ISSN 2757-847X I e-ISSN 2718-0964

EAMS

Experimental and Applied Medical Science

Offical Journal of Gaziantep Islam Science and Technology University, Faculty of Medicine
July 2024, Volume 5, Issue 3

GAZİANTEP İSLAM BİLİM VE TEKNOLOJİ ÜNİVERSİTESİ TIP FAKÜLTESİ

GAZİANTEP ISLAM SCIENCE AND TECHNOLOGY UNIVERSITY FACULTY OF MEDICINE

Experimental and Applied Medical Science

Volume 5, Issue 3

Official Journal of Gaziantep Islam Science and Technology University, Faculty of Medicine

ISSN: 2757-847X

e-ISSN: 2718-0964

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Dizinler/Indexing

Türkiye Atıf Dizini, Türk Medline, Google Scholar, Europub, Scilit, ASOS indeks, Advanced Science Index, Academic Resource Index, Eurasian Scientific Journal Index, Crossref, General Impact Factor

Publishing date: 30.07.2024
Yayın tarihi: 30.07.2024

Aim

Experimental and Applied Medical Science aims at being a current and easily accessible academic publication in which striking research results that will improve the quality of life and are unique from every field of medical sciences.

Amaç

Experimental and Applied Medical Science, yaşam kalitesini arttıracak çarpıcı araştırma sonuçlarının sunulduğu, tıp bilimlerinin her alanında benzersiz, güncel ve kolay erişilebilir bir akademik yayın olmayı hedeflemektedir.

Scope

Experimental and Applied Medical Science is an open-access, internationally double-blind peer reviewed academic medical journal which is published in English four times a year, under the auspices of Medical Faculty of Gaziantep Islam Science and Technology University. The journal receives manuscripts for consideration to be publishing in the form of research articles, reviews, letter to editor, brief notification, summary notification etc. which could have been presented from within the country or abroad and including experimental animal studies related to the pathogenesis of diseases, pharmacological, clinical, epidemiological and deontological studies, also studies in the fields of improving public health, health services or health insurance.

During evaluation or publication no charge is demanded from authors. The journal is published every 3 months (March, July, September and December) with 4 issues per year. The literary language of the journal is English. Abstract part of the manuscript only should also be submitted in Turkish.

Kapsam

Experimental and Applied Medical Science, Gaziantep İslam Bilim ve Teknoloji Üniversitesi Tıp Fakültesi himayesinde yılda dört kez İngilizce olarak yayınlanan açık erişimli, uluslararası çift kör hakemli bir akademik tıp dergisidir. Dergi, yurt içinden veya yurt dışından, hastalık patogenezleri ile ilişkili deneysel hayvan çalışmaları, klinik, farmakolojik, epidemiyolojik, deontolojik çalışmalar ile beraber halk sağlığının geliştirilmesi amacı taşıyan ve sağlık hizmetleri veya sağlık sigortaları konularında araştırma makaleleri, derlemeler, vaka sunumları, kısa bildirimleri, özet bildirimleri vs. yayınlamak için değerlendirmeye kabul etmektedir. Değerlendirme veya yayın sırasında yazarlardan herhangi bir ücret talep edilmez.

Dergi 3 ayda bir (Mart, Temmuz, Eylül ve Aralık) yılda 4 sayı olarak yayımlanır. Derginin yazı dili İngilizcedir. Makalenin sadece özet kısmı Türkçe olarak da gönderilmelidir.

Ethical Principles and Publication Policy

Manuscripts are only considered for publication provided that they are original, not under consideration simultaneously by another journal, or have not been previously published. Direct quotations, tables, or illustrations that have extracted from any copyrighted material must be accompanied by written authority for their use from the copyright owners. All manuscripts are subject to review by the editors and referees. Deserving to be publishing is based on significance, and originality of the material. If any manuscript is considered to deserve publishing, it may be subject to editorial revisions to aid clarity and understanding without changing the data presented.

Experimental and Applied Medical Science strictly adheres to the principles set forth by "Helsinki Declaration" whose web address is below.

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Editorial Board declares that all reported or submitted studies conducted with "human beings" should be in accordance with those principles.

Manuscripts presenting data obtained from a study design conducted with human participants must contain affirmation statements in the *Material and Methods* section indicating approval of the study by the institutional ethical review committee and "informed consent" was obtained from each participant. Also all manuscripts reporting experiments in which laboratory animals have been used should include an affirmation statement in the *Material and*

Etik İlkeler ve Yayın Politikası

Makaleler, orijinal/özgün olmaları, eş zamanlı olarak başka bir dergi tarafından incelenmemeleri veya daha önce yayınlanmamış olmaları koşuluyla yayına kabul edilir. Telif hakkıyla korunan herhangi bir materyalden alınan doğrudan alıntılar, tablolar veya resimler, kullanımları için telif hakkı sahiplerinden alınan yazılı izinle birlikte sunulmalıdır. Tüm yazılar editörler ve hakemler tarafından incelemeye tabidir. Yayınlanmaya hak kazanılması, materyalin önemine ve özgünlüğüne bağlıdır. Herhangi bir makalenin yayınlanmayı hak ettiği düşünülürse, sunulan veriler değiştirilmeden netlik ve anlayışa yardımcı olmak için editör revizyonlarına tabi tutulabilir.

Experimental and Applied Medical Science, internet adresi aşağıda yer alan "Helsinki Deklarasyonu" ile belirlenen ilkelere sıkı sıkıya bağlıdır.

