAS study (headache and anxiety depressive disorder comorbidity), a frequent combination was shown of TTH and psychiatric disorders. In the current study, TTH was seen to be accompanied by psychopathologies, primarily depression, followed by anxiety, panic disorder and obsessive compulsive disorder. Depressive disorder has been reported in 68.3% of TTH patients and anxiety disorder in 19.3% [27]. In a study by Mustelin *et al*. [28], it was reported that eating disorders in migraine patients could be explained by concomitant major depression. Büyükgöze-Kavas [29] reported a significant relationship between general eating attitudes and depression symptoms. In the current study, both the BDI and BAI points were determined to be statistically significantly higher in both the migraine and TTH patients compared to the control group ($p = 0.001$ and $p = 0.002$, respectively).

Limitations

Limitations of the current study were that the sample size was small, it was a single centre study and the scales used do not have diagnostic properties.

CONCLUSION

The results of the current study showed that the risk of eating disorders in patients with migraine and TTH is higher than that of the general population. In the follow-up and treatment of migraine patients, when it is considered that some foodstuffs can trigger headache, the presence of eating disorders or a poor attitude to eating becomes more important. This type

of screening in respect of eating disorders should be applied to this group of patients so that early diagnosis would allow the possibility of the necessary treatment.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] Karlı N, Zarifoğlu M, Erteş M, Saip S, Öztürk V, Neyal M, et al. Economic impact of primary headaches in Turkey: a university hospital based study: part II. J Headache Pain 2006;7:75-82.
[2] Bradley WG, Daroff BR, Fenichel GM, Jankovic J, Ed: Tan E, Özdemir SE. Neurology in Clinical Practice. 5. Baskı, Ankara: Kalkan Matbaacılık, 2008; 134-210, 2011-2059.
[3] Ropper HA, Samuels MA, Ed: Emre M. Adams and Victor's Principles of Neurology, 9th ed. Ankara: Detail printing press. 2011;162-188.
[4] Jensen RH. Tension−type headache--The normal and most prevalent headache. Headache 2018;58:339-45.
[5] Avraham Y, Hao S, Mendelson S, Berry EM. Tyrosine improves appetite, cognition, and exercise tolerance in activity anorexia. Med Sci Sports Exerc 2001;33:2104-10.
[6] D'Andrea G, Ostuzzi R, Bolner A, Colavito D, Leon A. Is migraine a risk factor for the occurrence of eating disorders? Prevalence and biochemical evidences. Neurol Sci 2012;33:71-76.
[7] Garner DM, Garfinkel PE. The Eating Attitudes Test: an index of the symptoms of anorexia nervosa. Psychol Med 1979;9:273-9.
[8] Savaşır I, Erol N. Eating Attitude Test: Anorexia Nervosa Symptom Index. Psychol J 1989;7:19-25.
[9] Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561-71.
[10] Hisli N. The validity and reliability of the Beck Depression Inventory for university students. J Psychol 1989;7:3-13.
[11] Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: Psychometric properties. J Consult Clin Psychol 1988;56:893-7.
[12] Ulusoy M, Şahin N, Erkmen H. Turkish version of The Beck Anxiety Inventory: Psychometric properties. J Cogn Psychother 1998;12:28-35.
[13] Baykan B. Headaches. Neurology. Second edition, Istanbul: Nobel Medical Bookstore, 2011;373-93.
[14] Carbaat PA, Couturier EG. [Headache: classification and diagnosis]. Ned Tijdschr Tandheelkd 2016;123:539-44. [Article in Dutch]
[15] Martin PR, Forsyth MR, Reece J. Cognitive-behavioral therapy versus temporal pulse amplitude biofeedback training for recurrent headache. Behav Therapy 2007;38:350-63.
[16] D'Andrea G, Ostuzzi R, Francesconi F, Musco F, Bolner A, D'Onofrio F, et al. Migraine prevalence in eating disorders and pathophysiological correlations. Neurol Sci 2009;30:55-9.
[17] D'Andrea G, Ostuzzi R, Bolner A, Francesconi F, Musco F, d'Onofrio F, et al. Study of tyrosine metabolism in eating disorders. Possible correlation with migraine. Neurol Sci 2008;29:88-92.
[18] Demirci K, Demirci S, Akpinar A, Demirdaş A, Atay İM. Evaluation of eating attitude in patients with migraine. Noro Psikiyatr Ars 2015;52:367-70.
[19] Brewerton TD, George MS. Is migraine related to the eating disorders? Int J Eat Disord 1993;14:75-79.
[20] Alstadhaug KB. Migraine and the hypothalamus. Cephalalgia 2009;29:809-17.
[21] Fava A, Pirritano D, Consoli D, Plastino M, Casalinuovo F, Cristofaro S, et al. Chronic migraine in women is associated with insulin resistance: A crosssectionalstudy. Eur J Neurol 2014;21:267-72.
[22] Bigal EM, Lipton BR. Obesity is a risk factor for transformed migraine but not chronic tension-type headache. Neurology 2006;67:252-7.
[23] Peterlin BL, Rosso AL, Williams MA, Rosenberg JR, Haythornthwaite JA, Merikangas KR, et al. Episodic migraine and obesity and the influence of age, race, and sex. Neurology 2013;81:1314-21.
[24] Bond DS, Roth J, Nash JM, Wing RR. Migraine and obesity: epidemiology, possible mechanisms and the potential role of weight loss treatment. Obes Rev 2011;12:362-71.
[25] Seidel S, Karwautz A, Wagner G, Zormann A, Eder H, Huemer J, et al. Migraine in patients with eating disorders: a study usinga sister-pair comparison design. Headache 2011;51:220-5.
[26] Baskin SM, Smitherman TA. Migraine and psychiatric disorders: Comorbidities, mechanisms, and clinical applications. Neurol Sci 2009;30:S61-5.
[27] Beghi E, Allais G, Cortelli P, D'Amico D, De Simone R, d'Onofrio F, et al. Headache and anxiety-depressive disorder comorbidity: the HADAS study. Neurol Sci 2007;28 Suppl 2:S217-9.
[28] Mustelin L, Raevuori A, Kaprio J, Keski-Rahkonen A. Association between eating disorders and migraine may be explained by major depression. Int J Eat Disord 2014;47:884-7.
[29] Büyükgöze-Kavas A. Eating attitudes and depression in a Turkish sample. Eur Eat Disord Rev 2007;15:305-10.

The European Research Journal 2019;5(3):490-496 ORIGINAL ARTICLE

Increased TIMI frame count of coronary arteries in patients with myocardial bridging

Ekrem Aksu, Hakan Güneş

Department of Cardiology, Kahramanmaraş Sütçü İmam University School of Medicine, Kahramanmaraş, Turkey

DOI: 10.18621/eurj.388556

ABSTRACT

Objectives: Myocardial bridging (MB) is associated with recurrent chest pain and cardiovascular events. Recently it has been proposed that MB has the features of vasospastic coronary artery characterized with reduced coronary flow reserve and endothelial dysfunction. In this study, an evaluation was made of the angiographic Thrombolysis in Myocardial Infarction (TIMI) frame counts (TFCs) of patients with normal angiogram and those with MB.

Methods: The study was conducted as a retrospective analysis of the demographic, laboratory, and angiographic features of consecutive patients who underwent coronary angiography between January 2014 and December 2017 in Necip Fazıl City Hospital and Sütçü Imam University, Kahramanmaraş, Turkey.

Results: The except for age (51.1 ± 11.6 years vs 56.8 ± 11.4 years) ($p = 0.011$), no difference was determined between the groups in respect of laboratory parameters and demographic features. TFCs of LAD (42.9 ± 6.1 vs 54.5 ± 11.5. $p < 0.001$), Cx (19.4 ± 4.5 vs 24.4 ± 7.1, $p < 0.001$), and RCA (26.8 ± 6.2 vs 32.5 ± 8.9, $p < 0.001$), and corrected TFC of LAD artery (25.2 ± 3.6 vs 32.0 ± 6.8, $p < 0.001$) were observed to be significantly increased in patients with MB compared to patients with normal coronary flow. Multiple regression analysis revealed that MB was the only determinant of increased corrected TFC of LAD artery (r=0.537, Adjusted r=0.281, $p < 0.001$).

Conclusions: Patients with MB had abnormally slow coronary flow demonstrated by increased TFC. This finding may explain the recurrent angina and cardiovascular events of patients with MB. It may also explain the reversible myocardial perfusion defects which are associated with recurrent cardiovascular events in patients with MB.

Keywords: Myocardial bridging, thrombolysis in myocardial infarction, TIMI frame count, coronary flow, recurrent angina

Received: February 1, 2018; Accepted: March 2, 2018; Published Online: June 1, 2018

Myocardial bridging (MB) of coronary artery disease may be associated with widely varying signs and symptoms of myocardial ischemia. Those signs and symptoms may develop due to either systolic compression of the coronary artery that can be detected on angiography or various hemodynamic abnormalities of coronary flow which can be documented on intracoronary Doppler assessment [1]. Abnormally increased pressure gradient during the systolic and diastolic period of coronary flow on the arterial segment proximal to the MB is the essential hemodynamic abnormality. Coronary flow reserve is

Address for correspondence: *Hakan Güneş, MD., Assistant Professor, Kahramanmaraş Sütçü İmam University School of Medicine, Department of Cardiology, Kahramanmaraş, Turkey*
E-mail: drhakangunes83@hotmail.com, Tel: +90 344 3003376, Fax:+90 344 300 3409

e-ISSN: 2149-3189

also reduced due to those intracoronary hemodynamic abnormalities induced by MB [2].

Recent studies have documented that the response to the acetylcholine test was more pronounced in patients with MB and caused diffuse spasm of the coronary artery where MB was present [3]. This is probably associated with the recurrence of signs and symptoms and cardiovascular events in those patients with MB. Postmortem studies have documented that the proximal arterial segments of a bridged coronary artery were stripped of endothelial lining compared to the other arterial walls [4]. Thus, endothelial dysfunction is a significant pathophysiological abnormality observed in patients with MB [5]. An abnormally paradoxical vasospastic response to adenosine infusion detected on angiography is significant evidence of endothelial dysfunction [6]. Therefore, MB may be one of the significant causes in the etiology of angina pectoris and myocardial ischemia in non-obstructive coronary artery disease [7]. All these hemodynamic and pathological abnormalities inevitably produce coronary flow abnormalities which can be assessed by the coronary flow quantification method defined as Thrombolysis in Myocardial Infarction (TIMI) frame count (TFC) [8]. Quantifying the coronary flow with TFC may allow the cardiologist to decide whether there is an underlying coronary flow abnormality in the etiology of signs and symptoms and to predict the long-term outcomes for patients with MB [8].

In this study it was aimed to evaluate the coronary flow properties by assessing the TFC of the coronary arteries on the coronary angiography of patients with MB.

METHODS

The study was conducted as a retrospective analysis of the demographic, laboratory, and angiographic features of consecutive patients who underwent coronary angiography between January 2014 and December 2017 in Necip Fazıl City Hospital and Sütçü İmam University, Kahramanmaraş, Turkey. Informed consent was obtained from all the patients. Approval for the study was granted by the Local Ethics Committee of Sütçü İmam University School of Medicine, Kahramanmaraş, Turkey.

Study Groups

All the patients were applied with coronary angiography for a diagnosis of stable coronary angiograph due to a positive treadmill test, recurrent chest pain despite medical therapy, previous dynamic ECG changes during chest pain, and patient request. The control group comprised patients with no apparent coronary artery stenosis as luminal irregularities, < 20% stenosis or normal coronary anatomy [9]. Patients with systolic compression of at least 25% luminal narrowing due to myocardial bridging in the proximal or middle segments of the left anterior descending artery were assigned to the myocardial bridging group.

Patients with previous myocardial infarction, atherosclerotic coronary artery disease, hypertension, diabetes, acute coronary syndromes including unstable angina pectoris, non-ST/ST segment elevated myocardial infarction, myocarditis, acute or chronic systemic inflammatory disease, chronic liver disease, and also congestive heart failure with reduced or preserved ejection fraction, or chronic renal failure were excluded from the study. In addition, patients with a moderate or higher daily alcohol intake, age < 25 years or > 70 years, were excluded from the study.

Laboratory Measurements

Serum levels of laboratory parameters were measured from the venous blood samples obtained at 08.00 in the morning after a 12-hour fasting period. Samples collected in tubes containing K^3 EDTA were rested for 20 minutes and then centrifuged at 3500 rpm for 15 minutes. Total plasma cholesterol, triglyceride, and high-density lipoprotein [HDL] cholesterol, uric acid and glucose concentrations were measured with the Cobas c501 (Roche Diagnostics, USA) using the spectrophotometric technique. Low density lipoprotein [LDL] cholesterol levels were calculated with the Friedwald formula.

Complete blood count measurement and cell differentiation were performed by Sysmex XE-5000 using the diode laser bench and fluorescent flow cytometry technique. Leukocytes, neutrophils, lymphocytes, and monocytes were presented as ($nx10^3/mm^3$). Hemoglobin (Hb) and Hematocrit (Hct) were presented as g/dL and %, respectively. Platelet count (Plt) were presented as $nx10^3/mm^3$.

Coronary Angiography Procedure

The standard angiographic procedure was applied to all patients. With the patient in a supine position, a 6F arterial sheath was introduced to the femoral artery using the Seldinger technique. 6F right and left Judkins catheters were used to image the coronary arteries. Angiography was performed as a standardized procedure including coronary imaging from 4 positions (left caudal, right caudal, and left cranial, right cranial) for the left coronary system and from 2 positions (left and right cranial) for the right coronary artery. The contrast media used during angiography was Iohexol (Omnipaque-350/100 ml, Opakim, Turkey) which was injected as 6-8 mL during each image shot.

TIMI Frame Count (TFC)

TFCs of LAD, Cx, and RCA arteries were calculated as the difference of the last and first frames of those arteries. The first frames of the arteries were accepted as the entrance of the contrast dye to at least 70% of the arterial lumen. The last landmarks were the opacification of the distal branching for LAD, and the first branching of the posterolateral artery for RCA, and the distal branching for Cx artery on the left lateral wall [11]. The LAD and Cx arteries were assessed on the angiographic projection of the right anterior oblique with caudal angulation and the RCA was assessed on the angiographic projection of the left anterior oblique with cranial angulation. TFC of LAD was corrected with a factor of 1.7 which had been previously defined [10].

The angiographic images were analyzed by two independent cardiologists blinded to the study project. The interobserver variability of the two cardiologists was tested using the results of the TFC calculations from the LAD artery recordings of the first fifteen patients. Cronbach's Alpha was calculated as 0.976 and intraclass correlation of analyses was 0.975 ($p < 0.001$).

Statistical Analysis

Statistical analyses of the study data were applied using IBM SPSS 15.0 software (IL, USA). The conformity to normal distribution of the data was tested using the Kolmogorov Smirnov test. Continuous variables with normal distribution were compared with parametric tests e.g. Independent Samples *t* test while those variables without normal distribution were compared with non-parametric tests. The distribution of categorized variables was analyzed using the Chi-Square test. Correlation analysis of continuous and categorized variables was applied by the Pearson and Spearman tests, respectively. A value of $p < 0.05$ was accepted as statistically significant.

RESULTS

Demographic features of body weight and height, systolic and diastolic blood pressure, and BMI were not different between the groups. Age was determined to be significantly higher in patients with MB (51.1 ± 11.6 years vs 56.8 ± 11.4 years, $p = 0.011$) (Table 1). Complete blood count and laboratory parameters were not different in the comparison of the two groups, with

Table 1. Demographic characteristics of the patients

Characteristics	Patients with normal coronary angiography (n = 62)	Patients with MB on angiography (n = 54)	*p*
Age (years)	51.1 ± 11.6	56.8 ± 11.4	**0.011**
Weight (kg)	82.5 ± 8.9	84.2 ± 9.7	0.361
Height (cm)	170.0 ± 4.3	171.5 ± 5.3	0.119
BMI (kg/m^2)	28.6 ± 3.4	28.6 ± 3.3	0.959
SBP (mmHg)	125.6 ± 5.3	127.2 ± 7.8	0.233
DBP (mmHg9	74.9 ± 6.7	76.2 ± 7.5	0.350

Data are shown as mean±standard deviation. BMI = body mass index, DBP = diastolic blood pressure, MB = myocardial bridging, SBP = systolic blood pressure

Table 2. Laboratory findings of the patients

	Patients with normal coronary angiography (n = 62)	Patients with MB on angiography (n = 54)	*p*
Hb (g/dL)	13.4 ± 1.3	14.1 ± 1.7	**0.030**
Hct (%)	41.1 ± 3.5	42.2 ± 4.8	0.200
Leukocyte (x10^3)	7.9 ± 2.2	8.0 ± 1.6	0.850
Neutrophil (x10^3)	5.0 ± 1.9	4.8 ± 1.5	0.461
Lymphocyte (x10^3)	2.2 ± 0.7	2.1 ± 0.6	0.355
Monocyte (x10^3)	0.6 ± 0.2	0.7 ± 0.3	0.079
Platelet (x10^3)	237.9 ± 65.0	230.0 ± 52.2	0.485
Glucose (g/dL)	93.8 ± 10.2	92.1 ± 9.9	0.388
Urea (mg/dL)	28.9 ± 10.4	28.7 ± 6.3	0.953
Creatinine (mg/dL)	0.8 ± 0.2	0.8 ± 0.1	0.527
AST (IU/L)	23.2 ± 6.3	24.0 ± 6.7	0.504
ALT (IU/L)	23.1 ± 9.9	23.4 ± 7.9	0.880
Total cholesterol (mg/dL)	179.4 ± 37.0	179.2 ± 42.6	0.974
LDL cholesterol (mg/dL)	112.4 ± 29.5	114.9 ± 39.9	0.697
HDL cholesterol (mg/dL)	45.3 ± 15.8	37.8 ± 7.2	**0.002**
TG (mg/dL)	153.8 ± 101.3	188.7 ± 105.6	0.082
Na (mEq/L)	140.7 ± 2.3	140.0 ± 2.3	0.107
K (mEq/L)	4.5 ± 0.4	4.4 ± 0.4	0.106

Data are shown as mean±standard deviation. ALT = alanine aminotransferase, AST = aspartate aminotransferase, Hb = hemoglobin, Hct = hematocrit, HDL = high-density lipoprotein, K = potassium, LDL = low density lipoprotein, Na =sodium, TG = triglyceride

the exception of Hb (13.4 ± 1.3 vs 14.1 ± 1.7, p = 0.030) and serum levels of HDL (45.3 ± 15.8 vs 37.8 ± 7.2, p = 0.002) (Table 2).

TFCs of LAD (42.9 ± 6.1 vs 54.5 ± 11.5, $p < 0.001$), Cx (19.4 ± 4.5 vs 24.4 ± 7.1, $p < 0.001$), and RCA (26.8 ± 6.2 vs 32.5 ± 8.9, $p < 0.001$), and corrected TFC of LAD artery (25.2 ± 3.6 vs 32.0 ± 6.8, $p < 0.001$) were significantly increased in patients with MB compared to patients with normal coronary flow (Table 3).

Table 3. TIMI frame counts of the patients

TIMI frame counts	Patients with normal coronary angiography (n = 62)	Patients with MB on angiography (n = 54)	*p*
Corrected TFC	25.2 ± 3.6	32.0 ± 6.8	**< 0.001**
LAD TFC	42.9 ± 6.1	54.5 ± 11.5	**< 0.001**
Cx TFC	19.4 ± 4.5	24.4 ± 7.1	**< 0.001**
RCA TFC	26.8 ± 6.2	32.5 ± 8.9	**< 0.001**

Data are shown as mean±standard deviation. Cx = circumflex coronary artery, LAD = left anterior descending coronary artery, TFC = TIMI frame count, TIMI = Thrombolysis in Myocardial Infarction, RCA = right coronary artery

In correlation analysis, corrected TFC was positively correlated with the presence of MB (r=0.537, p = 0.537) and Hb (r=0.212, p = 0.027), and male gender (r=0.240, p = 0.012). In multivariate linear regression analysis with a stepwise model, only the presence of MB was determined to be significantly correlated with corrected TFC of LAD artery (r=0.537, Adjusted r=0.281, p < 0.001) and no correlation was determined in respect of gender and Hb level.

DISCUSSION

The most significant result of this study was that coronary flow quantified by TFC was observed to be reduced in patients with MB compared to patients with normal coronary anatomy. TFC is a well validated technique to quantify coronary flow in angina or chest pain syndromes associated with non-obstructed coronary artery disease. TFC may quantify not only the epicardial coronary flow but also distal microvasculature and resistance, providing an objective and sensitive evaluation of the flow changes of the coronary artery [11]. The most interesting result of this study was that the slowing of the coronary blood flow was not limited only to the coronary artery where there is MB. Increased TFC is a global abnormality of coronary arteries in both the right and left coronary system. Although similar findings were reported by Barutcu *et al*. [12], they stated that TFC was significantly increased only on the LAD artery associated with MB but not on the RCA or Cx artery. On close examination of the results of that study, cTFC was seen to be significantly higher (24.7 ± 2.1 vs 22.1 ± 1.9, p = 0.001) in the LAD artery while TFC tended to be higher in the Cx artery (22.1 ± 2.4 vs 21.3 ± 2.3, p = 0.18) and was no different in the RCA (23.1 ± 2.2 vs 23.4 ± 2.1, p = 0.7) in patients with MB in the LAD artery. Coronary flow was significantly decreased irrespective of the degree of systolic narrowing and other clinical and echocardiographic features of the patients. That the number of patients was limited in that study may have been the reason why the results did not reach a level of statistical significance. In the current study, a larger population was evaluated, which may have contributed to the statistical significance of the data.

In this context, the hypothesis that coronary flow abnormality or pressure gradients are due to anatomic restrictions induced by MB could not mechanistically explain why TFC significantly increased not only in the LAD artery but also in the Cx and RCA. Therefore, the global increase of TFC on LAD and remote coronary arteries could be explained by several hormonal or autonomic dysfunctıons triggered by MB. In several cases, it has been reported that MB is associated with paradoxically worsening of coronary vasospasm following intracoronary adenosine or nitroglycerine infusion [6, 13]. It has also been demonstrated that adding oral nitrate treatment worsened the stable angina of a subject with MB [10]. This phenomenon was attributed to the endothelial dysfunction due to pressure gradient and vascular shear stress induced by MB. Endothelial dysfunction is a significant cause of reversible myocardial perfusion defects detected in patients with non-obstructive coronary artery disease as in patients with MB [14]. MB is one of the significant causes of reversible myocardial perfusion defects. Although Brolin *et al*. [15] reported that prevalence of MB did not differ in patients with MINOCA (myocardial infarction due to non-critically obstructed coronary artery disease) or Takotsubo syndrome, recurrent sign and symptoms of ischemia, angina, and myocardial infarction in patients with MB renders the diagnosis of MB essential in the management of those patients. The results of the current study may highlight those recurrent clinical characteristics due to MB. Since slow coronary flow associated with MB is seen in all coronary arteries, it may explain why localization of reversible perfusion defects on the myocardium may vary and present heterogeneity on the perfusion tests in patients with MB. Those reversible and non-homogeneous defects which were formerly called "false positive" have been associated with endothelial and microvascular dysfunction which may be caused by myocardial bridging and not confined to the territory of one coronary artery [16]. Slow coronary flow on different remote coronary arteries may also partially explain the reason why reversible perfusion defects can be detected on irrelevant myocardial segments. This phenomenon may explain to critics why myocardial perfusion tests were not performed and ischemia not documented since those perfusion defects could not be induced on every test. This entity may be a unique clinical feature of endothelial and

microvascular dysfunction induced by MB. MB causes recurrent angina resistant to therapy and may be complicated with myocardial infarction or malignant arrhythmia.[17] Therefore, the signs and symptoms of patients with MB may be different from stable angina pectoris and not predictable or reproducible. Sometimes it may be diagnosed as variant angina due to recurrent coronary vasospasm in daily clinical practice [18]. The current authors have previously suggested that recurrent vasospasm may develop due to increased Ca accumulation on the arterial wall proximal to the coronary segment with MB, as documented in postmortem studies [4, 19]. Moreover, smooth muscle cells found in the subendothelial layers of pre- and post-MB segments of coronary artery have shown increased migratory and proliferative activity [20]. All those histolopathological findings may contribute to the increased vasospastic response of a coronary artery with MB and may account for the recurrent signs and symptoms and the cardiovascular events due to MB.

Limitations

The retrospective design of this study may be one of the limitations of this study. All the patients in the MB group had MB in the proximal or mid segment of the LAD artery, which is consistent with previously reported data [21]. Although it may appear to be a limitation of this study, the prevalences of MB in the Cx or RCA arteries reported in previous autopsy or angiographic studies have not been of sufficient significance to warrant the design of any groups of those coronary arteries with MB. Intracoronary pressure gradients could have been measured using intracoronary Doppler measurements and the comparison made according to the pressure gradient. However, this is an invasive method and may require a further prospective study with more complex hemodynamic monitoring. Challenge tests for coronary vasospasm (e.g. acetylcholine test, adenosine) could have been applied to evaluate the association between the vasospastic response of the coronary artery with MB and TFC, but this could be tested in another future prospective study. Although patients with acute or chronic systemic inflammatory diseases were excluded, no evaluation was made of the laboratory parameters of the systemic inflammatory state in this study.

CONCLUSION

Patients with myocardial bridging had significantly slower coronary flow compared to patients with normal coronary anatomy. Endothelial dysfunction, coronary hemodynamic abnormalities and pressure gradients induced by the presence of MB may account for this slow coronary flow. This finding may be one of the mechanisms accounting for the recurrent signs and symptoms of ischemia and cardiovascular events in patients with MB.

Author contributions

All authors contributed to: (1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, and, (3) final approval of the version to be published.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] Bourassa MG, Butnaru A, Lespérance J, Tardif JC. Symptomatic myocardial bridges: overview of ischemic mechanisms and current diagnostic and treatment strategies. J Am Coll Cardiol 2003;41:351-9.
[2] Klues HG, Schwarz ER, vom Dahl J, Reffelmann T, Reul H, Potthast K, et al. Disturbed intracoronary hemodynamics in myocardial bridging: early normalization by intracoronary stent placement. Circulation 1997;96:2905-13.
[3] Im SI, Rha SW, Choi BG, Choi SY, Kim SW, Na JO, et al. Angiographic and clinical characteristics according to intracoronary acetylcholine dose in patients with myocardial bridge. Cardiology 2013;125:250-7.
[4] Tohno Y, Tohno S, Minami T, Pakdeewong-Ongkana N, Suwannahoy P, Quiggins R. Different accumulation of elements in proximal and distal parts of the left anterior descending artery beneath the myocardial bridge. Biol Trace Elem Res 2016;171:17-25.
[5] Zoghi M, Duygu H, Nalbantgil S, Kirilmaz B, Turk U, Ozerkan F, et al. Impaired endothelial function in patients with myocardial bridge. Echocardiography 2006;23:577-81.
[6] Farag A, Al-Najjar Y, Eichhöfer J. Adenosine-induced vasospasticity in a myocardial bridge. Endothelial dysfunction? JACC Cardiovasc Interv 2015;8:21-2.

[7] Radico F, Ciccihitti V, Zimarino M, De Caterina R. Angina pectoris and myocardial ischemia in the absence of obstructive coronary artery disease: practical considerations for diagnostic tests. J Am Coll Cardiol Intv 2014;7:453-63.
[8] Vijayalakshmi K, De Belder MA. Angiographic and physiologic assessment of coronary flow and myocardial perfusion in the cardiac catheterization laboratory. Acute Card Care 2008;10:69-78.
[9] Maddox TM, Stanislawski MA, Grunwald GK, Bradley SM, Ho PM, Tsai TT, et al. Nonobstructive coronary artery disease and risk of myocardial infarction. JAMA 2014;312:1754-63.
[10] Gibson CM, Cannon CP, Daley WL, Dodge JT Jr, Alexander B Jr, Marble SJ, et al. TIMI frame count: a quantitative method of assessing coronary artery flow. Circulation 1996;93:879-88.
[11] Kunadian V, Harrigan C, Zorkun C, Palmer AM, Ogando KJ, Biller LH, et al. Use of the TIMI frame count in the assessment of coronary artery blood flow and microvascular function over the past 15years. J Thromb Thrombolysis 2009;27:316-28.
[12] Barutcu I, Sezgin AT, Gullu H, Turkmen M, Esen AM. Assessing coronary blood flow with TIMI frame count method in isolated myocardial bridging. Angiology 2007; 58:283-8.
[13] Durukan M, Aksu T, Çolak A, Güray Ü. [Augmentation of vessel narrowing by nitroglycerine in a case with myocardial bridge]. Anadolu Kardiyol Derg 2011;11:464-6. [Article in Turkish]
[14] Van De Wiele C, Rimbu A, Belhocine T, DE Spiegeleer B, Sathekge M, Maes A. Reversible mycordial perfusion defects in patients not suffering from obstructive epicardial coronary artery disease as assessed by coronary angiography: a review of the literature. Q J Nucl Med Mol Imaging 2016 Mar 23.
[15] Brolin EB, Brismar TB, Collste O, Y-Hassan S, Henareh L, Tornvall P et al. Prevalence of myocardial bridging in patients with myocardial infarction and nonobstructed coronary arteries. Am J Cardiol 2015;116:1833-9.
[16] Wieneke H, Zander C, Eising EG, Haude M, Bockisch A, Erbel R. Non-invasive characterization of cardiac microvascular disease by nuclear medicine using single-photon emission tomography. Herz 1999;24:515-21.
[17] Kim SS, Jeong MH, Kim HK, Kim MC, Cho KH, Lee MG, et al. Long-term clinical course of patients with isolated myocardial bridge. Circ J 2010;74:538-43.
[18] Nardi F, Verna E, Secco GG, Rognoni A, Sante Bongo A, Iraghi G,et al. Variant angina associated with coronary artery endothelial dysfunction and myocardial bridge: a case report and review of the literature. Intern Med 2011;50:2601-6.
[19] Aparci M, Yalcin M, Isilak Z. Accumulation of Ca+2 at arterial segments proximal to myocardial bridging may influence the vascular dynamics of coronary artery. Int J Cardiol 2016;202:782-83.
[20] Loukas M, Bhatnagar A, Arumugam S, Smith K, Matusz P, Gielecki J, et al. Histologic and immunohistochemical analysis of the antiatherogenic effects of myocardial bridging in the adult human heart. Cardiovasc Pathol 2014;23:198-203.
[21] Cay S, Oztürk S, Cihan G, Kisacik HL, Korkmaz S. Angiographic prevalence of myocardial bridging. Anadolu Kardiyol Derg 2006;6:9-12.

The European Research Journal 2019;5(3):497-501 ORIGINAL ARTICLE

Could there be any relationship between nutritional deficiencies and idiopathic chest pain in children?

Şeyma Kayalı[1], Nuran Belder[2], Dilek Gürlek Gökçebay[3]

[1]Department of Pediatric Cardiology, University of Health Sciences, Keçiören Training and Research Hospital, Ankara, Turkey
[2]Department of Pediatrics, University of Health Sciences, Keçiören Training and Research Hospital, Ankara, Turkey, Turkey
[3]Department of Pediatric Hematology and Oncology, University of Health Sciences, Keçiören Training and Research Hospital, Ankara, Turkey

DOI: 10.18621/eurj.391401

ABSTRACT

Objectives: Chest pain in childhood is a frequent cause of referral to pediatric cardiology departments although cardiac etiology is very rare. Etiology is usually unidentified and named as 'idiopatic chest pain'. It is also well known fact that chronic pain is associated with insuffiency of some nutritional factors even in childhood. Our aim was to investigate if there is a relationship between nutritional defiencies with idiopathic chest pain in children.

Methods: We retrospectively reviewed 364 patients who were referred pediatric cardiology department in one year period due to experienced chest pain more than one time. Among these patients, a total of 109 patients who had complete blood count, serum ferritin, vitamin B 12 and 25-(OH) vitamin D levels in pediatric outpatient clinics before and the etiology was still unidentified after a detailed cardiac and other examinations formed the study group. Age and sex matched 59 healthy children without chest pain formed the control group. All participants had been evaluated with a detailed physical examination and patients in chest pain group also had an electrocardiographic ve echocardiographic evaluation.

Results: Vitamin B12 and Vitamin D levels were lower in noncardiac chest pain group while there was no difference between groups in term of ferritin levels and complete blood count parameters. These difference is statistically significant particularly in vitamin D levels.

Conclusions: Our results showed that low Vitamin D levels is associated with chronic chest pain in children. The present study provide the necessity of evaluating nutritional parameters in children with noncardiac chest pain.

Keywords: Chest pain, children, ferritin, vitamin B12, vitamin D

Received: February 7, 2018; Accepted: June 22, 2018; Published Online: June 27, 2018

Even in developed countries, nutritional deficiencies are worlwide common cause of anemia and various disorders [1-4]. In recent years, there are several studies that report the assosication between nutritional insuffiencies and diverse ilnesses, chronic pain syndromes [4-6]. In particular, low vitamin D level has been linked to chronic pain and there is a growing body of literature about this subject in recent years. The possible underlying mechanism of relationship between chronic pain and vitamin D

Address for correspondence: *Şeyma Kayalı, MD., University of Health Sciences, Keçiören Training and Research Hospital, Department of Pediatric Cardiology, Pınarbaşı Mah., Sanatoryum Cad., Ardahan Sok., No:25, 06380 Keçiören, Ankara, Turkey*
E-mail: ak-seyma@hotmail.com, Tel: +90 (312) 356 90 00, Fax: +90 (312) 356 90 02

e-ISSN: 2149-3189

deficiency is that vitamin D has been found to act as a neuroactive steroid, interfere with the creation and role of neurotrophins, influence prostaglandin action, effect inflammatory pathways, and inhibit nitric oxide synthase and T-helper cells [7]. Studies reported that even mild vitamin D deficiency may produce a variety of musculoskeletal pains such as fibromyalgia-like pain, low back pain, and arthralgia [8]. However, many tissues express vitamin D receptors and like other hormones, vitamin D plays a role in a wide range of processes in the body and the relationship between vitamin D deficiency and different pain types such as nociceptive and inflamatuary pain has also been proven [9]. In addition to this, vitamin B12 has been regarded as painkilling vitamin for decades and has been used in the treatment of pain which is particularly neuropatic [10].

In respect of iron, iron status is an important risk factor for cardiovascular health and clinical spectrum of iron deficiency range from asymptomatic to heart failure [1] and analghesic effect of iron oxide particles in inflamatuary pain sydrome were showed in a recent mice study [11]. On the other hand, chest pain is one of the main causes of recurrent referral to pediatric emergency and pediatric cardiology departments and the most common etiology is still unknown and called as'idiopathic' with a percentage of 21-59 % [12]. Different studies were made to enlight this unknown etiology to this date [13-16]. However, there has been no published studies that evaluated the relationship between idiopathic chest pain and nutritional deficiencies according to our knowledge.

The aim of this study was to contribute the management of children with chest pain by examining the serum levels of iron, vitamin B12 and vitamin D in these children and relationship between nutritional deficiencies and presence of idiopathic chest pain.

METHODS

The patients who were referred to pediatric cardiology because of recurrent chest pain between the dates of December 2016 to December 2017 were retrospectively reviewed. All participants with chest pain were screened with a detailed procedure including history, physical exam, electrocardiogram, transthorasic echocardiogram and were also evaluated for other possible causes of chest pain including gastroeusophageal reflux, costochondritis and pneumonia. A total of 109 patients who showed no evidence of obvious medical pathology and provided the condition of having complete blood count, serum ferritin, vitamin B12 and 25-(OH) vitamin D levels in pediatric outpatient clinics were considered eligible for the study group. Randomly chosen, age and sex matched healthy children without chest pain who was admitted pediatrics department for routine control formed the control group. Excluded from the study were any children with structural heart disease, hematologic disease (thalessemia, sicle cell anemia, etc.), dysrhythmia, chronic ilness or were taking any regular medications.

The serum levels of ferritin, vitamin B12 and 25-(OH) vitamin D was measured by chemiluminescent immunoassay method (Architect, Abbott, USA). Ferritin was lower than 25 ng/ml was considered as low iron storage [1]. Vitamin B12 deficiency was defined as serum level of vitamin B12 was 200 pg/ml [17]. Vitamin D insuffiency and vitamin D deficiency were considered when 25-(OH) vitamin D levels were level between 12-20 ng/ml and lower than 12 ng/ml respectively [18].

The present study was approved by a scientific committee comprising the hospital administration and the lecturers and performed in accordance with the Declaration of Helsinki.

Statistical Analysis

The data were recorded with the Statistical Package for the Social Sciences program version 21 (SPSS, Inc., Chicago, IL, USA). The distributions of continuous variables were analyzed with the Shapiro-Wilk test. The descriptive statistics were defined as mean ± standard deviation for normally distributing data and as median (minimum-maximum) for non-normally distributing data. The significance of the differences in mean values between two independent groups was analyzed with the Student t-test and the significance of the differences in median values between two independent groups was analyzed with the Mann-Whitney U test. Relationships between variables were tested with Pearson or Spearman correlation analysis where appropriate. A value of $p < 0.05$ was taken to statistical significance.

Table 1. Demographic and hematologic feaures of participants

	Study group (n =109)	Control group (n = 59)	*p* value
Age (years)	12.4 ± 3.6	11 ± 4.6	0.14
Gender	71 (65.1%)	30 (50.8%)	0.07
Hb (g/dl)	13.8 ± 1.37	13.6 ± 1.33	0.13
Hct (%)	41.4 ± 5.3	40.1 ± 3.9	0.08
RBC (10^6/μL)	4882.7 ± 367.6	4880.6 ± 377.2	0.6
Ferritin (ng/ml)	36.1±42.7	27.2±16.4	0.5

Data are shown as mean±standard deviation or number (%). Hb = Hemoglobin, Hct = Hematocrit, RBC = Red blood cell count

RESULTS

A total of 364 children were admitted pediatric cardiology department due to recurrent chest pain in one year period. A total of 109 children who diagnosed with idiopathic chest pain had complete blood count, serum levels of ferritin, vitamin B12 and vitamin D in pediatric outpatient clinics and formed study group. The average age of study and control group was 12.4 ± 3.6 years and 11 ± 4.6 years, respectively. There were 71 (65.1%) girls in study group while there were 30 (50.8%) girls in control group. There were no difference between groups in terms of age and gender ($p = 0.14$ and $p = 0.07$, respectively) (Table 1). There were no difference between groups in terms of serum ferritin levels and hemoglobin, hematocrit, red blood cell values ($p > 0.05$) (see Table 1).

The serum vitamin B12 levels of study group was lower than control group although was not statistically significant ($p = 0.1$) (Table 2). There were 14 (12.8%) children in study group with vitamin B12 deficiency while there were 8 (13.6%) children vitamin B12 deficiency in control group.

Serum level of 25-(OH) vitamin D was significantly lower in study group (p = 0.001). There were 65 (57.8%) children with vitamin D insufficiency in study group while there were 18 (30.5%) children with vitamin D insufficiency in control group. In addition to this, 40 (36.7%) of children in study group had vitamin D deficiency and 3 (5.1%) of children in control group had vitamin D deficiency ($p < 0.01$) (Table 2).