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Editör Kurulu, "insan" ile yapılan tüm raporlanan veya sunulan çalışmaların bu ilkelere uygun olması gerektiğini beyan eder. İnsan katılımcılarla yürütülen bir çalışma tasarımından elde edilen verileri sunan makaleler, *Gereç ve Yöntemler* bölümünde çalışmanın kurumsal etik inceleme komitesi tarafından onaylandığını ve her katılımcıdan "bilgilendirilmiş onam" alındığını belirten onay ifadeleri kullanmalıdır. Ayrıca laboratuvar hayvanlarının kullanıldığı deneyleri bildiren tüm yazılar, *Gereç ve Yöntemler* bölümünde, internet adresi aşağıda

Methods section validating that all animals have received human care in compliance with the "Guide for the Care and Use of Laboratory Animals" whose web address is below and reveal approval by the institutional ethical review board. https://www.gibtu.edu.tr/Medya/Birim/Dosya/20210818130308_dca61056.pdf

If there is a commercial relation that contributes to the study process or there is an institution that provides financial support for the study; the authors must declare that they have no commercial relationship with the commercial product, drug, company used, or what kind of relationship (consultant or any other agreement) they have, if any.

Processing and publication are free of charge with the journal. No fees are requested from the authors at any point throughout the evaluation and publication process. All manuscripts must be submitted via the online submission system, which is available at https://dergipark.org.tr/tr/pub/eams. The journal guidelines, technical information, and the required forms are available on the journal's web page.

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belirtilmiş olan "Laboratuvar Hayvanlarının Bakımı ve Kullanımı Kılavuzu"na uygun olarak tüm hayvanların insanî bir bakım aldığını doğrulayan bir beyan ile kurumsal etik inceleme kurulunun onayını içermelidir. https://www.gibtu.edu.tr/Medya/Birim/Dosya/20210818130308_dca61056.pdf

Çalışma sürecine katkı sağlayan ticari bir ilişki veya çalışmaya maddi destek sağlayan bir kurum varsa; yazarlar ticari ürün, ilaç, aracılık eden şirket ile ticari bir ilişkilerinin olmadığını veya varsa ne tür bir ilişkisi (danışmanlık veya başka bir anlaşma) olduğunu beyan etmelidir.

Değerlendirme ve yayınlama süreçleri ücretsizdir. Değerlendirme ve yayın sürecinin hiçbir aşamasında yazarlardan ücret talep edilmez. Tüm yazılar https://dergipark.org.tr/tr/pub/eams adresinde bulunan çevrimiçi başvuru sistemi üzerinden gönderilmelidir. Dergi ile ilgili kullanım kılavuzları, teknik bilgiler ve gerekli formlar derginin internet sayfasında yer almaktadır.

Derginin tüm masrafları Gaziantep İslam Bilim ve Teknoloji Üniversitesi Tıp Fakültesi tarafından karşılanmaktadır. Reklam vermeyi düşüne kişi veya kurumlar yayın ofisi ile iletişime geçmelidir. Reklam görselleri sadece Baş Editör'ün onayı ile yayınlanabilir.

Tüm araştırmacılar, makaleye doğrudan akademik veya bilimsel olarak katkıda bulunmuş olmalıdır. Yazarlar, makalenin planlanması, uygulanması, yazılması veya gözden geçirilmesi aşamalarından birine veya birkaçına katkıda bulunmuş olmalıdır. Tüm yazarlar nihai versiyonu onaylamalıdır. Bilimsel kriterlere uygun bir makale hazırlamak yazarların sorumluluğundadır.

the final version. It is the authors' responsibility to prepare a manuscript that meets scientific criterias.

Statements or opinions expressed in the manuscripts published in the journal reflect the views of the author(s) and not the opinions of the Medical Faculty of Gaziantep Islam Science and Technology University, editors, editorial board, and/or publisher; the editors, editorial board, and publisher disclaim any responsibility or liability for such materials.

All manuscripts involving a research study must be evaluated in terms of biostatistics and it must be presented altogether with appropriate study design, analysis and results. ***p*** values must be given clearly in the manuscripts. Other than research articles, reviews, case reports, letters to the editor, etc. should also be original and up to date, and the references and, if any, their biostatistical parts should be clear, understandable and satisfactory.

The publication language of the journal is English. In addition, the abstract part of the article must be uploaded in both Turkish and English. Manuscripts should be evaluated by a linguist before being sent to the journal.

All manuscripts and editorial correspondence must be submitted online to the editorial office, https://dergipark.org.tr/tr/pub/eams.

According to the Law on Intellectual and Artistic Works, which was first published in the Official Gazette with the law number 5846 on 13/12/1951, whose web address is below, and on which subsequently various changes have been made or novel parts have been added in time, all kinds of publication rights of the articles accepted

Dergide yayınlanan yazılarda ifade edilenler veya görüşler, Gaziantep İslam Bilim ve Teknoloji Üniversitesi Tıp Fakültesi, editörler, yayın kurulu ve/veya yayıncının görüşlerini değil, yazar(lar)ın görüşlerini yansıtır; editörler, yayın kurulu ve yayıncı bu tür materyaller için herhangi bir sorumluluk veya yükümlülük kabul etmez.

Araştırma çalışması içeren tüm yazılar biyoistatistiksel açıdan değerlendirilmeli ve uygun çalışma düzeni, verilerin analizi ve sonuçları ile birlikte sunulmalıdır. ***p*** değerleri yazılarda açık olarak verilmelidir. Araştırma makaleleri dışında derlemeler, olgu sunumları, editöre mektuplar vb. de orijinal/özgün ve güncel olmalı, kaynaklar ve varsa biyoistatistiksel kısımlar açık, anlaşılır ve tatmin edici olmalıdır.

Derginin yayın dili İngilizce'dir. Ayrıca makalenin özet kısmı hem Türkçe hem de İngilizce olarak yüklenmelidir. Yazılar dergiye gönderilmeden önce bir dilbilimci/konunun uzmanı tarafından değerlendirilmelidir.

Bütün çalışmalar ve editör kurulu ile yazışmalar çevrimiçi olarak, https://dergipark.org.tr/tr/pub/eams adresi üzerinde yayın ofisine gönderilmelidir.

İnternet adresi aşağıda belirtilmiş olan, ilk olarak 13/12/1951 tarih ve 5846 sayılı Kanun ile Resmi Gazete'de yayımlanan, sonraları üzerinde değişiklikler yapılmış veya yeni kısımlar eklenmiş olan Fikir ve Sanat Eserleri Kanunu'na göre; yayına kabul edilen makalelerin her türlü yayın hakkı dergiyi yayınlayan kuruma aittir. Ancak makalelerdeki düşünce ve öneriler tamamen yazarların sorumluluğundadır. https://www.gibtu.edu.tr/Medya/Birim/Dosya/20210818145630_406d24df.pdf

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Author Guidelines

Submission of a paper will be taken to imply that it has not previously been published and that it is not being considered for publication elsewhere. Decision as to publication of papers submitted to the Experimental and Applied Medical Science will be based on the opinion of the Editorial Board as to the significance and originality of the work.

Manuscripts should be prepared electronically using an appropriate “office word” compatible text-processing package, formatted for A4 size, double-spaced throughout, and using a “Times New Roman” 12 point font. Articles must be written in English. Abstracts must be written in both Turkish and English. Text should flush left, and not be justified. Words should not be hyphenated. Pages should be numbered sequentially.

There should be a separate title page with:

a) The title

b) The authors' names

c) The laboratory of origin, with complete address of each author

d) A running title

e) Corresponding author and e-mail

f) Conflict of interest

g) Acknowledgements

The main body of full-length paper should be divided into:

1. Abstract

2. Introduction

3. Material and Methods

4. Results

5. Discussion

Yazım Kuralları

Bir çalışmanın dergimize gönderilmesi için bu çalışmanın daha önce yayınlanmamış veya başka bir akademik dergide şu anda yayınlanmak üzere değerlendirilmiyor olması koşulu ile mümkündür. Experimental and Applied Medical Science’a gönderilen her türlü çalışmanın yayınlanmasına ilişkin karar, Yayın Kurulu'nun çalışmanın önemi ve özgünlüğü konusundaki görüşüne dayanacaktır.

Çalışmalar, ya “office word” programı ile ya da bu program ile uyumlu uygun bir metin işleme programı kullanılarak, A4 boyutunda hazırlanmalı, baştan sona çift aralıklı ve “Times New Roman” tarzında 12 punto yazı tipi kullanılarak elektronik ortamda yazılmalıdır. Makaleler İngilizce yazılmalıdır. Özetler hem Türkçe hem de İngilizce olarak yazılmalıdır. Metin iki yana yaslandırılmamalı, sadece sola yaslanmamalıdır. Kelimeler kısa çizgi ile hecelenmemelidir. Sayfalar sırayla numaralandırılmalıdır.

Aşağıdakileri içeren ayrı bir başlık sayfası olmalıdır:

a) Başlık

b) Yazarların isimleri

c) Her yazarın tam adresi ile birlikte çalıştıkları laboratuarlar

d) Kısa başlık

e) İletişimdeki yazar ve iletişim bilgileri

f) Çıkar çatışması beyanı

g) Teşekkür, bilgilendirme

Tam uzunluktaki kağıdın ana gövdesi şu bölümlere ayrılmalıdır:

1. Özet

2. Giriş

6. Conclusion
7. Conflict of interest
8. Acknowledgement
9. References

In general, there are no specific word lengths for any manuscript. The general principle is that a manuscript can be as long as necessary to communicate clearly and most effectively the scientific message, but should be as short as possible to achieve a complete presentation of the information without undue repetition or redundancy.

In the *Materials and Methods* section, the source of all compounds, equipment or software should be identified by the full name of the supplier, city, state/country. The chemical names of any drug should precede the trade name.

Papers describing animal experiments must define species, strain, sex, age, supplier and number of animals used. An ethical statement concerning the use of animals, or the details of ethical approvals, consent and recruitment of human subjects should be clearly stated. *Results* and *Discussion* can be broken down into subsections for improving the comprehensibility. The Results should not repeat methodological details and should avoid the discussion of the data.

The results of statistical tests should be incorporated in the body of the text, typically in the *Results* section, rather than in figure legends. Adequate description of statistical analysis should be provided. Statistical measures of variation in the text, illustrations and tables, should be identified. All dimensions and measurements must be

3. Gereç ve Yöntemler
4. Sonuçlar
5. Tartışma
6. Bağlam
7. Çıkar çatışması
8. Teşekkür, bilgilendirme
9. Kaynaklar

Genel olarak, herhangi çalışma için şart koşulan belirli bir kelime sayısı/metin uzunluğu yoktur. Genel ilke; bir makalenin bilimsel mesajı açık ve etkili bir şekilde iletmek için gerektiği kadar uzun olabileceği, ancak gereksiz tekrar veya fazlalık olmadan bilgilerin eksiksiz bir sunumunu elde etmek için mümkün olduğunca kısa olması gerektiğidir.

Gereçler ve Yöntemler bölümünde, tüm bileşiklerin, malzemelerin veya yazılımların kaynağı, tedarikçinin tam adı, şehir, eyalet/ülke ile tanımlanmalıdır. Herhangi bir ilacın kimyasal isimleri ticari isminden önce gelmelidir.