DISCUSSION

In this retrospective study we found that vitamin D level was significantly lower in children with idiopathic chest pain whereas there were no difference in terms of ferritin and vitamin B 12 levels.

The association of vitamin D deficiency with multiple forms of chronic pain are reported by several studies such as musculoscelatal, nociceptive, inflammatuary, cancer pain, etc.,[9, 19-24]. Although,

Table 2. Comparison of vitamin levels between groups

	Study group (n =109)	Control group (n = 59)	*p* value
Vitamin B12 (pg/ml)	326 ± 125.7	374.6 ± 168	0.1
25-(OH) Vitamin D (ng/ml)	20.5 ± 12.6	26.6 ± 14.4	**0.001**
Vitamin D deficieny	40 (36.7%)	3 (5.1%)	**< 0.01**
Vitamin B12 deficiency	14 (12.8%)	8 (13.6%)	0.9

Data are shown as mean±standard deviation or number (%).

not yet fully elucidated, possible mechanism for vitamin D in pain management are the anti-inflammatory effects mediated by reduced cytokine and prostaglandin release and effects on T-cell responses [7]. For this reason, vitamin D deficiency may lead to increased pain sensation, increased excitability and poor muscle function because of the lack of antiinflamatuary effect and its effect on nerve function [8, 9, 21]. Recent studies have been shown that vitamin D reduces pain severity, improves musculosceletal mobility [21-23]. Apart from vitamin D's effects on musculosceletal system it has been implicated that vitamin D supplementation is also useful to reduce headache with its neuroprotective effect even in pediatric age [23, 24].

In accordance with previous studies which evaluated vitamin D levels and different pain types, our study has showed that vitamin D levels are lower in children with idiopathic chest pain. Although the most common cause of chest pain in pediatric age is idiopathic chest pain, musculosceletal problems have also an important role in the etiology with a wide range of 12.8%-64% [24, 25]. Apart from the ilnesses like costocondritis, precordial catch syndrome etc., some musculosceletal problems may not have spesific anamnestic features or physical examination findings and may be diagnosed as idiopathic chest pain. Recent studies have been showed that vitamin D deficiency is related to growing pains and nonspesific musculosceletal pain in children [22, 28]. According to these findings, we defend that children with nonspesific musculosceletal pain as a result of the lack of vitamin D can also be presented as chest pain.

Vitamin B 12 is needed to make blood cells and to provide bone density. In addition to this, it is also a well known pain killing vitamin for decades [10]. However, underlying mechanism of its the analgesic effect is poorly understood. In case of vitamin B12 deficiency, neurologic dysfunction and chronic pain can be occured [5]. Vitamin B12 deficiency is mostly related with neuropathic chronic pain like diabetic neuropathies and different types of neuralgia [10]. In the present study, vitamin B12 levels were lower in chest pain group, however this difference were not statistically significant. The present result is also, because neuropathic pain is unexpected, etiology of chest pain in children.

There is very limited data about the relationship between iron status and pain. A recent animal study has been showed the analghesic effect of iron oxide particles in inflamatuary pain sydrome [11]. However, it is a well known fact that iron status is very important for cardiovascular health and clinical spectrum of iron deficiency range from asymptomatic to heart failure [1]. For this reason, ferritin levels also were evaluated in case of related any concealed cardiac problem that could cause chest pain. Our results did not show any relationship between chest pain and iron deficiency. In addition to this result, all patients had normal electrocardiographic and echocardiographic evalution.

Limitations

The present study has some limitations. As this was a single-center study, the number of cases was very small. Due to the retrospective nature of this study, follow-up information and the effect of vitamin deficiency treatment were not been collected. Although, only detailed history and electrocardiography is enough for excluding cardiac etiology in children with chest pain, echocardiographic examination was performed because of forming the study group from the cases evaluated at pediatric emergency and/or other departments before and referred to pediatric cardiology department. Further studies should be performed with a larger number of subjects.

CONCLUSION

Children are not small size of adults and have a growing and developing nature. During this growing period, musculusceletal health which vitamin D is a major component is very important. Our study showed that low vitamin D levels are associated with idiopathic chest pain in children. We believe that most idiopathic chest pain cases may have nonspesific musculosceletal pain and measuring vitamin D levels provides to diagnose and avoid unnecessary further cardiac and other unnecessary medical testing .This study emphasized the necessity of evaluating nutritional parameters especially vitamin D levels in children with idiopathic chest pain.

Authors' contribution

SK = Study design, statistical analysis, manuscript writing, NB = Study design, data collection, DGG = Study design, review of manuscript.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

T, et al. Low iron stores in otherwise healthy children affect electrocardiographic markers of important cardiac events. Pediatr Cardiol 2017;38:909-14.
[2] Stoltzfus RJ. Iron deficiency: global prevalence and consequences. Food Nutr Bull 2003;24(4 Suppl):99-103.
[3] Ghishan FK, Kiela PR. Vitamins and minerals in inflammatory bowel disease. Gastroenterol Clin N Am 2017;46:797-808.
[4] Koduah P, Paul F, Dörr JM. Vitamin D in theprevention, predictionand treatment of neurodegenerative and neuroinflammatory diseases. EPMA J 2017;8:313-25.
[5] Tick H. Nutrition and pain. Phys Med Rehabil Clin N Am 2015;26:309-20.
[6] Straube S, Moore AR, Derry S, Mc Quay HJ. Vitamin D and chronic pain. Pain 2009;141:10-3.
[7] Shipton EA, Shipton EE. Vitamin D and pain: Vitamin D and its role in the etiology and maintenance of chronic pain states and associated comorbidities. Pain Res Treat 2015;2015:904967.
[8] Abbasi M, Hashemipour S, Hajmanuchehri F, Kazemifar AM. Is vitamin D deficiency associated with non specific musculoskeletal pain? Glob J Health Sci 2012;5:107-11.
[9] Helde-Frankling M, Björkhem-Bergman L. Vitamin D in pain management. Int J Mol Sci 2017;18. pii:E2170.
[10] Park MJ, Lee J, Lee JK, Joo SY. Prevalence of vitamin D deficiency in Korean children presenting with nonspecific lower-extremity pain. Yonsei Med J 2015;56:1384-8.
[11] Zhang M, Han W, Hu S, Xu H. Methylcobalamin: a potential vitamin of pain killer. Neural Plast 2013;2013:424651.
[12] Wu PC, Hsiao HT, Lin YC, Shieh DB, Liu YC. The analgesia efficiency of ultrasmall magnetic iron oxide nanoparticles in mice chronic inflammatory pain model. Nanomedicine 2017;13:1975-81.
[13] Chun JH, Kim TH, Han MY, Kim NY, Yoon KL. Analysis of clinical characteristics and causes of chest pain in children and adolescents. Korean J Pediatr 2015;58:440-5.
[14] Eslick GD, Jones MP, Talley NJ. Non-cardiac chest pain: prevalence, risk factors, impact and consulting - a population-based study. Aliment Pharmacol Ther 2003;17:1115-24.
[15] Friedman KG, Kane DA, Rathod RH, Renaud A, Farias M, Geggel R, et al. Management of pediatric chest pain using a standardized assessment and management plan. Pediatrics 2011;128:239-45.
[16] Evangelista JA, Parsons M, Renneburg AK. Chest pain in children: diagnosis through history and physical examination. J Pediatr Health Care 2000;14:3-8.
[17] Hvas AM, Nexo E. Diagnosis and treatment of vitamin B12 deficiency--an update. Haematologica 2006;91:1506-12.
[18] Munns CF, Shaw N, Kiely M, Specker BL, Thacher TD, Ozono K, et al. Global Consensus Recommendations on Prevention and Management of Nutritional Rickets. J Clin Endocrinol Metab 2016;101:394-415.
[19] Zadro J, Shirley D, Ferreira M, Carvalho-Silva AP, Lamb SE, Cooper C, et al. Mapping the association between vitamin D and low back pain: a systematic review and meta-analysis of observational studies. Pain Physician 2017;20:611-40.
[20] Heuch I, Heuch I, Hagen K, Mai XM, Langhammer A, Zwart JA. Is there an association between vitamin D status and risk of chronic low back pain? A nested case-control analysis in the Nord-Trøndelag Health Study. BMJ Open 2017;7:e018521.
[21] Plotnikoff GA, Quigley JM. Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculo skeletal pain. Mayo Clin Proc 2003;78:1463-70.
[22] Blagojevic Z, Nikolic V, Kisic-Tepavcevic D, Terzic Supic Z, Kovacevic R, Zivkovic Z, et al. Musculoskeletal pain and vitamin D defciency in children: a pilot follow-up study of vitamin D therapy in musculoskeletal/orthopedic conditions. Acta Chir Orthop Traumatol Cech 2016;83:21-6.
[23] Ward KA, Das G, Berry JL, Roberts SA, Rawer R, Adams JE, et al. Vitamin D status and muscle function in post-menarchal adolescent girls. J Clin Endocrinol Metab 2009;94:559-63.
[24] Cayir A, Turan MI, Tan H. Effect of Vitamin D therapy in addition to amitriptyline on migraine attacks in pediatric patients. Braz J Med Biol Res. 2014;47:349-54.
[25] Lawrence DW, Sharma B. A review of the neuroprotective role of vitamin D in traumatic brain injury with implications supplementation post-concussion. Brain Inj 2016;30:960-8.
[26] Massin MM, Bourguignont A, Coremans C, Comté L, Lepage P, Gérard P. Chest pain in pediatric patients presenting to an emergency department or to a cardiac clinic. Clin Pediatr (Phila) 2004;43:231-8.
[27] Hambrook JT, Kimball TR, Khoury P, Cnota J. Disparities exist in the Emergency Department evaluation of pediatric chest pain. Congenit Heart Dis 2010;5:285-91.
[28] Qamar S, Akbani S, Shamim S, Khan G. Vitamin D levels in children with growing pains. J Coll Physicians Surg Pak 2011;21:284-7.

The European Research Journal 2019;5(3):502-509 ORIGINAL ARTICLE

Effect of coronary artery bypass surgery on ventricular functions in patients with poor left ventricular function

Cüneyd Öztürk[1], Şenol Yavuz[2]

[1]*Department of Cardiovascular Surgery, Kadıköy Florence Nightingale Hospital, İstanbul, Turkey*
[2]*Department of Cardiovascular Surgery, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey*

DOI: 10.18621/eurj.519917

ABSTRACT

Objectives: The aim of the present study was to compare preoperative / postoperative ventricular functions of patients with ventricular dysfunction who were planned for coronary artery bypass grafting (CABG) using echocardiography and angiography, and to evaluate whether there was a significant improvement in ventricular function.

Methods: This prospective study included 30 patients with poor ventricular function who had undergone CABG at the Cardiovascular Surgery Clinics of Bursa Yüksek Ihtisas Hospital. The patients' ventricular functions were compared preoperatively and postoperatively at the 2nd, 6th and 12th months.

Results: Of the patients, 28 were males, and the mean age was 60.1 ± 8 years (range 39-71). In these cases, functional capacity improved within the early postoperative period, and global ventricular functions improved within the postoperative first year. The improvement in ejection fraction results was statistically significant at 6 months and 12 months ($p < 0.05$). A significant decrease was observed in left ventricular enddiastolic pressures within one year ($p < 0.001$). For the performance score, improvement was significant from the 2nd month ($p < 0.05$).

Conclusions: Our findings show that CABG improves ventricular function in terms of EF, PS, LVEDP and NYHA classification. In conclusion, we consider that CABG is a significantly effective option in patients with poor ventricular function.

Keywords: Coronary artery bypass grafting, poor left ventricular function, ischemic heart disease

Received: January 31, 2019; Accepted: February 28, 2019; Published Online: March 11, 2019

Ischemic heart disease is caused by insufficient transport of oxygenated blood in myocardium. The regional distribution of highly constricted and occluded lesions results in myocardial ischemia or infarction. Therefore, myocardial function abnormalities are generally segmental or regional in patients with ischemic heart disease. When very common myocardial damage occurs due to high degree of stenosis and obstruction in many places of the coronary arteries, the entire left ventricle may show reduced contraction strength. In acute coronary occlusion, there is systolic curvature or dyskinesia at the center of the relevant region, hypokinesia- or akinesia-induced contraction in the adjacent region, and compensatory hyperfunction in the intact myocardium. 80% decrease in blood flow causes akinesia, and 95% decrease in dyskinesia. If

Address for correspondence: *Cüneyd Öztürk, MD., Assistant Professor, Kadıköy Florence Nightingale Hospital, Department of Cardiovascular Surgery, İstanbul, Turkey*
E-mail: cuneydozturk@gmail.com, Fax: +90 216 4500303

e-ISSN: 2149-3189

the affected myocardium is small, the regional left ventricular dysfunction is balanced by the hyperfunction of the intact region, and the global left ventricular function is preserved [1, 2]. Each abnormality of the affected ventricular wall motion as a result of disruption of blood flow creates an additional burden for each ventricle. This dysfunction of the heart may be major and minor changes depending on the condition of the vessel occlusion and the extent of the affected area. The best method for the diagnosis of vascular occlusion is selective coronary arteriography. After the occlusion, left ventricle and its function are the most important region and function affected [1-3].

Knowing left ventricular performance in ischemic heart disease is of great importance for the management of the treatment. To assess left ventricular performance, the extent and severity of regional contraction abnormalities should be determined. For this purpose, end diastolic volume (EDV) after heart contraction, blood volume (stroke volume [SV]) and residual volume at end of systole (End-sistolic volume [ESV]) are important information about this subject. Ejection fraction (EF) reflects left ventricular pump function [1-4]. The results of these measurements show the performance of left ventricle, and the effectiveness of the treatment is followed according to these results. Coronary artery surgery studies so far have shown that patients with severe left ventricular dysfunction benefit from coronary revascularization [3, 4]. Some studies reported failure in regional wall movements after treatment, and these evaluations led to questions in clinicians' minds [4-7].

The aim of the present study was to compare preoperative/postoperative ventricular functions of in patients with ventricular dysfunction who were planned for coronary artery bypass grafting (CABG) using echocardiography and angiography, and to evaluate whether there was a significant improvement in ventricular function.

METHODS

Selection of patients

Thirty patients with coronary artery disease who were considered to have poor ventricular function were enrolled in the study at the Cardiovascular Surgery Department of Bursa Yüksek Ihtisas Training and Research Hospital. EF, left ventricular enddiastolic pressures (LVEDP), functional capacities (FC) and performance scores (PS) were used as criteria. CABG was performed on the patients with severe left ventricular failure who were met with these criteria and who had coronary artery disease.

Evaluation

Preoperative and postoperative ventricular function results of the patients were compared. In ventricular function was evaluated as poor using; (i) EF < 35%, preoperative and postoperative LVEDP, M-mode, 2D echocardiography were measured, (ii) LVEDP > 20 mmHg criteria were determined, and LVEDP was measured preoperatively and postoperatively at 12th months, and (iii) Performance score > 15 was accepted. Performance score is not a criterion alone, but it is meaningful when the analysis of each segment is performed together with other criteria. Although widespread hypokinesia is a low performance score, it is clinically poor in terms of ventricular function. The ventricular aneurysm in the two segments shows a high performance score, but has a better ventricular function than the common hypokinesia.

The performance score was calculated as 1-6 points by dividing the heart into seven segments. The total score of seven segments was added after each score was calculated for each segment. According to these points, the subjects included in this study had moderate and severe dysfunctional ventricular functions. Functional capacities of the patients were evaluated preoperatively and postoperatively according to the New York Heart Association (NYHA) criteria [1-3, 7]. In addition, risk factors of patients, previous myocardial infarction, type of angina, cardiothoracic index, vascular lesions, echocardiography and wall movements of angiography, postop used inotrope, pacemaker, IABA, the drugs they used were questioned.

The patients' morbidity and mortality rates were determined. Operative death was defined as death at the postoperative 30th day or at the time of hospitalization. The new Q-wave or CK-MB elevation of perioperative MI was defined by the fact that MB isoenzyme was greater than 50 U/L or greater than 8%

of total CK. Preoperative and postoperative ECGs were evaluated. A preoperative intraaortic balloon pump (IABP) was placed in unstable angina that did not respond to medical therapy or unstable angina with ventricular dysfunction or ECG changes in the operating room. Low-output syndrome was diagnosed in cases where IABP was needed to increase circulating system, or when inotropic medication was needed to keep cardiac index greater than 2L/min. Preoperative balloons were diagnosed with low-output when postoperative inotropic treatment was required.

Coronary revascularization

Mild hypothermia (34°C) and membrane oxygenator were used in all patients undergoing CABG. In all cases, distal anostomosis between the native coronary artery and the graft was performed under the cross-clamp, and the heart was stopped using blood cardioplegia at the room temparature, and under proximal anostomosis under the cross-clamp. Blood cardioplegia was given regularly in 20 minutes. A total of 1-5 coronary bypass grafts were applied to the cases. Preoperative angina and heart failure symptoms were evaluated according to NYHA classification. All living cases were checked at the 2nd, 6th and 12th months. Echocardiography was performed preoperatively. LVEDP was measured, and after approximately 12 months, all these patients were repeated.

Statistical Analysis

Statistical analysis was made using the SPSS version 25.0 software (SPSS IBM, Chicago, IL, USA). Descriptive statistics was given as a mean±standard deviation for continuous variables, and the normality test of the numerical variables was checked by Kolmogorov Smirnov test. Independent Samples t test was used in the comparison of two independent groups. Categorical variables werre given as number and percentage. Preoperative values and postoperative results were evaluated using Paired Samples t test. $p < 0.05$ was considered statistically significant.

RESULTS

Of the patients, 28 were males, and two were females. The mean age was 60.1 ± 8 years (range 39-71 years). All patients had angina pectoris (Grade III and IV according to the NYHA). Thirty patients had myocardial infarction (MI) at least once. A total of 22 patients had congestive heart failure (CHF) consisted of dyspnea, orthopnea, and clinical and radiological findings of pulmonary congestion. These patients were under digital+diuretic therapy. The preoperative clinical findings of the patients are summarized in Table 1.

Mean EF values of patients who underwent coronary bypass surgery were insignificant in the second month ($p = 0.718$). However, the improvement in mean EF results was statistically significant at 6 months and 12 months ($p = 0.011$ and $p = 0.004$, respectively) (Table 2). Mean LVEDP values were significantly decreased in coronary bypass patients in one year ($p < 0.001$) (Table 3). The improvement of mean performance scores (PS) for coronary bypass patients after the 2nd month was statistically significant ($p = 0.012$, $p = 0.007$ and $p < 0.001$, respectively for each measurement period) (Table 4). In patients with coronary bypasses, improvement was also statistically significant after 2 months according to the mean NYHA Classification ($p < 0.001$ for each measurement period) (Table 5).

Table 1. Preoperative clinical findings of the patients

Baseline characteristics	Data (n = 30)
Age (years)	60.1 ± 8
range	39-71
Gender, male	28 (94%)
Chest CTI	
Increased	18 (60%)
Borderline	12 (40%)
MI history	
Anteroseptal	15 (50%)
Inferior	15 (50%)
Hipertension	17 (56.6%)
Diabetes Mellitus	3 (10%)
Smoking	22 (73%)
Heredity	5 (16.6%)
High cholestherol	10 (33.3%)

CTI = cardio-thoracic index, MI = myocard infarction

Table 2. Distribution of preoperative and postoperative ejection fraction values

EF values (%)	Preoperative (n)	Postoperative 2nd month (n)	Postoperative 6th month (n)	Postoperative 12th month (n)
> 35	0	0	3	9
31-35	16	2	17	12
26-30	9	11	6	8
21-25	4	5	4	8
< 21	1	3	0	0
Mean EF	29.233	28.56	31.6	33.8
p* value (between mean EFs)	-	0.718	**0.011**	**0.002**

EF = ejection fraction. **p* values were calculated in comparison to the preoperative mean EF values.

Coronary revascularization

One (3.3%) of the cases had one, four (13.3%) had bilateral, 12 had (40%) triplet, nine (30%) had four, four (13.3%) had five, and 21 patients (70%) had internal mammary artery used for the operation. The time of the aortic cross-clamp and the time of cardiopulmonary bypass were 61 ± 19 min and 97 ± 27 min, respectively. The mean extubation time was 3.4 days. Average days of stay in intensive care unit are 5.6 days; the mean hospital stay was 15.8 days.

Table 3. Distribution of preoperative and postoperative left ventricle enddiastolic pressure values.

LVEDP (mmHg)	Preoperative (n)	Postoperative 12th month (n)	*p* value
31-35	4	4	-
26-30	18	2	-
20-25	8	24	-
Mean LVEDP	27.966	21.9	**< 0.001**

LVEDP = left ventricle enddiastolic pressure

Surgical complications

The operative mortality was 9%. These cases were excluded from the study. Five patients (16.6%) underwent IABP due to perioperative low cardiac output. Femoral embolectomy was performed in 4 (10.3%) patients with IABP. Five patients (16.6%) had peroperative Q wave myocardial infarction detected by postoperative ECG.

Table 4. Distribution of preoperative and postoperative performance scores

PS values (points)	Preoperative (n)	Postoperative 2nd month (n)	Postoperative 6th month (n)	Postoperative 12th month (n)
< 15	0	4	5	5
15-20	17	21	23	21
21-25	12	5	2	1
26-30	1	0	0	0
Mean PS	19.76	18.7	17.26	6.83
p* value (between mean PS values)	-	**0.012**	**0.007**	**< 0.001**

PS = performance scoring. **p* values were calculated in comparison to the preoperative mean PS values.

Table 5. Distribution of preoperative and postoperative functional capacity according to NYHA Classification

	Preoperative (n)	Postoperative 2nd month (n)	Postoperative 6th month (n)	Postoperative 12th month (n)
NYHA Class I	0	0	0	0
NYHA Class II	3	10	12	13
NYHA Class III	19	14	13	13
NYHA Class IV	8	6	5	4
Mean	3.23	2.86	2.76	2.7
p* value (between mean NYHA values)	-	**< 0.001**	**< 0.001**	**< 0.001**

NYHA = New York Heart Association. **p* values were calculated in comparison to the preoperative mean NYHA values.

DISCUSSION

Coronary artery surgery is the most effective and common method of left ventricular performance. This surgical method has been applied to the patients in the high risk group safely. Mortality after coronary artery surgery of about 3% before 70s decreased to 0.4-0.5% in the early 80s [3]. Coronary artery surgery studies so far have shown that patients with severe left ventricular dysfunction benefit from coronary revascularization [4]. Some studies reported failure in regional wall movements after treatment, and these evaluations led to questions in clinicians' minds. Correction of left ventricular functions, one of the most important factors for the survival of a patient with coronary artery disease, is one of the aims of CABG [5-8]. To date, contradictory studies on the left ventricular function of CABG have been published. Some studies reported failure in the regional wall movements after surgery, while others reported improvement in the dysfunction zone with or without total ventricular performance improvement [4-7].

Patients with CABG have a higher mortality rate in patients with severe left ventricular failure compared to those with normal left ventricular function. This rate has been reported to vary from 5% to 80% [9-11]. Hung *et al*. [9] reported that the operative mortality rate was 12% in their studies. This rate is 1-2% in patients with normal LV function. In these series, the identification of LV failure was emphasized as radiological cardiomegaly, ejection fraction was < 0.35, and the majority of patients were emphasized as congestive heart failure. Some studies have included aneurysmectomy cases [10] while some studies reported the results have changed from weak to good [3-7]. Our study included 30 living patients with preoperative severe left ventricular failure. Preoperative and postoperative clinical status of the patients and objective evaluations of left ventricular functions were compared.

Researchers report different types of poor ventricular function defines with improved operation results. Inamdar *et al*. [12] evaluated EF < 40% as poor ventricular function. CASS defines EF as < 36% [13]. According to Makkar *et al*. [14] EF was < 20%. In their three-year study, Kron *et al*. [15] reported a three-year survival rate of 83% after coronary revascularization in ischemic cardiomyopathy patients with 20% of EF, and reported that myocardial revascularization should be tested for patients with severe ischemic cardiomyopathy prior to transplantation. Louie *et al*. [16] reported a three-year survival rate as 72 ± 10% for patients undergoing revascularization or transplantation as a result of ischemic cardiomyopathy, and as 73 ± 6% for the transplantation-patients. In the same report; preoperative EFs were 26 ± 9%, left ventricular end diastolic dimension (LVEDD) was 68 ± 3 mm, and NYHA class was 3.9 ± 0.4 preoperatively. LVEDP was reported to be as 36 ± 9%, LVEDD was 64 ± 6 mm, and NYHA class was 1.2 ± 0.4 compared to postoperative values. As a result, they stated that successful coronary revascularization could be performed with coronary artery and operative

mortality was acceptable in the patients with (i) LVEDD < 70 mm, (ii) coronaries appropriate for bypass, and (iii) reversible myocardial ischemia in PET [16].

Because left ventricle bilateral performance could be changed significantly within the postoperative first year, Mintz *et al*. [17] summarized their findings as; (i) not to use wide-interval evaluations in determining the operation results in the same category, (ii) studies conducted at postoperative 2nd months or after could not take the early postoperative period with rapid changes as the subject, (iii) left ventricular performance with frequent sequential studies to evaluate the results of a single patient, and (iv) the wall movements in the previous infarct areas could be improved with CABG. The mechanism of low enddiastolic volume observed in the early postoperative period is the diastolic filling time, which is reduced by tachycardia after CABG. Since the pericardium is wide open during surgery, it is normal for the end-diastolic volume not to be affected as no reposition is performed. The change in left ventricular compliance (due to intra-opioid) seems to not limit the end-diastolic volume because these changes are resolved within postoperative 24 hours, and our earliest study was not within this time [17]. Operative mortality (9%) is a generally acceptable mortality in patients with poor ventricular disease according to the criteria we used. In order to reduce the need for O2, ischemic myocardium slows down segmental wall movements, leading to hemodynamic changes starting from elevation in LVEDP. This results as the clinical symptoms. However, it is thought that vascular tissue can function normally by revascularizing the segment, and hence the clinical manifestation may improve.

Almost all of alternative treatment methods in extremely limited ventricle (cardiac transplantation, asist device methods, cardiomyoplasty, etc.) have certain morbidity and mortality. The cost effect ratio of these methods should be discussed. Because the costs are quite high. In the countries with donor problems similar to Turkey, CABG may still be considered the most radical solution in the severe ventricular group. In our study group, preoperative ventricular functions were compared with the postoperative period. Therefore, the study was carried out in the living patients.

Among the methods of revascularization, the method called beating heart and the use of mini-thoracotomy methods without the need for sternotomy in recent years, especially the bad effects of the cardiopulmonary bypass on poor ventricular function is possible in selected cases. Long-term outcomes in patients with severe ventricular dysfunction are better in surgery than in medical treatment. Operative mortality rate varies between 1.6-50% in high-risk patients. This ratio should be kept as low as possible [18]. Louie *et al*. [16] concluded that successful coronary revascularization could be performed for patients with coronary artery bypass grafting and LVEDP < 70 and reversible myocardial ischemia on PET and operative mortality was acceptable. In our study, the first improvement in early postoperative period (within the first 2 months) was seen in functional capacity (FC) (according to the NYHA) and angina classification (Canadian). Although there is no revascularized myocardial ischemic pain, there is no global improvement in ventricular function in the early period, and the exercise capacity is improved. At the postoperative 2nd month, EF decreased below the preoperative value, but increased to preoperative value at 6 months. Performance score (PS) starts to improve since the postoperative 2nd month. The cleavage of the ischemic region also starts to improve in segmental movements, but it affects the EF globally in 6 months. The postoperative course of the patients in terms of both clinical and ventricular functions can reach at the best condition in 6-12 months. However, in LVEDP (30 mmHg) cases, LVEDP has not decreased despite the clinical improvement. This is probably due to the low stay of stiff tissue-induced ventricular compliance secondary to ischemia.

In our study, two patients with LVEDPs of 30 mmHg and 35 mmHg and EFs of 24% and 26% were operated urgently due to acute pulmonary edema and cardiogenic shock. Both of these cases had 2nd- and 6th-month echocardiographic measurements as LVEDPs of 50 mmHg and 50% mmHg and EFs of 45% and 46%. If there is angina in patients with severe LV failure, the operation relieves the angina and provides long-term survival. If CHF is a major symptom, CABG disappoints the results [9]. In our study, there was no improvement in the very high LVEDP group at the postoperative 12th month. We

used blood cardioplegia in all of our cases, we underwent proximal anostomosis under the cross-clamp, and thought to minimize reperfusion injury. We tried to emphasize the importance of myocardial protection and surgical procedure in extremely limited ventricles.

Christakis *et al*. [18] reported that myocardial protection type has a role on operative mortality in patients with EF of < 20-40%, and that they had better results in high-risk cases when they switched from crystalloid to blood cardioplegia. In recent years, they used warm induction as warm terminal cardioplegic infusion, and they reported that they had positive results with a continuous warm antegrade or combination of antegrade and retrograde. In patients with severe LV insufficiency with CAD, CABG can be applied because of the reduction of angina and long-term survival in patients [18]. Concerning the effects of myocardial revascularization in diffuse LV insufficiency, Mundth *et al*. [10] have reported improved LV contractions in 4 of 5 patients reevaluated with LV angiography. Kloner *et al*. [19] observed an increase in ejection fraction in some patients, but they did not specify a number. In our study, there was no change in EDV in patients with open and closed grafts. Some studies found no change in postoperative EDV. However, some studies found a decrease and increased in postoperative EDV in EF-depressed patients found decreased postoperative EDV in completely revascularized patients [18-21]. Christakis *et al*. [18] reported that patients with severe ventricular dysfunction who had isolated CABG were at high risk, and their risk was due to the urgency of the operation. They emphasized that efforts to improve outcomes should be intensified in patient selection, in the development of myocardial protection, and in the treatment of preoperative less aggressive myocardial ischemia. They also demonstrated EF, the urgency, reoperation, advanced age, left main coronary artery stenosis, and use of crystalloid cardioplegia as the factors for increasing operative mortality in patients with EF of < 20% [16]. In the group called poor ventricle, inotropic use, IABP usage, duration of mechanical ventilation support, duration of intubation, duration of stay in hospital and longer hospital stay are longer than in the group with good ventricular ischemic group. Complications related to IABP and infection complications were more frequent.

Limitations

There are some limiting aspects of our work. The study has the disadvantages of being retrospective and uncontrolled and thus produces an uncertain hypothesis. Since echocardiograms are not routinely taken after CABG surgery, selection may be a mistake. Echocardiographic measurements were performed only three times in individual patients, so we cannot say whether these changes show consistency in the long term. In addition, echocardiography is not the best way to evaluate cardiac measurement, the observed variability in EF measurement between observers is 6% [21]. The study is a thesis study based on observations of cases. Case differences may vary according to time, location and region.

CONCLUSION

In conclusion, CABG can be performed with an acceptable mortality and morbidity in patients with ischemia-induced poor ventricular function. In these cases, preoperative functional capacity and global ventricular function improved. While functional capacity is improved in the early postoperative period, recovery of global ventricular functions is in the process of postoperative 1st year. In patients with a LVEDP of more than 30 mmHg, FC (NYHA) is recovering, whereas global ventricular function does not show a significant change. However, even in these cases the quality of life is significantly increased. CABG is considered as the first choice in this group of patients that modern surgery techniques, cardiopulmonary bypass and transplantation under intensive care conditions are discussed, especially in our country.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The author disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] Ahmadi A, Stone GW, Leipsic J, Shaw LJ, Villines TC, Kern

MJ, et al. Prognostic determinants of coronary atherosclerosis in stable ischemic heart disease: anatomy, physiology, or morphology? Circ Res 2016;119:317-29.
[2] Denktas AE, Paniagua D, Jneid H. Coronary physiology assessment for the diagnosis and treatment of stable ischemic heart disease. Curr Atheroscler Rep 2016;18:62.
[3] Koene RJ, Kealhofer JV, Adabag S, Vakil K, Florea VG. Effect of coronary artery bypass graft surgery on left ventricular systolic function. J Thorac Dis 2017;9:262-70.
[4] Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, et al; American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013;62:e147-239.
[5] Kim MS, Lee JH, Cho HJ, Cho JY, Choi JO, Hwang KK, et al. KSHF Guidelines for the Management of Acute Heart Failure: Part III. Specific management of acute heart failure according to the etiology and co-morbidity. Korean Circ J 2019;49:46-68.
[6] Velazquez EJ, Bonow RO. Revascularization in severe left ventricular dysfunction. J Am Coll Cardiol 2015:17;65:615-24.
[7] Nizamic T, Murad MH, Allen LA, McIlvennan CK, Wordingham SE, Matlock DD, et al. Ambulatory inotrope infusions in advanced heart failure: a systematic review and meta-analysis. JACC Heart Fail 2018;6:757-67.
[8] Sobolev BG, Fradet G, Hayden R, Kuramoto L, Levy AR, Fitzgerald MJ. Survival benefit of coronary-artery bypass grafting accounted for deaths in those who remained untreated. J Cardiothorac Surg 2008;3:47.
[9] Hung J, Kelly DT, Baird DK, Hendel PN, Leckie BD, Grant AF, et al. Aorta-coronary bypass grafting in patients with severe left ventricular dysfunction. J Thorac Cardiovasc Surg 1980;79:718-23.
[10] Mundth ED, Harthorne JW, Buckley MJ, Dinsmore R, Austen WG: Direct coronary arterial revascularization. Treatment of cardiac failure associated with coronary artery disease. Arch Surg 1971;103:529-34.
[11] Pepper J. Managing heart failure patients with multivessel disease--Coronary Artery Bypass Graft versus Percutaneous Coronary Intervention. Card Fail Rev 2015;1:118-22.
[12] Inamdar AA, Inamdar AC. Heart failure: diagnosis, management and utilization. J Clin Med 2016;5:62.
[13] Zipes DP, Libby P, Bonow RO, Mann DL, Tomaselli GF. Braunwald's Heart Disease E-Book: A Textbook of Cardiovascular Medicine. International edition, 11th ed, Elsevier, 2018.
[14] Makkar RR, Smith RR, Cheng K, Malliaras K, Thomson LE, Berman D, et al. Intracoronary cardiosphere-derived cells for heart regeneration after myocardial infarction (CADUCEUS): A prospective, randomised phase 1 trial. Lancet 2012;379:895-904.
[15] Kron IL, Flanagan TL, Blackbourne LH, Schroeder RA, Nolan SP. Coronary revascularization rather than cardiac transplantation for chronic ischemic cardiomyopathy. Ann Surg 1989;210:348-54.
[16] Louie HW, Laks H, Milgalter E, Drinkwater DC Jr, Hamilton MA, Brunken RC, et al. Ischemic cardiomyopathy. Criteria for coronary revascularization and cardiac transplantation. Circulation 1991;84:290-5.
[17] Mintz LJ, Ingels NB, Daughters GT, Stinson EB, Alderman EL. Sequential studies of left ventricular function and wall motion after coronary arterial bypass surgery. Am J Cardiol 1980,45:210-6.
[18] Christakis GT, Weisel RD, Fremes SE, Ivanov J, David TE, Goldman BS, et al. Coronary artery bypass grafting in patients with poor ventricular function. Cardiovascular Surgeons of the University of Toronto. J Thorac Cardiovasc Surg 1992;103:1083-92.
[19] Kloner RA, Przyklenk K, Kay GL. Clinical evidence for stunned myocardium after coronary artery bypass surgery. J Card Surg 1994;9:397-402.
[20] Hillis LD, Smith PK, Anderson JL, Bittl JA, Bridges CR, Byrne JG, et al. 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2011;124:2610-42.
[21] Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, et al. ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. Circulation 2011;124:2574-609.

The European Research Journal 2019;5(3):510-514 ORIGINAL ARTICLE

Distribution of causes of acute abdominal pain in children that presented to a state hospital radiology unit according to age, gender and pathology origin

Betül Tiryaki Baştuğ

Department of Radiology, Eskişehir Osmangazi University School of Medicine, Eskişehir, Turkey

DOI: 10.18621/eurj.380401

ABSTRACT

Objectives: The term "acute abdomen" refers to any sudden non-traumatic disorder whose chief manifestations are located within the abdominal area. In this condition, urgent operation may be necessary. The aim of this study was to investigate the distribution of causes of acute abdominal pain in children according to their age, gender and origin of pathology, who presented to a state hospital radiology unit in Turkey that had undergone standardised abdominal sonography and computed tomography imaging if necessary.

Methods: This study was designed as a retrospective investigation. A sample of 1000 patients (568 males and 432 females) were selected from a pool of 3452 paediatric patients between 2014 and 2016.

Results: Acute abdomen in the paediatric age group occurred more frequently in males than females. The most common age of presentation with acute abdominal pain was between 7 and 15 years. The most common medical cause was mesenteric lymphadenitis (11%). In females, mesenteric lymphadenitis, acute appendicitis and ovarian cyst rupture were the predominant causes, whereas mesenteric lymphadenitis, acute appendicitis and urinary system pathologies were predominant in males.

Conclusions: When evaluating a child with acute abdominal pain, the most important components include taking a thorough patient history and performing repeated physical examinations. Selective use of appropriate laboratory and radiological investigations may be necessary in order to establish a specific diagnosis.

Keywords: Paediatric, acute abdomen, distribution of cause

Received: January 17, 2018; Accepted: July 31, 2018; Published Online: September 6, 2018

Abdominal pain is a common complaint in the emergency department. Trauma, appendicitis and intussusception are the most common reasons for emergency abdominal imaging in paediatric patients. The term "acute abdomen" refers to any sudden non-traumatic disorder whose chief manifestations are located within the abdominal area. For patients in this condition, urgent operation may be necessary. Delay in diagnosis and treatment affects the outcome [1]. The aim of this study was to determine the distribution of causes of acute abdominal pain in children that presented to a state hospital radiology unit according to age, gender and origin of pathology that had undergone standardised abdominal sonography and compued tomography imaging if necessary.

METHODS

The study was designed as a retrospective

Address for correspondence: *Betül Tiryaki Baştuğ, MD., Assistant Professor, Eskişehir Osmangazi University School of Medicine, Department of Radiology, Eskişehir, Turkey*
E-mail: betultryak@yahoo.com

e-ISSN: 2149-3189

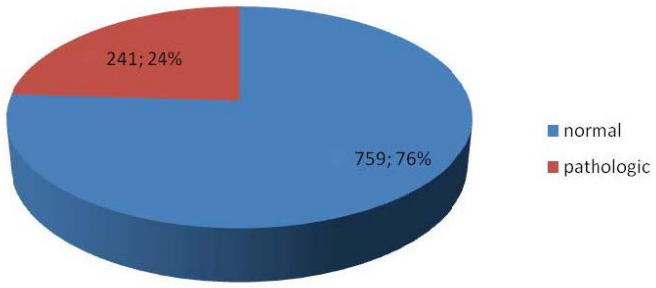


Figure 1. Distribution of patients according to normal or pathologic radiologic findings.