Hayvan deneylerini açıklayan makaleler, tür, soy, cinsiyet, yaş, tedarikçi ve kullanılan hayvan sayısını açıkça tanımlamalıdır. Hayvanların kullanımına ilişkin bir etik beyan veya insan deneklerin etik kurul onayları, bilgilendirilmiş onamları ve çalışmaya dâhil edilmelerine ilişkin ayrıntılar açıkça belirtilmelidir. *Sonuçlar ve Tartışma* bölümleri, anlaşılırlığı artırmak için alt bölümlere ayrılabilir. Sonuçlar, metodolojik ayrıntıları tekrarlamamalı ve verilerin tartışılmasından kaçınmalıdır.

İstatistiksel testlerin sonuçları, şekillerin altındaki açıklama kısımlarından ziyade metnin gövdesine, tipik olarak Sonuçlar bölümüne dâhil edilmelidir. İstatistiksel analizin yeterli bir şekilde açıklaması sağlanmalıdır. Metinde, resimlerde ve

specified in the metric system.

All subscripts, superscripts, Greek letters and unusual characters must be clearly identified.

In the text, abbreviations should be used consistently. Abbreviations should be defined on first use.

References should be designed in “Vancouver” style. While writing references, “Times New Roman” 10 point font should be used. Multiple authors should be separated by a comma. If there are more than three authors, after the 3rd author, "et al." should be inserted without a comma for both article and book references. If reference is made from a chapter in a book and there are many authors belonging only to this chapter, the title and chapter of the book are indicated, the first three of the chapter authors are written, and "et al." statement is added for subsequent authors.

Example:

1. Perell KL, Nelson A, Goldman RL, et al. Fall risk assessment measures: an analytic review. The journals of gerontology Series A, Biological sciences and medical sciences. 2001;56(12):M761-6.

2. Ha H, Han C, Kim B. Can Obesity Cause Depression? A Pseudo-panel Analysis. Journal of preventive medicine and public health = Yebang Uihakhoe chi. 2017;50(4):262-7.

3. Çekmen MB, Turgut M, Türköz Y, et al. Nitrik Oksit (NO) ve Nitrik Oksit Sentaz (NOS)'ın Fizyolojik ve Patolojik Özellikleri. Türkiye Klinikleri Journal of Pediatrics. 2001;10(4):226-35.

4. Parlakpınar H, Örüm MH, Acet A. Kafeik asit fenetil ester (KAFE) ve miyokardiyal

tablolarda istatistiksel varyasyon ölçütleri tanımlanmalıdır.

Tüm boyutlar ve ölçüler metrik sistemde belirtilmelidir.

Tüm alt simgeler, üst simgeler, Yunan harfleri ve olağandışı karakterler açıkça tanımlanmalıdır.

Metinde kısaltmalar tutarlı bir şekilde kullanılmalıdır. Kısaltmalar ilk kullanımda tanımlanmalıdır.

Kaynaklar “Vancouver” tarzında yazılmalıdır. Kaynaklar yazılırken, “Times New Roman” 10 punto kullanılmalıdır. Birden çok yazar virgülle ayrılmalıdır. Hem makale hem de kitap referanslarında, eğer üçten çok yazar varsa, 3. Yazardan sonra virgül ve “et al.” ifadesi kullanılmalıdır. Kitapta bir bölümden referans yapılıyorsa ve sadece bu bölüme ait çok sayıda yazar varsa, kitabın başlığı ve bölümü belirtilip, bölüm yazarlarının ilk üçü yazılıp ve ardından sonraki yazarlar için “et al.” ifadesi eklenmelidir.

Örnek:

1. Perell KL, Nelson A, Goldman RL, et al. Fall risk assessment measures: an analytic review. The journals of gerontology Series A, Biological sciences and medical sciences. 2001;56(12):M761-6.

2. Ha H, Han C, Kim B. Can Obesity Cause Depression? A Pseudo-panel Analysis. Journal of preventive medicine and public health = Yebang Uihakhoe chi. 2017;50(4):262-7.

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iskemi reperfüzyon (Mİ/R) hasarı. İnönü Üniversitesi Sağlık Bilimleri Dergisi 2012; 1: 10-5.
5. Yıldırım AB. The effects of maternal hypothyroidism on the immunoreactivity of cytochrome p450 aromatase in the postnatal rat testes. 2015; Doctoral thesis.
6. https://hsgm.saglik.gov.tr/depo/birimler/kanserdb/istatistik/Trkiye_Kanser_statistikleri_2016.pdf (Last access date: 21.09.2020).
7. Kuran O, İstanbul, Filiz Kitabevi. Sistematik Anatomi. 1983 p. 76-9.
8. Abbas AK, Andrew H Lichtman, Shiv Pillai. Cellular and Molecular Immunology. 6th ed. Philadelphia: Saunders Elsevier; 2007 p. 121-56.
Submit illustrations as separate files, only as TIFF or EPS files, with a minimum resolution of 300dpi.
Tables of numerical data should each be typed with double spacing on separate pages numbered in sequence in numerals, provided with a heading, and referred to in the text, as Table 1, Table 2, etc. Each table should have a brief but descriptive heading. Explanatory matter should be included in footnotes to the table.
We accept electronic supplementary material to support and enhance your scientific research. Supplementary files offer the author additional possibilities to publish supporting applications, movies, animation sequences, high-resolution images, background datasets, sound clips and more.