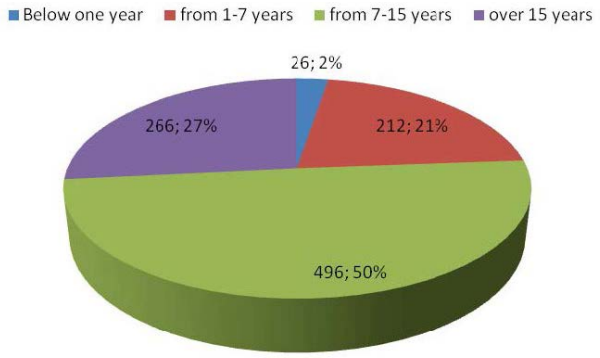


Figure 2. Distribution of patients according to age.

investigation. The sample included 1000 patients (568 males and 432 females) that were randomly selected from a pool of 3452 paediatric patients that had undergone standardised abdominal sonography between 2014 and 2016. The inclusion criteria were patients aged between 0 and 18 years and the presence of acute abdominal pain before or during consultation with the physician. The exclusion criteria were patients aged over 18 years or the absence of acute abdominal pain as a symptom before or during the examination.

Statistical Analysis

In the data analyses, frequency analysis was performed and percentages were calculated. Analyses were performed with SPSS 22.0 software. The images were created with Microsoft Excel 2017 software.

RESULTS

There was no pathology identified in 76% (n = 759) of the patients, with normal results obtained in both the sonography and CT exams. Figure 1 shows the distribution of patients according to normal or pathologic radiologic findings.

In the study group, the minimum age was 0 years and maximum was 17 years. According to age, children were divided into the following (four) groups: (1) patients aged younger than 1 year old (26/1000, 2.6%; 20 (2.0%) males and 6 (0.6%) females); (2) patients aged from 1-7 years old (212/1000, 21.2%; 176 (17.6%) males and 36 (3.6%) females); (3) patients aged from 7-15 years (496/1000, 49.6%; 310 (31%) males and 186 (18.6%) females); and (4) patients aged over 15 years (266/1000, 26.6%; 150

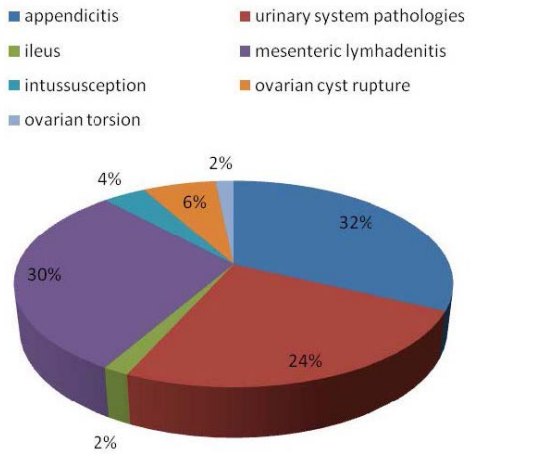


Figure 3. Distribution of patients according to pathology.

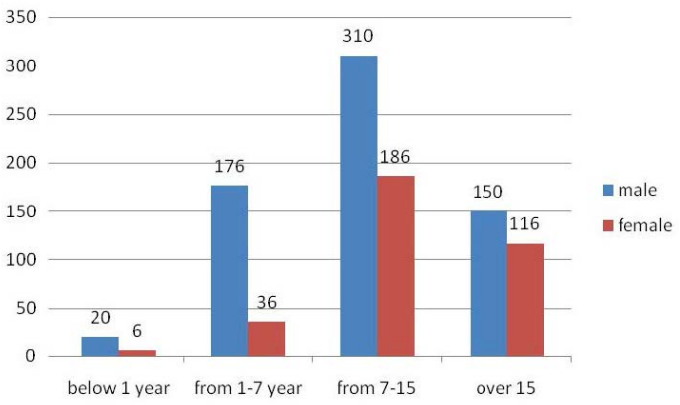


Figure 4. Distribution of patients according to gender.

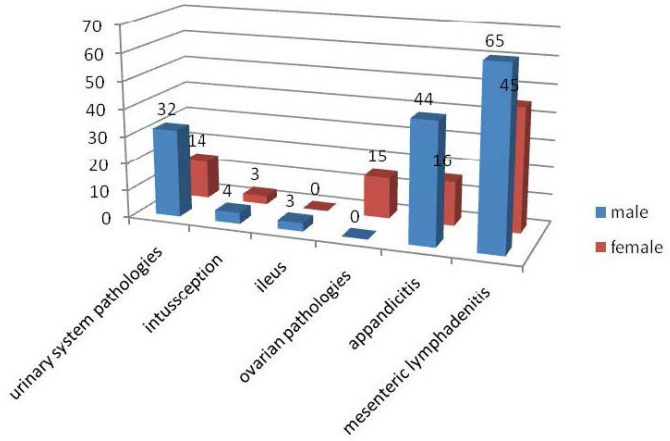


Figure 5. Distribution of patients according to gender and pathology origin.

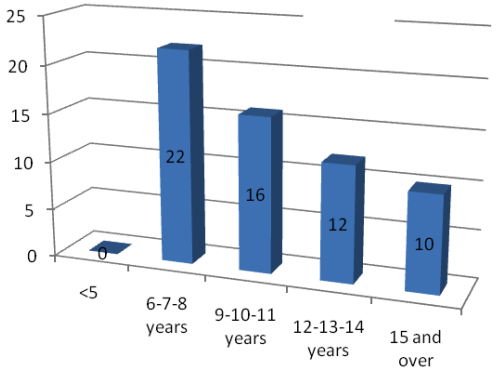


Figure 6. Distribution of appendicitis detected patients according to age.

(15%) males and 116 (11.6%) females). Figure 2 shows the distribution of patients according to age. Acute abdomen in the paediatric age group was more prevalent in males than in females. Figure 3 shows the distribution of patients according to gender.

Abdominal pain and vomiting were the most common clinical symptoms. Of the 1000 patients, 45 had appendicitis, 30 had urinary system pathologies, 3 had ileus, 110 had mesenteric lymhadenitis, 7 had intussusception, 12 had an ovarian cyst rupture and 3 patients showed ovarian torsion, as detected by ultrasound. Figure 4 shows the distribution of patients according to pathology, and Figure 5 shows the distribution of patients according to gender and origin of pathology.

The highest frequency of cases was represented by mesenteric lymphadenitis (110 patients, 11%). Figure 6 shows the distribution of mesenteric lymphadenitis among patients according to age. Figure 7 shows the distribution of ovarian pathologies according to patient age.

Ultrasonography should still be the first imaging modality for detecting the underlying pathology of the paediatric abdominal emergency. In 45 patients, CT was performed. Ureteral calculi was detected by CT scans in 16 patients and appendicitis in 15 patients, which were considered together with secondary findings from a previous ultrasound. Figure 8 shows the distribution of appendicitis in patients according to age, and Figure 9 shows the distribution of urinary pathologies in patients according to age. In three patients, ileus was verified by CT.

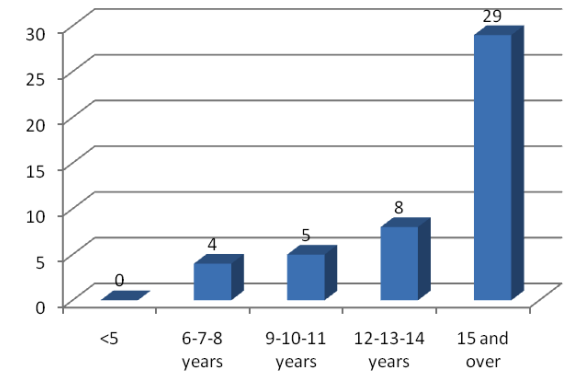


Figure 7. Distribution of urinary pathology detected patients according to age

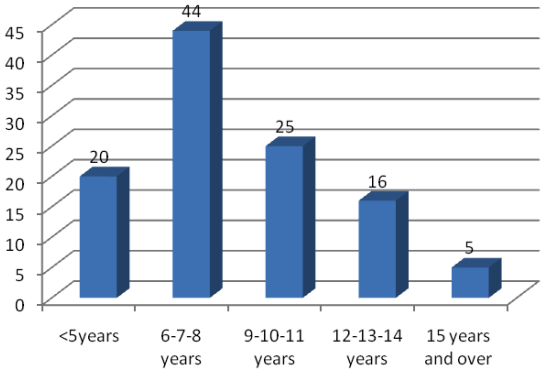


Figure 8. Distribution of mesenteric lymphadenitis detected patients according to age

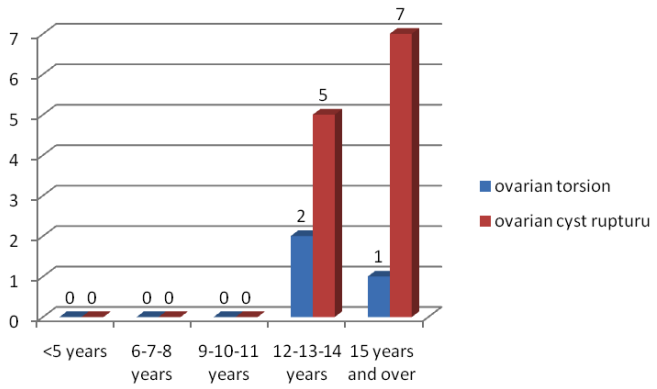


Figure 9. Distribution of ovarian pathologies detected patients according to age

DISCUSSION

Acute abdominal pain is one of the most common complaints in childhood, and one that frequently requires rapid diagnosis and treatment in the emergency department. The term acute abdominal pain refers to non-traumatic abdominal pain of rapid onset with duration of less than five days [2]. Acute abdominal pain can be divided in urgent and non-urgent conditions. Urgent causes require treatment within 24 hours to prevent serious complications whereas for non-urgent conditions treatment is not necessitated within a fixed period [3]. Although acute abdominal pain is typically self-limiting and benign, there are potentially life-threatening conditions that require urgent management, such as appendicitis, intussusception or bowel obstruction. The most difficult challenge is making a timely diagnosis so that treatment can be initiated to prevent morbidity [4].
Viruses or bacteria can be a reason of abdominal pain. Viral infections tend to be off quickly, while bacterial infections may want an antibiotic. Food poisoning, food allergies, eating excessive food, or gas production can cause pain. Surgical problems include appendicitis or blockage of the bowels. Medical causes for example diabetes can be a reason of abdominal pain.

Most simple causes of abdominal pain do not last long and usually gone within 24 hours. Any abdominal pain that continues longer than 24 hours should be evaluated by a physician. Most simple pains are located in the center of the abdomen. Pain felt in other areas especially located low and down on the right side of the abdomen. is more concerning. Until proven otherwise this should be considered as appendicitis.
Children vomit quite frequently with abdominal pain. Vomiting does not always indicate a important problem. Vomiting for longer than 24 hours is a rightful reason to call the physician. Diarrhea is also common with abdominal pain . This generally points out that a virus is the cause. This can continue for several days but usually only lasts less than 72 hours.

The presence of fever does not always shows a serious problem. Indeed, a normal temperature can be seen with the more serious causes of abdominal pain. One critical point is that an abdominal pain actually can come from somewhere else. Testicular torsion can be given as an example for this situation [5]. Abdominal pain associated with any trouble urinating, could show an infection.
Age is a key factor when evaluating the cause, as the incidence and symptoms of different conditions vary greatly over paediatric age groups. Differential diagnosis of the acute abdominal pain is influenced by many factors, especially patient age.

In the emergency department, ultrasound and computed tomography are widely used to identify the cause of abdominal pain [6, 7]. Although computed tomography is more accurate than ultrasound, ultrasound is the preferred imaging modality for the initial evaluation of potential causes of paediatric abdominal pain because it is non-invasive, radiation-free and less expensive [8].

In the current study, acute abdomen in the paediatric age group was found to occur more frequently in males than females. The most common age of presentation with acute abdominal pain was between 7-15 years of age. The most common medical cause was mesenteric lymphadenitis (11%). In the 7-15 and over 15 age groups, acute appendicitis, mesenteric lymphadenitis, ovarian follicular cysts and urinary system pathologies were the predominant causes. In the 0-4 age group, intussusception was predominant. Intestinal obstruction was more frequent in patients aged under 5 years. In females, mesenteric lymphadenitis, acute appendicitis and ovarian cyst rupture were the main causes of acute abdomen, whereas in males mesenteric lymphadenitis, acute appendicitis and urinary system pathologies were predominant.

CONCLUSION

When evaluating a child with acute abdominal pain age, gender, the onset of the pain, pain duration, pain location and associated clinical findings are key factors as the incidence and symptoms of different conditions vary greatly over paediatric age groups. In this state the most important components are taking a comprehensive patient history and repeated physical examinations. Selective use of appropriate laboratory and radiological investigations may be necessary in order to establish a specific diagnosis.

Conflict of interest

The author disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The author disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] Boey JH. Acute abdomen in current surgical diagnosis and treatment. 9th ed. 1991.
[2] Laméris W, van Randen A, Dijkgraaf MGW, Bossuyt PMM, Stoker J, Boermeester MA. Optimization of diagnostic imaging use in patients with acute abdominal pain (OPTIMA): Design and rationale. BMC Emerg Med 2007;7:9.
[3] Hill BC, Johnson SC, Owens EK, Gerber JL, Senagore AJ. CT scan for suspected acute abdominal process: impact of combinations of IV, oral, and rectal contrast. World J Surg 2010;34:699-703.
[4] Leung AKC, Sigalet DL. Acute abdominal pain in children. Am Fam Phys 2003;67:2321-8.
[5] Ferry F. Jr., Abdominal pain in children. emedicinehealth. Accessed:11/20/2017
[6] Vignault F, Filiatrault D, Brandt ML, Garel L, Grignon A, Ouimet A. Acute appendicitis in children: evaluation with US. Radiology 1990;176:501-4.
[7] Soundappan SV, Holland AJ, Cass DT, Lam A. Diagnostic accuracy of surgeon-performed focused abdominal sonography (FAST) in blunt paediatric trauma. Injury 2005;36:970-5.
[8] Reich JD, Brogdon B, Ray WE, Eckert J, Gorell H. Use of CT scan in the diagnosis of pediatric acute appendicitis. Pediatr Emerg Care 2000;16:241-3.

The European Research Journal 2019;5(3):515-521 ORIGINAL ARTICLE

Comparison of laboratory and imaging methods associated with bone metabolism in patients with or without renal failure under the age of 45 years with elevated parathyroid hormone levels

Hande Peynirci[1], Canan Ersoy[2], Vildan Gürsoy[3], Ayten Girgin[3], Mehmet Ali Aşık[3], Ahmet Gültepe[3], Güven Özkaya[4], Emel Işıktaş Sayılar[5], Alparslan Ersoy[6]

[1]Department of Internal Medicine, Division of Endocrinology and Metabolism, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Turkey
[2]Department of Internal Medicine, Division of Endocrinology and Metabolism, Uludağ University School of Medicine, Bursa, Turkey
[3]Department of Internal Medicine, Uludağ University School of Medicine, Bursa, Turkey
[4]Department of Statistics, Uludağ University School of Medicine, Bursa, Turkey
[5]Department of Internal Medicine, Division of Nephrology, Edirne State Hospital, Edirne, Turkey
[6]Department of Internal Medicine, Division of Nephrology, Uludağ University School of Medicine, Bursa, Turkey

DOI: 10.18621/eurj.378720

ABSTRACT

Objectives: Although bone biopsy is considered the gold standard for the definitive diagnosis of renal osteodystrophy; it is not suitable for routine clinical practice due to its invasive nature. The present study was aimed to evaluate and compare the bone mineral status using dual energy X-ray absorptiometry of patients with or without chronic kidney disease in young population with elevated parathyroid hormone levels.

Methods: This was a single center, cross-sectional, retrospective study conducted in patients younger than 45 years of age. The study was performed in the outpatient clinic of a university hospital. Patients with elevated parathyroid hormone levels were included.

Results: Among them, 29 had renal insufficiency, 158 had normal renal function. Measured bone mineral density with dual energy X-ray absorptiometry and laboratory values were collected from patient files. The primary end point was to assess the efficiacy of dual energy X-ray absorptiometry in patients with or without renal failure. Except Z score at Ward's triangle, all of the T and Z scores at lomber, femur neck, trochanteric, and intertrochanteric areas were found significantly lower in patients with chronic kidney disease compared to those without ($p < 0.001$).

Conclusion: Dual energy X-ray absorptiometry seemed to be a reliable method for detection of osteoporosis in premenopausal female and male patients younger than 45 years of age with or without renal failure with elevated parathyroid hormone levels.

Keywords: hyperparathyroidism, renal insufficiency, osteoporosis, dual energy X-ray absorptiometry

Received: January 23, 2018; Accepted: March 21, 2018; Published Online: June 4, 2018

Address for correspondence: *Hande Peynirci, MD., Kanuni Sultan Süleyman Training and Research Hospital, Department of Internal Medicine, Division of Endocrinology and Metabolism, Atakent Street, No: 46/1, 34303 Küçükçekmece, İstanbul, Turkey*
E-mail: handepeynirci@yahoo.com.tr, Tel: +90 212 4041500, Fax: +90 212 5714790

e-ISSN: 2149-3189

Chronic kidney disease (CKD) is a functional definition which is characterized by irreversible and progressive decrement in renal functions. Renal function impairment has many negative effects on cardiovascular, hematopoietic, and gastrointestinal system as well as bone metabolism [1]. Changes in mineral metabolism and bone structure develop early in the course of CKD and worsen with progressive loss of kidney function. The Kidney Disease: Improving Global Outcomes (KDIGO) committee refined CKD-mineral and bone disorders (CKD-MBD), as a systemic disorder of mineral and bone metabolism due to CKD and manifested by either one or a combination of (i) abnormalities of calcium, phosphorous, parathyroid hormone (PTH) or vitamin D metabolism; (ii) abnormalities of bone turnover, mineralization, volume, linear growth, or strength; and (iii) vascular or other soft tissue calcification [2]. Hyperparathyroid-mediated high-turnover bone disease (osteitis fibrosa cystica), and adynamic bone disease are the bone diseases related to CKD.

Osteoporosis in CKD patients is only a part of a wider spectrum of metabolic bone problems. Osteoporosis is defined as a skeletal disorder characterized by compromised bone strength that leads to an increased risk of fracture [3]. Bone biopsy is considered the gold standard for the definitive diagnosis of renal osteodystrophy; however, it is not suitable for routine clinical practice due to its invasive nature. Also, requirement for special equipment and expertise are other limiting factors. For that reason, most clinicians perform bone biopsies for clinical research [4-6]. Although dual energy X-ray absorptiometry (DXA) does not discriminate between CKD-MBD, it has been widely used for the assesment of bone mineral deficiency status in renal insufficient patients. Diagnostic accuracy, the short exposure time and the low radiation dose are the advantages of this imaging method [7, 8].

Postmenopausal period and advanced age are the other important unmodifiable risk factors for osteoporosis. In this study, we aimed to evaluate and compare the laboratory, imaging, and treatment methods associated with bone metabolism in patients with or without renal failure in premenopausal women and men younger than 45 years with elevated PTH levels.

METHODS

Study population

After getting an approval from the local ethics committee, patients with or without renal failure younger than 45 years with elevated PTH levels who applied to internal medicine, endocrinology and nephrology outpatient clinics of Uludağ University School og Medicine Hospital between January 2011 and January 2012 were searched retrospectively and included in the study. The study was conducted in accordance with the Declaration of Helsinki. Patients aged 18-45 years, having parathyroid hormon increasement and files fulfilling the laboratory and imaging data were included while patients aged > 45 years, who had malignancy, having the diagnosis of diseases known to affect bone metabolism (such as hyperthyroidism, rheumatological disease), who had undergone hysterectomy, who were using steroids and who were on therapy for osteoporosis were excluded from the study.

Study protocol

Patients with elevated PTH levels were divided into two groups depending on whether they had renal insufficiency or not. Patients' age, gender, co-morbidities, and the type and duration of dialysis if present were recorded. Serum urea, creatinine, albumin, sodium, potassium, chloride, calcium, phosphorus, PTH and 25-OH-vitamin D with 24-hour urinary excretion of calcium and phosphorus values were determined. Chemiluminescent method was used for determination of PTH and 25-OH-vitamin D. ARCHITECT assay (Abbott Diagnostics, Abbott Park, IL, USA) were performed for their measurement. T and Z scores of the lumbar vertebrae 1-2-3-4, total lumbar, femur neck, trochanteric and intertrochanteric area, Ward's triangle and total femur monitored by DXA (Hologic) were recorded from patients' files. The side of the parathyroid adenoma determined by neck ultrasonography (USG) and/or parathyroid scintigraphy and the histopathological diagnosis of the patients who had undergone surgery were evaluated. The treatment modalities as well as the frequency of follow-up visits were analyzed.

Statistical Analysis

Statistical analysis was performed using SPSS

software version 20.0. Shapiro Wilk test was used to determine normality. Mann Whitney U test and Kruskal Wallis tests were used for comparison of non normally distributed data. The categorical data were analyzed with Pearson Chi-Square Test and Fisher's Exact test. The level of significance was defined as $p < 0.05$.

RESULTS

The records of 300 patients were analyzed and 187 patients fulfilling the inclusion criteria were enrolled to the study. Among all patients with elevated PTH, 29 had renal insufficiency while 158 had normal renal function. Sixteen of CKD patients (55.2%) were women, and 13 (44.8%) were men and the mean age was 40.5 (range 20-48) years. Among the patients without CKD, 143 (90.5%) were women, and 15 (9.5%) were men and the mean age was 36 (22-47) years. Except one patient with compansated CKD, 4 patients were managed with peritoneal dialysis, 19 with hemodialysis, and 5 with both. During follow-up, 17 patients underwent renal transplantation. The causes of CKD were hypertension (HT) in 7 patients, glomerulonephritis in 5, vesicoureteral reflux in 4, polycystic kidney disease in 2, neurogenic bladder in 1, both kidney agenesia + nephrectomy in 1, analgesic nephropathy in 1, and tacrolimus nephropathy in 1. The primary kidney diseases of 7 patients were not known. Duration of dialysis ranged from 3 years to 24 years, mean duration was 11.78 years. The most common comorbidity was HT (62.07%) in patients with CKD, and thyroid disease in those without CKD (24.7%). None of the patients had hyperthyroidism that may affect DXA results.

The laboratory data of the patients with and without renal failure was shown in Table 1. Serum urea, creatinine, phosphorus, PTH, and 25-OH-D levels were statistically significantly elevated and chloride level were statistically significantly decreased in patients with CKD compared to those without.

T and Z scores of lumbar 1-2-3-4, total lumbar, femur neck, trochanteric, intertrochanteric area, Ward's triangle, and total femur of the patients monitored by DXA were shown in Table 2. DXA imaging were performed before transplant procedure for 17 patients who underwent renal transplantation.

Table 1. The laboratory values of the patients with or without chronic kidney disease and their comparisons

	Normal Reference Interval	Patients with CKD (min-max)	Patients without CKD (min-max)	*p* value
Urea (mg/dL)	10-50	82.5 (27-277)	24 (11-63)	**< 0.001**
Creatinine (mg/dL)	0.6-1.3	6.15 (0.6-15.1)	0.7 (0.4-1.1)	**< 0.001**
Albumin (g/dL)	3.5-5.0	4 (2.9-4.7)	4.1 (2.8-5.1)	0.062
Sodium (mmol/L)	136-145	138.5 (109-143)	139 (133-147)	0.249
Potassium (mmol/L)	3.5-5.1	4.45 (3.3-7.3)	4.3 (3.1-5.4)	0.265
Chloride (mmol/L)	98-107	103 (96-112)	105 (97-141)	**0.002**
Calcium (mg/dL)	8.4-10.2	9.7 (7.5-12.2)	9.9 (7.6-18.9)	0.285
Phosphorus (mg/dL)	2.3-4.7	3.9 (2.4-7.5)	3 (1.1-4.6)	**< 0.001**
Parathormone (pg /mL)	15-68.3	824 (99-2839)	125.1 (54-2600)	**< 0.001**
25-OH-vitamin D (µg/L)	> 30	16 (3.7-35)	10.3 (2-48.87)	**0.024**
Urinary calcium excretion (mg/ day)	80-320	155 (24-417)	204 (14-1137)	0.405
Urinary phosphorus excretion (mg/ day)	250-1000	558 (290-558)	693 (0-1930)	0.170

CKD = chronic kidney disease

Table 2. The T and Z scores of the patients with or without with or without chronic kidney disease and their comparisons

	Patients with CKD (min-max)	Patients without CKD (min-max)	*p* value
Lumbar 1 T score	-1.6 (-3.4 - 0.6)	-0.7 (-6.30 - 6.5)	**0.022**
Lumbar 2 T score	-1.5 (-4.3 - 0)	-0.3 (-6.9 - 17)	**< 0.001**
Lumbar 3 T score	-2.15 (-5.4 - 0.2)	-0.9 (-7.4 - 5)	**< 0.001**
Lumbar 4 T score	-2.5 (-5.1 - 0.1)	-1.1 (-7.8 - 4.2)	**< 0.001**
Total lumbar T score	-2.1 (-4.2 - 0.1)	-0.9 (-7.2 - 5.3)	**< 0.001**
Lumbar 1 Z score	-1.15 (-3.4 - 0.7)	-0.4 (-6.6 - 6.5)	**0.015**
Lumbar 2 Z score	-1.6 (-4.1 - 0.7)	-0.5 (-6.5 - 5.8)	**< 0.001**
Lumbar 3 Z score	-1.9 (-4.6 - 0.3)	-0.7 (-7 - 5)	**< 0.001**
Lumbar 4 Z score	-2.35 (-5.1 - 0.9)	-0.8 (-7.5 - 4.3)	**< 0.001**
Total Lumbar Z score	-1.9 (-3.6 - 0.3)	-0.7 (-6.8 - 5.3)	**< 0.001**
Femur neck T score	-1.75 (-2.7 - 4.2)	-0.7 (-5.3 - 5)	**0.003**
Femur trochanteric T score	-1.55 (-2.8 - 0.2)	-0.8 (-5.7 - 5.9)	**< 0.001**
Femur intertrochanteric T score	-1.1 (-2.5 - 0.5)	-0.1 (-3.9 - 4)	**< 0.001**
Femur wards T score	-1.35 (-3 - 0.3)	-0.9 (-4.6 - 8)	**0.048**
Femur total T score	-1.4 (-3 - 0.3)	-0.2 (-4.7 - 5.3)	**< 0.001**
Femur neck Z score	-1.2 (-2.4 - 4.5)	-0.4 (-5 - 5.1)	**0.031**
Femur trochanteric Z score	-1.35 (-2.4 - 0.3)	-0.6 (-5.5 - 5.9)	**0.001**
Femur intertrochanteric Z score	-0.85 (-2.6 - 0.5)	0 (-3.8 - 4.1)	**< 0.001**
Femur wards Z score	-0.6 (-2.5 - 0.7)	-0.1 (-3.9 - 8.1)	0.066
Femur total Z score	-0.95 (-3.9 - 0.5)	0.1 (-4.5 - 5.3)	**< 0.001**

DXA = Dual energy X-ray absorptiometry, CKD = chronic kidney disease

Except Z score at Ward's triangle, all of the T and Z scores were statistically significantly lower in CKD patients.

Twenty-one (72.4%) of 29 patients with CKD had neck USG. Among 13 patients who had parathyroid adenomas, 4 had on the right side, 3 on the left side, and 6 on both sides. Twenty-two patients (75.9%) were scanned with parathyroid scintigraphy and parathyroid adenomas were detected in 10 of them. Four of these 10 patients had on the right side, 3 on the left side, and 2 on both sides. The information about localization was missing in 1 patient.

Ninety-nine of 158 (67.7%) patients without CKD were examined by neck USG for detecting parathyroid adenomas. Adenomas were not detected in 51 patients. Among 48 patients with parathyroid adenomas, 31 patients had on the right side, 15 on the left, and 1 on both sides and information about localization was missing in 1 patient. One hundred and eighteen (74.7%) patients were scanned with parathyroid scintigraphy and parathyroid adenomas were found in 46 of them. Twenty-seven patients had on the right side, 15 on the left side, and 1 patient on both sides. The information about localization was missing in 3 patients.

Thirteen of the 29 patients (44.8%) with CKD had parathyroidectomy. Histopathological examination revealed 2 adenomas, 10 hyperplasias, and 1 normal parathyroid tissue. Except 1 patient who was lost to follow up and 1 patient who had recurrent disease, there weren't any problems during follow-up visits of the rest of the patients. Forty-five of 158 patients without CKD (27.8%) underwent surgery and had 34 (75.6%) adenomas, 3 hyperplasias, 1 carcinoma and 7

normal parathyroid tissue on pathological examination. In 37 patients (90.2%) recurrence was not detected and 3 patients lost follow-up.

DISCUSSION

Osteoporosis is a condition of the skeleton characterized by an increased risk of bone fracture resulting from deficient mechanical resistance. The mechanical resistance of bones is conditioned by bone mineral density (BMD) and the quality of bone tissue [9]. Osteoporosis criteria according to the World Health Organization are based on the BMD evaluation of the proximal end of the femur (hip) or vertebrae in postmenopausal women, given as the T−score expressed as the number of standard deviations (SD); the baseline is the maximum bone mass: >−1 SD: normal value, from −1 to –2.5 SD: osteopenia, <−2.5 SD: osteoporosis, <−2.5 SD and osteoporotic fracture: advanced osteoporosis. The Z−score should be considered in children and premenopausal female and male subjects; the normal values are obtained from normal sex and age matched reference population [10].

Senility and postmenopausal status are important unchangeable risk factors for osteoporosis [11]. CKD is also an additional facilitiating factor. Mineral and bone disorders related to CKD result from the imbalance between calcium, phosphorus, PTH, and vitamin D. Decreased renal synthesis of 1,25(OH)2D3, phosphorus accumulation, increased fibroblast-growth factor (FGF)-23, decreased intestinal calcium, bone resistance to PTH action, hypocalcemia, chronic metabolic acidosis, and vitamin D deficiency are the metabolic disturbances related to the pathophysiology of CKD-MBD [12-15].

In this study we evaluated and compared the bone mineral status of patients with or without CKD in young population with elevated PTH levels. We used DXA for evaluating bone mineral status. Although DXA is the most commonly used technique to assess BMD in patients with and without CKD, it has some limitations. DXA measures areal BMD, rather than volumetric BMD. In addition, it cannot distinguish between cortical and trabecular bone, and it cannot assess bone microarchitecture or bone turnover [16, 17].

A study performed to determine the prevalence and associated risk factors of CKD between 1999-2004 in the United States has been reported to occur more frequently in men over 60 years old [18]. Of our patients, 55.2% were female. It may be due to the selected group or the number of the patients with CKD. The most common cause of CKD is diabetes mellitus (DM) and the second one is HT [18, 19]. In our study, HT was the most common cause of CKD. This result may be related to the younger age of our patients because type 2 DM is usually diagnosed at a later age. Besides, it takes approximately 10 years in patients with type 2 DM and 20 in patients with type 1 DM to develop renal failure.

Serum urea, creatinine, phosphorus, PTH, and 25-OH-D levels were statistically significantly elevated and chloride level was statistically significantly decreased in patients with CKD compared to those without. Vitamin D deficiency was shown to be more prevalent even in the early stages of CKD in comparison to the general population [20]. In contrast to the expected, 25-OH-D levels were statistically significantly elevated in our patients with CKD probably due to the replacement therapies. Another important result of our study was that, 25-OH-D levels in patients without CKD were low although our country has advantage of sunshine exposure. Our finding is also in line with the data from one of the largest studies done in Turkey by Satman *et al*. [21]. They found that the overall prevalence rate of vitamin D deficiency was 93%, with the highest rate seen in younger (< 40 years) age group (96.2%) in women, and elderly (≥ 65 years) age group (91.9%) in men [21].

Effect of CKD on bone mineral density using DXA has not yet been clearly elucidated. Some studies have shown that low BMD measurements were more prevalent in patients with CKD like our findings while several other studies have reported no relationship between CKD and low BMD measurements [22-25]. In our study, except Z score at Ward's triangle, all of the T and Z scores were found statistically significantly lower in CKD patients especially T and Z scores at lumbar 3 and 4 [7, 26-28]. In our study, we found that the BMD measurement at L2-L4 region was significantly higher than that at femur neck in both genders ($p < 0.01$). Although, Z-scores were affected more in some studies that were done in

postmenopausal women with CKD, in our study we found T scores to be affected as much as Z-scores in premenopausal women and men. In addition, postmenopausal and senile osteoporosis may coexist with all forms of bone disease in kidney dysfunction. Most of the studies were done in postmenopausal women in the literature. In our study we chose a group that was not influenced by menopause and senility. In the patients wihout CKD, there was no risk factor other than vitamin D deficiency.

Although dual-phase dual-isotope iodine 123 (^{123}I)/technetium Tc 99m (^{99}mTc) sestamibi scintigraphy and ultrasonography and their comparison for determination of enlarged parathyroid glands in primary hyperparathyroidism has been discussed in many studies, their utility in renal hyperparathyroidism is rarely addressed [29, 30]. Périé *et al*. [31] reported that a series of 20 patients consecutively referred for parathyroidectomy, hyperplastic parathyroid glands were detected by USG in 75%, dual-phase ^{123}I/^{99}mTc sestamibi scintigraphy in 66%, and both methods in 88%. Most missed glands at scintigraphy corresponded to superior glands, whereas false-negative results at USG correlated with low gland weight [31]. In another study which aimed to detect the usefulness of the combination of USG and 99mTc-sestamibi scintigraphy in the preoperative evaluation of uremic secondary hyperparathyroidism it was reported that the sensitivities of scintigraphy and USG were 62% and 55% respectively, and the specificity was 95% for both procedures. The sensitivity of combined techniques was 73% [32]. In our study, 21 (72.4%) of 29 patients with CKD had neck USG and 13 patients had parathyroid adenomas. Twenty-two patients (75.9%) were scanned with parathyroid scintigraphy and parathyroid adenomas were detected in 10 of them. It was seen that 99 of 158 (67.7%) patients without CKD examined with neck USG and 48 patients had adenomas. It was found that 118 (74.7%) patients were scanned with parathyroid scintigraphy and parathyroid adenomas were found in 46 of them. From these results cervical USG and parathyroid sintigraphy seem to be useful radiologic techniques to localize parathyroid lesion before considering surgery.

Limitations

The limitations of our study are the cross-sectional design and the relatively small sample size in CKD group. They precluded us from drawing certain causal conclusions.

CONCLUSION

The patients with CKD have lower BMD scores (both T and Z scores at all sites) and higher levels of vitamin D may be observed due to replacement therapies. Low vitamin D level seemed to be an additional risk factor for osteoporosis in patients without CKD although our country has advantage for sunshine exposure. Besides, DXA seemed to be a reliable method for osteoporosis detection in both groups.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] Eknoyan G, Lameire N, Barsoum R, Eckardt KU, Levin A, Levin N, et al. The burden of kidney disease: improving global outcomes. Kidney Int 2004;66:1310-4.
[2] Ketteler M, Block GA, Evenepoel P, Fukagawa M, Herzog CA, McCann L, et al. Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder: Synopsis of the Kidney Disease: Improving Global Outcomes 2017 Clinical Practice Guideline Update. Ann Intern Med 2018;168:422-30.
[3] Riggs BL, Melton LJ 3rd. The worldwide problem of osteoporosis: insights afforded by epidemiology. Bone 1995;17(5 Suppl):S505-11.
[4] Malluche HH, Mawad HW, Monier-Faugere MC. Renal osteodystrophy in the first decade of the new millennium: analysis of 630 bone biopsies in black and white patients. J Bone Miner Res 2011;26:1368-76.
[5] Miller PD. The role of bone biopsy in patients with chronic renal failure. Clin J Am Soc Nephrol 2008;3 Suppl 3:S140-50.
[6] Fontaine MA, Albert A, Dubois B, Saint-Remy A, Rorive G. Fracture and bone mineral density in hemodialysis patients. Clin Nephrol 2000;54:218-26.
[7] Khan MI, Syed GM, Khan AI, Sirwal IA, Anwar SK, Al-Oufi AR, et al. Mean bone mineral density and frequency of occurrence of osteopenia and osteoporosis in patients on hemodialysis: a single-center study. Saudi J Kidney Dis Transpl 2014;25:38-43.
[8] Jannot M, Mac-Way F, Lapierre V, Lafage-Proust MH. The use of bone mineral density measured by dual energy X-ray absorptiometry (DXA) and peripheral quantitative computed microtomography in

chronic kidney disease. J Nephrol 2017;30:635-43.
[9] Rachner TD, Khosla S, Hofbauer LC. Osteoporosis: now and the future. Lancet 2011;377:1276-87.
[10] NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. JAMA 2001;285:785-95.
[11] O'Connor KM. Evaluation and treatment of osteoporosis. Med Clin North Am 2016;100:807-26.
[12] Lima GA, Paranhos Neto Fde P, Pereira GR, Gomes CP, Farias ML. Osteoporosis management in patient with renal function impairment. Arq Bras Endocrinol Metabol 2014;58:530-9.
[13] Ford ML, Smith ER, Tomlinson LA, Chatterjee PK, Rajkumar C, Holt SG. FGF-23 and osteoprotegerin are independently associated with myocardial damage in chronic kidney disease stages 3 and 4. Another link between chronic kidney disease-mineral bone disorder and the heart. Nephrol Dial Transplant 2012;27:727-33.
[14] Kovesdy CY, Anderson JE, Kalantar-Zadeh K. Association of serum bicarbonate levels with mortality in patients with non-dialysis-dependent CKD. Nephrol Dial Transplant 2009;24:1232-7.
[15] Tolouian R, Hernandez GT, Chiang WY, Gupta A. A new approach for evaluating bone turnover in chronic kidney disease. Eur J Intern Med 2010;21:230-2.
[16] Nickolas TL, Leonard MB, Shane E. Chronic kidney disease and bone fracture: a growing concern. Kidney Int 2008;74:721-31.
[17] Seeman E. Clinical review 137: sexual dimorphism in skeletal size, density, and strength. J Clin Endocrinol Metab 2001;86: 4576-84.
[18] Centers for Disease Control and Prevention (CDC). Prevalence of chronic kidney disease and associated risk factors--United States, 1999-2004. MMWR Morb Mortal Wkly Rep 2007;56:161-5.
[19] Nadim MK, Dua R, Campese VM. Antihypertensive drugs and the kidney. Curr Cardiol Rep 2004;6:403-8.
[20] Jean G, Souberbielle JC, Chazot C. Vitamin D in chronic kidney disease and dialysis patients. Nutrients 2017;9(4). pii: E328.
[21] Satman I, Ozbey N, Boztepe H, Kalaca S, Omer B, Tanakol R, et al. Prevalence and correlates of vitamin D deficiency in Turkish adults. Endocrine Abstracts 2013;32:P135.
[22] Klawansky S, Komaroff E, Cavanaugh PF Jr, Mitchell DY, Gordon MJ, Connelly JE, et al. Relationship between age, renal function and bone mineral density in the US population. Osteoporos Int 2003;14:570-6.
[23] Jassal SK, von Muhlen D, Barrett-Connor E. Measures of renal function, BMD, bone loss, and osteoporotic fracture in older adults: the Rancho Bernardo study. J Bone Miner Res 2007;22:203-10.
[24] Hsu CY, Cummings SR, McCulloch CE, Chertow GM. Bone mineral density is not diminished by mild to moderate chronic renal insufficiency. Kidney Int 2002;61:1814-20.
[25] Jamal SA, Swan VJ, Brown JP, Hanley DA, Prior JC, Papaioannou A, et al. Kidney function and rate of bone loss at the hip and spine: the Canadian Multicentre Osteoporosis Study. Am J Kidney Dis 2010;55:291-9.
[26] Grzegorzewska AE, Młot-Michalska M. Influence of age and sex on bone mineral density in dialysis patients. Adv Perit Dial 2007;23:77-81.
[27] Dooly AC, Weiss NS, Kestenbaum B. Increased risk of hip fracture among men with CKD. Am J Kidney Dis 2008;51:38-44.
[28] Hesegawa K, Hasegawa Y, Nagano A. Estimation of bone mineral density and architectural parameters in the distal radius in hemodialysis patients using peripheral quantitative computed tomography. J Biomechan 2004;37:751-6.
[29] Billy HT, Rimkus DR, Hartzman S, Latimer RG. Technetium-99m-sestamibi single agent localization versus high resolution ultrasonography for the preoperative localization of parathyroid glands in patients with primary hyperparathyroidism. Am Surg 1995;61:882-8.
[30] Haber RS, Kim CK, Inabnet WB. Ultrasonography for preoperative localization of enlarged parathyroid glands in primary hyperparathyroidism: comparison with (99m) technetium sestamibi scintigraphy. Clin Endocrinol (Oxf) 2002;57:241-9.
[31] Périé S, Fessi H, Tassart M, Younsi N, Poli I, St Guily JL, et al. Usefulness of combination of high-resolution ultrasonography and dual-phase dual-isotope iodine 123/technetium Tc 99m sestamibi scintigraphy for the preoperative localization of hyperplastic parathyroid glands in renal hyperparathyroidism. Am J Kidney Dis 2005;45:344-52.
[32] Vulpio C, Bossola M, De Gaetano A, Maresca G, Bruno I, Fadda G, et al. Usefulness of the combination of ultrasonography and 99mTc-sestamibi scintigraphy in the preoperative evaluation of uremic secondary hyperparathyroidism. Head Neck 2010;32:1226-35.