4. Parlakpınar H, Örüm MH, Acet A. Kafeik asit fenetil ester (KAFE) ve miyokardiyal iskemi reperfüzyon (Mİ/R) hasarı. İnönü Üniversitesi Sağlık Bilimleri Dergisi 2012; 1: 10-5.
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6. https://hsgm.saglik.gov.tr/depo/birimler/kanserdb/istatistik/Trkiye_Kanser_statistikleri_2016.pdf (Last access date: 21.09.2020).
7. Kuran O, İstanbul, Filiz Kitabevi. Sistematik Anatomi. 1983 p. 76-9.
8. Abbas AK, Andrew H Lichtman, Shiv Pillai. Cellular and Molecular Immunology. 6th ed. Philadelphia: Saunders Elsevier; 2007 p. 121-56.
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Sayısal veri tablolarının her biri, sayılarla sırayla numaralandırılmış bir başlık ile birlikte ve metinde Tablo 1, Tablo 2, vb. olarak atıfta bulunulmuş halde, ayrı sayfalarda çift aralıkla hazırlanmalıdır. Her tablonun kısa ama açıklayıcı bir başlığı olmalıdır. Tablo dipnotlarında açıklayıcı hususlara yer verilmelidir.
Bilimsel araştırmalarınızı desteklemek ve geliştirmek için elektronik ek materyaller kabul edilmektedir. Ek dosyalar, yazara, destekleyici uygulamaları, filmleri, animasyon dizilerini, yüksek çözünürlüklü

Disclosure of conflict of interest and financial support is required at the time of submission. The authors are responsible for informing the Journal of any additional conflicts of interest or financial support that may arise prior to the date of publication of their paper. All authors must individually disclose all potential conflicts of interest and financial support, whether or not directly related to the subject of their paper.

görüntüleri, arka plan veri kümelerini, ses kayıtlarını ve daha fazlasını yayınlamak için ek olanaklar sunmaktadır.

Başvuru sırasında çıkar çatışmasının ve mali destek konularının açıklanması elzemdir. Yazarlar, makalelerinin yayımlanma tarihinden önce ortaya çıkabilecek ek çıkar çatışmalarını veya bulunan mali destekleri dergiye bildirmekle yükümlüdür. Tüm yazarlar, makalelerinin konusuyla doğrudan ilgili olsun ya da olmasın, tüm olası çıkar çatışmalarını ve mali desteği bireysel olarak açıklamalıdır.

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Judges Board /Sayı Hakemleri

Contents/İçindekiler

129 **Elderly Patients in the Emergency Department: Risks, Vulnerabilities, and Fragility**

Serdar ÖZDEMİR

131 **Strengthening The Roadmap of Antimicrobial Stewardship/Evolution of Artificial Intelligence**

Sumeyra KOCTURK

137 **The Promise and the Challenge: Large Language Models for Patient Education - Are We There Yet?**

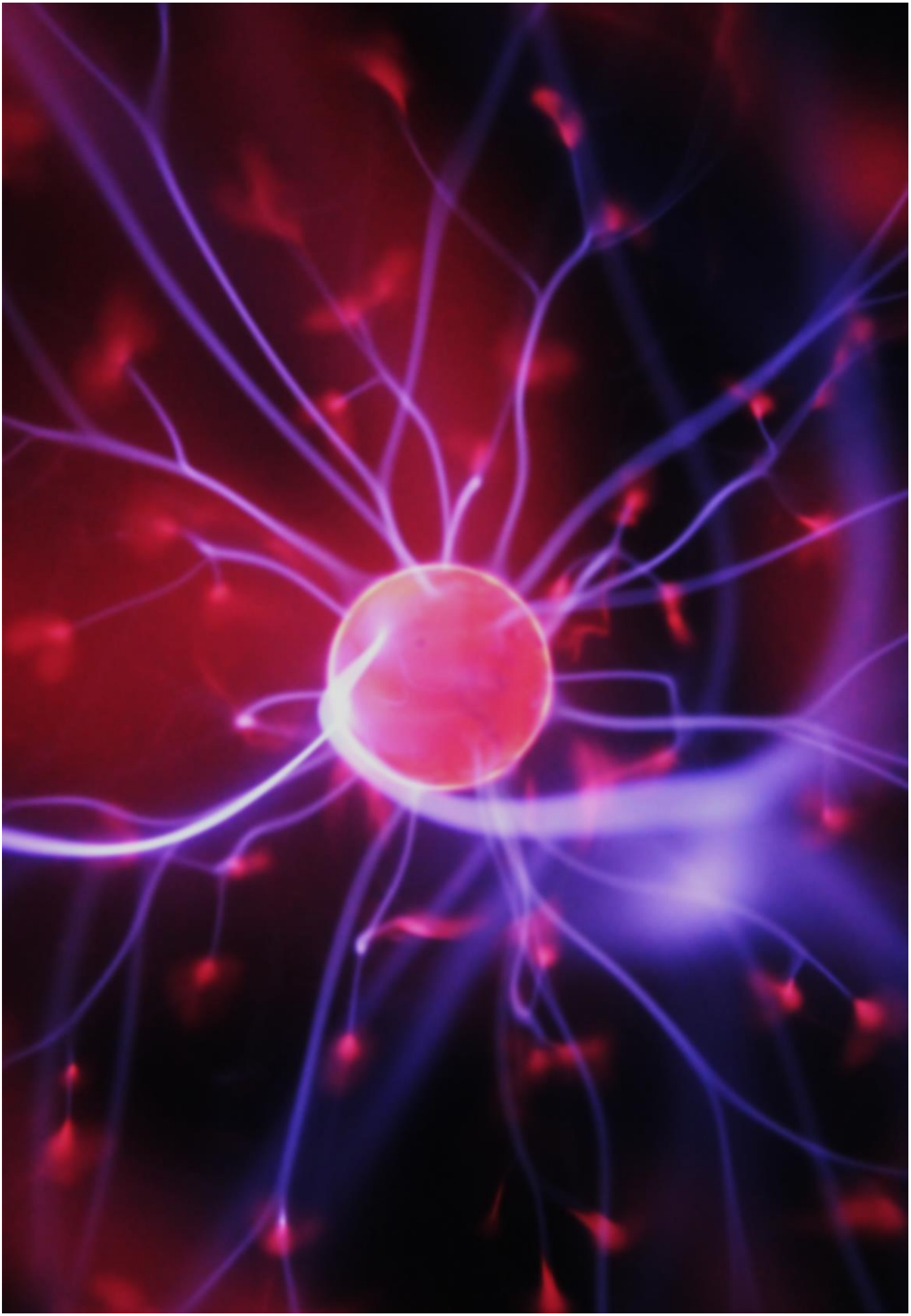
İbrahim Edhem YILMAZ

150 **Reliability of Thyroid Imaging Reporting and Data Systems' Scoring in the Evaluation of Thyroid Nodules**