Evaluation of plasma catestatin levels in patient with coronary slow flow

Dursun Topal[1], Bedrettin Boyraz[2], Alkame Akgümüş[3], Tezcan Peker[4], Mustafa Yılmaz[5], Fahriye Vatansever Ağca[1], Selçuk Kanat[1], Ömür Aydın[6], Burhan Arslan[7]

[1]Department of Cardiology, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey
[2]Department of Cardiology, Bitlis Tatvan State Hospital, Bitlis, Turkey
[3]Department of Cardiology, Gemlik State Hospital, Bursa, Turkey
[4]Department of Cardiology, Bursa Doruk Hospital, Bursa, Turkey
[5]Department of Cardiology, Uludağ University School of Medicine, Bursa, Turkey
[6]Department of Cardiology, Kilis State Hospital, Kilis, Turkey
[7]Department of Cardiology, Mardin Kızıltepe State Hospital, Mardin, Turkey

DOI: 10.18621/eurj.372631

ABSTRACT

Objectives: Coronary slow flow (CSF) is characterized by delayed opasification of the coronary arteries in the absence of obstructive coronary disease. Catestatin has several cardiovasculer actions, in addition to diminihed sympato-adrenal flow. The study was to investigated associations between CSF and plasma catestatin levels.

Methods: This study included 45 CSF patients (37 males, mean age 48 ± 9.5 years) and 30 control individuals (24 males, mean age 48.4 ± 9 years). Coronary flow was quantified according to the TIMI (Thrombolysis in Myocardial Infarction) frame count method for coronary arteries. Serum catestatin levels taken from blood samples were measured by ELISA method. These parameters were compared between the groups.

Results: When compared with to the control group the serum catestatin levels was found higher in the CSF group. In addition to this, mean platelet volume was also significantly higher in patients with coronary slow flow.

Conclusions: Our study revealed that catestatin levels are increased in patients with CSF. Coronary slow flow that increased catecholaminergic sympathetic system activities seem to be among the reasons of endothelial dysfunction.

Keywords: Catestatin, coronary slow flow, coronary artery disease

Received: December 29, 2017; Accepted: March 30, 2018; Published Online: May 21, 2018

The coronary slow flow (CSF) phenomenon which was first described by Tambe *et al.* [1] in 1972 is characterized by delayed opacification of the distal vascularture in patients with normal coronary arteries. Endothelial dysfunction, occlusive disease of small coronary arteries, increase of vasomotor resistance have been suggested [2-5].

Endothelin-1 (ET-1) acts by reversing the effect of nitric oxide and it is known as the most potent vasoconstrictor agent. ET-1 has positive inotropic effects on cardiomyocytes and is mitogenic for smooth muscle cells. Increased ET-1 levels and increased

Address for correspondence: *Dursun Topal, MD., University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Department of Cardiology,Bursa, Turkey, E-mail: dursuntopal@yahoo.com*

e-ISSN: 2149-3189

catecholaminergic activity are responsible for microvascular resistance [6, 7].

Catestatin is a 21 aminoacidic hydrofobic neuroendocrine peptide that is formed by dissociation of chromogranin-A [8]. It is co-stored in the secretory granule and co-released with catecholamine in adrenal chromaffin cells and adrenergic neurons. It is non-competitively inhibites nicotinic acetylcholine receptors and catecholamine secretion [9]. Besides, it was shown to have a direct negative inotrophic effect, catestatin shows an adverse effect towards ET-1's positive inotropic, lusinotropic and constrictor effect on coronary arteries. In addition to this; hypertrophic, mitogenetic and angiogenetic effects of ET-1 on vascular smooth muscle cells, are also inhibited by catestatin [10, 11]. Catestatin also distrupts contraction coupling over the calcium pathway by inhibiting phosphorization of Phospholamban by protein phosphokinase. In this way catestatin contributes to vasodilation in microvascular area [10].

In this study, we aimed to investigate the relation between CSF and plasma catestatin levels.

METHODS

The study included 45 patients (group I) with CSF (37 males/8 females, mean age 48 ± 9.5 years) and 30 patients (group II) with normal coronary arteries (24 males, mean age 48.4 ± 9 years). The study was approved by the Institutional Ethics Committee, and written consent was obtained from all patients. All patients were evaluated in terms of cardiovascular risk factors. Patients with acute or chronic renal failure, unregulated hypertension, occlusive coronary artery disease diagnosed in the past or recent angiography or who had been surgically or percutaneously treated for this diagnosis, patients with an open heart surgery history, patients with an active infection, patients below 18 years old, pregnants, patients have systolic dysfunction and patients with dysrhythmia have been excluded from the study.

Hyperlipidemia was defined as low-density cholesterol (LDL) was greater than 100 mg/dl or lipid-lowering medication was used. Blood pressure was measured of all patients. Hypertension was defined systolic blood pressure equal or greater than 140 mmHg and/or diastolic blood pressure equal or greater than 90 mmHg or under control by using antihypertansive drugs. Diabetes mellitus was defined as the fasting glucose level exceeding 126 mg/ dl on two seperate measurement or using of antidiabetic treatment.

All patients underwent coronary angiography due to stable angina pectoris in our clinic and preliminary diagnosis of ischemic heart disease and diagnosed as having normal coronary arteries. Coronary angiographies of the patients were evaluated and two groups were separated as having coronary slow flow according to the TIMI (Thrombolysis in Myocardial Infarction) frame countmethod and having normal coronary artery. Blood samples were obtained for basic hematological and biochemical parameters.

Plasma Catestastin Measurement

Samples taken for the measurement of catestatin levels were centrifuged for 10 minutes at 10.000 cycle than stored at -80°C until analysed. Obtained samples were measured by human catestatin Elisa kit and cathestatin levels were analysed.

Echocardiograhy

Echocardiography images were examined in the left lateral decubitus position. The measurements were examined after patients' admission to the hospital, with 3,5 MHz transduser and GE Vivid 7 Pro equipment, according to the guidelines of the American Society of Echocardiography [12]. Left ventricle end-diastolic diameters (LVEDd), left ventricle end-systolic diameters (LVESd) and left ventricle ejection fraction (LVEF) were obtained with modified Simpson method from apical 4 chamber views.

Documentation of Coronary Slow Flow

All the patients underwent selective coronary angiography in elective conditions with the standard technique. For imaging, lohexol (Omnipaque) was used as the contrast agent. TIMI frame count method first described by Gibson *et al*. [13] was used for documenting of coronary flow rates of all subjects and was determined for each major coronary artery in each patient and control subject.

Quantitative coronary angiographic measurements were examined with ACOM PC Lite version 2.0 (Siemens, München, Germany) programme. Flow

velocity was calculated by observing angiographic records taped at 15 square (15 fps) speed. For each coronary artery, elapsed time for the contrast to reach distal determinant points was defined as the frame count. As the starting point, the point where the contrast touches both sides of the coronary artery was taken. As the final point, mustage was taken for left anterior descending artery (LAD), first distal bifurcation of the longest branch was taken for circumflex artery (Cx) and the point where posterior descending artery (PD) branch gave its first sub branch, was taken for right coronary artery (RCA). TIMI frame count was normalized by comparing the length of LAD with RCA and Cx and corrected TIMI frame count (cTFC) was found. cTFC was obtained by dividing total sine frame count of LAD to 1.7. For LAD 36 ± 1, for Cx 22 ± 2 and for RCA 20 ± 3 average reference values were obtained. Since our angiography records were at 15 fps (frame speed per minute), obtained values were doubled and standardized according to the 30 fps velocity. Mean reference values above two standard deviation was accepted as CSF.

Statistical Analysis

Statistical analyses were made with IBM SPSS (Statistical Package for the Social Sciences ver. 16.0, SPSS Inc, Chicago, Illinois, USA) statistical analysis package programme. Continuous variables were defined as mean ± standard deviation whereas categorical variables were defined as percentage (%). Among groups, parametric variables that show comparability to the normal range, were compared by Student t test while non-parametric variables that do not show comparability to the normal range, were compared by Mann-Withney U test. Correlation between continuous variables was determined by Pearson correlation coefficients. For statistical evaluations, $p < 0.05$ value was considered as significant for all the statistical analyses.

RESULTS

In both groups, male gender was observed significantly higher. In the CSF group, 8 (17.7%) of 45 patients whereas in the control group, 6 (20%) of 30 patients were female. No significant difference was found between these two groups ($p > 0.05$).Baseline clinical and demograhic parameters were similar. (Table 1).

When compared in terms of echocardiographic parameters, both groups were similar in left ventricular chamber diameters and systolic pulmoner arterial pressure parameters. Moderate or severe valvular insufficiencies or stenosis was not observed in all groups (Table 2).

Mean platelet volume (MPV) in the CSF group was found to be higher and statistically significant ($p = 0.01$) compared to the control group; in CSF group MPV was 8.04 ± 0.91 fL, and incontrol group MPV was 7.55 ± 0.53 fL. There was no significant difference between the groups, in terms of routine hematologic and biochemical parameters except MPV (Table 3).

Catestatin levels in CSF (2.1 ± 0.65 ng/ml) group

Table 1. Comparison of the clinical and demographic properties in coronary slow flow patients and controls

Variables	Group 1 (CSF) (n = 45)	Group 2 (CONTROL) (n = 30)	*p* value
Age (year)	48 ± 9.5	48.4 ± 9	0.841
Diabetes Mellitus (%)	6 (13.3%)	5 (16.6%)	0.910
Hypertension (%)	16 (35.5%)	10 (33.3%)	0.699
Dyslipidaemia (%)	4 (8.8%)	5 (16.6%)	0.721
(BMI) (kg/m^2)	30 ± 1.7	29.6 ± 1.9	0.271

Data are presented as mean ± standard deviation. CSF = coronary slow flow, BMI = body mass index

Table 2. Comparison of conventional echocardiographic parameters of coronary slow flow and control groups

Variables	Group 1 (CSF) (n = 45)	Group 2 (CONTROL) (n = 30)	*p* value
LVEF (mm)	62.5 ± 2.5	61.6 ± 2.3	0.120
IVST (mm)	10.2 ± 0.6	10 ± 0.6	0.260
LVEDd (mm)	48.3 ± 3.2	47.4 ± 1.9	0.170
LVESd (mm)	28.7 ± 1.5	28.31 ± 1.9	0.150
sPAP (mmHg)	22.3 ± 6.1	24.2 ± 3.5	0.250

Data are presented as mean ± standard deviation. LVEF = left ventricular ejection fraction, IVST = interventricular septum thickness, LVEDd = left ventricular end-diastolic diameter, LVESd = left ventricular end-systolic diameter, sPAP = systolic pulmonary artery pressure

was found to be statistically significantly higher compared to the control group (1.80 ± 0.41 ng/ml) (p = 0.016) (Table 3).

In the correlation analysis, we found a strong and positive linear relationship between TIMI frame count and serum catestatin levels (r = 0.417, p = 0.004). (Table 4).

DISCUSSION

As a result of this study, catestatin levels in patients having CSF was found to be higher compared to the patients with a normal coronary angiography. In addition to this, in CSF patients with a higher TIMI frame count, catestatin levels were found to be higher

Table 3. Comparison of hematologic and biochemical parameters of coronary slow flow and control groups

Variables	Group 1 (CSF) (n = 45)	Group 2 (CONTROL) (n = 30)	*p* value
Leukocytes, /mm3	6,860 ± 1,161	6,423 ± 940	0.90
Hemoglobin, g/dL	14.2 ± 1.2	14 ± 1.2	0.470
Platelet, 10^3 /mm^3	249,620 ± 56,100	252,200 ± 36,210	0.820
Glucose, mg/dL	101 ± 23.8	96.3 ± 21	0.380
Urea, mg/dL	16.2 ± 5.1	17.3 ± 4.1	0.340
Creatinin, mg/dL	0.78 ± 0.1	0.84 ± 0.1	0110
Sodium, mg/dL	138.8 ± 2	141.9 ± 1.8	0.250
Potassium,mg/dL	4.1 ± 0.3	4 ± 0.3	0.120
AST, U/L	27.6 ± 7.8	28.6 ± 5.1	0.970
ALT, U/L	25.8 ± 8.2	25.9 ± 6.4	0.570
MPV, f/L	8.04 ± 0.9	7.55 ± 0.7	**0.01**
CRP, mg/dL	1.2 ± 0.6	1.2 ± 0.6	0.970
Catestatin, ng/ml	2.10 ± 0.6	1.80 ± 0.4	**0.016**

Data are presented as mean ± standard deviation. AST = aspartate transaminase, ALT = alanine transaminase, MPV = mean platelet volume, CRP = c-reactive protein

Table 4. Correlatioon between TIMI frame count and catestatin levels

		TIMI Frame Count	Serum Catestatin Levels
TIMI Frame Count	Pearson Correlation	1	0.417
	Sig. (2-tailed)		**0.004**
	N	45	45
Serum Catestatin Levels	Pearson Correlation	0.417	1
	Sig. (2-tailed)	**0.004**	
	N	45	45

**Correlation is significant at the 0.01 level (2-tailed). TIMI = Thrombolysis in Myocardial Infarction, N = number of the patients (Group 1)

than the patients having a lower TIMI frame count.

Endothelium normally secretes vasoconstrictor and vasodilator substances to regulate blood flow. In some situations this regulation is impaired and coronary blood flow is adversely affected.

While still carrying some question marks in its etiopathogenesis, CSF is a phenomenon characterized by late opacification of distal vasculartur of the epicardial coronary arteries without occlusive disease. Various mechanisms have been proposed for CSF phenomenon in terms of underlying pathology such as endothelial dysfunction, occlusive disease of small coronary arteries, increased vasomotor resistance [2-5].

Increased ET-1 concentrations in the small coronary arteries, increase coronary resistance by vasoconstrictive effect and cause myocardial ischemia in patients having angina pectoris and normal coronary angiography [13, 14].

Catestatin is a 21 aminoasitic peptide formed as a result of the hydrolysis of chromogranin A and is stored with catecholamines and released via exocytosis [15, 16]. Catestatin inhibites the catecholamine release, via non-competitive blockage of nicotinic receptors. It reverses ET-1's positive inotropic, lusinotropic and vasospastic effect on coronary arteries [9, 10].

Elevated serum catestatin levels have been shown in many studies in situations where catecholamine release is increased such as heart failure and myocardial infarction. In a study patients having heart failure, the group having NYHA (NewYork Heart Association) class 3-4 symptoms have significantly higher serum catestatin levels compared to the control group and group with NYHA class 1-2 symptoms [18, 19].

Besides, catestatin has cardioprotective effects on the cardiovascular system and these effects was shown in some studies. Catestatin's cardioprotective effect mainly occurs as a negative inotropic and antihypertansive effect via Ca++ metabolism on myocardium. In a study by Penna C *et al*. [19] in 2010, catestatin was found to improve post-infarction LV function and to decrease ischemia-reperfusion injury. It also has cardioprotective effect on endothelium. Catestatin blocks vasoconstructive effect of endothelin by inhibiting ET-1 receptor and causes vasodilation by two separate pathways; by stimulating histamin release via H1 receptor and by stimulating nitric oxide (NO) synthetase leading to NO formation.

There are studies suggesting that endothelin and catecholamines are associated with slow coronary flow. Yazıcı *et al*. [20] investigated the relationship between plasma ET-1 levels and corrected TIMI frame counts in patients with CSF. They found that the corrected TIMI frame counts measured in LAD and Cx arteries was independent predictor of ET-1 level in patients with CSF. This result implies that the increase in ET-1 level may be responsible for increase in corrected TIMI frame count or CSF [20]. In another study, it was aimed to investigate the role of adrenergic activity in patients with CSF and its relationship to TIMI frame count on the pathogenesis of CSF. Correlation analysis established that both adrenalin and noradrenalin levels were correlated with TIMI frame counts of LAD and Cx arteries. Higher noradrenalin and adrenalin levels and correlation between TIMI frame count and ischemia in patients

with CSF suggest that increased adrenergic activity may be the manifestation of coronary slow flow [21].

In our study, catestatin levels were found to be significantly higher in the CSF patient group. In addition, in the CSF patient group, as the TIMI frame count increased, plasma catestatin levels increased as well. On the other hand, MPV was also significantly higher in patients with coronary slow flow according to literature [22]. Examining the pathogenesis of CSF, one of the possible causes is considered to be vasoconstruction at microvascular level. In this patient group, catestatin may be trying to reverse the vasoconstrictive effect of ET-1 and catecholamines and catestatin levels may be found increased in proportion to the severity of the disease. Besides, elevated catestatin levels may have a predictive value in understanding the severity of the disease in CSF. On the other hand, elevated catestatin levels can be considered as an indirect indicator of an increased catecholaminergic activity and increased coronary vasospastic presentation in this group. However, catestatin may be considered to be one of the factors affecting microvascular circulation. There is a need for more extensive studies.

CONCLUSION

Many reasons that might cause endothelium disfunction, are considered responsible for CSF pathophsiology. Increased catecholaminergic activity and sympathatic system activity are possible reasons of CSF vasospastic period. In our study, we found serum catestatin levels to be high in CSF patients. In addition to this, we also found that an increase in TIMI frame count is related with elevated catestatin levels in the CSF patient group. Plasma catestatin levels can be an indirect indicator of increased catecholaminergic activity and increased coronary vasospastic presentation. On the other hand, elevated serum catestatin levels in CSF may have a predictive value in understanding the severity of the disease.

Authorship Declaration

All authors listed meet the authorship criteria according to the latest guidelines of the International Committee of Medical Journal Editors, and all authors are in agreement with the manuscript.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] Tambe AA, Demany MA, Zimmerman HA, Mascarenhas E. Angina pectoris and slow flow velocity of dye in coronary arteries --a new angiographic finding. Am Heart J 1972;84:66-71.
[2] Lierde JV, Vrolix M, Sionis D, De Geest H, et al. Piessens J. Lack of evidence for small vessel disease in a patient with 'slow dye progression' in the coronary arteries. Cathet Cardiovasc Diagn 1991;23:117-20.
[3] Fung MM, Salem RM, Mehtani P, Thomas B, Lu CF, Perez B, et al. Direct vasoactive effects of the chromogranin A (CHGA) peptide catestatin in humans in vivo. Clin Exp Hypertens 2010;32: 278-87.
[4] Mahapatra NR. Catestatin is a novel endogenous peptide that regulates cardiac function and blood pressure. Cardiovasc Res 2008;80:330-8.
[5] Brunner F, Bras-Silva C, Cerdeira AS,Leite-Moreira AF. Cardiovascular endothelins: essential regulators of cardiovascular homeostasis. Pharmacol Ther 2006;111:508-31.
[6] Luscher TF, Tanner FC. Endothelial regulation of vascular tone and growth. Am J Hypertens 1993;6(7 Pt 2):283-93.
[7] Tamirisa P, Frishman WH, Kumar A. Endothelin and endothelin antagonism: roles in cardiovascular health and disease. Am Heart J 1995;130(3 Pt 1):601-10.
[8] Mahata SK, O'Connor DT, Mahata M, Yoo SH, Taupenot L, Wu H, et al. Novel autocrine feedback control of catecholamine release. A discrete chromogranin a fragment is a noncompetitive nicotinic cholinergic antagonist. J Clin Invest 1997;100:1623-33.
[9] Angelone T, Quintieri AM, Brar BK, Limchaiyawat PT, Tota B, Mahata SK, et al. The antihypertensive chromogranin A peptide catestatin acts as a novel endocrine/paracrine modulator of cardiac inotropism and lusitropism. Endocrinology 2008;149:4780-93.
[10] Liu L, Ding W, Li R, Ye X, Zhao J, Jiang J, et al. Plasma levels and diagnostic value of catestatin in patients with heart failure. Peptides 2013;46:20-5.
[11] Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am SocEchocardiogr 1989;2:358-67.
[12] Gibson CM, Cannon CP, Daley WL, Dodge JT Jr, Alexander B Jr, Marble SJ, et al. TIMI frame count: a quantitative method of assessing coronary artery flow. Circulation 1996;93:879-88.
[13] Kaski JC, Elliott PM, Salomone O, Dickinson K, Gordon D, Hann C, et al. Concentration of circulating plasma endothelin in patients with angına and normal coronary angiograms. Br Heart J 1995;74:620-4.
[14] Kaski JC, Cox ID, Crook JR, Salomone OA, Fredericks S, Hann C, et al. Differential plasma endothelin concentrations in subgroups of patients with angına and angiographically normal coronary arteries: Coronary artery Disease Research Group. Am Heart J 1998;136:412-7.
[15] Taupenot L, Harper KL, O'Connor DT. Mechanisms of disease: the chromogranin-secretogranin family. N Engl J Med 2003;348:1134-49.

[16] Helle KB, Corti A, Metz-Boutigue MH, Tota B. The endocrine role for chromogranin A: a prohormone for peptides with regulatory properties. Cell Mol Life Sci 2007;64:2863-86.
[17] Schiffrin EL, Deng LY, Larochelle P. Effects of a beta-blocker or a converting enzyme inhibitor on resistance arteries in essential hypertension. Hypertension 1994;23:83-91.
[18] Zhu D, Xie H, Wang X, Liang Y, Yu H, Gao W. Correlation of plasma catestatin level and the prognosis of patients with acute myocardial infarction. PLoS One 2015;10:e0122993.
[19] Penna C, Alloatti G, Gallo PM, Cerra MC, Levi R, Tullio F, et al. Catestatin improves post-ischemic left ventricular function and decreases ischemia/reperfusion injury in heart. Cell Mol Neurobiol 2010;30:1171-9.
[20] Yazıcı M, Balcı B, Demircan S, Yeşildağ O, Sağkan O, Şahin M, et al. [Relationship between plasma endothelin-1 levels and corrected TIMI frame count in patients with slow coronary artery flow]. Türk Kardiyoloji Dern Arş 2002;30:466-72. [Article in Turkish]
[21] Yazıcı M, Demircan S, Durna K, Şahin M. The role of adrenergic activity in slow coronary flow its relationship to TIMI frame count. Angiology 2007;58:393-400.
[22] Nurkalem Z, Alper AT, Orhan AL, Zencirci AE, Sari I, Erer B, et al. Mean platelet volume in patients with slow coronary flow and its relationship with clinical presentation. Turk Kardiyol Dern Ars 2008;36:363-7.

The European Research Journal 2019;5(3):529-534 ORIGINAL ARTICLE

Semi-wrapping lateral cartilage to a square edged strut perpendicularly to prevent collapse in external nasal valve dysfunction: pseudodome technique

Muhammed Yanılmaz[1], **Davut Akduman**[2]

[1]*Department of Otorhinolaryngology, Medient Hospital, İstanbul, Turkey*
[2]*Department of Otorhinolaryngology, Düzce University School of Medicine, Düzce, Turkey*

DOI: 10.18621/eurj.376421

ABSTRACT

Objectives: During inhalation through the nose, the weakness of lateral cartilage may cause the collapse of nasal vestibule and sidewall, causing the complaint of difficult breathing through the nose. We aimed to support the lateral cartilage with a square edged strut to resolve this problem.

Methods: We described a technique in 8 cases (5 males, 3 females). In this technique the lateral cartilage is semi wrapped from the underside to a square edged strut, and arched to outside with an open approach rhinoplasty. As it was only a physical support and did not create a new canting up through the skin, we named this maneuver as *pseudodome* technique.

Results: All patients experienced relief of symptoms and no complications observed. The reinforcement effect of the strut was effective in preventing collapse of the nasal alar sidewall as well as did not cause contour irregularities.

Conclusions: *Pseudodome* technique can be performed for acquired or congenital nasal sidewall collapse caused by lower lateral cartilage structural weaknesses successfully.

Keywords: .nasal valve, lateral cartilage, *pseudodome* technique, open approach rhinoplasty

Received: January 9, 2018; Accepted: January 29, 2018; Published Online: May 24, 2018

Nasal septum, lateral nasal walls, and nasal mucosa interact as static and dynamic forces during the nasal breathing. The most important variable in nasal airflow for a patient with nasal obstruction is the diameter of the nasal passage.

The term nasal valve was introduced by Mink in 1903 [1]. It is divided into external and internal portions. Internal nasal valve is located in the area of transition between the skin and respiratory epithelium. It is the narrowest part of the nasal passage, and often referred to as the nasal valve. External nasal valve is a dynamic structure that lies caudal to the internal valve. It is formed by columella, nasal floor, and caudal border of the lower lateral cartilage (nasal rim). The level of support for the external nasal valve is determined by the size, shape, flexibility, and orientation of the lower lateral cartilage and alar muscles [2].

Nasal valve collapse can be classified as congenital, traumatic, senile, mucosal, neurogenic, or idiopathic [3]. It is primarily diagnosed by clinical evaluation using the Cottle maneuver or Bachmann

Address for correspondence: *Davut Akduman, MD., Associate Professor, Düzce University School of Medicine, Department of Otorhinolaryngology, Düzce, Turkey, E-mail: dr.akduman@gmail.com*

e-ISSN: 2149-3189

test [4], whereas rhinomanometry and acoustic rhinomanometry may assist in diagnosis [5-7]. Several surgical reconstruction techniques have been proposed to resolve this problem, with varied results [8-14].

Nasal valves may function as collapsible tubes attached to rigid tubes (Starling resistors) [15]. The transmural pressure increases as the airflow velocity increases, which leads to collapse of nasal passage and a decrease in airflow. In individuals with an external valve collapse caused by weakness of lateral cartilage, this mechanism functions at a low transmural pressure, which leads to premature collapse of alar sidewall and difficulty with nasal breathing. Beeson [16] also has outlined Ohm's law, Bernoulli's principle, Venturi effect, and Poiseuille's law as the key concepts relating to nasal physiology.

Herein we described a different technique to support the weakness of lateral cartilage to prevent alar sidewall collapse during forced inhalation. In this technique the lateral cartilage is semi wrapped from the underside to a square edged strut, and arched to outside.

METHODS

Patients

Between 2012 and 2013, a total of 8 patients (3 female and 5 male) were enrolled in the study. All patients had a complaint of difficulty breathing through the nose, and had the nasal valve collapse during forced inspiration through the nose.

A total of 8 patients (5 males, 3 femeles) with the complaint of difficulty breathing through the nose that had external nasal valve pathology in the ENT examination and underwent nasal valve surgery in our clinic between 2012-2013 years were included in the study. The study was approved by institutional review board of the study center. Patient's informed consent for photograph release obtained from the patient.

Of the 8 patients, only one male patient had a rhinoplasty operation five years ago and the others had congenital nasal sidewall collapse caused by lower lateral cartilage structural weaknesses. All patients had nasal valve collapse and difficulty in breathing during respiration. One patient had bilateral (rhinoplasty case) and 7 patients had unilateral lower lateral cartilage structural weaknesses. A Bachmann test [4] was used to have positive predictive value, when there was an inspiratory collapse. Prior to topicalization of the internal nose, the back end of a Q-tip or some other small instrument was used to elevate the alar sidewall of the nose approximately 1-2 mm. When definite benefit was reported from this maneuver, the patientwas evaluated for the surgery [17].

Surgical Technique

This technique is best suited for acquired or congenital nasal sidewall collapse caused by lower lateral cartilage structural weaknesses. This includes cartilage defects that cause the collapse of nasal sidewall during forced inhalation through the nose.

The local anesthetic solution (1% lidocaine with epinephrine, 1 mg/100 mL) wasinjectedas defined for open approach rhinoplasty [18]. Nasal bridge and lower lateral cartilages were exposed with an open approach technique.

A vertical tunnel at the undersurface of weakest point of lateral cartilage from caudal to the cephalic margin, beneath the mucoperichondrium was dissected with a pair of short curved delicate Metzenbaum scissors and advanced with a Killian elevator. The mucosal integrity was preserved to prevent postoperative scar formation. A square edged strut graft which harvested from nasal septum was prepared and sized to the vertical length of lateral cartilage. The weak and collapsed part of lateral cartilage was semi-wrapped from the underside to that strut. The suture was initiated by inserting the needle from outside the lateral cartilage from one side, slightly farther from the strut graft. Then, passed under the strut graft and removed inside out on the opposite side, where it exits the cartilage. The needle was placed backwards in the needle driver, inserted into the cartilage about 2 mm beyond of that point the needle has just been passed through, and passed from the far side back to the first insertion side. The needle exited the cartilage about 2 mm near the first insertion site. Finally the suture was tied gently on the side of the wound where the suturing began, and completed as a horizontal mattress stitch. The square edged strut graft was fixed with 3 horizontal mattress stitches, and a support point between the medial and lateral portions of the lower lateral cartilage was created. Care was taken not to enter the mucoperichondrium lying undersurface of the lateral cartilage while suturing

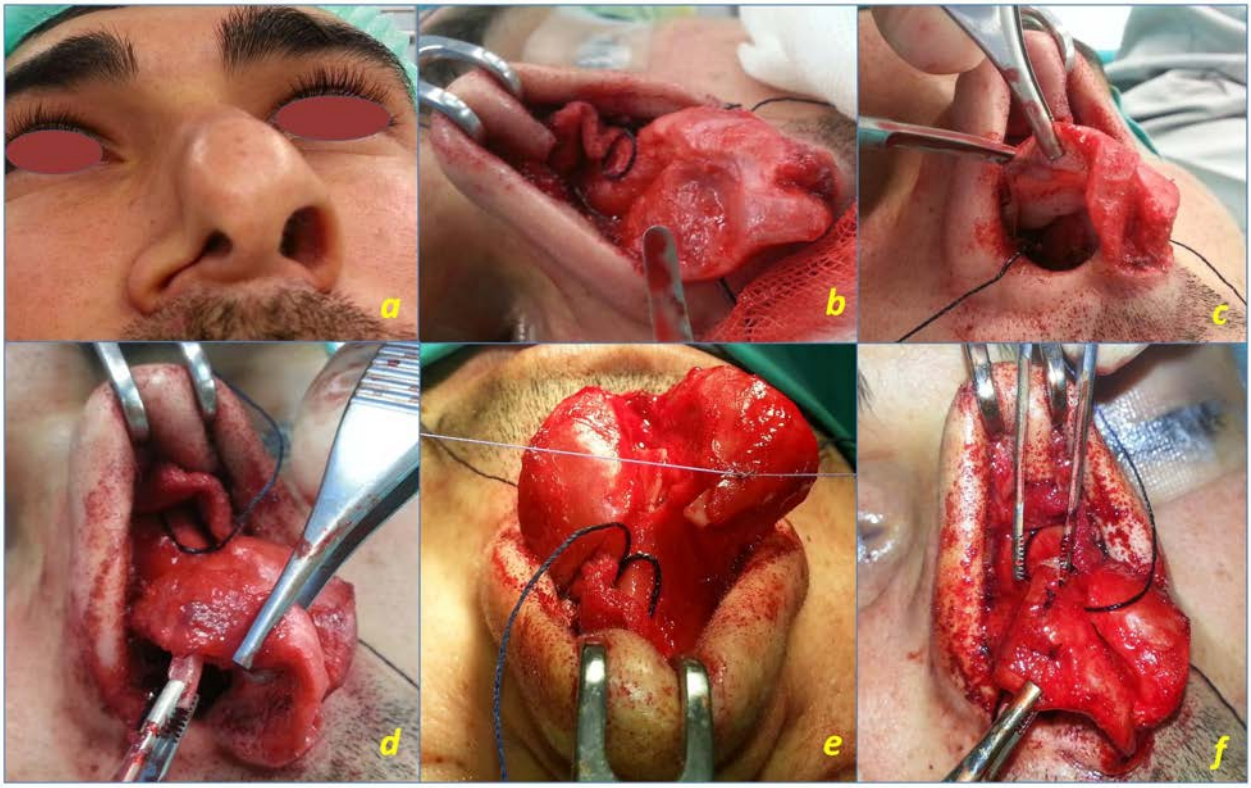


Figure 1. Preoperative nasal valve collapse during forced inspiration through the nose (a). Intraoperative implementation of pseudodome technique: Identifying the weakest point of lateral cartilage (b), creating a vertical tunnel at the undersurface of weakest point of lateral cartilage from caudal to the cephalic margin, beneath the mucoperichondrium (c), semi-wrapping the weakest and collapsed part of lateral cartilage from the underside to a square edged strut graft which was harvested from nasal septum (d), creating a support point between the medial and lateral portions of the lower lateral cartilage with 3 horizontal mattress stitches (e, f).

(Figure 1). After other required surgical manipulations, the skin incisions were closed with 5.0 prolene suture and the operation was completed. Bilateral intranasal packing were applied with a half of longitudinally divided and thinned Merocel® per nasal cavity for about 48 hours, and a silicone splined splint for about one week. If the procedure was performed in conjunction with a rhinoplasty operation, a thermoplastic or aluminum external nasal splint was used to immobilize the nose after the operation, otherwise only plaster strips were used.

The patients were followed-up for at least 12 months postoperatively. The result of the surgery was evaluated by a forced inspirium maneuver. A nasal sidewall collapse at rest or during physical exertion and forced inspiration accepted as the surgical failure.

RESULTS

We have utilized this technique on a case series of eight patients successfully to repair alar sidewall insufficiency with optimal functional and cosmetic outcomes (Figure 2). The patients included in the study were both 5 males and 3 females ranging in age from 22 to 38 years.

No patients experienced nasal sidewall collapse at rest or during physical exertion and forced inspiration. All of the patients were followed for more than 12 months and did not note any delayed undesirable depression of the graft or compromise of the nasal vestibule. The reinforcement effect of the strut was effective in preventing collapse of the nasal alar sidewall as well as did not cause contour irregularities.

DISCUSSION

The lateral cartilage defects that cause the collapse of the nasal sidewall during forced inhalation through the nose may be due to a developmental defect which are somewhat more apparent or after rhinoplasty

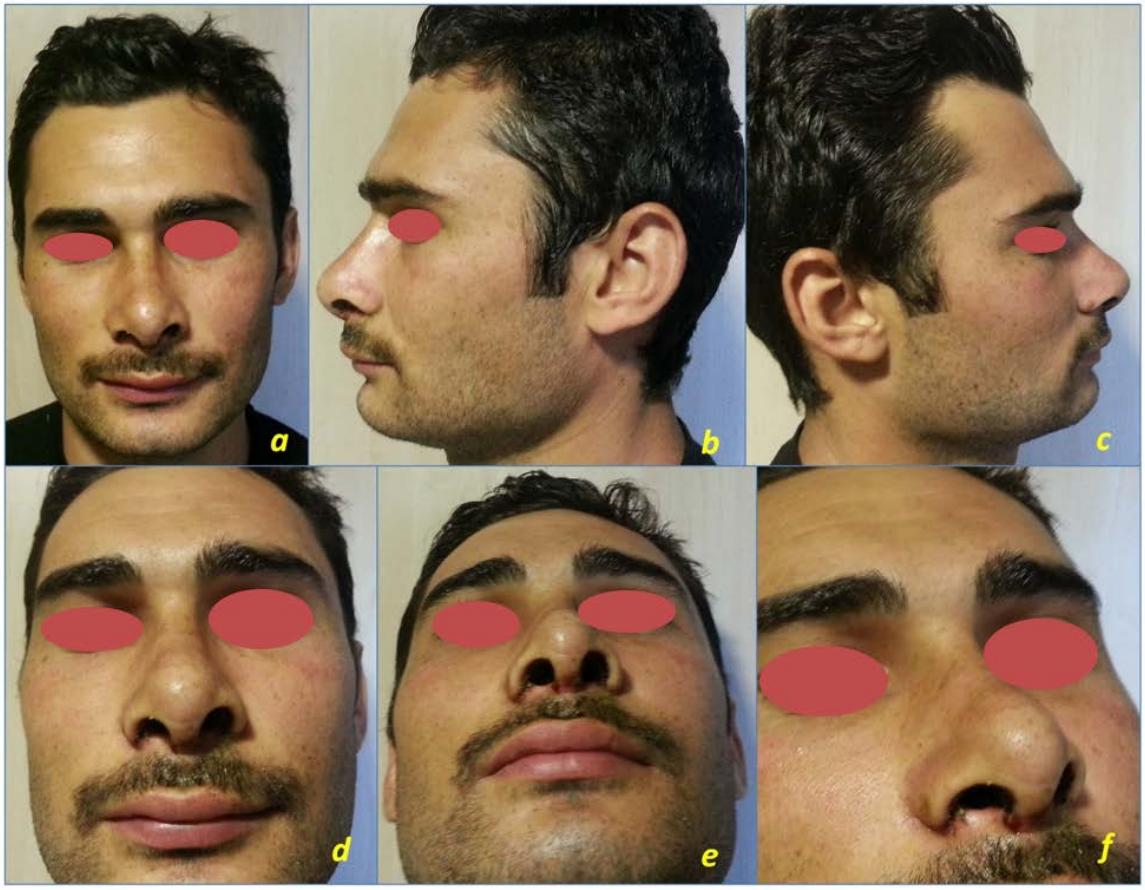


Figure 2. Postoperative anterior (a), left (b), right (c), antero-inferior (d), inferior (e) and right-inferolateral (f) photographic views of a male patient.

operations. The most important variable in the nasal airflow is the diameter of nasal passage. The interaction of static and dynamic forces, including the nasal septum, turbinates, lateral nasal walls, and nasal mucosa interacts during normal nasal breathing [19]. Kern and Wang [20] classified the etiologies of nasal valve dysfunction as mucocutaneous and skeletal/structural disorders. Secondary to infectious, allergic or vasomotor rhinitis the cross-sectional area of the nasal valve may decrease due to mucosal swelling, and it may reduce nasal airway patency. The skeletal/structural components of nasal valve (septum, upper and lower lateral cartilages, fibroareolar lateral tissue, piriform aperture, head of the inferior turbinate, and nasal floor) may also contribute to lateral nasal valve collapse during inspiratory activity especially at sport activities.