Zeynep ERGENC, Hasan ERGENC, Erkan AKSOY, Özlem KARACA OCAK, Kerim GÜZEL, Feyzi GÖKOSMANOĞLU

160 **The Relationship between Posture and Muscle Stiffness with Blood Flow in Cervicogenic Headache**

Meltem UZUN, Yasemin EKMEKYAPAR FIRAT, Mehmet Ali İKİDAĞ, Nevin ERGUN, Türkan AKBAYRAK



Experimental and Applied Medical Science, 5, 3: 129-130, 2024. DOI: 10.46871/eams.1435394

Elderly Patients in the Emergency Department: Risks, Vulnerabilities, and Fragility

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Dear Editor,

Elderly patients, due to their advanced age and often frail health status, are particularly vulnerable when they require overnight stays in the emergency department. The fragility of these individuals amplifies the risks associated with prolonged stays in this environment.

Firstly, the physical fragility of elderly patients predisposes them to various complications during their stay in the emergency department. Frail individuals may have weakened immune systems, making them more susceptible to infections acquired in hospital settings. Moreover, their fragile skin is prone to breakdown when exposed to prolonged pressure from hospital beds or medical equipment, leading to pressure ulcers (1).

Secondly, the cognitive fragility of elderly patients can exacerbate their vulnerability during overnight stays in the emergency department. Conditions such as dementia or delirium may be exacerbated by the unfamiliar and chaotic environment of the emergency department, increasing the risk of agitation, disorientation, and falls. These cognitive impairments can also hinder effective communication between healthcare providers and patients, leading to misunderstandings or errors in care (2,3).

Additionally, the social fragility of elderly patients further complicates their situation in the emergency department. Many elderly individuals live alone or lack strong social support networks, making them more vulnerable to feelings of loneliness, anxiety, and depression during their overnight stay. Furthermore, issues such as transportation difficulties or financial constraints may hinder their ability to access follow-up care after discharge, increasing their risk of adverse outcomes and readmissions (4).

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Furthermore, the interaction between these various forms of fragility can create a vicious cycle that further compromises the health and well-being of elderly patients. For example, a physically frail patient who develops a hospital-acquired infection may experience increased cognitive decline due to the illness, which in turn exacerbates their physical frailty and increases their risk of further complications (5).

In conclusion, the fragility of elderly patients amplifies the risks associated with overnight stays in the emergency department, making them particularly vulnerable to adverse outcomes. Addressing the unique needs and vulnerabilities of this population is essential to providing safe and effective care in emergency settings. Strategies aimed at minimizing physical discomfort, optimizing communication and cognitive support, and providing comprehensive social services can help mitigate the risks and improve outcomes for elderly patients requiring overnight stays in the emergency department.

References

1. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013 Mar 2;381(9868):752-62. doi: 10.1016/S0140-6736(12)62167-9.
2. Gower LE, Gatewood MO, Kang CS. Emergency department management of delirium in the elderly. West J Emerg Med. 2012 May;13(2):194-201. doi: 10.5811/westjem.2011.10.6654.
3. Akça HŞ, Özdemir S, Algin A, Kar E, Altunok İ. Evaluation of The Efficacy of The Clinical Frailty Scale in The Prediction of Prognosis In Geriatric Patients Presenting To The Emergency Department With Acute Abdominal Pathologies: A Prospective Study. KTD. January 2023;24(1):36-42. doi:10.18229/kocatepetip.985311.
4. Singh A, Misra N. Loneliness, depression and sociability in old age. Ind Psychiatry J. 2009 Jan;18(1):51-5. doi: 10.4103/0972-6748.57861.
5. Angulo J, El Assar M, Álvarez-Bustos A, Rodríguez-Mañas L. Physical activity and exercise: Strategies to manage frailty. Redox Biol. 2020 Aug;35:101513. doi: 10.1016/j.redox.2020.101513.

Experimental and Applied Medical Science, 5, 3: 131-136, 2024. DOI: 10.46871/eams.1431345

Strengthening The Roadmap of Antimicrobial Stewardship/Evolution of Artificial Intelligence

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Abstract

The World Health Organization (WHO) is taking a "One Health" approach to address the ten major threats to global health, recognizing the interdependency of human, animal, plant, and environmental health, particularly in relation to antimicrobial resistance.

Failure to address antimicrobial resistance can have significant impacts on agriculture, economy, and food security, with low- and middle-income countries being the most affected. Strategies for antimicrobial stewardship programs have mainly focused on mandatory antimicrobial use, cost, and resistance rates. An ideal system should be able to detect microorganisms, display test results, and compare them to reference microorganisms.

The use of artificial intelligence is anticipated to be crucial in saving time and energy, and new techniques based on AI are expected to play a vital role in combating antimicrobial resistance.

Key words: *Antimicrobial resistance, Antimicrobial stewardship, Artificial intelligence.*

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Introduction

The World Health Organization considers antimicrobial resistance in humans and animals to be one of the top ten threats to global health. It is estimated that there could be up to 10 million deaths a year by 2050, with a knock-on effect on economies and more people in poverty. Another opinion in this are a is the use of the "One Health" approach, which recognizes that the health of humans, animals, plants, and the environment are closely interdependent, and antimicrobial resistance can be successfully addressed. If antimicrobial resistance is not assessed here; agricultural production could also be significantly impacted, affecting the economy and food security, with low and middle-income countries bearing most of the burden (1). Agriculture, economy and health facilities are most affected by this issue.