The patient may experience a dynamic collapse of nasal valve during inspiration and it may lead to airway obstruction. The etiology of insufficiency is generally congenital structural defects or surgery or trauma to the skeletal and soft tissue components. The upper lateral cartilages partially collapse at a ventilatory flow rate of 30 L/min in healthy individuals [19]. While a normal nasal valve may collapse with extreme inspiratory effort, a patient with dynamic nasal valve dysfunction often has a weakened lateral nasal wall and it may collapse even during normal nasal breathing.

External nasal valve collapse can be diagnosed based on the observation of nostril margin to determine if the alar collapse is present or a Bachmann test may be used. In this test alar sidewall of the nose is elevated approximately 1-2 mm with the use of back end of a Q-tip or some other small instrument prior to topicalization of the internal nose [4]. The patient with a flaccid or collapsible valve usually appreciates an immediate improvement in airflow with this maneuver.

Many different techniques has recently put forth to resolve nasal valve insufficiency. However, due to the variety of pathologies in the nasal valve area, any

technique does not provide the same benefits to every patient.

Alar batten graft was a simple choice for alar rim a decade ago. As the large grafts provide support, it often obscures the alar crease or causes altered symmetry. Lateral crural strut grafts have replaced alar batten grafts in the majority of primary rhinoplasty cases [21]. Lateral crural strut grafts were developed to reshape, reposition or reconstruct the lateral crura. Straight strong pieces of cartilage measuring 3-4 mm in width by 14-20 mm length are used in different ways. The medial portion of graft is sutured to the undersurface of the lateral crura (alar cartilage) while the distal end is placed in a lateral pocket in to one of three locations: pyriform, alar base, or nostril rim depending upon indication [21]. Transposition of lateral crura is a tip decision, whereas the position of a lateral crural strut graft is a functional decision. Controlled nasal tip rotation via the lateral crural overlay technique which was described by Kridel and Konior [22] also may be used to support lateral crural weakness or concavity.

As for severely concave or weak lateral crura we propose a different technique to straighten and support alar cartilage to prevent collapse of lateral nasal sidewall during inspirium especially at exercise. Although extreme forced inspiration may cause some collapse in most people, a part of lateral cartilage is thinner and weaker in some cases, and it may collapse into nasal cavity during inhalation for this reason. This technique helps to reinforce alar sidewalls of the nose by supporting only lower lateral cartilage from the underside to prevent the sidewalls from collapsing, resulting in maximized airflow. Weakest point of lateral cartilage is semi wrapped from the underside to a square edged strut and fixed with 2 or 3 mattress sutures defined in the surgical technique.

There was a weakness in the lateral cartilage in all patients in this study. We performed a minimum cephalic trimming to ensure the symmetry between two sides when necessary and reconstructed the defective part of lateral cartilage with this technique.

The weakened or concavity formatted part of lateral cartilage was semi wrapped from the underside to a square edged strut which was harvested from the nasal septum and sized to the vertical length of lateral cartilage. In fact, we created a new dome on the lower lateral cartilage with this technique. As it was only a physical support and did not create a new canting up through the skin, we named this maneuver as *pseudodome* technique. For all that, the small number of cases presented in the study may be a lack of the study.

CONCLUSION

Pseudodome technique can be suggested for acquired or congenital nasal sidewall collapse caused by lower lateral cartilage structural weaknesses. However, this technique may not be sufficient for inferomedial displacement of the upper lateral cartilage after rhinoplasty operation.

Informed consent

Written informed consent was obtained from the patient for the publication of photographs in this article

Author Contributions:

MY: surgeon, data collection, writing manuscript; DA: editing, analyzing data, writing manuscript.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] Mink PJ. Le nezcommevoierespiratoire. Presse Otolaryngol Belg 1903;21:481-96.
[2] Chand MS and Toriumi DM: Nasal physiology and management of the nasal airway. In; Dallas Rhinoplasty-Nasal Surgery by the Masters, Gunter JP, Rohrich RJ, Adams WP Jr. eds., Quality Medical Publishing, Inc: St. Louis, Missouri, 2002, pp.643-61.
[3] O'Halloran LR. The lateral crural J-flap repair of nasal valve collapse. Otolaryngol Head Neck Surg 2003;128:640-9.
[4] Bloching MB. Disorders of the nasal valve area. GMS Curr Top Otorhinolaryngol Head Neck Surg 2007;6:Doc07.
[5] Roithmann R, Chapnik J, Zamel N, Barreto SM, Cole P. Acoustic rhinometric assessment of the nasal valve. Am J Rhinol 1997;11:379-85.
[6] Ricci E, Palonta F, Preti G, Vione N, Nazionale G, Albera R, et al. Role of nasal valve in the surgically corrected nasal respiratory obstruction: evaluation through rhinomanometry. Am J Rhinol

2001;15:307-10.
[7] Cakmak O, Coşkun M, Celik H, Büyüklü F, Ozlüoğlu LN. Value of acousticrhinometry for measuring nasal valve area. Laryngoscope 2003;113:295-302.
[8] Ozturan O, Miman MC, Kizilay A. Bending of the upper lateral cartilages for nasal valve collapse. Arch Facial Plast Surg 2002;4:258-61.
[9] Paniello RC. Nasal valve suspension. An effective treatment for nasal valve collapse. Arch Otolaryngol Head Neck Surg l996;122:1342-6.
[10] Schlosser RJ, Park SS. Functional nasal surgery. Otolaryngol Clin North Am 1999;32:37-51.
[11] Park SS. The flaring suture to augment the repair of the dysfunctional nasal valve. Plast Reconstr Surg 1998;101:1120-2.
[12] Stucker FJ, Lian T, Sanders K. Management of severe bilateral nasal wall collapse. Am J Rhinol 2002;16:243-8.
[13] Guyuron B, Michelow BJ, Englebardt C. Upper lateral splay graft. Plast Reconstr Surg 1998;102:2169-77.
[14] Teichgraeber JF, Wainwright DJ. The treatment of nasal valve obstruction. Plast Reconstr Surg 1994;93:1174-82.
[15] Farré R, Peslin R, Montserrat JM, Rotger M, Navajas D. Flow-dependent positive airway pressure to maintain airway patency in sleep apnea-hypopnea syndrome. Am J Respir Crit Care Med 1998;157:1855-63.
[16] Beeson WH. The nasal septum. Otolaryngol Clin North Am 1987;20:743-67.
[17] Akduman D, Yanılmaz M, Haksever M, Doner F, Sayar Z. Patients` evaluation for the surgical management of nasal obstruction. Rhinology 2013;51:361-7.
[18] Toriumi DM, Becker DG. Injection. In; Rhinoplasty Dissection Manual, Lippincott-Williams&Wilkins, 1999:pp. 25-9.
[19] Romo T 3rd, Moutran HA, Pearson JM, Presti P, Yalamanchilli H. Postrhinoplasty Nasal Obstruction Rhinoplasty. Medscape. At available: http://emedicine.medscape.com/article/841574-overview#showall.
[20] Kern EB, Wang TD. Nasal valve surgery. In: Daniel RK, Regnault P, eds. Aesthetic Plastic Surgery - Rhinoplasty. 1st ed. Baltimore, MD: Lippincott Williams&Wilkins; 1993:pp. 613-30.
[21] Daniel K Rollin, Mastering Rhinoplasty. A Comprehensive Atlas of Surgical Techniques with Integrated Video Clips. Springer Science & Business Media, NY, 2010.
[22] Kridel RW, Konior RJ. Controlled nasal tip rotation via the lateral crural overlay technique. Arch Otolaryngol Head Neck Surg 1991;117:411-5.

The European Research Journal 2019;5(3):535-539 ORIGINAL ARTICLE

Evaluation of hearing results in Behçet's disease

Cem Bayraktar[1], Özlem Yağız Aghayarov[1], Sedat Doğan[1], Demet Işık Bayraktar[2], Ahmet Altuntaş[1]

[1]Department of Otolaryngology, Head and Neck Surgery, Adıyaman University Training and Research Hospital, Adıyaman, Turkey
[2]Department of Internal Medicine, Adıyaman University Training and Research Hospital, Adıyaman, Turkey

DOI: 10.18621/eurj.379685

ABSTRACT

Objectives: Behçet's disease is an inflammatory rheumatic disease with recurrent scarring in the oral and genital area, as well as skin, eye, joint, vein, and nerve involvement. The aim of the study was to investigate the level of hearing in Behçet's disease and whether there is a change in hearing levels as the level of the disease increases.

Methosd: In this study we examined 32 patients with Behçet's disease and 50 healthy volunteers. All patients were evaluated with audiometry, tympanometry and acoustic reflex tests, as well as detailed ear, nose, and throat examinations.

Results: Sensorineural hearing loss was observed in 9.3% of the patients with Behçet's disease, according to the audiological data, and all patients were bilateral. We also observed sensorineural hearing loss to be the fifth most common symptom in our study. Especially in high frequencies, there was positive correlation between hearing levels and disease exposure time ($p < 0.05$).

Conclusions: We think that the audiological examinations should be included in the routine check-ups of Behçet's patients. In addition, a follow-up assessment of the hearing level of these patients with high frequency audiometry may be more meaningful.

Keywords: Behçet's disease, hearing loss, audiometry

Received: January 16, 2018; Accepted: March 7, 2018; Published Online: June 3, 2018

Behçet's disease is a systemic and complex disease thought to be caused by autoimmune and autoinflammatory mechanisms. It was described as an oral aphthae, genital ulcer and recurrent uveitis triad by Turkish dermatologist Hulusi Behçet in 1937. Geographical differences are observed in the prevalence of Behçet's disease. It is estimated that there are about 2000 patients in the UK, while this ratio is much higher in Japan (10 in 100.000) and Turkey (8-38 in 100 000) [1-3].

Gastrointestinal, renal, pulmonary, cardiovascular, and musculoskeletal system involvement may be seen in addition to the triad described in patients with Behçet's disease [4]. In rare cases, vena cava superior syndrome [5], optic perineuritis [6], oculopalatal tremor [7], and audiovestibular symptoms have also been reported [8].

There are many studies in the literature about inner ear involvement. The incidence of hearing loss in these studies ranges from 12% to 80% [9-14].

Address for correspondence: *Cem Bayraktar, MD., Adıyaman University Training and Research Hospital, Department of Otolaryngology, Head and Neck Surgery, 02000 Adıyaman, Turkey*
E-mail: cem_dr23@hotmail.com, Fax: +90 416 2145599

e-ISSN: 2149-3189

Behçet's disease is a systemic vasculitis which may have cochlear involvement. The aim of this study was to investigate the relationship between Behçet's disease and hearing loss, determine the effect of disease duration on hearing loss; and emphasize the importance of hearing loss in these patients.

METHODS

This study was carried out with 32 patients (64 ears, 12 females and 20 males) who were diagnosed with Behçet's disease at the Department of Internal Medicine in the Adıyaman University Training and Research Hospital. This study was approved by the Ethics Committee of Adıyaman University, and informed patient consent was obtained. This study was carried out between April 2017 and December 2017. Demographic data, such as the age and sex of the patients, were recorded. Clinical findings that could be observed during the course of Behçet's disease were investigated, and accompanying symptoms were recorded. Exclusion criterias are : previous ear surgery, known hearing loss stories, head trauma, autotoxic drug use stories, under 18 years of age, other systemic diseases that could lead to hearing loss. Fifty (100 ears) voluntary patients (14 females, 36 males) who were referred to our out-patient clinic for non-ear reasons were included in the study as a control group with respect to gender and age. After the otological examination, chronic noise exposure and the use of ototoxic drugs were investigated as causes and excluded. Pure tone audiometry, tympanometry and acoustic reflex tests were performed. Patients who were not complaining of hearing loss, were acoustically reflex positive, and had type A curve in tympanometrywere included in the control group. Hearing thresholds at frequencies between 250-8000 Hz were analyzed between the patient group and the control group, comparing the right and left ears. Pure tone average value was calculated by adding the thresholds obtained at 500, 1000, 2000, and 4000 Hz frequencies and dividing the result by four.

Statistical Analysis

The SPSS 15.0 (Chicago, USA) program was used for the analysis of the data. The Student's t-test and Fisher's exact test were used for the demographic characteristics of the groups. The two group averages were compared with the Mann-Whitney U test, as the data distribution of hearing results was not normal. The relationship between the duration of the disease and the average of frequencies was analyzed with a Pearson correlation test. A p value < 0.05 was considered statistically significant.

RESULTS

The ages of the patient group (12 males and 20 females, range 20 to 55) ranged from 20 to 55, with a mean of 39.56 ± 8.94. The ages of the control group (14 females and 36 males) ranged from 30 to 55, with a mean of 42.68 ± 8.04 (Table 1).

The most common symptom was oral aphthous ulcers (87%). Other symptoms were genital ulcers (68%), ocular findings (uveitis, 34%), neurological involvement (12%), and skin involvement and hearing loss (6%).

Over 25 dB very mild sensorineural hearing loss was detected in only 3 (9.3%) patients, according to pure tone averages at 500, 1000, 2000 and 4000 Hz. All of these patients had bilateral hearing loss. Disease duration wasbetween 2 and 30 years, with an average of 9.50 ± 7.75 years. Significant differences were observed between the control and the patient groups

Table 1. Demographic characteristics of the groups

	Control group (n = 50)	Patient group (n = 32)	*p* value
Age	42.68 ± 8.04	39.56 ± 8.94	0.105‡
Gender			
Female, n (%)	14 (28 %)	12 (37.5 %)	0.467¥

‡ Student t- test, ¥ Fisher's exact test

Table 2. The comparisons of average frequency values in the study and control groups

		Control group (n = 50)	Patient group (n = 32)	*p* value‡
Left ear	250 Hz	20.20 ± 5.88	21.25 ± 6.09	0.425
	500 Hz	17.40 ± 5.55	20.47 ± 4.28	**0.006**
	1000 Hz	15.80 ± 4.20	19.22 ± 5.55	**0.005**
	2000 Hz	16.50 ± 5.46	19.06 ± 5.45	**0.035**
	4000 Hz	22.60 ± 7.90	22.97 ± 11.69	0.340
	8000 Hz	23.40 ± 8.10	32.81 ± 18.48	**0.041**
Right ear	250 Hz	20.10 ± 5.66	21.09 ± 6.18	0.705
	500 Hz	17.70 ± 5.17	20.00 ± 4.21	**0.046**
	1000 Hz	16.30 ± 4.01	19.38 ± 5.35	**0.006**
	2000 Hz	17.30 ± 5.26	19.06 ± 5.88	0.119
	4000 Hz	22.00 ± 8.57	24.84 ± 11.32	0.346
	8000 Hz	26.00 ± 8.74	35.78 ± 15.66	**0.001**

‡ Mann Whitney U test

at frequencies of 500, 1000, 2000 and 8000 Hz in the left ear; and 500, 1000 and 8000 Hz in the right ear. There was no significant difference in the left ear at 4000 Hz, or in the right ear at 2000 and 4000 Hz (Table 2). In addition, we found a significant correlation between the duration of the illness and hearing loss in both ears at 4000 and 8000 Hz in our study. (left 4000 Hz: r = 0.575; $p = 0.001$, left 8000 Hz: r = 0.528; $p = 0.002$, right 4000 Hz: r = 0.582; $p < 0.001$, right 8000 Hz: r = 0.438; $p = 0.012$) (Table 3).

Table 3. The correlation between average frequencies and duration of disease

		r	*p value**
Left ear	250 Hz	-0.062	0.738
	500 Hz	-0.090	0.624
	1000 Hz	-0.242	0.182
	2000 Hz	-0.168	0.358
	4000 Hz	0.575*	**0.001**
	8000 Hz	0.528*	**0.002**
Right ear	250 Hz	-0.079	0.667
	500 Hz	0.089	0.628
	1000 Hz	-0.202	0.267
	2000 Hz	-0.046	0.803
	4000 Hz	0.582*	**< 0.001**
	8000 Hz	0.438*	**0.012**

*Pearson correlation coefficient. Statistically significance showed with bold characters

DISCUSSION

Although Behçet's disease has long been accepted as an oculo-oral-genital syndrome, it is now described as a vasculitis that can affect all systems. The presence of autoantibodies in the oral mucosa of approximately half of the patients suggests anautoimmune etiology [15].

In addition, infection and coagulation disorders can trigger T-cell proliferation and cytokine release, and cause neutrophil activation and endothelial damage in the vasculitis [16, 17].

Berrettini *et al*. [18] and Hagiwara *et al*. [19] reported sudden hearing loss cases that were completely remedied by steroid and immunosuppressive therapy. These findings support the theory of immunologic and vasculitic processes in the inner ear involvement of Behçet's patients [18, 19]. The cochlea feeds with a single terminal branchartery from the posterior cerebral circulation [20]. For this

reason, the most common cause of hearing loss in Behçet's disease may be vascular in nature.

Hearing loss was observed in 12% of cases by Belkahia *et al*. [21], 28% by Andreoli and Savastano [22], 55% by Gemigrani *et al*. [23], and 80% by Elidan *et al*. [10].

In our study, sensorineural hearing loss was observed in only three patients (9.3%). These cases were bilateral and very mild, and were compatible with the typical descending curve audiogram as noted in some studies in the literature [24, 25].

Soylu *et al*. [26] found significant differences in hearing thresholds at frequencies of 250, 500, 2000 and 4000 Hz in patients with Behçet's disease; Ak *et al*. [25] found a statistically significant difference at 250, 500, 4000, 6000 and 8000 Hz. Aslan *et al*. [27] stated that there was a significant difference between patient and control group at 250, 1000, 2000, 4000 and 8000 Hz. In our study, we observed statistically significant differences in frequencies of 500, 1000, 2000 and 8000 Hz in the left ear, and 500, 1000 and 8000 Hz in the right ($p < 0.05$).

A child with external ear canal necrosis, facial paralysis, Horner's syndrome and internal carotid artery rupture, in addition to inner ear involvement, has been reported by Miura *et al*. [28]. All of the patients in our study group underwent ear, nose, and throat examinations that proved normal.

This study did not use the SISI (short increment sensitivity index) and Metz recruitment tests to confirm the cochlear pathology as in Ak *et al*. [25], nor the TonDecay test to exclude retrocochlear pathology, nor the Auditory Brainstem Response (ABR) test as in Mahdi *et al*. [29] and Sonbay *et al*. [30]. Evereklioğlu *et al*. [31] reported that ABR, SISI, and ToneDecay tests produced no results when applied to Behçet's disease patients, so we did not add suchtime consuming and high cost tests to our study.

When we look at the relationship between the duration of the illness and hearing loss, Brama and Fainaru [32] found a relationship in the 1980 study, but no relationship was found in most studies in the following years [2, 10]. Ak *et al*. [25] found no relationship between hearing loss and duration of illness, but found that there was a relationship between the average age of the patients and hearing loss. In our study, we observed positive significant correlation between hearing loss and duration of illness in high frequencies.

Sonbay *et al*. [30] have shown that the age at the onset of the disease is higher in patients with hearing loss, and they have explained this with a more severe course in the early stages of the disease.

Hearing loss was the third or fourth most common clinical finding in the cases in some studies [3, 25, 33-35]. In our study, hearing loss emerged as the fifth most common along with other skin lesions, following oral and genital ulcers, ocular lesions, and neurological manifestations. Only two of the patients recognized and identified hearing loss, but the test results showed hearing loss in three (9.3%) patients. This suggests that these patients should be tested for hearing loss, whether or not they have a hearing complaint, and should be referred to the ENT physician if they are diagnosed.

Limitations

There are some limitations in this study. First of all, the number of the study group is small. Secondly, assessments were performed according to audiometry results and objective hearing tests were not used in comparisons. And finally, adding high frequency audiometry to the test battery may be more meaningful in these patients.

CONCLUSION

In Behçet's disease, hearing levels are significantly worse at high frequencies (4000 Hz and 8000 Hz), and this correlateswith disease duration. Significant hearing loss was observed in different frequencies in both ears in the control and study groups. It should be kept in mind that the loss of hearing in these patients may develop over thetime. It may also be beneficial to include hearing tests in routine follow-up charts.

As it is possible to detect early hearing loss at very high frequencies due to small vessel involvement, a comparison of high frequency audiometry with the control group may be proposed as a new study topic in the future.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] Marshall SE. Behçet's disease. Best Pract Res Clin Rheumatol 2004;18:291-311.
[2] Soylu M, Ersoz TR, Erken E. The association between HLA B5 and ocular involvement in Behçet's disease in southern Turkey. Acta Ophthalmol (Copenh) 1992;70:786-9.
[3] Dagli M, Eryilmaz A, Tanrikulu S, Aydın A, Gonul M, Gul U, et al. Evaluation of cochlear involvement by distortion product otoacoustic emission in Behçet's disease. Auris Nasus Larynx 2008;35:333-7.
[4] Zeidan MJ, Saadoun D, Garrido M, Klatzmann D, Six A, Cacoub P. Behçet's disease physiopathology: a contemporary review. Auto Immun Highlights 2016;7:4.
[5] Sarr SA, Fall PD, Mboup MC, Dia K, Bodian M, Jobe M. Superior vena cava syndrome revealing a Behçet's disease. Thromb J 2015;13:7.
[6] Lai C, Sun Y, Wang J, Purvin VA, He Y, Yang Q, et al. Optic perineuritis in Behçet disease. J Neuroophthalmol 2015;35:342-7.
[7] Morgan ML, EspinoBarros Palau A, Lee AG, Foroozan R. Neuro-Behçet disease presenting with oculopalatal tremor. J Neuroophthalmol 2015;35:51-3.
[8] White AS, Taylor RL, McNeill C, Garsia R, Welgampola MS. Behçet's disease presenting as a peripheralvestibulopathy. J ClinNeurosci 2014;21:1060-3.
[9] Alajouanine T, Castaigne V, Lhermitte F, Gambier J, Gautier JC. La meningo-encephalite de la maladie de Behçet. Presse Med 1961;69:2579-82.
[10] Elidan J, Levi H, Cohen E, BenEzra D. Effect of cyclosporine A on the hearing loss in Behçet's disease. Ann Otol Rhinol Laryngol 1991;100:464-8.
[11] International Study Group for Behçet's Disease. Evaluation of diagnostic (classification) criteria in Behçet's disease-to wards internationally agreed criteria. Br J Rheumatol 1992;31:299-308.
[12] Yazici H, Yurdakul S, Hamuryudan V. Behçet'ssyndrome. In: Maddison PJ, Isenberg DA, Woo P, Glass DN, editors. Oxford textbook of rheumatology. 2nd ed. Oxford: Oxford Medical Publications; 1998:pp.1394-403.
[13] Chajek T, Fainaru M. Behçet'sdisease. Report of 41 cases and review of the literature. Medicine 1975;54:179-95.
[14] Nadeau SE, Watson RT. Neurologic manifestations of vasculitis and collagen vascular syndromes. In: Joynt RJ, editor. Clinical neurology. Philadelphia: JB Lippincott. 1992:pp.1-166.
[15] Ehrlich GE. Vasculitis in Behçet's disease. Int Rev Immunol 1997;14:81-8.
[16] Hirohata S, Kikuchi H. Behçet's disease. Arthritis Res Ther 2003;5:139-46.
[17] Onder M, Gürer MA. The multiple faces of Behçet's disease and its aetiological factors. J Eur Acad Dermatol Venereol 2001;15:126-36.
[18] Berrettini S, Bruschini P, Sellari Franceschini S, Mita L, Olivieri I, Gemignani G. [Sudden deafness and Behçet's disease]. Acta Otorhinolaryngol Belg 1989;43:221-9. [Article in French].
[19] Hagiwara N, Harashima S, Tukamoto H, Horiuchi T. [A case of Behçet's disease with chronic and repeated sudden hearing loss: successful treatment with intravenous cyclophosphamide pulse therapy]. Ryumachi 2001;41:858-63. [Article in Japanese]
[20] Arts HA. Sensorineural hearing loss: evaluation and management in adults. In: Cummings CW, Flint PW, Harker LA, Haughey BH, Richardson MA, Robbins KT, et al., eds. Cummings Otolaryngology-Head and NeckSurgery, 4th ed. Philadelphia: Mosby. 2005:pp.3535-61.
[21] Belkahia A, Ben Ayed H, Ben H'Mida M, Hamza M. [Auditory and vestibular lesions in Behcet's disease]. Ann Otolaryngol Chir Cervicofac 1982;99:469-76. [Article in French]
[22] Andreoli C, Savastano M. Audiologicpathology in Behçet's syndrome. Ann J Otol 1989;10:466-67.
[23] Gemignani G, Berrettini S, Bruschini P, Sellari-Franceschini S, Fusari P, Piragine F, et al. Hearing and vestibular disturbances in Behçet's syndrome. Ann Otol Rhinol Laryngol 1991;100:459-63.
[24] Bayazit YA, Yilmaz M, Gunduz B, Altinyay S, Kemaloglu YK, Onder M, et al. Distortion product otoacoustice mission findings in Behcet's disease and rheumatoid arthritis. ORL J Otorhinolaryngol Relat Spec 2007;69:233-8.
[25] Ak E, Harputluoglu U, Oghan F, Baykal B. Behcet's disease and hearing loss. Auris Nasus Larynx 2004;31:29-33.
[26] Soylu L, Aydogan B, Soylu M, Ozsahinoglu C. Hearing loss in Behçet'sdisease. Ann Otol Rhinol Laryngol 1995;104:864-7.
[27] Aslan S, Serarslan G, Savas N, Teksoz E, Dagli S. Hearing loss in patients with Behçet's disease: an audiological and transient evoked otoacoustice mission study. J Laryngol Otol 2010;124:10-5.
[28] Miura MS, LubiancaNeto JF, Krumenauer RC, Prates K, de Castro R, Saffer M. Behçet's disease: external ear involvement. Int J Pediatr Otorhinolaryngol 2004;68: 817-21.
[29] Bakhshaee M, Ghasemi MM, Hatef MR, Talebmehr M, Shakeri MT. Hearing loss in Behçet syndrome. Otolaryngol Head Neck Surg 2007;137:439-42.
[30] Sonbay ND, Saka C, Tatlican S, Vuralkan E, Aygener N, Eren C, et al. Audiological evaluation in patients with Behçet's disease. J Laryngol Otol 2014;128:694-7.
[31] Evereklioglu C, Cokkeser Y, Doganay S, Er H, Kizilay A. Audio-vestibular evaluation in patients with Behçet's syndrome. J Laryngol Otol 2001;115:704-8.
[32] Brama I, Fainaru M. Inner ear involvement in Behçet's disease. Arch Otolaryngol 1980;106:215-7.
[33] Sota J, Vitale A, Orlando I, Lopalco G, Franceschini R, Fabiani C, et al. Auditory involvement in Behcet's disease: relationship with demographic, clinical, and therapeutic characteristics. Clin Rheumatol 2017;36:445-9.
[34] Kulahli I, Balci K, Koseoglu E, Yuce I, Cagli S, Senturk M. Audio-vestibular disturbances in Behcet's patients: report of 62 cases. Hear Res 2005;203:28-31.
[35] Erbek S, Erbek SS, Yilmaz S, Yucel E, Ozluoglu LN. Vestibular evoked myogenic potentials in Behcet's disease. Eur Arch Otorhinolaryngol 2008;265:1315-20.

The European Research Journal 2019;5(3):540-544 ORIGINAL ARTICLE

Antibiotic prescription before and after rapid antigen detection test (RADT) for beta-hemolytic streptococci

Baki Derhem[1], Süleyman Özsarı[2], Selman Erturhan[1]

[1]*Yıldızeli Family Health Center, Sivas, Turkey*
[2]*Bolu Provincial Health Directorate, Bolu, Turkey*

DOI: 10.18621/eurj.376503

ABSTRACT

Objectives: Acute pharyngo-tonsillitis is one of the diseases that pediatricians and general practitioners most frequently experienced and only a small percentage of patients (20%-30% of pediatric patients, even less in adults) are actually suffering from pharyngo-tonsillitis by group A beta-hemolytic *Streptococcus* (GABHS). Also three quarters of pharyngitis patients have been treated with inappropriate antibiotics even these patients have viral infections. The aim of this study was to assess the effectiveness of the rapid antigen detection test (RADT) on the percentage of antibiotic prescriptions amongst patients with sore throat at a primary health care center in rural area.

Methods: Retrospective Cohort Study was designed to compare antibiotic prescription in patients with sore throats in two groups, one with the use of RADT and other with the clinical desicions of physicians. The x^2 test was used between two nominal variables to assess the impact of RADT on antibiotic prescription. For comparison of more than two independent variables, the ANOVA test was used and to identify the differences between groups, the Post-Hoc test was processed.

Results: Of the 580 patients, the avarage age of the study population was 25.8 years old while the median age was 21 years (min.=3, max.=65). There was a significant difference between two groups who had tested with RADT or not in terms of antibiotic prescription ($p < 0.001$). There was a significant difference between 3-14 years of age and 15-44 years of age ($p = 0.001$) as well as 3-14 years of age and 45-65 years of age ($p = 0.009$), however there was no significant difference between 15-44 and 45-65 years of age ($p = 1.00$).

Conclusions: Using the RADT is truly effective in reducing the percentage of antibiotic prescriptions in our setting. We believe that, the tools like RADTs which are quickly results and easy to use are really useful in practising (particularly in rural area).

Keywords: Rapid antigen detection test, *Streptococcus*, sore throat, antibiotic prescription

Received: January 9, 2018; Accepted: April 18, 2018; Published Online: May 27, 2018

Acute pharyngo-tonsillitis is one of the diseases that pediatricians and general practitioners most frequently encounter (15 million visits per year in the US alone), only a small percentage of patients (20%-30% of pediatric patients, even less in adults) are actually have pharyngo-tonsillitis by group A beta-hemolytic *Streptococcus* (GABHS) [1]. These are rare in children under 3 years of age, peak with the highest incidence between the ages of 3-15, and very rare in people over 50. With the exception of other rare

Address for correspondence: *Baki Derhem, MD., Sivas Provincial Health Directorate Yildizeli Family Health Center, Atatürk Cad. Yıldızeli, Sivas, Turkey*
E-mail: dr.baki71@gmail.com

e-ISSN: 2149-3189

bacterial infections of pharynx (caused by *Corynybacterium diphtheriae and Neisseria ghonorrhoeae*), antibiotic therapy is unnecessary for acute pharyngo-tonsillitis caused by other organisms than GABHS even more so because most cases are caused by viruses (in particular adenovirus, influenza and parainfluenza viruses). It is extremely important to make the diagnosis accurately to avoid unnecessary and potentially harmful antibiotic prescriptions [2, 3].

Inappropriate antibiotic prescriptions for treatment of pharyngitis have contributed to the emergence of resistant strains of oropharyngeal human flora and it causes increased morbidity, mortality and healthcare costs [4]. Approximately three quarters of pharyngitis patients have recieved inappropriate antibiotic prescriptions by antibiotics for viral infections [5, 6].

The aim of this study was to assess effectiveness of the rapid antigen detection test (RADT) on percentage of antibiotic prescriptions amongst patients with sore throat at a primary health care center in rural area.

METHODS

Study Setting

The study was conducted in a rural area -Yildizeli Family Health Center in Sivas (Turkey)- which has 6 family physicians. Informed permission were obtained from patients by clinic physicians. Retrospective Cohort Study was designed to compare antibiotic presicription in patients with sore throats in two groups, one with use of RADT and other with clinical desicions of physicians.

Participants

All patients between the ages of 3 and 65 years old with sore throat were asked to participate in the study between February and June 2017. Patients over 18 years old were given an informed permission and under 18 years old, informative sheet of study was given to their parents. For control group, all patients with sore throat between 3 and 65 years of age between February and June 2016 were selected. Ages are grouped as 3-14, 15-44 and 45-65 years of age.

Inclusion Criteria

- Males and females aged 3 to 65 years old.

- At least one symptom of acute pharyngitis (fever, sore throat, tonsillar exudates, tender servical nodes, absence of cough).

Exclusion Criteria

- Patients who did not consent to participate.

- Patients younger than 3 years and over 65 years old.

- Immunsuppressed condition such as neoplasm, AIDS (acquired immunodeficiency syndrome), reception of chemotherapy, radiotherapy, coticosteroids and immunsuppressive therapy (1 patients with recently received chemotherapy).

- Rheumatic hearth disease, hearth valve disease (4 patients with rheumatic hearth disease).

- Toncillectomy (12 patients).

- Patients who received antibiotics in previous two weeks (26 patients).

Samples

Samples were taken by family physicians who have trained previously to perform the correcttechnique (a throat swab was collected using a sterile swab from posterior pharynx, tonsils and/orinflamed areas). Samples were processed using the TOYO in vitro diagnostic test for GABHS (Türklab, Izmir, Turkey). According the manufacturer's instruction, this test has a 99% specificity and 97.3% sensitivity.

Statistical Analysis

Statistical analyses were performed using SPSS 22 for Windows. x2 test was used between twonominal variables to assess the impact of RADT on antibiotic prescription. For comparison of morethan two independent variables, the ANOVA test was used and to identify the differences betweengroups, the Post-Hoc test was processed. The statistical distrubutions of age and gender were specifiedin numbers and percentage values. P values of 0.05 or less were considered statistically significant.

RESULTS

Five hundreds and eighty patients participated in our study. The patients' demographics were shown in Table 1. In total, positive test results were obtained in

Table 1. Patient demographics

Variables	Data
Males, n(%)	307 (52.9%)
Females, n (%)	273 (47.1%)
Age (years)	25.8 ± 18.06
Median Age (min.- max.)	21 (3-65)
Assessed with RADT, n (%)	271 (46.7%)
Assessed with clinical decision, n (%)	309 (53.2%)
Total number of patients in the study, n (%)	580 (100%)

Data are shown as mean ± standard deviation or number (%). min = minimum, max = maximum, RADT = rapid antigen detection test

75 (27.7%) of the 271 patients who were tested with RATD and they were treated with antibiotics. One hundred and seventy-six (57%) of 309 patients who were not tested with RADT were treated with antibiotics according to clinical evaluation. There was a significant difference between two groups who had tested with RADT or not in terms of antibiotic prescription ($p < 0.001$). No statistically significant difference of antibiotic prescription was found by comparing patients by gender ($p = 0.184$). The patients were grouped as 3-14, 15-44 and 45-65 years of age and we compared them between each other with antibiotic prescription. There was a significant difference between 3-14 years of age and 15-44 years of age ($p = 0.001$) as well as 3-14 years of age and 45-65years of age ($p = 0.009$), however there was no significant difference between 15-44 and 45-65 years ofage ($p = 1.00$).

Table 2. Antibiotic preference

Prefered antibiotic prescriptions	Data
Penicillin, n (%)	215 (85.6%)
-Amoxicillin clavulanate	201 (80.0%)
-Penicillin-G	7 (2.7%)
-Amoxicilin	7 (2.7%)
Cephalosporins, n (%)	31 (12.3%)
-1. generation	7 (2.7%)
-2. generation	20 (7.9%)
-3. generation	4 (1.6%)
Macrolide, n (%)	4 (1.6%)
Tetracycline, n (%)	1 (0.3%)

Data are shown as number (%).

Antibiotics were prescribed to 251 patients. Among these prescriptions, penicillin was the most frequently preferred class (85.6%). Within this class, majority of prescriptions were amoxicillin clavulanate (80.0%), penicillin-G and amoxicillin were also prescribed (2.7% and 2.7% repectively). Twelve point three percent (12.3%) of the prescriptions were cephalosporins, with the first generation cephalosporins account for 2.7%, second-generation cephalosporins acount for 7.9% and third-generation cephalosporins account for 1.6%. Macrolides (1.6%) and tetracyclines (0.4%) were the less prefered groups of antibiotics (Table 2).

DISCUSSION

Most phayngo-tonsillitis cases are viral and with nasal congestion, low grade fever, cough, dysphonia, headache and myalgia. The process of bacterial pharyngo-tonsillitis is acute onset of high fever with chills, severe odynophagia and dysphagia but no cough. None of signs and symptoms are specific to acute pharyngitis caused by GABHS, so that the clinical criteria are of poorly use.

Various studies reported that, GABHS is the most common bacterial cause of acute pharyngitis and responsible for 5%-15% of sore throat visits in adults and 20%-30% in children [7].

Diagnosis

The culture is the gold standard for diagnosis but requires 18-24 hours of incubation at 37°C, causing a delay in identification of GABHS [8]. The time period for reading culture is its main limitations about using sistematically. Thus, to improve the diagnostic criteria, several scoring systems have been developed to predict, on a clinical basis, whether patients have bacterial or viral pharyngitis. Among many devised clinical scores, the Centor criteria has reliable predictors of GABHS pharyngitis. They include evaluating patients for tonsillar exudates, tender anterior servical lymphadenopathy or lymphadenitis, absence of cough and fever (oral temperature higher than 38.3 C; 101 F) [9]. More recently, the Centor score was modified by incorporating patient's age, which allows the physician to classify patient in low-

, moderate-, or high-risk groups [10]. On the other hand, Mistik *et al*. [12] have developed a scoring system (called Mistik Score) to diagnose viral sore throats. Within the last two decades, RADT) have become commercially available for the detection of *Streptococcus*. pyogenes using throat swabs. These tests offer an advantage of diagnosing streptococcal pharyngitis within a few minutes [12]. Although their specificity is more than 95%, sensitivity of test vary, which ranges from 65% to 95%. Several guidelines have been published on diagnosis and treatment of streptococcal pharyngitis, however not all are in agreement. The American College of Phsyician's (ACP) guideline endorsed by Center for Disease Control (CDC), American Academy of Family Phsyicians and the American Society of Internal Medicine recommends that patient with low Centor scores of "0" or "1" (low risk for streptococcal pharyngitis) do not require any testing or antibiotic prescription. For patients with Centor scores "2" and "3", guidelines suggest using a RADT and prescribing antibiotics to patients with positive tests. Empirical antibiotic treatment is recommended for patients with Centor score of "4" [13, 14].

Treatment

Patient with acute GABHS pharyngitis should be treated with an appropriate antibiotic at an appropriate dose for a duration likely to eradicate the organism from pharnx (usually 10 days). Based on their limited spectrums of activity, infrequency of adverse reactions and small costs penicillin or amoxicillin is recommended drug of choice for those non-allergic to these agents. Treatment of GABHS pharyngitis in penicillin allergic individuals should include a first generation cephalosporin for 10 days, clindamycin or clarithromycin for 10 days or azithromycin for 5 days [15].