Systematic approaches to improving the use of antimicrobials across the spectrum of healthcare are referred to as antimicrobial stewardship. Most studies of antimicrobial stewardship program strategies have looked at prescribed antimicrobial use, antimicrobial costs and rates of antimicrobial resistance. However, many of these studies have been insufficiently powered to detect differences between groups in clinical cure rates, length of hospital stay, and mortality rates; often there was frequently been no difference between the antimicrobial stewardship group and the control groups (2).

While questioning the implementation of these strategies; each government regulates institutions to track and also report stewardship metrics. Instutions uses the data analysis programs include all antimicrobial sensitivity tests confirmed and completed in the laboratory. It should provide the ability to obtain test results along with the requirements listed below. Preferably, the system should be able to display the sample results even if antimicrobial testing of the detected microorganisms (if any) has not been performed (3). For identification of specimens sent to laboratories for purposes other than diagnosis of infection (e.g., infection control, quality control, proficiency testing, screening, surveillance) the system must have a separate mechanism. These quality assurance parameters are also included in standardized protocols. By the way; we create cumulative antibiograms; another parameter of antimicrobial stewardship; to predict empiric therapy. When generating the cumulative antibiogram; i.e., antibiotic susceptibility, only the first isolate of each species isolated from a patient in each evaluation period (e.g., one year), at the

body site where it was isolated, should be included in the data, regardless of profile or other phenotypic characteristics (e.g., biotype) (4).

At present, antimicrobial resistance is spreading throughout the world, and new mechanisms of resistance to older agents are emerging with resistance to new antibiotics (5). This topic has been the subject of numerous high-quality and timely scientific, economic, public health, and educational reports (6,7). While these reports deal with AST (antibiotic susceptibility testing), there are two basic diagnostic requirements related to AST. It is important for physicians to quickly identify antibiotics that can effectively treat patients infected with bacterial pathogens. Second, epidemiological application is required, that is, detection of phenotypic resistance mechanisms and surveillance of spread. AST monitoring provides surveillance data and helps develop strategies to control the spread of antimicrobial resistance (AMR) .The need to overcome barriers to the introduction of diagnostic devices (8,9). Among these following factors are barriers against adoption to antimicrobial stewardship so affecting income expense balance; each of which can be a paragraph on its own.

-Expertise of laboratory personel,

-Communication between clinicians and diagnosticians

-High cost of test

-Continous availability of the laboratory

-Lack of clinical outcome results' reports

-Cost of scientific studies

-Cost of development

-Poor info management and poor electronic records

-Finding clinical research partners (clinicians, laboratory directors, researchers, etc.)

-Intellectual complience on multiple innovations

-Decentralization of laboratories and non-networked steward ship teams

-Lack of appropriate pre-marketengagement

-Quality and availability of materials

-Admitting to the authorities about developmental processes

-Sample collection problems

-Transfer of samples

-Knowledge differences among clinicians about antimicrobial resistance

-Lack of funding

-Storage,transport,and stability of the test

-The limited exchange between diagnostic and pharmaceutical companies

-Lack of speed

-Availability of the test

-FDA validationand European certification (CE) including differences between -countries

-Biological hazard

-Ethical issues

-The insufficient exchange between the public and private sector
-Environmental aspects
-Health practices
-Communication (or lack there of)
-Lack of support programs

The implementation of new technological criteria is what we need to address at this point (8,9). Smart antibiograms should be created to incorporate a wide range of patient search parameters and demographic data into their calculations. This will facilitate the automatic fine-tuning of the smart antibiogram algorithms and increase their value in predicting the correct empirical antibiotic therapy for individual microorganisms detected in different clinical samples at different times in different wards and in different populations. Using past experience and intelligent databases, statistical approaches will be necessary to predict the correct antibiotic treatment. Several goals were achieved, such as; increased efficiency, digitally shifting tasks and addressing staffing bottlenecks, population health applications to enable targeted and differentiated services, earlier disease detection, improving the quality of clinical decision-making, continuous patient monitoring, and artificial intelligence (AI) applications used in pharmacy practice that can be categorized as prevention, diagnosis, and treatment.

For example the techniques presented with machine learning (ML) allows to anticipate the sensitivity results of the microbiology laboratory. Early identification of patients at high risk for resistance to specific antibiotics could provide clinicians with useful information for prescribing empiric therapy based on the local antibiotic resistance pattern. Implementation of such prescribing practices could have a significant impact on antimicrobial stewardship (10).

Another example is the gradient-doped decision tree (GBDT) model formed to predict the presence of isolates resistant to co-amoxiclav, ciprofloxacin, meropenem and piperacillin-tazobactam antimicrobial drugs. Predicting susceptibility to antimicrobials was a key consideration. The methodology can be used to help physicians reduce inappropriate use of antibiotic drugs (drugs unsuitable for a case being identified by high probability of AMR at admission) and select (11). In rapid diagnosis, cost-effectiveness and rapid and accurate screening of many samples at the same time are very important in the diagnosis and treatment of diseases. Mass spectrometry systems (eg, MALDI-TOF MS, Bruker) produced to meet these goals are a highly sensitive, very fast and low-cost, high-efficiency technology product used in the identification of microorganisms in the microbiology laboratory (12, 13). With this

system, after ionizing the biomolecules and large organic molecules of microorganisms, protein profiles are obtained by passing them through electric and magnetic fields. The graphical images obtained in this way are compared with the reference microorganisms in the database of the system and identifies the factors on the basis of genus and species according to their compatibility. MALDI-TOF MS creates fingerprints from proteins specific to each microorganism and thus identifies microorganisms (14).