The overconsumption of antibiotics for sore throat is main problem that is showed by several studies. In Athens, Maltezou *et al*. [12] stated that, diagnosis of streptococcal pharyngitis using clinical criteria only led to high rates of antibiotic prescription among children managed empirically (72.2%) [12]. In Pakistan, Palla *et al*. [16] stated that, antibiotics for suspected pharyngitis were prescribed to 98.5% of all patients included in the study. In Poland, Nitsch-Osuch *et al*. [17] stated that, the antibiotic therapy was ordered for 58% patients with influenza. Like these studies, our study showed, 57% of all patients with sore throat were treated with antibiotics according to clinical evaluation. These empirically managements may be the result of physicians' concerns about complications and their defensive approaches because of increasing malpractice lawsuits [18].

In our population, antibiotic prescription was reduced by 48.5% using the RADT compared with empirical management of patients. Similarly, in Greece Maltezou *et al*. [12] reported, the reduction is 61% with using RADT and McIsaac *et al*. [19] reported a 45% reduction in antibiotic prescription in adults using a RADT compared with empirical treatment.

In this study, when comparing antibiotic prescribing rates with age groups, there was a statistically significant difference between 3-14 years of age and 15-44 years of age ($p = 0.001$) and between 3-14 years of age and 45-65 years of age ($p = 0.009$). Prescribing more antibiotics to 3-14 years of age groups may be caused by; 1) the prevalance of GABHS is higher in this age group, 2) the family pressure for prescribing antibiotics, 3) the physicians' concerns and defensive approach to this group of age. The most commonly prefered antibiotics were penicillin and amoxicillin followed by cephalosporins and macrolides in our study setting. Our treatment choices are compatible with clinical guidelines [4, 15].

CONCLUSION

There are many conducted study in literature relevant with how to reduce inappropriate antibiotic prescriptions. It reveals that, throat swab is gold standart for diagnose GABHS; but not all physicians possess this opportunity while practising (particularly in rural area). In this situation, streptococcal pharyngitis is diagnosed with physicians' clinical experiment and/or clinical scoring systems like Centor. On the other hand, a lot of studies performed about RADT's sensitivity, specificity, positive and negative predictive values and it's insufficient sensitivity values (ranges from 65%- 5%).

In our study, we aimed not to calculate RADT's sensitivity, specificity, PPV or NPV while we aimed to evaluate RADT's impact on antibiotic prescriptions

and our study revealed that, using the RADT is truly effective in reducing the percentage of antibiotic prescriptions in our setting. We believe that, the tools like RADTs which are quickly results and easy to use are really useful in practising (particularly in rural area).

Author Contributions

Study Design: BD; Statistical Analysis: BD, SÖ; Data Interpretation: BD, SÖ; Data Collection: BD, SE; Manuscript Preparation: BD, SE; Literature Search: BD, SE; Funds Collection: BD.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] Cots JM, Alos JI, Barcena M, Boleda X, Canada JL, Gomez N, et al. Recommendations for management of acute pharyngitis in adults. Acta Otorrinolaringol Esp 2015;66:159-70.
[2] Kim S. Optimal diagnosis and treatment of group A streptococcal pharyngitis. Infect Chemother 2015;47:202-4.
[3] Agarwal M, Raghuwanshi SK, Asati DP. Antibiotic use in sore throat: are we judicious? Indian J Otolaryngol Head Neck Surg 2015;67:267-70.
[4] Bisno AL, Gerber MA, Gwaltney JM Jr, Kaplan EL, Schwartz RH. Practice guidelines for the diagnosis and management of group A streptococcal pharyngitis. Clin Infect Dis 2002;35:113-25.
[5] Ayranci U, Akgun Y, Unluoglu I, Kiremitci A. Antibiotic prescribing patterns for sore throat infections in a University-based primary care clinic. Ann Saudi Med 2005;25:22-8.
[6] Linder JA, Stafford RS. Antibiotic treatment of adults with sore throat by community primary care physicians: a national survey, 1989-1999. JAMA 2001;286:1181-6.
[7] Ebell MH, Smith MA, Barry HC, Ives K, Carey M. Does this patient have strep throat? JAMA 2000;284:2912-8.
[8] Regoli M, Chiappini E, Bonsignori F, Galli L, de Martino M. Update on the management of acute pharyngitis in children. Ital J Pediatr 2011;37:10.
[9] Aalbers J, O'Brien KK, Chan WS, Falk GA, Teljeur C, Dimitrov BD, et al. Predicting streptococcal pharyngitis in adults in primary care: a systematic review of the diagnostic accuracy of symptoms and signs and validation of the Centor score. BMC Med 2011;9:67.
[10] McIsaac WJ, Goel V, To T, Low DE. The validity of a sore throat score in family practice. CMAJ 2000;163:811-5.
[11] Mistik S, Gokahmetoglu S, Balci E, Onuk FA. Sore throat in primary care project: a clinical score to diagnose viral sore throat. Fam Pract 2015;32:263-8.
[12] Maltezou HC, Tsagris V, Antoniadou A, Galani L, Douros C, Katsarolis I, et al. Evaluation of a rapid antigen detection test in the diagnosis of streptococcal pharyngitis in children and its impact on antibiotic prescription. J Antimicrob Chemother 2008;62:1407-12.
[13] Cooper RJ, Hoffman JR, Bartlett JG, Besser RE, Gonzales R, Hickner JM, et al. Principles of appropriate antibiotic use for acute pharyngitis in adults: background. Ann Emerg Med 2001;37:711-9.
[14] Snow V, Mottur-Pilson C, Cooper RJ, Hoffman JR. Principles of appropriate antibiotic use for acutepharyngitis in adults. Ann Intern Med 2001;134:506-8.
[15] Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee G, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. Clin Infect Dis 2012;55:e86-102.
[16] Palla AH, Khan RA, Gilani AH, Marra F. Over prescription of antibiotics for adult pharyngitis is prevalent in developing countries but can be reduced using McIsaac modification of Centor scores: a cross-sectional study. BMC Pulm Med 2012;12:70.
[17] Nitsch-Osuch A, Gyrczuk E, Wardyn A, Zycinska K, Brydak L. Antibiotic prescription practices among children with influenza. Adv Exp Med Biol 2016;20:25-31.
[18] Derhem B, Ungan M. General practitioners' level of knowledge about their rights andcriminal liabilities according to legislation in Turkey. Fam Med Prim Care Rev 2017;19:357-60.
[19] McIsaac WJ, Kellner JD, Aufricht P, Vanjaka A, Low DE. Empirical validation of guidelines for the management of pharyngitis in children and adults. JAMA 2004;291:1587-95.

Epidemiologic, clinical findings and risk factors of recurrent herpes labialis in healthy adult patients: a case-control study

Mohammad Nassaji[1], Raheb Ghorbani[2], Ramin Taheri[3], Maryam Azizzadeh[3], Fatemeh Abbassyan[4]

[1]Department of Infectious Diseases, Semnan University of Medical Sciences, Research Center for Social Determinants of Health, Semnan, Iran
[2]Department of Community Medicine, Semnan University of Medical Sciences, Faculty of Medicine, Research Center for Social Determinants of Health, Semnan, Iran
[3]Department of Dermatology, Semnan University of Medical Sciences, Kowsar Hospital, Semnan, Iran
[4]General Physician, Semnan University of Medical Sciences, Kowsar Hospital, Semnan, Iran

DOI: 10.18621/eurj.384806

ABSTRACT

Objectives: Herpes labialis is a common viral infection and characterized by recurrent vesicular lesion primarily on the lips and perioral skin. The aim of this study was to determine the epidemiological, clinical characteristics and trigger factors associated with recurrence herpes labialis in adult patients.

Methods: This case-control study was conducted with the participation of one hundred adult patients and the same number of control. Data collected about demographics, clinical, as well as trigger factors from individuals who met inclusion criteria.

Results: Seventy-four percent of cases and 34% of controls were female that showed significant difference ($p < 0.001$). Mean body mass index of patients was significantly higher than controls (25.9 ± 2.9 kg/m^2 versus 22.0 ± 2.9 kg/m^2, $p < 0.001$). The most common location of the lesions during the last episode of infection was upper lip (65%). The number of lesions was single in 58% and multiple in 42% of patients. The frequency of episodes per year was more than two attacks each year in most patients (83%). Positive family history of recurrence herpes labialis was found in 50% and 20% of cases and controls respectively ($p < 0.001$). Emotional stress (61%), sunlight exposure (54%) and flu (37%) were the main triggering factors reported by the patients.

Conclusions: This study revealed that recurrence herpes labialis is more common in women and on the upper lip. Family history of recurrence herpes labialis was positive significantly in patients. The most common trigger factors were stress, sunlight exposure, flu. Higher body mass index was a probable risk factors for recurrence herpes labialis.

Keywords: Recurrence herpes labialis, adult, epidemiology, trigger factors

Received: January 27, 2018; Accepted: March 15, 2018; Published Online: June 2, 2018

Recurrence herpes labialis (RHL) is one of the most prevalent and clinically common viral infectious diseases in general population [1]. It is caused by the reactivation of latent infection of herpes simplex virus-1 (HSV-1). About 45% to 98% of the world population are infected by HSV-1 and 15 to 40% of infected people may develop RHL [2]. The primary HSV-1 infection typically occurs in early

Address for correspondence: *Mohammad Nassaji, MD., Associate Professor, Semnan University of Medical Sciences, Research Center for Social Determinants of Health, Kowsar Hospital, Department of Infectious Diseases, Basij Blvd, Semnan, Iran*
E-mail: hnassaji@yahoo.com, Tel: +98 2333437844, Mobile: +989121318640, Fax: +982333437837

e-ISSN: 2149-3189

childhood and is asymptomatic or can causes herpetic gingivostomatitis. After the primary infection, the virus ascends the sensory nerve axons and establishes chronic, latent infection in trigeminal ganglion [3]. Recrudescent disease is a consequence of centrifugal migration of the reactivated virus from the trigeminal ganglion to the periphery and its local replication. Recurrent lesions are common on the mucocutaneous junction of the lips and less common intraorally [4].

Most patients experience prodromal symptoms prior to the appearance of lesions which is associated with pain, itching, burning, tingling and paresthesia. After about 24 hours lesions appear and characterized by erythema, papules and blisters. The lesions crust over and heal without scarring over a period of 1-2 weeks [5]. The diagnosis of RHL is based on the history, classic location and clinical appearance of the lesions [6].

RHL vary in severity from patient-to-patient. In some individuals, infection is infrequent and considered a minor problem. But in others, episodes of recurrences are frequent and may be painful, long-lasting, disfiguring and negatively affect the patient's quality of life [7, 8]. The factors that trigger the outbreak of RHL are not completely understood. The most important are stress, fever, dental manipulation, upper respiratory tract infections, ultraviolet light, menstruation, trauma and immune incompetence [9].

Studies about RHL in adults have been equivocal in identifying some of the risk factors. The present study was designed to examine epidemiological andclinical characteristics of the disease in a group of adult patients and comparing findings of patients with a control group. Another aim of the study was to evaluate some risk factors associated with RHL.

METHODS

This case-control study was conducted from February 2016 to May 2017 in Semnan, Iran. All adult patients (≥ 18 years) with diagnosis of RHLwho were visited in Dermatology and Infectious diseases clinics of Semnan University of Medical Sciences considered for participation in the study. RHL was defined as at least one episodes during recent year.

Control group were selected from adult individuals without history of RHLby the systematic sampling. Subjects with history of connective tissue disorders, receiving immunosuppressive drugs and those with non- ascertainable clinical status were excluded.

A structured data collection sheet was used to obtain information about demographics, clinical, as well as trigger factors from individuals who met inclusion criteria.Basic data collected included age, gender, blood group and body mass index (BMI). During the visit patients were clinically examined to confirm its presence and the location of lesion. Also, participants were asked to indicate the age at first episode of RHL, perceived precipitating factors, number of lesions (single or multiple), duration of lesions to heal, annual recurrence rate and family history of RHL. A short verbal stress ratingscale was used for measuring the perception of stress [10]. Sunlight exposure was defined as being outdoor more than one ours for three days before to the appearance of lesions.

Informed consent was obtained from all participant before enrollment. The study protocol was approved by Research Council and Ethical Committee of the Semnan University of Medical Sciences.

Statistical Analysis

Data were analyzed by Kolmogorov-Smirnov, Chi Square,student's t tests and logistic regression analysis using SPSS 18.0. A p value less than 0.05 considered statistically significant.

RESULTS

Finally, 100 patients with diagnosis of RHL met inclusion criteria and were enrolled. Same numbers of controls were selected. The mean age of patients was 37.1 ± 13.4years and for the controls was 28.2 ± 7.2 years ($p < 0.001$). Seventy-four percent of cases and 34% of controls were female that showed significant difference ($p < 0.001$). Mean BMI of patients was significantly higher than controls (25.9 ± 2.9 kg/m^2 versus 22.0 ± 2.9 kg/m^2, $p < 0.001$). The most common blood group among the patients and controls was A (44% and 55% respectively). But distribution of ABO blood groups in the patients with RHL was not significantly different from of control group ($p = 0.109$). Basic characteristics of cases and controls are

Table 1. Distribution of basic characteristics in individuals with and without recurrent herpes labialis

Characteristics	Study Group		*p* value
	Patients (n = 100)	Control (n = 100)	
Age (year)			**< 0.001**
< 40	22	14	
40-59	9	1	
≥ 60	69	85	
Gender			**< 0.001**
Male	26	66	
Female	74	34	
Body Mass Index (kg/m^2)			**< 0.001**
< 18.5	0	9	
18.5-24.9	37	76	
25-29.9	58	13	
≥ 30	5	2	
Family History			**< 0.001**
+	50	20	
-	50	80	
Blood Group			0.109
A$^+$	44	55	
B$^+$	15	16	
AB$^+$	20	20	
O$^+$	21	9	

given in Table 1.

The number of lesions was single in 58% and multiple in 42% of patients. The location of the RHL lesions during the last episode of infection arelisted in Table 2. The mean duration of suffering from RHL in patients was 12.10 ± 11.03 years. The mean duration of each episode was 7.24 days. The mean interval between attacks was 12.04 ± 9.37 months. The frequency of episodes per year was more than two attacks each year in most patients (83%). Positive family history of RHL was found in 50% and 20% of cases and controls respectively ($p < 0.001$).

The most common trigger factors reported by participants were stress, sunlight exposure and flu (Table 3). The results of logistic regression analysis showed that BMI (OR=2.1, 95% CI:1.16-2.8, $p < 0.001$) was significantly higher in patients with RHL.

Table 2. Distribution of herpes labialis lesions at the time of examination

Location	Percentage
Upper lip	65
Lower lip	40
Nose	13
Cheek	1

Table 3. Perceived triggers for the episode of herpes labialis among the patients

Trigger	Percent
Stress	61
Sunlight exposure	54
Flu	37
Fever	33
Trauma	2
Menstruation (in women)	9

DISCUSSION

Recurrence herpes labialis is a very common disease worldwide. The relationship between some risk factors and the occurrence of the disease is somehow complex. Also, the prevalence of predisposing factors may vary between different populations which has led to discordant findings among studies.

A striking finding in our study was the significantly higher BMI in patients with RHL compared with controls. Based our knowledge no previous study evaluated this variable. Obesity has some effects on the immune response through a variety of immune mediators. It has been suggested that the adipose tissue participates actively in inflammation and immunity by releasing a variety of proinflammatory and anti-inflammatory factors. This leads to dysregulated immune response and may leads to susceptibility or reactivation of infections in individuals with high BMI [11]. Several studies in adult suggest that BMI was associated with the risk of some infections including skin, respiratory, urinary tract and nosocomial infections [12]. Bernstein *et al*. [13] reported that having a larger BMI was associated with higher human herpes virus type 8 infections.

According to our results, RHLwas more common in females. Similarly, this sex difference has been reported in some other studies[14-16]. In contrast in Embil *et al*'s study [17] RHL prevalence was found to be higher among men than among women. On the other hand, some other researcher reported that RHLwas not statistically significant difference between two genders [18, 19].

In the present study the lesions were more common on the upper lip than lower lip that showed comparable patternwith some other studies [20, 21]. The results of the Sawair *et al*. [22] study showed a slight higher occurrence of the lesions on the lower lip (51.9%) than upper lip (46.2%).

Information from our patients indicated that most individual experienced more than two episodes of herpes labialis per year. Similarly, Axell *et al*. [21] reported more than two episodes per year. This finding is in contrast with most previous reports stated that majority of patients experienced ≤2 episodes of herpes labialis per year [18, 23, 24]. One probable explanation for this difference is that patients with one or two episodes may not seeking medical care for their problem.

Studies in adults about the trigger factors of RHL showed different results. The most common factors reported by the participants in this study were stress, sunlight, flu and fever. Similarly, a higher level of perceived stress was the most common associated risk factors of RHL [18, 25] or one of more common trigger factors in some studies [20, 22]. Suggested biologic mechanism is the association between changes in stress and immune and neuroendocrine markers especially the modulations of T-lymphocyte function that can leads to virus reactivation [26, 27]. Psychological stress, through its suppression of both innate and adaptive immune responses, especially CD8+ T cell control of latent HSV-1 infections may be an important factor in the reactivation of herpes infections [28]. Other studies reported different trigger as the most common provocative factors of RHL [16, 23]. The difference in these findings might at least partly be explained by differences in the study design, patients' selection, and number of samples.

According to the patients, the mean duration of each episode was 7.24 days that is in accordance with Sawair *et al*.'s study [22] (mean 7.15± 3.1 days). A shorter healing time was reported by Axell *et al*.'s study [21] in most cases. Positive family history of RHL was significantly more common in patients. Most previous studies confirmed this finding [18, 22, 23].

Limitations

Our study has several limitations that should be taken into account in interpreting the findings. First, the eligible patient number is relatively small in this study. Second, we assessed patients in university affiliated hospital, so that referral bias may be occurred. Third, because of the difficulty in remembering past events, the likelihood of recall bias is present.

CONCLUSION

Our study revealed that RHL is more common in women and on the upper lip. Family history of RHL was positive significantly in patients. The most common trigger factors were stress, sunlight exposure,

flu and fever. Higher BMI was a probable risk factors for RHL. Controlling of stress, sunlight exposure, fever and BMI may lead to reducing episode of the diseases.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

Acknowledgement

The research was supported by Research Committee of Semnan University of Medical science.

REFERENCES

[1] Whitley RJ, Roizman B. Herpes simplex virus infections. Lancet 2001;12;357:1513-8.
[2] Fatahzadeh M2, Schwartz RA. Human herpes simplex virus infections: epidemiology, pathogenesis, symptomatology, diagnosis, and management. J Am Acad Dermatol 2007;57:737-63; quiz 764-6.
[3] Arduino PG, Porter SR. Herpes Simplex Virus Type 1 infection: overview on relevant clinico-pathological features. J Oral Pathol Med 2008;37:107-21.
[4] Worrall G. Herpes labialis. BMJ Clin Evid 2009;2009. pii: 1704.
[5] Higgins CR, Schofield JK, Tatnall FM, Leigh IM. Natural history, management and complications of herpes labialis. J MedVirol 1993 41(Suppl 1):22-6.
[6] Siegel MA. Diagnosis and management of recurrent herpes simplex infections. J Am Dent Assoc 2002;133:1245-9.
[7] Fatahzadeh M, Schwartz RA. Human herpes simplex labialis. Clin Exp Dermatol 2007;32:625-30.
[8] Dreno B, Malkin JE, Saiag P. Understanding recurrent herpes labialis management and impact on patients' quality of life: The HERPESCOPE study. Eur J Dermatol 2013;23:491-9.
[9] Glick M. Clinical aspects of recurrent oral herpes simplex virus infection. Compend Contin Educ Dent 2002; 23:4-8.
[10] Alfvén G, Nilsson S. Validity and reliability of a new short verbal rating scale for stress for use in clinical practice. Acta Paediatr 2014;103:e173-5.
[11] Milner JJ, Beck MA. The impact of obesity on the immune response to infection. Proc Nutr Soc 2012;71:298-306.
[12] Dobner J, Kaser S. Body mass index and the risk of infection - from underweight to obesity. Clin Microbiol Infect 2018;24:24-28.
[13] Bernstein KT, Jacobson LP, Jenkins FJ, Vlahov D, Armenian HK. Factors associated with human herpesvirus type 8 infection in an injecting drug user cohort. Sex Transm Dis 2003;30:199-204.
[14] Löwhagen GB, Bonde E, Eriksson B, Nordin P, Tunbäck P, Krantz I.Self-reported herpes labialis in a Swedish population. Scand J Infect Dis 2002;34:664-7.
[15] Shulman JD, Carpenter WM, Lewis DL. The prevalence of recurrent herpes labialis during an Army hot weather exercise. J Public Health Dent 1992;52:198-203.
[16] Katz J, Chaushu G, Peretz B. Recurrent oral ulcerations associated with recurrent herpes labialis – two distinct entities? Community Dent Oral Epidemiol 2001;29:260-3.
[17] Embil JA, Stephens RG, Manuel FR. Prevalence of recurrent herpes labialis and aphthous ulcers among young adults on six continents. Can Med Assoc J 1975;113:627-30.
[18] Celik M, Sucakli MH, Kirecci E, Ucmak H, Ekerbicer HC, Ozturk P. Recurrent herpes labialis among health school students in Kahramanmaras, Turkey: a cross-sectional survey. Dermatol Sin 2013;31:64-7.
[19] Shulman JD.Recurrent herpes labialis in US children and youth. Community Dent Oral Epidemiol 2004;32:402-9.
[20] Lorette G, Crochard A, Mimaud V, Wolkenstein P, Stalder JF, El Hasnaoui A. A survey on the prevalence of orofacial herpes in France: the INSTANT Study. J Am Acad Dermatol 2006;55:225-32.
[21] Axéll T, Liedholm R.Occurrence of recurrent herpes labialis in an adult Swedish population. Acta Odontol Scand 1990;48:119-23.
[22] Sawair FA, Jassim ZA, Malkawi ZA, Jamani KD. Epidemiologic aspects of recurrent herpes labialis among Jordanian university students. Saudi Med J 2010;31:808-13.
[23] Azodo CC, Umoh AO. Herpes labialis among dental healthcare providers in Nigeria. Indian J Dent 2015;6:116-20.
[24] Chi CC, Wang SH, Delamere FM, Wojnarowska F, Peters MC, Kanjirath PP. Interventions for prevention of herpes simplex labialis (cold sores on the lips). Cochrane Database Syst Rev 2015;(8):CD010095.
[25] Stock C, Guillén-Grima F, de Mendoza JH, Marin-Fernandez B, Aguinaga-Ontoso I, Krämer A. Risk factors of herpes simplex type 1 (HSV-1) infection and lifestyle factors associated with HSV-1 manifestations. Eur J Epidemiol 2001;17:885-90.
[26] Chida Y, Mao X. Does psychosocial stress predict symptomatic herpes simplex virus recurrence? A meta-analytic investigation on prospective studies. Brain Behav Immun 2009;23:917-25.
[27] Sainz B, Loutsch JM, Marquart ME, Hill JM. Stress-associated immunomodulation and herpes simplex virus infections. Med Hypotheses 200;56:348-56.
[28] Freeman ML, Sheridan BS, Bonneau RH, Hendricks RL. Psychological stress compromises CD8+ T cell control of latent herpes simplex virus type 1 infections. J Immunol 2007;179:322-328.

The European Research Journal 2019;5(3):550-556 ORIGINAL ARTICLE

Complications in patients with spinal cord injuries: a clinical study from a third level rehabilitation center in Turkey

Tuba Tülay Koca, Burhan Fatih Koçyiğit, Ejder Berk, Vedat Nacitarhan

Department of Physical Medicine and Rehabilitation, Sütçü İmam University School of Medicine, Kahramanmaraş, Turkey

DOI: 10.18621/eurj.395651

ABSTRACT

Objectives: Normal lifespan can be achieved by avoiding complications in patients with spinal cord injuries (SCIs). We aimed to characterize our spinal cord injured patients and to obtain necessary information to prevent complications.

Methods: This retrospective, cross-sectional study included 44 patients with subacute/chronic SCIs, who were included in an inpatient rehabilitation program from 2012 to 2017. The patients' epidemiological data, etiology, neurological examinations, complications, and accompaying conditions were analyzed. The neurological level, functional ambulatory scale (FAS), and American Spinal Cord Injury Association (ASIA) impairment scale were used for the classification of patients.

Results: A total of 44 patients between 16 and 81 years of age (median: 35) were included in the study. Of these, 65.9% were male. The most common etiologies were falling down from a height (31.8%), spinal surgery (29.5%), and traffic accidents (15.9%) respectively. When we look the neurological status of these patients, FAS: 0 (38.6%) and ASIA: C (40.9%) were the most common cases seen in the population. Eighteen patients (40.9%) were wheelchair-bound. Urinary (34.1%), dermatologic (29.5%), and psychiatric (22.7%) complications were the most common in the patients. Patients with low FAS levels were young (in early period), and their spasticity, urinary incontinence, and urinary and dermatological pathologies were found to be high. The wheelchair-bound patients were mostly young, and they had significantly high urinary incontinence, urinary and dermatological pathologies.

Conclusions: In our rehabilitation clinic, subacute/chronic SCI diagnosis is most commonly seen in young men, with thoracic vertebrae being the most common, followed by falling from a height. The most common complications were urinary and dermatological pathologies. The present study found higher rates of complications in patients with higher grades of injuries and in patients with lower functional levels.

Keywords: complication, morbidity, rehabilitation, spinal cord injury

Received: February 16, 2018; Accepted: March 13, 2018; Published Online: June 28, 2018

Spinal cord injuries (SCIs) are seen in various countries, with incidence rates varying from 15% to 40%. Traffic accidents, violence-related injuries, leisure activities, or work accidents are the leading causes apart from country differences. SCI pathophysiology is gradually being clarified over the past 30-40 years [1-3].

Along with motor and sensory deficits, instabilities of the cardiovascular, thermoregulatory and broncho-pulmonary system are common after a

Address for correspondence: *Tuba Tülay Koca, MD., Assistant Professor, Sütçü İmam University School of Medicine, Department of Physical Medicine and Rehabilitation, Kahramanmaraş, Turkey*
E-mail: tuba_baglan@yahoo.com

e-ISSN: 2149-3189

SCI. Disturbances of the urinary and gastrointestinal systems are typical as well as sexual dysfunction. Frequent complications of cervical and high thoracic SCI are neurogenic shock, bradyarrhythmias, hypotension, ectopic beats, abnormal temperature control and disturbance of sweating, vasodilatation and autonomic dysreflexia. Autonomic dysreflexia is an abrupt, uncontrolled sympathetic response, elicited by stimuli below the level of injury. The symptoms may be mild like skin rash or slight headache, but can cause severe hypertension, cerebral haemorrhage and death [4].

Patients may experience normal lifespan by avoiding these medical complications. According to the literature, pressure sores and respiratory complications are the most common complications. Respiratory complications are more common in the tetraplegic group and are the most common cause of mortality [1-3].

This study aimed to analyze the functional levels, the use of orthosis and assistive devices, and the follow-up complications of patients with SCI who were hospitalized and treated during acute/chronic periods in a tertiary rehabilitation clinic.

METHODS

This retrospective study included 44 patients with subacute/chronic SCI who were also included in an inpatient rehabilitation program between the years 2012 and 2017. The data of the study were collected retrospectively by analyzing patient records. Local ethics committee approval was obtained. The patients' epidemiological data, etiology, neurological examinations, complications, and accompaying conditions were analyzed. The neurological level, functional ambulatory scale (FAS) [5], and American Spical Cord Injury Association (ASIA) [6] impairment scale were used for the classification of patients. The patients were questioned for urinary and fecal incontinence, spasticity, neuropathic pain, deep vein thrombosis, pulmonary pathology, skin pathology, psychiatric findings, urinary pathology, cardiac pathology, gastrointestinal pathology, vertebral fracture, and accompanying diseases. In addition, the patients' orthosis use and Botox-A application were recorded. The Modified Ashworth Spasticity Scale (grades 0-4) was used to assess the severity of spasticity [7]. Further, the probability of suicide was also questioned.

Functional ambulatory scale (FAS)

Grade 1: Nonfunctional Ambulator
Grade 2: Ambulator - Dependent for Physical Assistance (level 2)
Grade 3: Ambulator - Dependent for Physical Assistance (level 1)
Grade 4: Ambulator - Dependent for Supervision
Grade 5: Ambulator - Independent, Level surfaces only
Grade 6: Ambulator - Independent

American Spical Cord Injury Association (ASIA)

A = Complete: No sensory or motor function is preserved in sacral segments S4-S5
B = Incomplete: Sensory, but not motor, function is preserved below the neurologic level and extends through sacral segments S4-S5
C = Incomplete: Motor function is preserved below the neurologic level, and most key muscles below the neurologic level have a muscle grade of less than 3
D = Incomplete: Motor function is preserved below the neurologic level, and most key muscles below the neurologic level have a muscle grade that is greater than or equal to 3
E = Normal: Sensory and motor functions are normal

Modified Asworth Spasticity Scale

0- No increase in muscle tone
1- Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension
1+- Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM
2- More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved
3- Considerable increase in muscle tone, passive movement difficult
4- Affected part(s) rigid in flexion or extension

Statistical Analysis

All statistical analyses were carried out using IBM SPSS version 19 (IBM Corp., NY, USA). Descriptive

Table 1. Etiology and duration of the injury

Etiology	**n (%)**
Traffic accident	7 (15.9%)
Falling	14 (31.8%)
Spinal surgery (including spinal tumor)	13 (29.5%)
Work-related injury	1 (2.3%)
Spinal infection	3 (6.8%)
Violent injury	4 (9%)
Spinal vascular pathology	2 (4.5%)
Duration	
< 1 year	24 (54.5%)
1-3 year	3 (6.8%)
2-3 year	4 (9.1%)
3-4 year	4 (9.1%)
> 4 year	9 (20.5%)

Table 2. FAS, ASIA scores and use of asistive device

	n (%)
FAS	
0	17 (38.6%)
1	5 (11.4%)
2	13 (29.5%)
3	4 (9.1%)
4	4 (9.1%)
5	1 (2.2%)
ASIA	
A	7 (15.9%)
B	6 (13.6%)
C	18 (40.9%)
D	13 (29.5%)
Assistive devices	
Walker	12 (27.5%)
Canadian	12 (27.5%)
Wheelchair	18 (40.9%)
Orthosis (AFO, splint, long walking device)	6 (13.6%)

FAS = functional ambulatory scale; ASIA = American spinal cord injury association scale, AFO = ankle foot orthosis

data were presented as mean ± standard deviation (SD) or median scores. The coherence of variables to normal contribution (normality) was analyzed using the Kolmogorov-Smirnov test. Spearman's correlation analysis was used to analyze the level of correlation between the variables.

Categorical data were reported as percentages and compared using the chi-squared. Continuous data were reported as mean with SD or median with minimum and maximum and compared by using the t test or Mann Whitney U test according to being normal distribution. Finally, a logistic regression analysis was performed to explore the predictors of ambulation. A p value of < 0.05 was considered statistically significant.

RESULTS

A total of 44 patients between 16 and 81 years of age (median: 35) were included in the study. Of these, 65.9% were male. The most common etiologies were falling from a height (31.8%), spinal surgery (29.5%), and traffic accidents (15.9%). Of the injuries, 54.5% occurred within the first year (Table 1).

When we look the neurological status of these patients, FAS: 0 (38.6%) and ASIA: C (40.9%) were the most common cases seen in the population. Eighteen patients (40.9) were wheelchair-bound. The anatomic damage was at the C5 level (25%), followed by thoracic (42.3%) and cervical (25%) involvement. Urinary incontinence was 63.6% and fecal incontinence was 31.8%. Urinary (34.1%), dermatologic (29.5%), and psychiatric (22.7%) complications were the most common complications seen in the patients. The spasticity rate was 45.5% and grade 3 was the most common type.

Patients with low FAS levels were young (in early period), and their spasticity, urinary incontinence, urinary, and dermatological pathologies were found to be high (Figure 1). Wheelchair-bound patients were mostly young, and they had significantly high urinary incontinence and urinary and dermatological pathologies. Table 3 summarizes the complications in all the cases. The percentage of nonvertebral fractures including the scapula, phalanx, clavicula and pelvis was 13.6.

FAS values were significantly related with age (p

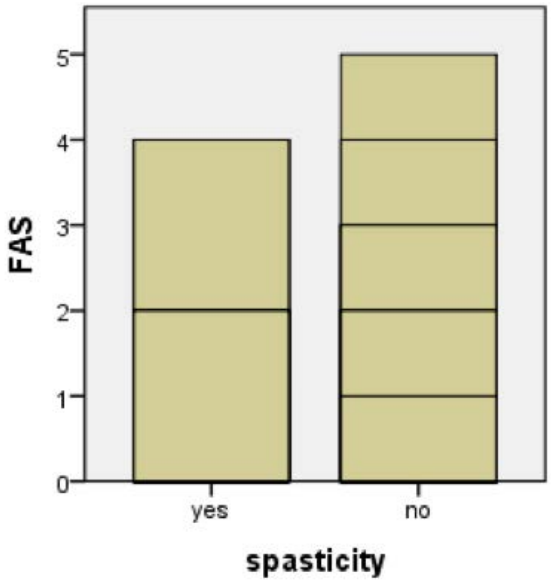


Figure 1. The relation between ambulation and spasticity existence. FAS = functional ambulatory scale.

= 0.001), spasticity (p = 0.03), injury duration (p = 0.043), dermatological pathology (p = 0.023), urinary pathology (p < 0.01), and urinary incontinence (p < 0.01). According to these results, patients with low FAS levels were young (in early period) and had high spasticity, urinary incontinence, urinary and dermatological pathologies.

ASIA scores were significantly related with etiology (p = 0.005). Wheelchair-bound patients were mostly young (p = 0.035), and they had significantly high urinary incontinence (p = 0.04), urinary pathology (p < 0.01), and dermatologic pathology (p = 0.016). No parameters were found to be predictive for wheelchair dependence in regression analysis. The FAS and ASIA scores were found to be related (p < 0.01). In addition, the FAS value was found to be positively related with age (p = 0.014). FAS ve ASIA scores and use of assistive device and orthosis of the cases are summarized in Table 2.

DISCUSSION

SCI is seen in various countries with incidence rates of 15% to 40%. Traffic accidents, violence-related injuries, leisure activities, or work accidents are the leading causes.[1,2] The differences between international studies occur based on differences in identification, classification, inclusion criteria, pretreatment, and hospital treatment. In some countries, the use of two-wheelers and bicycles is the most common reason behind the prevalence.[1-3] Unlike other countries, the most common etiological cause of SCI in Turkey is falling from a height [8, 9].

It is necessary to investigate the reasons for this difference and to take precautions. The results of the present study showed that falling down from a height was found to be the most common cause of SCI in the young male population. Conversely, the study found that spinal pathology/surgery was the most common cause of SCI in patients of advanced age. Further, better mobility and lower wheelchair dependence were found in the these group.

The ASIA impairment scale was used to assess the stage of the disease. SCI is a situation with long-term results. The most common causes of deaths related to SCI are pulmonary issues, heart diseases, and suicide [3]. Preventive methods are needed because treatment is not yet available. Implementing tight security measures in these activities will reduce the prevalence of SCI [10-12].

Calcium, free radicals, sodium, excretory aminoacids, vascular mediators, and apoptosis are thought to be responsible for the pathophysiology of SCI in both primary and secondary mechanisms. Various studies have reported that pressure ulcers (most frequently of the foot) and pulmonary complications are associated with the length of hospital stay in patients with SCI in the acute phase [1, 10-12]. Pressure ulcers are especially seen in body parts exposed to pressure. These ulcers can be avoided by taking some precautions such as nutrition, frequent position change, and skin care. Implications for rehabilitation prevention education for targeting pressure ulcers can be effective in reducing incidence of this important complication in persons with SCI [13].

Unlike in other studies, urinary pathologies were the first cause of SCIs in the present study. This was followed by skin and psychiatric pathologies. This result can be attributed to the fact that the patients were in the subacute/chronic phase, were hemodynamically stable, and participated in an exercise program.

Bradyarrhythmia, hypotension, vasovagal reflexes, supraventricular ectopic beats, vasodilatation,

and venous stasis may occur during the acute phase of SCI. In particular, orthostatic hypotension, blood pressure, blood volume, and body temperature irregularities are seen during the chronic period. Autonomic dysreflexia is usually encountered, especially in tetraplegic patients. This is characterized by a sudden elevation in blood pressure, an uncontrolled sympathetic response, headaches, and erythema in the upper part of the trunk. In addition, these patients are prone to atherosclerotic disease due to excessive weight, lipid disorders, metabolic syndrome, diabetes, as well as thrombolytic emboli due to venous stasis and hypercoagulopathy [14-16]. Apart from sensory and motor deficits, autonomous nervous system insufficiency, which is found in many organ and metabolic pathways, may also develop in patients with SCI. The patient group in the current study consisted of patients who had passed the acute period and those who were within the first year. These patients were found to be hemodynamically stable. No serious cardiovascular pathology was seen in any patient. This can be attributed to the fact that thepatients were in the subacute/chronic phase.

Werthagen *et al*. [17] found that the most common complications in patients with SCI who survived for more than 25 years were found to be pressure ulcers (62%), neuropathic pain (32%), and respiratory ailments (25%).

Pain is very common in patients with SCI, and it affects physical function, mood, and participation in work, leisure, and social activities. A variety of pain types can be seen following central neuropathic pain after SCI [18]. Similar to that in the literature, neuropathic pain was found in one third of the patients in the present study. These patients should be questioned regarding their neuropathic pain, and diagnosis should not be neglected.

Respiratory complications (atelectasis, pneumonia, and respiratory failure) negatively affect acute and long-term morbidity along with the level of damage and motor loss. Sleep apnea is also very common in the chronic period and adversely affects the rehabilitation process [19-21]. Severe respiratory pathology was not detected in patients in the present study.

Spasticity develops in 70% of patients with SCI damage. Causes such as full bladder, constipation, acute infections, syringomyelia, or bone fractures may affect the degree of spasticity in these patients. Severe spasticity affects the mobilization and rehabilitation process negatively. Spasticity was present in half the patients in the present study. In patients with spasticity, active exercise, physiotherapy and oral medication, botulinum toxin injection, intrathecal baclofen, and surgery are performed in selected patients [22-24].

Deep and venous thrombosis can develop in patients with SCI, with an increasing severity of paralysis, especially in the acute phase [25]. Depression is the most common psychiatric condition and has a negative effect on disease severity. Depression in patients with SCI was reported at rates of up to 24%, and more psychiatric comorbidity, drug use, and greater health care admission rates were observed in depressed patients with SCI [26]. A similar depression rate was observed in this study too. SCI should also be investigated in terms of nonvertebral fractures. Most of the times, no fracture assessment was done on the pleural extremity.

In developed countries, patients with SCI are urgently transferred to special rehabilitation units from the standard trauma centers [27, 28]. Rehabilitation of patients with SCI is important for functional and psychosocial recovery. Patients with SCI can have a normal lifespan by preventing medical complications. Nowadays, steroids are not used routinely. In prospective trials, early spine stabilization in the first 24 h caused a decrease in secondary complication rates [29, 30]. Treatment in the acute phase is done by airway, oxygenation, blood pressure, and circulatory control [29]. In these patients, the degree of damage is important for morbidity and mortality. In particular, tetraplegic patients have high mortality rates after severe pulmonary complications [31]. The present study found higher rates of complications in patients with higher grades of injuries and in patients with lower functional levels. The metaanalysis done by Ma *et al*. [32], provide evidence that the body-weight-supported treadmill and robotic-assisted gait training plus conventional over-ground training might have the best efficacy in the treatment of SCI, and the venlafaxine XR and GM-1 ganglioside showed adequate safety for SCI.

With limited extremity function, these individuals find it challenging to perform activities of daily living (ADLs) such as self-feeding, bathing, dressing, and toileting. As a result, they often require outside

assistance in the form of caretakers and assistive devices. To enable independence of individuals with tetraplegia, clinicians and researchers provide tools to help regain or compensate for lost extremity function [33, 34]. In our study, nearly half of the patients were wheelchair dependent and one in ten was using upper /lower limb orthotics. The use of orthosis in paraplegic individuals is necessary for joint protection, prevention of deformities and energy saving. In the treatment of spasticity, Botox-A administration was observed in 5 patients in patient files.

Limitations

Because this study was based solely on the database of one outpatient treatment clinic, enough information was not available on all patients with SCI. This dataset includes no data about patients with SCI who died in the first 3 months after hospitalization, causing a deficit in study results. In addition, since the registration files were filled in by a physician, the examination of the leukomotor system was detailed, and sufficient data about other possible complications could not be recorded.

CONCLUSION

SCI is a condition with high morbidity and mortality in the young male population. The pathogenesis and progression of the disease have not yet been clarified fully. Complications in patients with SCI negatively affect the rehabilitation process. Consequently, the etiology and complications of patients must be identified well and precautions should be taken to combat SCI. In our study, subacute/chronic SCI diagnosis is most commonly seen in young men, with thoracic vertebrae being the most common, followed by falling from a height. The most common complications were urinary and dermatological pathologies. The present study found higher rates of complications in patients with higher grades of injuries and in patients with lower functional levels.

Authorship declaration

All authors listed meet the authorship criteria according to the latest guidelines of the International Committee of Medical Journal Editors, and all authors are in agreement with the manuscript.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] Sekhon LH, Fehlings MG. Epidemiology, demographics, and pathophysiology of acute spinal cord injury. Spine (Phila Pa 1976) 2001;26(24 Suppl):S2-12.
[2] Hagen EM, Rekand T, Gilhus NE, Grønning M. Traumatic spinal cord injuries--incidence, mechanisms and course. Tidsskr Nor Laegeforen 2012;132:831-7.
[3] Kristinsdottir EA, Knutsdottir S, Sigvaldason K, Jonsson H Jr, Ingvarsson PE. [Epidemiology of spinal cord injury in Iceland from 1975 to 2014]. Laeknabladid 2016;102:491-6. [Article in Icelandic]
[4] Hagen EM. Acute complications of spinal cord injuries. World J Orthop 2015;6:17-23.
[5] Holden MK, Gill KM, Magliozzi MR, Nathan J, Baker LP. Clinical gait assessment in the neurologically impaired. Reliability and meaningfulness. Phys Ther 1984;64:35-40.
[6] American Spinal Injury Association. International Standards for Neurological Classifications of Spinal Cord Injury. revised ed. Chicago, Ill: American Spinal Injury Association, 2000., pp. 1-23.
[7] Bohannon R, Smith M. Interrater reliability of a modified Ashworth scale of muscle spasticity. Phys Ther 1987;67: 206-7.
[8] Karacan I, Koyuncu H, Pekel O, Sümbüloglu G, Kirnap M, Dursun H, et al. Traumatic spinal cord injuries in Turkey: a nation-wide epidemiological study. Spinal Cord 2000;38:697-701.
[9] Koçyiğit BF, Akaltun MS, Altındağ Ö, Aydeniz A, Gürsoy S, Gür A. Epidemiological and clinical data of patients with spinal cord injury: Five-year experience of our center. J Clin Exp Invest 2015;6:140-3.
[10] Hagen EM, Rekand T, Grønning M, Færestrand S. Cardiovascular complications of spinal cord injury. Tidsskr Nor Laegeforen 2012;132:1115-20.
[11] Wang H, Xiang Q, Li C, Zhou Y. Epidemiology of traumatic cervical spinal fractures and risk factors for traumatic cervical spinal cord injury in China. J Spinal Disord Tech 2013;26:E306-13.
[12] Aito S, Tucci L, Zidarich V, Werhagen L. Traumatic spinal cord injuries: evidence from 30 years in a single centre. Spinal Cord 2014;52:268-71.
[13] Chishtie J, Chishtie F, Yoshida K, Balogh R. Spinal cord injury rehabilitation and pressure ulcer prevention after the 2005 South Asian Earthquake: a CBR case study from Pakistan. Disabil Rehabil 2018 Mar 7:1-9. doi: 10.1080/09638288.2018.1445783. [Epub ahead of print]
[14] van Weert KC, Schouten EJ, Hofstede J, van de Meent H, Holtslag HR, van den Berg-Emons RJ. Acute phase complications following traumatic spinal cord injury in Dutch level 1 trauma centres. J Rehabil Med 2014;46:882-5.
[15] Joseph C, Nilsson Wikmar L. Prevalence of secondary medical complications and risk factors for pressure ulcers after traumatic spinal cord injury during acute care in South Africa. Spinal Cord 2016;54:535-9.
[16] Scheel-Sailer A, Wyss A, Boldt C, Post MW, Lay V. Prevalence, location, grade of pressure ulcers and association with specific patient characteristics in adult spinal cord injury patients during the hospital

stay: a prospective cohort study. Spinal Cord 2013;51:828-33.
[17] Werhagen L, Aito S, Tucci L, Strayer J, Hultling C. 25 years or more after spinal cord injury: clinical conditions of individuals in the Florence and Stockholm areas. Spinal Cord 2012;50:243-6.
[18] Siddall PJ, Middleton JW. Spinal cord injury-induced pain: mechanisms and treatments. Pain Manag 2015;5:493-507.
[19] Tollefsen E, Fondenes O. Respiratory complications associated with spinal cord injury. Tidsskr Nor Laegeforen 2012;132:1111-4.
[20] Spreyermann R, Michel F. [Long-term follow-up in patients with spinal cord injury - prevention and comprehensive care]. Praxis (Bern 1994) 2014;103:95-104. [Article in German]
[21] Saunders LL, Krause JS. Injuries and falls in an aging cohort with spinal cord injury: SCI Aging Study. Top Spinal Cord Inj Rehabil 2015;21:201-7.
[22] Rekand T, Hagen EM, Grønning M. Spasticity following spinal cord injury. Tidsskr Nor Laegeforen 2012;132:970-3.
[23] Chhabra HS, Arora M. Demographic profile of traumatic spinal cord injuries admitted at Indian Spinal Injuries Centre with special emphasis on mode of injury: a retrospective study. Spinal Cord 2012;50:745-54.
[24] Alshahri SS, Cripps RA, Lee BB, Al-Jadid MS. Traumatic spinal cord injury in Saudi Arabia: an epidemiological estimate from Riyadh. Spinal Cord 2012;50:882-4.
[25] Matsumoto S, Suda K, Iimoto S, Yasui K, Komatsu M, Ushiku C, et al. Prospective study of deep vein thrombosis in patients with spinal cord injury not receiving anticoagulant therapy. Spinal Cord 2015;53:306-9.
[26] Ullrich PM, Smith BM, Blow FC, Valenstein M, Weaver FM. Depression, healthcare utilization, and comorbid psychiatric disorders after spinal cord injury. J Spinal Cord Med 2014;37:40-5.
[27] Suarez NC, Levi R, Bullington J. Regaining health and wellbeing after traumatic spinal cord injury. J Rehabil Med 2013;45:1023-7.
[28] Shah N, Shrestha B, Subba K. Spinal cord injury rehabilitation in Nepal. JNMA J Nepal Med Assoc 2013;52:427-31.
[29] Stahel PF, VanderHeiden T, Finn MA. Management strategies for acute spinal cord injury: current options and future perspectives. Curr Opin Crit Care 2012;18:651-60.
[30] Knútsdóttir S, Thórisdóttir H, Sigvaldason K, Jónsson H Jr, Björnsson A, Ingvarsson P. Epidemiology of traumatic spinal cord injuries in Iceland from 1975 to 2009. Spinal Cord 2012;50:123-6.
[31] Alsaleh K, Bednar D, Farrokhyar F. Acute traumatic quadriplegia in adults: predictors of acute in-hospital mortality. Turk Neurosurg 2017;27:942-5.
[32] Ma DN, Zhang XQ, Ying J, Chen ZJ, Li LX. Efficacy and safety of 9 nonoperative regimens for the treatment of spinal cord injury: A network meta-analysis. Medicine (Baltimore) 2017;96:e8679.
[33] Portnova AA, Mukherjee G, Peters KM, Yamane A, Steele KM. Design of a 3D-printed, open-source wrist-driven orthosis for individuals with spinal cord injury. PLoS One 2018;13:e0193106.
[34] Arazpour M, Gholami M, Bahramizadeh M, Sharifi G, Bani MA. Influence of reciprocating link when using an isocentric reciprocating gait orthosis (IRGO) on walking in patients with spinal cord injury: a pilot study. Top Spinal Cord Inj Rehabil 2017;23:256-62.

The European Research Journal 2019;5(3):557-561 REVIEW

Current treatment options for carbon monoxide-induced neurological dysfunction

Ayush Dubey[1], Shubham Dubey[2]

[1]*Department of Neurology, SAIMS Medical College and PG Institute, Indore, India*
[2]*Department of Medicine, Gandhi Medical College and Hamidia Hospital, Bhopal, India*

DOI: 10.18621/eurj.414225

ABSTRACT

Carbon monoxide is an established dangerous toxicant with a complex mechanism of cellular toxicity. It is known to cause various neurological symptoms which can manifest both in acute as well as chronic forms. Delayed neurological deficits are often less recognizable. Radiological findings are also less specific. Hyperbaric oxygen therapy has been the mainstay of treatment over the years but is associated with its own list of complications and controversies. Current management for this important condition is discussed here.

Keywords: Carbon monoxide, hyperbaric oxygen therapy, neuroglobulin

Received: April 10, 2018; Accepted: July 10, 2018; Published Online: September 18, 2018

Carbon monoxide is a colorless, odorless and non-irritating gas produced by incomplete burning of carbon containing fossil fuels [1]. It is a leading cause of poisoning related mortality in the United States and is responsible for more than half of all the fatal poisonings occurring worldwide.

Its clinical symptoms are non specific and diverse including headache, chest pain, syncope, seizures and flu like illness. Thus, undiagnosed exposure may often lead to a significant morbidity and mortality [2, 3].

Environmental carbon monoxide exposure is usually less than 0.001% or around 10 ppm [4], but is even higher in urban areas. After cooking with a gas stove, the indoor air concentrations of carbon monoxide may reach 100 ppm [5]. Exposure to 70 ppm leads to carboxy-hemoglobin levels of 10% at equilibrium (approximately 4 hours) [2], while exposure to 350 ppm may lead to carboxy-hemoglobin levels of 40% at equilibrium [6]. Neurological manisfestations can be acute as well as chronic and depend upon the severity and duration of carbon monoxide exposure. Hypoxia is the main complication of this poisoning. Hence, oxygen therapy forms the mainstay of treatment.

Carbon Monoxide-Induced Neurological Dysfunctions

The clinical manifestations of carbon monoxide poisoning are variable and severity depends on the concentration of carbon monoxide in the inspired air, duration of exposure and general health of the involved person. The population at increased risk comprises of infants, elderly, patients with cardiovascular disorders, lung disorders, anaemia and increased basal metabolic rate [7]. The features of acute carbon monoxide poisoning are better known and more easily recognized than those having chronic exposure. Table 1 shows the clinical features manifested with the varying levels of blood carboxy-hemoglobin concentration [8]. During acute exposure, patients may complain of headache, dizziness, nausea, vomiting, emotional liability, confusion, impaired judgment, clumsiness and

Address for correspondence: *Ayush Dubey, MD., SAIMS Medical College and PG Institute, Department of Neurology, Indore, India*
E-mail: ayushdubey2@yahoo.co.in

e-ISSN: 2149-3189

Table 1. Levels of carboxy-hemoglobin with associated clinical manifestations

Blood carboxy-hemoglobin concentration (%)	Clinical manifestations
15-20	Mild headache, fatiguability
20-30	Impaired motor dexterity, blurred vision, irritability
30-40	Severe muscle weakness, vomiting, mental confusion, delirium
40-50	Tachycardia, irritability
50-60	Seizures, respiratory insufficiency
> 60	Coma, respiratory failure, death

syncope. Prolonged exposures resulting in seizures, altered mental status or coma, may be accompanied by retinal hemorrhages and lactic acidosis [9]. Myonecrosis can also occur but it rarely leads to renal failure. Cherry-red coloured skin which is associated with severe carbon monoxide poisoning, is seen in around 2-3% of symptomatic cases [10]. Severe poisoning often leads to hypotension and sometimes pulmonary oedema with the former being the most reliable marker of prognosis.

Neuropsychiatric issues may develop insidiously over weeks to months after recovery from carbon monoxide intoxication. These include intellectual deterioration, memory impairments, cerebral, cerebellar and midbrain damage, eg. Parkinsonism and akinetic mutism with changes in personality like increased irritability, verbal aggressiveness, impulsiveness, violence and moodiness [11]. Around two fifths of patients develop memory impairments and around one third suffer late deterioration of personality [12]. Chronic carbon monoxide poisoning is often misdiagnosed as chronic fatigue syndrome or chronic infection. Carboxy-haemoglobin levels are usually not excessively elevated in these cases.

Diagnosis

History

A meticulous history should be elicited for possible ways of exposure to carbon monoxide. Patients presenting with flu like symptoms must be asked about use of wood, coal or gas based heating appliances at home or work, especially in winters. Similar symptoms in the other housemates is helpful in getting to a diagnosis.

Carboxyhemoglobin Levels

Low levels may correlate with minor symptoms such as diffuse headache or nausea whereas high levels may be fatal too. carboxy-hemoglobin levels drop rapidly after the person inhales atmospheric air (containing around 21% oxygen) as well as with time and with oxygen therapy.

Laboratory Tests

This includes complete blood counts, serum electrolytes, cardiac markers, arterial blood gas analysis (may show metabolic acidosis because of the combination of hypoxia, cellular respiration inhibition and increased metabolic demand) and serum lactate levels which have been used as a marker for severe poisoning.

Other Tests

Chest radiographs may show non cardiogenic pulmonary edema. Drug level estimation for drugs showing similar symptoms should be assessed. ECG should be done to look for arrhythmias or signs of myocardial infarction.

Neuropsychiatric Testing

This includes Mini mental state examination, Weschlar memory scale, Weschlar adult intelligence scale, or other more specific tests such as Carbon Monoxide Neuropsychological Screening Battery (CONSB) [13]. Improvement on these tests after oxygen therapy is considered as an evidence of effectiveness of the therapy.

Brain Imaging

CT scan of brain may initially show signs of cerebral edema and may later show bilateral basal ganglia hypodensities, particularly in globus pallidus and substantia nigra [14]. MRI may show diffuse white matter involvement predominantly in periventricular areas al-

though basal ganglia, hippocampus and thalamus may also be involved. Patients may show symmetrical T2 and FLAIR hyperintensities in the globus pallidus which are often seen to resolve with time and after oxygen therapy [15]. Single Photon Emission Computed Tomography (SPECT), quantitative MRI and EEG have been used in carbon monoxide poisoning but more studies are needed to prove their specificities.

Management

After the correct diagnosis of carbon monoxide poisoning, first step should be the maintenance of airway, breathing and circulation. Patient should be advised bed rest to reduce oxygen demand and consumption.

There is no consensus currently regarding the optimal therapy of treatment in carbon monoxide poisoning for preventing acute symptoms as well as long term neurological sequelae. A bundle therapy therefore is advised which includes a combination of modalities to prevent the neurological damage [16].

Hypoxia is the most common complication of carbon monoxide poisoning. Oxygen therapy, thus is the most important measure to resolve the symptoms. Two types of oxygen therapy using 100% oxygen are used : Hyperbaric Oxygen Therapy (HBOT) and Normobaric Oxygen Therapy (NBOT). The choice of using the oxygen therapy out of these two is still controversial and lacks a robust data for either of them. The quality and results of clinical trials designed to assess the efficacy of HBOT in reducing the severity of delayed neurological symptoms have varied widely. Of several such studies, the two most important, double-blinded trials that included all patients regardless of poisoning severity came to contradictory conclusions [17, 18]. In HBOT, oxygen is at a pressure twice to thrice that of atmospheric pressure at sea level whereas it is equal to sea level atmospheric pressure in NBOT. In case of acute carbon monoxide poisoning, HBOT improves outcomes by several mechanisms. These mechanisms include acceleration of carbon monoxide elimination from hemoglobin and other heme-containing molecules, improved mitochondrial oxidative metabolism, inhibition of lipid peroxidation, inhibition of leukocyte adherence to injured microvessels and attenuation of immune-mediated delayed neurological dysfunction [19]. In addition to accelerating the rate of carbon monoxide elimination from hemoglobin, HBOT also enhances the removal of carbon monoxide from intracellular binding sites. It's timely administration prevents neuronal injury and prevents delayed neuropsychological sequelae by terminating the biological degradation [4]. If HBOT is used for delayed neuropsychiatric syndrome (DNS), the available literature suggests that benefit is greatest if treatment begins as early as possible, ideally within six hours. It is used in patients with serious intoxication showing loss of consciousness, neurological deficits, significant metabolic acidosis and carboxy-hemoglobin more than 25%. Despite its benefits, HBOT is associated with adverse effects such as cataracts, reversible myopia, tracheobronchial symptoms, self-limited seizures and barotraumas to the middle ear, the cranial sinuses or the lungs. Another limitation is that not all the hospitals are equipped with such a chamber. For patients with mild carbon monoxide poisoning (carboxy-hemoglobin level < 20%), a different regime involving 100% NBOT for 6 hours is appropriate.

Other treatment options include targeted temperature management with mild therapeutic hypothermia especially in patients with post cardiac arrest or hypoxic ischemic brain injury. Administration of sympatholytics may be useful for inhibition of the postganglionic functions of the sympathetic nervous system, thus minimizing the systemic response to acute stressor (carbon monoxide). Anti oxidants in the form of N-acetylcysteine can be used. It restores the intracellular levels of glutathione and the ability of cells to resist the reactive oxygen species. Potent anti inflammatory drugs and immune suppressant steroids such as dexamethasone or methylprednisolone could be used for severe inflammation in carbon monoxide poisoning [16].

Erythropoeitin is a glycoprotein hormone which produces red blood cells. In hypoxic states like stroke, it may be protective of neuronal cells by reducing S100B and preventing from neurological damage. In patients with carbon monoxide poisoning too, it has shown improved outcomes in management for prevention of delayed neurological sequelae [20]. Other drugs such as ziprasidone and donepezil have been used but lack data to support their use.

Latest studies suggest the introduction of a potential treatment for carbon monoxide poisoning based on near irreversible binding of carbon monoxide by an engineered neuroglobin (Ngb) with a mutated distal

histidine (H64Q). Ngb is a six-coordinate hemoprotein, with the heme iron coordinated by two histidine residues. Mutation of distal histidine to glutamine (H64Q) and substitution of three surface cysteines with less reactive amino acids forms a five-coordinate heme protein (Ngb-H64Q-CCC). This molecule exhibits an unusually high affinity for gaseous ligands, with a P50 (partial pressure of O2 at which hemoglobin is half-saturated) value for oxygen of 0.015 mmHg. Ngb-H64Q-CCC binds about 500 times more strongly than does hemoglobin. Incubation of Ngb-H64Q-CCC with 100% carbon monoxide-saturated hemoglobin, either cell-free or encapsulated in human red blood cells, reduces the half-life of carboxyhemoglobin to 0.11 and 0.41 min, respectively, from ≥ 200 min when the hemoglobin or red blood cells are exposed only to air. Infusion of Ngb-H64Q-CCC to carbon monoxide-poisoned mice enhanced carbon monoxide removal from red blood cells, restored heart rate and blood pressure, increased survival, and was followed by rapid renal elimination of carbon monoxide-bound Ngb-H64Q-CCC. Heme-based scavenger molecules with very high carbon monoxide binding affinity, such as this mutant five-coordinate Ngb, are potential antidotes for carbon monoxide poisoning by virtue of their ability to bind and eliminate carbon monoxide [21].

Also, carbon monoxide can be photodissociated and recombinated to wild type (WT) and H64Q Ngb. The distribution of carbon monoxide within the proteins differs substantially due to rearrangement of amino acids surrounding the distal heme pocket leading to the decrease of the distal pocket volume in H64Q Ngb in comparison to WT Ngb, trapping migrating carbon monoxide molecules in the distal pocket. This shows that the mutation implicates the shortening of the time scale of carbon monoxide geminate recombination, making H64Q Ngb 2.7 times more frequent binder than WT Ngb [22]. However, more studies are needed for the substantiation of this novel, yet promising therapy option.

Patients with carbon monoxide poisoning should be followed up periodically after discharge. The rate and extent of recovery after poisoning are variable, and recovery is complicated by the development of sequelae, which can persist after exposure or develop weeks after poisoning [4] and which can be permanent. Specific therapy for sequelae is not available. Such patients should have their symptoms treated, through psychiatric, vocational, cognitive, speech, occupational, and physical rehabilitation, although data on the effects of these interventions in patients with carbon monoxide related sequelae are lacking.

Prevention

During winters, carbon monoxide poisoning should be suspected in all patients presenting with flu-like symptoms (e.g., headache, nausea, dizziness),and with a doubtful history. Proper public education on the safe operation of heaters, appliances, fireplaces and internal combustion engines is necessary. Burn victims, with an evidence of smoke inhalation from enclosed fire, should undergo testing for carboxy-hemoglobin levels. Carbon monoxide detectors with alarms can also improve home and workplace safety [8].

CONCLUSION

There is currently no optimal treatment for carbon monoxide poisoning and its delayed neurological sequelae. Carboxy-hemoglobin has poorer correlates with severity of carbon monoxide poisoning. HBOT, which is a well known and widely used modality, has become controversial and it is unlikely that it will hold its place as the sole standard optimal treatment in future. So, in patient management, there is a need for new markers in monitoring and evaluation. A bundle therapy with targeted temperature management is the ideal way of management. Further research is necessary for novel agents which act depending on the underlying pathophysiological process of causation of delayed neurological sequelae.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

[1] Kao L, Nanagas K. Toxicity associated with carbon monoxide. Clin Lab Med 2006;26:99-125.
[2] Tomaszewski C. Carbon monoxide. In: Goldfrank LR, Flomenbaum NE, Lewin NA, et al, editors. Goldfrank's toxicologic emergencies. 7th edition. New York: McGraw-Hill; 2002. p. 1478-97.
[3] Cobb N, Etzel RA. Unintentional carbon monoxide-related deaths in the United States, 1979 through 1988. JAMA 1991;266:659-63.
[4] Ernst A, Zibrak JD. Carbon monoxide poisoning. N Engl J Med 1998;339:1603-8.
[5] Abelsohn A, Sanborn MD, Jessiman BJ, Weir E. Identifying and managing adverse environmental health effects. 6. Carbon monoxide poisoning. CMAJ 2002;166:1685-90.
[6] Raub JA, Mathieu-Nolf M, Hampson NB, Thom SR. Carbon monoxide poisoning--a public health perspective. Toxicology 2000;145:1-14.
[7] Stewart RD. The effect of carbon monoxide on humans. Annu Rev Pharmacol 1975;15:409-22.
[8] Mehta SR, Das S, Singh SK. Carbon monoxide poisoning. MJAFI 2007;63:362-5.
[9] Ely EW. Moorehead B, Haponik EF. Warehouse workers' headache: emergency evaluation and management of 30 patients with carbon monoxide poisoning. Am J Med 1995;98:145-55.
[10] Longo LD, Hill EP. Carbon monoxide uptake and elimination in fetal and maternal sheep. Am J Phsiol 1977;232:324-30.
[11] Gilbert GJ, Glaser GH. Neurologic manifestations of chronic carbon monoxide poisoning. N Eng J Med 1959;264:1217-220.
[12] Smith JS, Brandon S. Morbidity from acute carbon monoxide poisoning at three-year follow-up. Br Med J 1973;1:318-21.
[13] Messier LD, Myers RA. A neuropsychological screening battery for emergency assessment of carbon-monoxide-poisoned patients. J Clin Psychol 1991;47:675-84.
[14] Silver DA, Cross M, Fox B, Paxton RM. Computed tomography of the brain in acute carbon monoxide poisoning. Clin Radiol 1996;51:480-3.
[15] Kinoshita T, Sugihara S, Matsusue E, Fujii S, Ametani M, Ogawa T. Pallidoreticular damage in acute carbon monoxide poisoning: diffusion-weighted MR imaging findings. Am J Neuroradiol 2005;26:1845-8.
[16] Oh S, Choi SC. Acute carbon monoxide poisoning and delayed neurological sequelae: a potential neuroprotection bundle therapy. Neural Regen Res 2015;10:36-8.
[17] Weaver LK, Hopkins RO, Chan KJ, Churchill S, Elliott CG, Clemmer TP, et al. Hyperbaric oxygen for acute carbon monoxide poisoning. N Engl J Med 2002; 347:1057-67.
[18] Juurlink DN, Buckley NA, Stanbrook MB, Isbister GK, Bennett M, McGuigan MA. Hyperbaric oxygen for carbon monoxide poisoning. Cochrane Database Syst Rev 2005;(1):CD002041.
[19] Hampson NB, Mathieu D, Piantadosi CA, Thom SR, Weaver LK. Carbon monoxide poisoning: interpretation of randomized clinical trials and unresolved treatment issues. Undersea Hyperb Med 2001;28:157-64.
[20] Pang L, Bian M, Zang XX, Wu Y, Xu DH, Dong N, et al. Neuroprotective effects of erythropoietin in patients with carbon monoxide poisoning. J Biochem Mol Toxicol 2013;27:266-71.
[21] Azarov I, Wang L, Rose JJ, Xu Q, Huang XN, Belanger A, et al. Five-coordinate H64Q neuroglobin as a ligand-trap antidote for carbon monoxide poisoning. Sci Transl Med 2016;8:368ra173.
[22] Rydzewski J, Nowak W. Photoinduced transport in an H64Q neuroglobin antidote for carbon monoxide poisoning. J Chem Phys 2018;148:115101

The European Research Journal 2019;5(3):562-565 CASE REPORT

Are we familiar with this rare indicative of a higher risk for breast cancer?

Ayşegül Altunkeser[1], Fatma Zeynep Arslan[1], Ender Alkan[2], Tuğba Günler[3]

[1]Department of Radiology, University of Health Sciences, Konya Training and Research Hospital, Konya, Turkey
[2]Department of Radiology, Aksaray University, Aksaray Training and Research Hospital, Aksaray, Turkey
[3]Department of Pathology, University of Health Sciences, Konya Training and Research Hospital, Konya, Turkey

DOI: 10.18621/eurj.424563

ABSTRACT

Secretory adenosis (SA) of breast is rarely seen benign breast lesion, which might be associated with increased risk for breast carcinoma. SA is an extremely rare lesion, the cases reported in the literature and long-term follow-up studies are limited and radiological and histopathological diagnosis of SA is mostly challenging; it could be frequently misinterpreted as ductal carcinoma in situ. Because of these reasons; clinical significance and management of SA is still not fully understand and relative risk of SA is still not well-established. Herein; we presented mammography, ultrasound, magnetic resonance imaging and microscopic findings in a patient with SA of breast.

Keywords: breast carcinoma, magnetic resonance imaging, secretory adenosis

Received: May 17, 2018; Accepted: August 3, 2018; Published Online: January 18, 2019

Secretory adenosis (SA) of the breast is rarely seen type of sclera osing lesions [1, 2]. There is a significant increase in proliferation in both glandular epithelium and myoepithelial [3, 4]. There are only a few recent researches investigating the frequency of SA; prevalence of SA is reported as approximately 0.4% [5]. SA is an extremely rare lesion, the cases reported in the literature and long-term follow-up studies are limited and radiological and histopathological diagnosis of SA is mostly challenging; especially for SA with or without atypical could be frequently misinterpreted as ductal carcinoma in situ [6]. Because of these reasons; clinical significance and management of SA is still not fully understand and relative risk of SA is still not well-established. Considering the uncommon nature of SA and importance of reporting such unique lesions; we presented here a mammography, ultrasound, magnetic resonance imaging (MRI) and microscopic findings.

CASE PRESENTATION

A 44-year-old female admitted to our outpatient clinic with a palpable mass on the right breast. There was no known medical history and laboratory findings were normal. On physical examination; a palpable, soft and mobile mass was detected in outer quadrant of right breast. On mammography; encapsulated heterogeneous nodular density containing lucent areas in a size with 40 × 20 mm was observed (Figure 1). Sonographically; a well-circumscribed, heterogeneous hyperechoic lesion in a size with 40 × 20 mm was seen. Microcalcifications were observed within the

Address for correspondence: *Fatma Zeynep Arslan, MD., University of Health Sciences, Konya Training and Research Hospital, Department of Radiology, Konya, Turkey*
E-mail: Zzynep_a1002@hotmail.com, Fax: +90 332 323 67 23

e-ISSN: 2149-3189

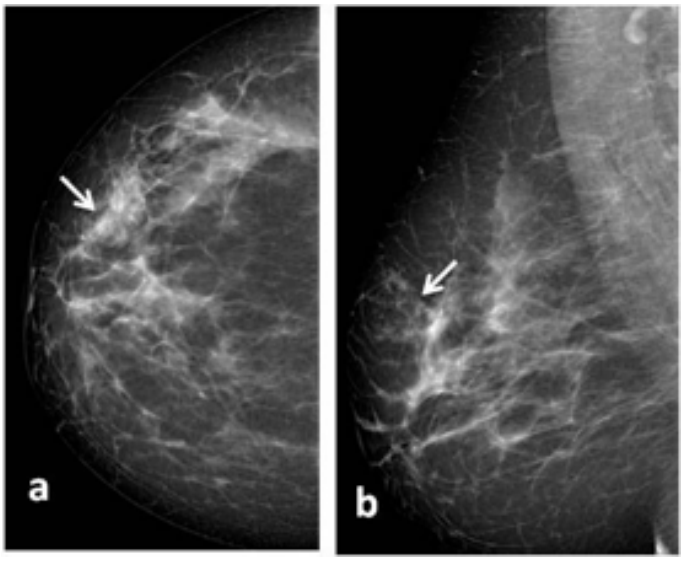


Figure 1. Craniocaudal (a) and mediolateral oblique (b) mammogram of the right breast has demonstrated an encapsulated heterogeneous nodular density containing lucent areas (arrow).

lesion. MRI demonstrated encapsulated nodular lesion of approximately 3 cm in diameter with early phase contrast enhancement and type 2 contrast enhancement pattern was seen in the late phase. Diffusion restriction was detected on diffusion-weighted imaging (Figure 2). Clinical and radiological data could not exclude malignancy, a core biopsy was taken with 16 Gauge needle. On histopathological examination, ductal structures are observed between the layer of adipose tissue, hyalinized stroma, and myoepithelial layers. Secretion was noted in the lumen of someducts. In the immunohistochemical study performed, positive staining for calponin was seen (Figure 3). Lesion is confirmed as secretory adenosis with marked cystic degeneration.

DISCUSSION

Secretary adenosis is mostly occurred in the salivary gland, skin, and parathyroid, breast is an unusual location [7]. SA affects both young and old women. SA can be seen with fibrocystic changes or can be observed as a pure entity [8]. While some important studies [5, 9] reported that SA is a benign, some studies found that there is a RR increase for developing future malignancy [10]. A research with a larger sample size found that there is an important relative risk increase about 5 times for future breast malignancy [10]. There is also some evidence in the literature that an excised SA may recur [11]. Literature

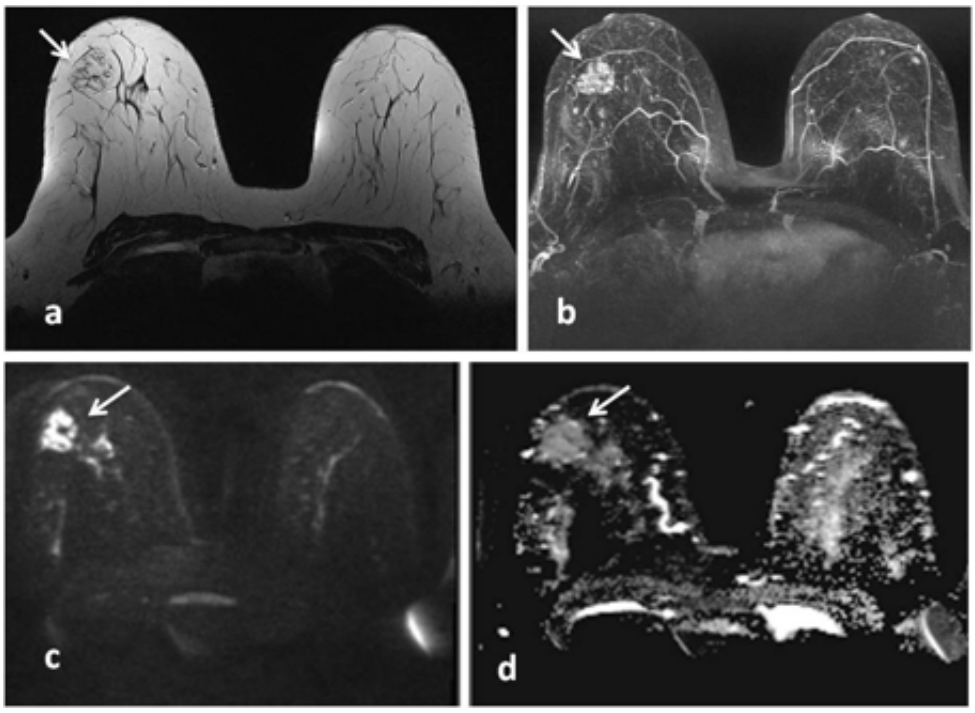


Figure 2. Axial T2 weighted image demonstrates an encapsulated mass (a), MIP imagehaverevealed a masswithtype 1 contrastenhancementpattern (b), DWI (c), and ADC mapping (d) demonstrates diffusion restriction of mass (arrow). MIP = maximum intensity projection, DWI = diffusion weighted imaging, ADC = apparent diffusion coefficient.

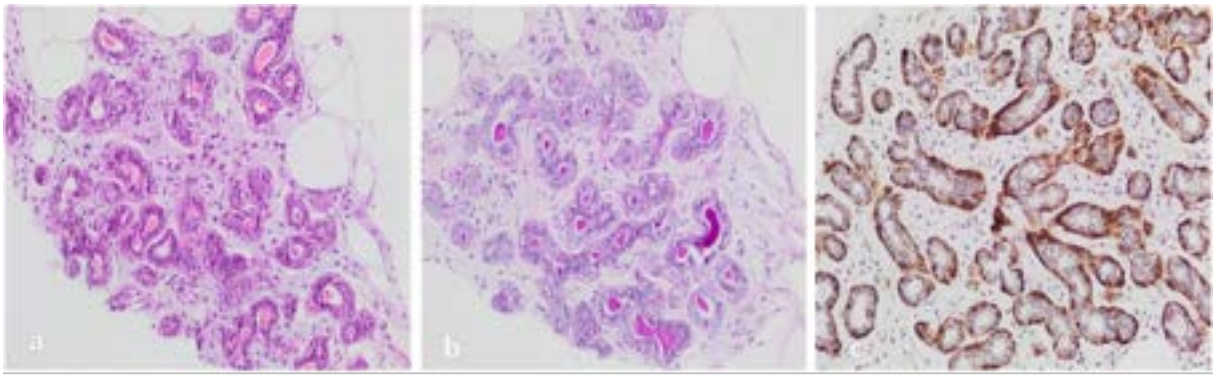


Figure 3. On Periodic acid-Schiff positive (a), diastase-resistant (b) sections, secretion is noted in small glands within traluminal eosinophilic secretions. Myoepithelial cells that are positively stained with the calponin around the secretory glands are seen (c).

data has revealed such various results; since lesion is rarely encountered and there are only few studies and case reports in the literature.

On physical examination a lump can be palpable in the breast, on mammography asymmetric focal density or mass lesion with diffuse or clustered microcalcifications with an irregular shape or spiculated borders, or display asymmetric focal density and focal architectural distortion may be seen, which could support the suspicion of breast cancer [12]. We also observed an encapsulated focal asymmetric density containing radiolucent areas on mammography. The mammographic appearance of lesion was similar to hamartoma. SA revealed that hypoechoic mass with a uncertain boundary or well circumscribed mass with microlobulated contours can be sonographically seen [12, 13]. We observed a well-circumscribed, heterogeneous hyperechoic lesion containing microcalcifications on ultrasound. Yet, no sonographically specific feature is described. It seems almost impossible to obtain accurate diagnosis based on mammographic and sonographic findings. Gity et al. [14] emphasized MRI as a usefull modality in characterizing lesions containing pure adenosis from mixed adenosis lesions. They also revealed that adenosis lesions are frequently false-positively reported as malign, since these lesions can show morphologic or dynamic border line features on MRI. In a vast majority of these adenosis showed oval/lobulated or irregular shapes, showed heterogeneous internal enhancement, all demonstrated a rapid initial rise then wash-out enhancement patterns on dynamic examination with varying enhancement patterns such as seg-mental or linear distribution and clumped internal enhancement [14]. In our patient; we detected a nodular lesion with an contrast enhancement in early phase and type 2 contrast enhancement pattern was seen in the late phase on dynamic MRI, too. A core needle biopsy and histopathological confirmation is necessary for the definitive diagnosis. On microscopic examination; haphazard proliferation of bland glands with apocrine differentiation with apocrine metaplasia in > 50% of adenosis area is seen [15]. On microscopic examination of our case, myoephitelial cells were seen. Treatment options include follow-up or excision of the lesion. The differential diagnosis also includes sclerosing adenosis, fibroadenoma, ductal carcinoma in situ and breast carcinoma.

CONCLUSION

In conclusion; SA is rare and there is only limited number of cases have been reported. Relative risk of developing possible future malignancy and interval to cancer diagnosis as mean time is yet not fully established. It is a great necessity to report these rare SA cases and to perform new researches could provide important informations for understanding SA.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

[1] Tavassoli FA, Soares J. Myoepithelial Lesion: World Health Organization classification of Tumors. Pathology& Genetics. Tumors of the breast and Female Genital Organs. Lyon: International Agency for Research on Cancer (IARC); 2003:86-8.
[2] Moinfar F. Adenosis. In Essentials of Diagnostic Breast Pathology. Edited by: Moinfar F. Berlin: Springer; 2007:31.
[3] Tsuda H, Mukai K, Fukutomi T, Hirohashi S. Malignant progression of adenomyoepithelial adenosis of the breast. Pathol Int 1994;44:475-9.
[4] Tavassoli FA. Myoepithelial lesion of the breast. Myoepitheliosis, adenomyoepithelioma, and myoepithelial carcinoma. Am J Surg Pathol 1991;15:554-68.
[5] Page DL, Dupont WD, Jensen RA. Papillary apocrine change of the breast: associations with atypical hyperplasia and risk of breast cancer. Cancer Epidemiol Biomarkers Prev 1996;5:29-32.
[6] Watanabe K, Nomura M, Hashimoto Y, Hanzawa M, Hoshi T. Fine needle aspiration cytology of apocrine adenosis of the breast: Report on three cases. Diagn Cytopathol 2007;35:296-9.
[7] Mitra B, Pal M, Saha TN, Maiti A. Adenomyoepithelial adenosis of breast: a rare case report. Turk Patoloji Derg 2017;33:240-3.
[8] Rosen PP. Rosen's Breast Pathology. 3rd ed. Philadelphia: Lippincott Williams &Wilkins; 2008.
[9] Calhoun BC, Booth NC. Atypical apocrine adenosis diagnosed on core biopsy: implications for management. Hum Pathol 2014;45:2130-5.
[10] Seidman JD, Ashton M, Lefkowitz M. Atypical apocrine adenosis of the breast: a clinico pathologic study of 37 patients with 8.7-year follow-up. Cancer 1996;77:2529-37.
[11] Erel S, Tuncbilek I, Kismet K, Kilicoglu B, Ozer E, Akkus MA. Ademomyoepithelial adenosis of the breast: clinical, radiological, and pathological findings for diffrential diagnosis. Breast Care 2008;3:427-30.
[12] Günhan-Bilgen I, Memiş A, Ustün EE, Ozdemir N, Erhan Y. Sclerosing adenosis: mammographic and ultrasonographic findings with clinical and histopathological correlation. Eur J Radiol 2002;44:232-8.
[13] Chen JH, Nalcioglu O, Su MY. Fibrocystic change of the breast presenting as a focal lesion mimicking breast cancer in MR imaging. J Magn Reson Imaging 2008;28:1499-505.
[14] Gity M, Arabkheradmand A, Taheri E, Shakiba M, Khademi Y, Bijan B, et al. Magnetic resonance imaging features of adenosis in the breast. J Breast Cancer 2015;18:187-94.
[15] Gillellamudi SB, Vellanki VS, Veeragandham S, Omar O. Apocrine adenosis of breast: a very rare case report. Int Surg J 2016;1:97-8.

The European Research Journal 2019;5(3):566-568 CASE REPORT

Gastric volvulus: a rare cause of gastric outlet obstruction in pediatric age

Burcu Güven[1], Burhan Beger[2], Enver Uslu[3], Ebüzer Düz[2]

[1]*Department of Pediatric Gastroenterology, Yüzüncü Yıl University School of Medicine, Van, Turkey*
[2]*Department of Pediatric Surgery, Yüzüncü Yıl University School of Medicine, Van, Turkey*
[3]*Department of Pediatrics, Yüzüncü Yıl University School of Medicine, Van, Turkey*

DOI: 10.18621/eurj.407805

ABSTRACT

Gastric volvulus is a rare disease in the pediatric population. Symptoms may change depending on the type of the disease, rotation degree, and the etiology. Early diagnosis and treatment are important especially in the acute type of the gastric volvulus. Here, it was presented a 10-month-old girl with non-bilious vomiting and abdominal distention in last 2 days, diagnosed gastric volvulus.

Keywords: gastric volvulus, pediatric

Received: March 19, 2018; Accepted: July 25, 2018; Published Online: July 26, 2018

Gastric outlet obstruction is a rare condition encountered in the pediatric age group of 2-5 years and its incidence is 1:1000 [1]. Due to the obstruction of the passage of the gastric content to the duodenum, persistent non-bilious vomiting followed by dehydration and electrolyte imbalance develops. The most common cause is idiopathic hypertrophic pyloric stenosis. Other rare causes are distal gastric antral webs, gastric duplication cysts, gastric polyps, neoplasms, Crohn's disease, bezoar, complications of the gastrostomy tube, malrotations and volvulus [1].

Gastric volvulus is a rare disease, especially in children. It was first defined by Berti in 1866 [2]. In a review published in 1980, 51 patients were described and 52% of these patients were under one year of age and 26% were less than 1 month old [2]. Less than 600 pediatric patients with gastric volvulus were reported until 2008 [3]. Although its incidence is unknown, it is evenly distributed regarding the gender and race [4].

CASE PRESENTATION

A 10-month-old girl was admitted to the clinic with the complaints of non- bilious vomiting and abdominal distention in last 2 days. She had vomited everything she had eaten. There was no special finding in her medical and family history and distension was observed in the left upper abdominal quadrant during the physical examination. Abdominal plain radiography revealed that left hemidiaphragm was elevated, the stomach was dilated and air passage to distal was obstructed (Figure 1). Abdominal ultrasonography showed a thick fluid in the gastric lumen and intense echogenic appearance partly with air-fluid levels. Esophagogastroduodenoscopy revealed abundant fluid in the corpus and a changed gastric configuration. Abdominal computed tomography showed that the gastroesophageal junction was dislocated and the pylorus moved to

Address for correspondence: *Burcu Güven, MD., Yüzüncü Yıl University School of Medicine, Department of Pediatric Gastroenterology, Dursun Odabaş Tıp Merkezi, 71450 Tuşba, Van, Turkey*
E-mail: burcuguven55@gmail.com

e-ISSN: 2149-3189

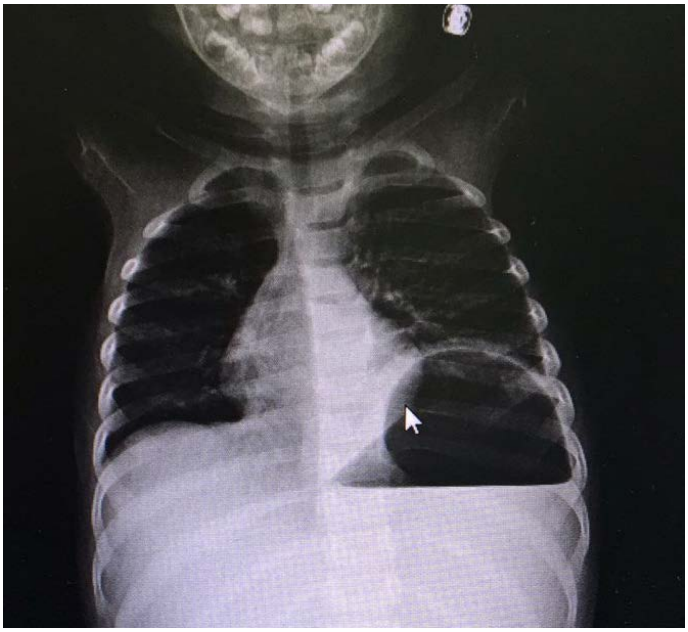


Figure 1. Abdominal plain radiography revealed that the left hemidiaphragm was elevated, the stomach was dilated and air passage to distal was obstructed.

anterior of the abdominal midline (Figure 2). In light of these findings, it was considered mesentero-axial gastric volvulus and referred to the pediatric surgery. During the operation, it was observed that the stomach had rotated clockwise about 360° in the longitudinal position. Gastric volvulus reduction and anterior gastropexy were performed. There was no problem with her follow-up.

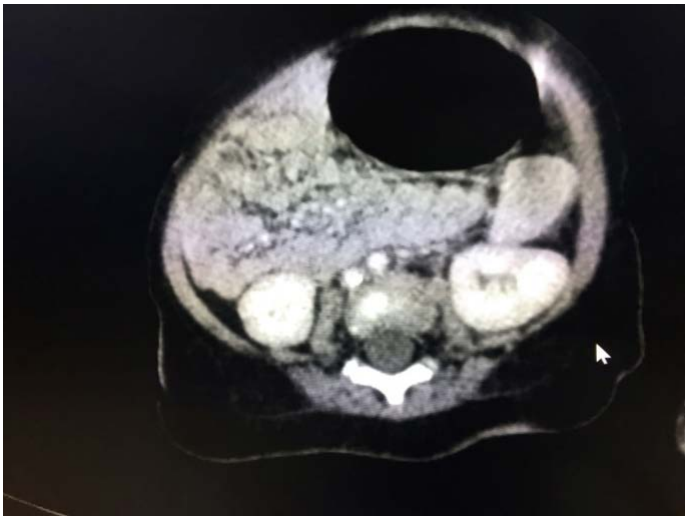


Figure 2. Abdominal computed tomography showed that the gastroesophageal junction was dislocated and the pylorus moved to anterior of the abdominal midline

DISCUSSION

Gastric volvulus is defined as a partial or complete rotation of the stomach of more than 180°. There are 3 types: organo-axial, mesentero-axial and combined. Organo-axial type is seen in 50-60% of the cases. In organo-axial volvulus, the stomach rotates around the longitudinal axis connecting the gastro-esophageal junction with the pylorus. The greater curvature of the stomach lies superior to the lesser curvature. In the mesentero-axial type, the stomach rotates around the transverse axis and pylorus lies superior to the gastroesophageal junction at anterior side. In the combined type, the rotation occurs in both longitudinal and transverse axes.

The stomach is normally fixed by four ligaments. These are gastrocolic, gastrohepatic, gastrophrenic and gastrosplenic ligaments. Agenesis, elongation or disruption of these ligaments leads to primary gastric volvulus [5]. The causes of the secondary gastric volvulus are a diaphragmatic hernia, asplenia, pyloric stenosis, phrenic nerve palsy or esophageal atresia operations [6].

Gastric volvulus causes gastric outlet obstruction. This obstruction may be acute, recurrent, intermittent or chronic. Acute gastric volvulus is a life-threatening condition, which should be diagnosed and treated as quickly as possible. These patients admit to the clinic with persistent, no bilious vomiting, epigastric pain, and distension. More rarely, they may present with dyspnea, cyanosis or hematemesis. Due to gastric outflow obstruction, hypochloremic hypokalemic alkalosis and dehydration can develop. As a result of the delayed diagnosis, 5-28% of the patients can present with ischemia, necrosis or perforation [7]. Gastro-intestinal bleeding and septic shock may be encountered in these patients. The mortality in gastric volvulus with necrosis and perforation increases up to 50% [8]. The symptoms are usually non-specific in chronic gastric volvulus. These patients often apply to the clinic with distention related to the eating, epigastric pain, vomiting, and weight loss [9]. Usually, anatomical defects are associated with the acute type. On the other hand, the loss of the ligament laxity is in the chronic gastric volvulus [10].

In chronic gastric volvulus patients with non-specific symptoms, the diagnosis may be delayed. An incidental diagnosis is common on an upper

gastrointestinal contrast study performed with reflux symptoms. In contrast study, it is usually detected a distended stomach lying in a horizontal and upright position. Some clues in the plain radiographs indicating gastric volvulus include air-fluid level in the epigastrium, abnormal gastric double-bubble sign and epigastric distention despite the presence of nasogastric tube [9]. Abdominal ultrasonography and upper gastrointestinal endoscopy may be not useful regarding the diagnosis [10]. Computed tomography is helpful in confirming the diagnosis of gastric volvulus. Although ionizing radiation has disadvantages, it is valuable in showing the anatomy [7].

The treatment depends on the type of the gastric volvulus. In acute gastric volvulus, following the decompression with a nasogastric tube, the patient must be referred to the acute surgery. In order to assure the normal gastric configuration, gastropexy is performed. Anatomical problems like a hiatal hernia may be corrected simultaneously during the operation. Untreated acute gastric volvulus may lead to strangulation, necrosis, and perforation [11]. The mortality rate is twice high in acute gastric volvulus compared to the chronic volvulus [5]. Secondary gastric volvulus may recover without gastropexy if the predisposing factors are eliminated [6]. In patients with chronic volvulus, the conservative treatments such as prone position (with head slightly up), prokinetics, antisecretory drugs and diet modification may be tried [10]. Al-Salem [12] reported that the conservative treatment was beneficial in 11 chronic volvulus patients with mild-moderate symptoms.

CONCLUSION

In conclusion, gastric volvulus is a rare disease in the pediatric population. Symptoms may change depending on the type of the disease, rotation degree, and the etiology. Early diagnosis and treatment are important especially in the acute type of the gastric volvulus.

Informed consent

Written informed consent was obtained from the patient's family for publication of this case report and any accompanying images.

Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

[1] Otjen JP, Iyer RS, Phillips GS, Parisi MT. Usual and unusual causes of pediatric gastric outlet obstruction. Pediatr Radiol 2012;42:728-37.
[2] Cameron AEP, Howard ER. Gastric volvulus in childhood. J Pediatr Surg 1987;22:944-7.
[3] Joshi M, Parelkar S, Sanghvi B, Agrawal A, Mishra P, Pradeep SH. Gastric volvulus in children: experience of 6 years at a tertiary care centre. Afr J Paediatr Surg 2010;7:2-4.
[4] Rashid F, Thangarajah T, Mulvey D, Larvin M, Iftikhar SY. A review article on gastric volvulus: a challenge to diagnosis and management. Int J Surg 2010;8:18-24.
[5] Cribbs RK, Gow KW, Wulkan ML. Gastric volvulus in infants and children. Pediatrics 2008;122:752-62.
[6] Mirza B, Ijaz L, Sheikh A. Gastric volvulus in children: our experience. Indian J Gastroenterol 2012;31:258-62.
[7] Trecroci I, Morabito G, Romano C, Salamone I. Gastric volvulus in children--a diagnostic problem: two case reports. J Med Case Rep 2016;10:138.
[8] Farag S, Fiallo V, Nash S, Navab F. Gastric perforation in a case of gastric volvulus. Am J Gastroenterol 1996;91:1863-4.
[9] Duman L, Savas MC, Büyükyavuz BI, Akcam M, Sandal G, Aktas AR. Early diagnostic clues in neonatal chronic gastric volvulus. Jpn J Radiol 2013;31:401-4.
[10] Porcaro F, Mattioli G, Romano C. Pediatric gastric volvulus: diagnostic and clinical approach. Case Rep Gastroenterol 2013;7:63-8.
[11] Carter R, Brewer LA, Hinshaw DB. Acute gastric volvulus. A study of 25 cases. Am J Surg 1980;140:99-106.
[12] Al-Salem AH. Acute and chronic gastric volvulus in infants and children: who should be treated surgically? Pediatr Surg Int 2007;23:1095-9.

The European Research Journal 2019;5(3):569-571 CASE REPORT

Rivaroxaban-induced acute pancreatitis

Özgür Sirkeci[1], Emel Erkuş Sirkeci[2], Belma Taşel[3]

[1]*Department of Internal Medicine, Near East University School of Medicine, Nicosia, Cyprus*
[2]*Department of Emergency Medicine, Near East University School of Medicine, Nicosia, Cyprus*
[3]*Department of Cardiology, Near East University School of Medicine, Nicosia, Cyprus*

DOI: 10.18621/eurj.417972

ABSTRACT

Rivaroxaban is a direct factor Xa inhibitor and has been safely used since 2008. It is used for the detection of atrial fibrillation and venous thromboembolism. Pancreatitis is one of the rare but dangerous side effects of rivaroxaban. The case of a 53-year-old female patient that developed in the third month of drug usage was evaluated, and it was confirmed after a full analysis was conducted that excluded all other factors, such as biliary calculus, alcohol usage, hypertriglyceridemia, biochemical parameters, ultrasonography and computed tomography that the patient's condition was caused by the use of Rivaroxaban. The aim of this case presentation is to indicate that awareness should be increased regarding the risks of using the drug Rivaroxaban, as it could lead to drug-induced pancreatitis, even though this is rare.

Keywords: drug-induced pancreatitis, rivaroxaban, drug safety

Received: April 24, 2018; Accepted: October 8, 2018; Published Online: November 16, 2018

Acute pancreatitis is an important disease that can cause morbidity. Approximately 80% of cases progress mildly, while severe pancreatitis is seen in 20% of cases. The most frequent causes are biliary calculus and alcohol, followed byhypertriglyceridemia and drugs [1]. Approximately 4%-5.3% of the condition is drug-induced pancreatitis and they generally progress in a mild form. It is argued that drugs may be a direct cause of pancreatitis by the way of idiosyncratic, direct toxic or angioedema [2].

Rivaroxaban direct factor Xa inhibitor began to be used in 2008 after it was approved by the FDA. It is used for atrial fibrillation, seizure prophylaxis and venous thromboembolic prophylaxis. According to FDA reports, 81,217 side effects were reported since its inception, of which 81 of these side effects were pancreatitis. Furthermore, 60.87% of the cases that developed pancreatitis showed symptoms of the disease in the first month, while 21.74% occurred between the first and sixth month of usage. A total of 49.3% of the patients were female and 50.7% were male. More than 50% of the patients were over the age of 60 [3].

CASE PRESENTATION

A 53-year-old female patient consulted the emergency service complaining of painthat had started suddenly after eating and had spread to the rear of the epigastric region. In her physical examination, sensitivity in the epigastric area and rebound were present. In her laboratory tests, the alanine aminotransferase, aspartate aminotransferase, gamma

Address for correspondence: *Özgür Sirkeci, MD., Near East University Hospital, Department of Internal Medicine, Nicosia, Cyprus*
E-mail: ozgursirkeci@hotmail.com

e-ISSN: 2149-3189

glutamyl transferase, bilirubin levels were all normal. Amylase was observed at 3,000 mg/dl. Kidney functions were normal. Gall bladder and biliary tracts were observed to be normal in the ultrasonography of the patient that was suspected of having pancreatitis. Oedematous pancreatitis findings were present in the contrast enhancement computed tomography (CT), while the gall bladder and biliary tracts had normal appearance (Figure 1). The patient had no history of alcohol or smoking. Triglyceride and calcium levels were normal. She had no abdominal trauma history. The patient had no suggestion of autoimmunity in either her family history or clinical findings. It was determined that she had been taking metoprolol 25 mg once per day for valvular heart disease for approximately 5 years, cytolopram 5 mg per day for anxiety disorder and had started to take 20 mg/a day of Rivaroxaban for paroxysmal atrial fibrillation diagnosis 3 months prior to the onset of the symptoms. Based on the existing findings, it was thought that she had acute pancreatitis. There were no biliary calculus findings in ultrasonography and CT scan, the gall bladder and biliary tracts were normal, no herbal medication had been consumed, there had been no alcohol use and the normal triglyceride level Indicated a high likelihood that the patient had drug-induced pancreatitis. As the patient had used metoprolol and cytolapram for 5 years with no symptoms of pancreatitis during this timeand had then started using Rivaroxaban 3 months prior to experiencing pain, this suggested that pancreatitis was associated with theRivaroxaban. The oral intake and current medications of the patient were stopped, and appropriate fluid replacement and analgesia was performed. Anticoagulation was provided with LMAH. On the third day of treatment, the patient had no pain complaints and oral intake started. On the fifth day, metopropol and cytolapram treatment started again. In accordance with the cardiology consultation, Apixaban 2×5 mg treatment started for the patient instead of Rivaroxaban. No complications developed and no further complaints were reported by the patient.

DISCUSSION

Rivaroxaban is an anticoagulant that has been safely used and is being increasingly utilised. According to FDA data, 81,271 patients experienced side effects to date and of these, only 81 experienced Acute Pancreatitis [2]. This is the 82nd case that was reported and the first in 2017. Drug-induced

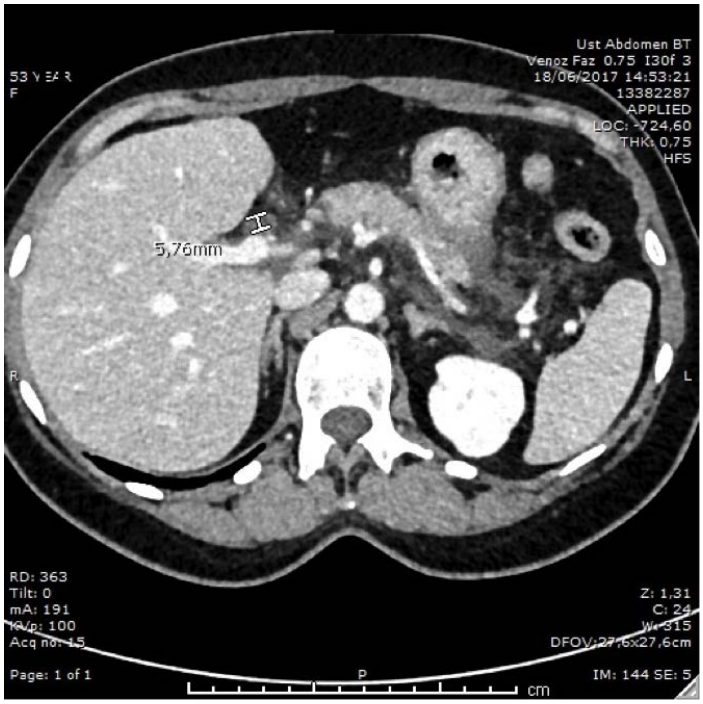


Figure 1. Abdominal computered tomography

pancreatitis is generally diagnosed according to four criteria: a) Pancreatitis development while using medication; b) Recovery of the patient by stopping the medication; c) Repetition of complaints by repeating usage of the medication; d) Exclusion of other pancreatitis causes [4, 5]. In this case, the symptoms developed while the patient was using the medication and complaints reduced when the patient stopped the medication; therefore, all other possibilities were excluded and the medication was not given again [4, 5]. Because the patient required the use of an anticoagulant, Apixaban treatment was started and there were no complaints or findings that would suggest pancreatitis in the follow-up. We started abixaban because it will provide enough anticoagulant effect and currently noabixaban induced pancreatitis reported yet. Pancreatitis conditions were light while under medication and the patient's complaints were rectified with supportive care by the fifth day and the patient was subsequently discharged. Drug-induced pancreatitis incidence has been reported in only 5.3% of patients with pancreatitis, although it is difficult to confirm this, as many patients do not provide honest answers on questionnaires [1]. In this case, it was evaluated that it was highly likely that the pancreatitis was related to Rivaroxaban as a idiosyncratic reaction. Because other reasons were excluded after proper examinations and the patient had not consumed alcohol and had no history of smoking, autoimmunity, hypercalcaemia history, herbal medication usage and had started to use Rivaroxaban recently. In the declared rivaroxaban related pancreatitis cases until today, 60.87% were observed to develop in the first month and 21.74% within 1-6 months. In the present case, pancreatitis developed in the third month.

CONCLUSION

In the drug-induced pancreatitis etiology, Rivaroxaban should be considered to be one of the causative factors and treatment should include stopping the medication. If anticoagulation is necessary, the other new oral anticoagulants like apixaban or dabigatran may be used during the treatment period however, they may cause pancreatitis.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

[1] Cappell MS. Acute pancreatitis: etiology, clinical presentation, diagnosis, and therapy. Med Clin North Am 2008;92:889-923.
[2] Badalov N, Baradarian R, Iswara K, Li J, Steinberg W, Tenner S. Drug-induced acute pancreatitis:an evidence-based review. Clin Gastroenterol Hepatol 2007;5:648-61.
[3] http://www.ehealthme.com/ds/xarelto/pancreatitis/
[4] Tenner S. Drug induced acute pancreatitis: Does it exist? World J Gastroenterol 2014;20:16529-34.
[5] Hung WY, Abreu Lanfranco O. Contemporary review of drug-induced pancreatitis: A different perspective. World J Gastrointest Pathophysiol 2014;5:405-15.

The European Research Journal 2019;5(3):572-575 CASE REPORT

Intradural extramedullary cystic schwannoma of the cervical spine

Elif Başaran Gündoğdu, Mehmet Ali Ekici

Department of Neurosurgery, University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey

DOI: 10.18621/eurj.384041

ABSTRACT

Giant cervical intradural extramedullary schwannoma with severe spinal cord compression is a rare entity. Tumor spread and size are very important for surgical approach. In this case, we report a 55-years-old male patient with a giant intradural-extramedullary cervical schwannoma extending between C5 and T1 and causing spinal cord compression that underwent total resection with laminoplasty at C5-6-7 levels. The patient developed no additional deficit. To preserve the cervical lordosis, the patient used a cervical collar for three months. There has been no recurrence during two years of follow-up. Using the appropriate surgical method is essential in patients with spinal tumor in order to avoid additional neurological deficits and achieve cure.

Keywords: cervical schwannoma, laminoplasty, intradural extramedullary tumor

Received: January 25, 2018; Accepted: July 5, 2018; Published Online: August 15, 2018

Spinal schwannomas are slow-growing tumors of benign origin, which represent approximately 30% of all primary spinal cord tumors. Spinal schwannomas are most commonly intradural [1]. Extradural involvement becomes more pronounced for the cervical schwannomas, since the intradural segment of the nerve root is shorter at the cervical region compared to the other areas of the spinal cord. The general approach is laminectomy for cervical schwannomas, or unilateral facetectomy may be performed if the lesion is located laterally [2].

Giant intradural extramedullary schwannoma of the cervical spine has a low incidence and causes severe spinal cord compression. These patients present progressive motor and/or sensory deterioration [3].

CASE PRESENTATION

A 55-year-old male patient who had numbness and pain in his right arm and numbness in his right leg was admitted to the outpatient clinic. The neurological examination revealed hyperactive upper and lower extremity deep tendon reflexes (DTRs) and a positive Rhomberg test. Bilateral hypoesthesia was present at the C5-6-7-T1 dermatomes, although it was more pronounced on the right side. There was 1-2/5 weakness of the right arm. A cervical MRI study was performed. On the cervical MRI, there was an intradural extramedullary solid mass including cystic areas, which was extending between C5 and T1, compressing the spinal cord from the left side, and

Address for correspondence: *Elif Başaran Gündoğdu, MD., University of Health Sciences, Bursa Yüksek İhtisas Training and Research Hospital, Department of Neurosurgery, Emniyet Caddesi No:35, 16115 Yıldırım, Bursa, Turkey*
E-mail:basaran.elif@hotmail.com, Phone: +90 224 2955000, Fax: +902243660416

e-ISSN: 2149-3189

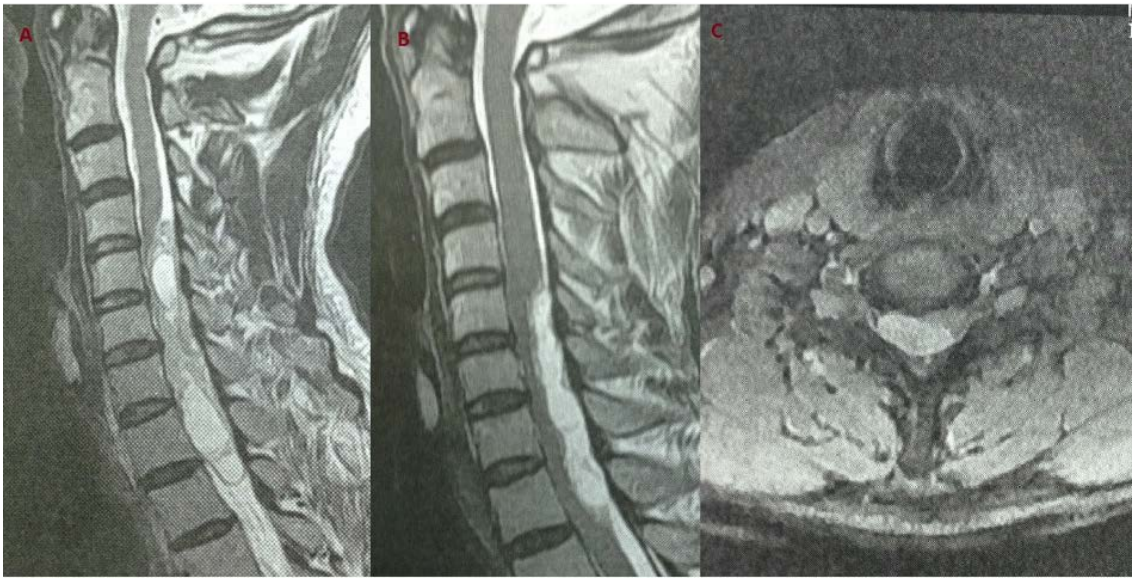


Figure 1. (A-B-C) Cervical MRI taken preoperatively.

enhancing homogeneously with gadolinium (Figure 1A, 1B and 1C). In the opeeration, after laminectomy at C5-6-7 levels (Figure 2A and 2B), a midline incision was made on the dura and gross total resection of the tumor mass was completed. On macroscopic examination, the specimen was a solid-to-cystic mass which was grayish-white in color and was partly adherent to the arachnoid (Figure 2C). Then the dura was sutured and laminoplasty was performed after hemostasis of the surgical area with cautious electrocautery (Figure 2D). On histopathological examination, hypo- and hypercellular areas (Figure

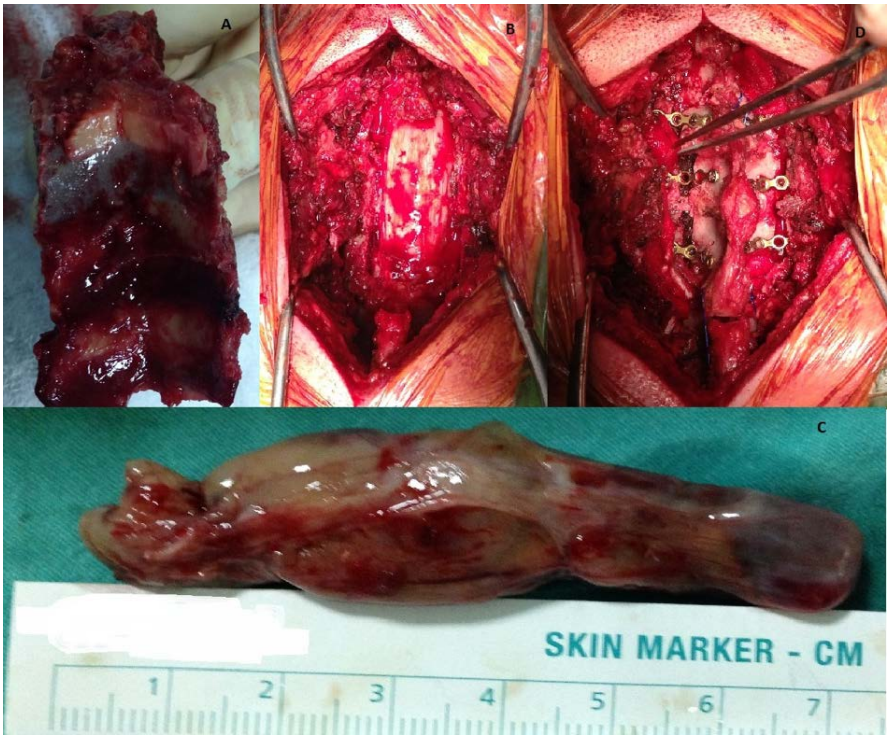


Figure 2. (A-B-C-D) During the operation laminoplasty and tumor mass.

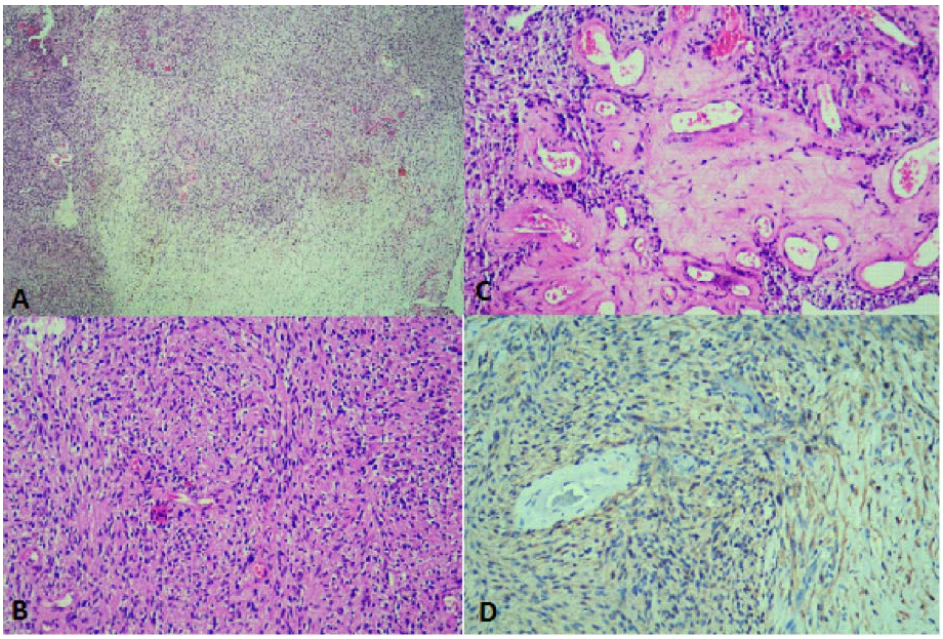


Figure 3. (A-B-C-D) Histopathological examination.

3A), Atoni A areas (Figure 3B), perivascular hyalinization (Figure 3C), and positive immunohistochemical staining for S-100 protein confirmed the diagnosis of schwannoma. During the first three months postoperatively, the patient used a cervical collar for preservation of the natural cervical lordosis. At the end of the postoperative third month, there was no severe kyphosis on the cervical X-ray (Figure 4A and 4B). The patient was followed up for two years with no recurrence.

DISCUSSION

Five-fifteen percent of all adult spinal cord tumors are primary [4]. One third of all primary spinal cord

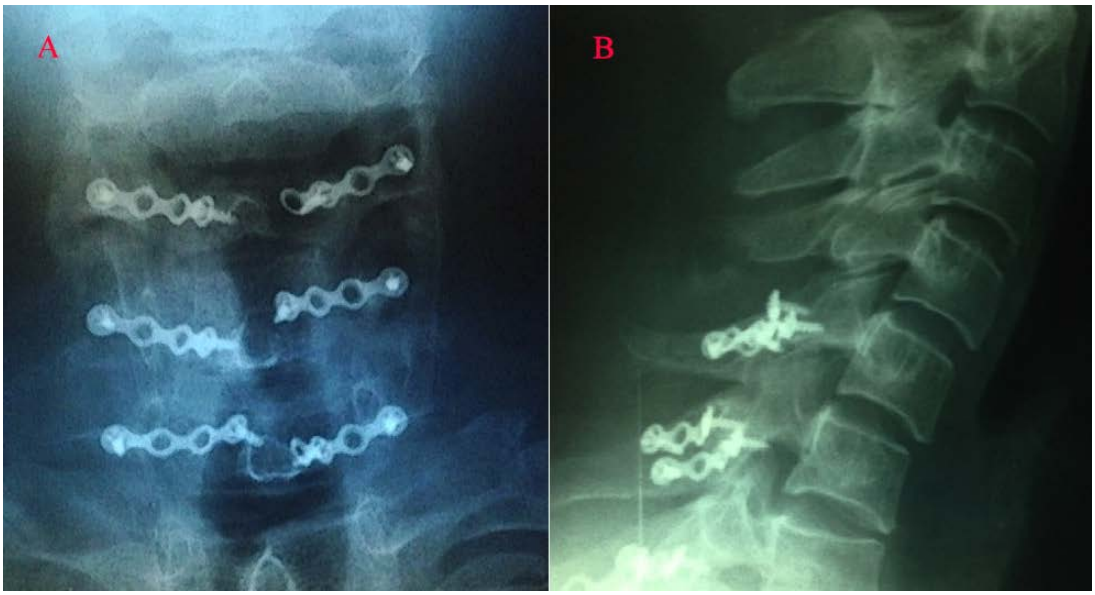


Figure 4. (A-B) Cervical x-ray taken postoperatively.

tumors are schwannomas. Also, schwannomas are benign tumors whose most common location is intradural extramedullary [5]. Intradural extramedullary schwannomas may demonstrate a cystic, solid, or mixed character. On MRI study, these lesions are visualized as hypo-/isointense on T1 images, and hyperintense on T2 sequence [5, 6]. Treatment options vary according to tumor localization, and the choice of surgery is determined by the surgeon's experience and dexterity. The preferred method may be tumor resection with laminectomy, with or without posterior stabilization. [7]. In the presented case, posterior stabilization was not preferred; instead, 3-level laminoplasty was performed, and there was no severe kyphosis on control X-ray at the end of the third postoperative month. The main advantages of minimal invasive surgery are reduced perioperative bleeding and shorter duration of postoperative hospital stay [8]. In our case, there was no need for erythrocyte replacement and the patient was discharged after two days. Another thing to consider for cervical schwannomas is that incidence of radicular dysfunction varies according to whether the tumor originates from the anterior or the posterior root. Tumor involvement in the anterior root is more likely to cause motor deficits [9]. In our case; there was no additional loss of motor and sensory function in the postoperative period.

CONCLUSION

In conclusion, giant cervical intradural extramedullary schwannoma with severe spinal cord compression is a rare entity. The presented case underwent total excision with laminoplasty, and developed no additional deficit. Also the cervical lordosis was mostly preserved without any need for stabilization. Laminoplasty is suitable in selected cases with relatively short segment involvement, especially if an appropriate cervical collar is used in the postoperative period.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

[1] Iacopino DG, Giugno A, Gulì C, Basile L, Graziano F, Maugeri R. Surgical nuances on the treatment of giant dumbbell cervical spine schwannomas: description of a challenging case and review of the literature. Spinal Cord Ser Cases 2016;2:15042.
[2] Mc.Cormick PC, Stein BM. Spinal Cord Tumors in Adults. In Youmans Julian R (Ed) Neurosurgical Surgery. 6th Edition. Volume 3, Ch 309. WB Saunders Company. 2011 (CD Edition).
[3] Quillo-Olvera J, Lin GX, Kim JS. Severe spinal cord compression by pure giant intradural schwannoma of cervical spine. World Neurosurg 2018;110:17-9.
[4] Pan E, Prados MD. Spinal cord tumors, in Kufe DW, Pollock RE, Weichselbaum RR, et al (eds): Holland-Frei Cancer Medicine, 6th ed. Hamilton, ON: BC Decker, 2003.
[5] Conti P, Pansini G, Mouchaty H, Capuano C, Conti R. Spinal neurinomas: retrospective analysis and long-term outcome of 179 consecutively operated cases and review of the literature. Surg Neurol 2004;61:34-43; discussion 44.
[6] De Verdelhan O, Haegelen C, Carsin-Nicol B, Riffaud L, Amlashi SF, Brassier G, et al. MR imaging features of spinal schwannomas and meningiomas. J Neuroradiol 2005;32:42-9.
[7] Gu BS, Park JH, Roh SW, Jeon SR, Jang JW, Hyun SJ, et al. Surgical strategies for removal of intra- and extraforaminal dumbbell-shaped schwannomas in the subaxial cervical spine. Eur Spine J 2015;24:2114-8.
[8] Kim SH, Doh JW, Yoon SM, Yun IG. Huge schwannoma extended from craniocervical junction to upper thoracic spine. J Korean Neurosurg Soc 2003;34:589-92.
[9] Wong AP, Lall RR, Dahdaleh NS, Lawton CD, Smith ZA, Wong RH, et al. Comparison of open and minimally invasive surgery for intradural-extramedullary spine tumors. Neurosurg Focus 2015;39:E11.

THE ASSOCIATION OF HEALTH
RESEARCH AND STRATEGY