Examples include: Nguyen et al. used machine learning to predict the minimum inhibitory concentrations (MICs) of Salmonella strains and predict their susceptibility to (15) antibiotics.1- Doctors Without Borders developed a microbiology tool for use in resource-limited settings that uses computer vision to read "zones of inhibition" to improve patient care. 2- Key factors to consider when evaluating an AI solution for healthcare (15).

Artificial intelligence (AI) systems can be utilized to differentiate individuals prone to COVID-19 by creating personalized and categorized systems. Characteristics such as underlying diseases (hypertension, heart failure, diabetes mellitus, etc.), blood test parameters (ACE2 expression level) and clinical data (age, respiratory parameters, viral load, etc.) of COVID-19 patients help to define risky situations, and by coding these data into systems, risk classification can be predicted by artificial intelligence systems. AI analysis of traits from asymptomatic, mild, or severe COVID-19 patients can be used to classify and predict people based on their vulnerability or resistance to potential COVID-19 infection (16). Regional differences of variant forms, which have recently been a serious threat in the COVID19 epidemic, can be followed instantly on websites such as ‘GSI-AD’ and ‘Nextstrain’, so the mutation/vaccine can be followed more closely (17).

Conclusion

The use of Big Data and the use of new techniques based on AI will become extremely important. As mentioned earlier, data is generated today from very different sources, with volumes on the order of exabytes; however, these must be exploited. Application of artificial intelligence in healthcareis not practised enough to be used efficiently. Moreover, ever since having covered the basics of AI, the question is how to apply these advanced technologies to healthcare.

References

1. Antimicrobial report- Bracing for Superbugs. UN environment reports United Nations Environment Programme. 2023;978-92-807-4006-6.
2. Baur D, Gladstone BP, Burkert F , et al. Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and Clostridium difficile infection:a systeatic review and meta-analysis. The Lancet infect. Disease. 2017;17(9) :990-1001.

3. A guide to antibiotic susceptibility data analysis and presentation formedical microbiologists. Klimud(ClinicalMicrobiologyAssociation)publ ications.2019; 15-20.
4. Kohlmann R., Gatermann SG. Analysis and presentation of cumulative antimicrobial susceptibility test data- The influence of different parameters in a routine clinical microbiology laboratory. Plos One 2016; 11(1).
5. Liu YY, Wang Y, Walsh TR, et al. Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. Lancet Infect. Dis. 2016;16, 161–8.
6. Lübbert C, Baars C, Dayakar A, et al. Environmental pollution with antimicrobial agents from bulk drug manufacturing industries in Hyderabad, South India, is associated with dissemination of extended-spectrum β-lactamase and carbapenemase- 2017 Aug; 45(4): 479-491.
7. Review on antimicrobial resistance. Tackling drug- resistant infections globally: final report and recommendations /AMR, 2016.
8. World Health Organization Library Cataloguing inPublication Data. Global action plan on antimicrobial resistance /WHO, 2015.
9. Rolfe R,Jr, Kwobah C, Muro F, et al. Barriers to implementing antimicrobial stewardship programs in three low- and middle-income country tertiary care settings: findings from a multi-site qualitative study. Antimicrob Resist Infect Control. 2021; 10:60.
10. Belkum AV, Bachmann TT, Lüdke G. Developmental roadmap for antimicrobial susceptibility testing systems.Nature Reviews Microbiology, volume /2019; 17:50-5.
11. Feretzakis G, Loupelis E, Sakagianni A, et al. Using Machine Learning Algorithms to Predict Antimicrobial Resistance and Assist Empirical Treatment The Importance of Health Informatics in Public Health during a Pandemic. 2020 June. doi:10.3233/SHTI200497
12. Cavallaro M., Moran E., Collyer B., et al. Informing antimicrobial stewardship with explainable AI. Plos Digital Health 2023 Jan 5. https://doi.org/10.1371/journal.pdig.0000162.
13. Croxatto A, Prod'hom G, Greub. Applications of MALDI-TOF Mass Spectrometry in Clinical Diagnostic Microbiology. FEMS Microbiol Rev. 2012;36(2): 380-407.
14. Wieser A, Schneider L, Jung J,et al. MALDI-TOF MS in Microbiological Diagnostics Identification of Microorganisms and Beyond. Appl Microbiol Biotechnol. 2012;93(3):965-74.
15. Anhalt JP, Fenselau C. Identification of Bacteria Using Mass Spectrometry. Anal Chem. 1975;47: 219-25.
16. Nguyen M, Long SW, McDermott PF, et al. Using Machine Learning to predict antimicrobial MICs and associated genomic features for Nontyphoidal Salmonella. J Clin Microbiol. 2019, 30;57(2):e01260-18.
17. Alimadadi A, Aryal S, Manandhar I, et al. Artificial Intelligence and Machine Learning to Fight COVID-19. Physiol Genomics. 2020 Apr 1;52(4):200-2.
18. Altindis M. Yapay zekanın mikrobiyolojide kullanımı. Sağlıkta yapay zeka. Medipol Üniversitesi yayınları 2021-58.

Experimental and Applied Medical Science, 5, 3: 137-149, 2024. DOI: 10.46871/eams.1456744

The Promise and the Challenge: Large Language Models for Patient Education - Are We There Yet?

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Abstract

Purpose: *This study aimed to evaluate the potential of large language models (LLMs) for delivering patient education materials.*

Methods: *Two LLMs, Gemini and ChatGPT 3.5, were analysed for their ability to provide clear and understandable information on the topic of blepharitis, a common eye condition.*

The understandability and actionability of the information provided by the LLMs in response to a set of questions were evaluated using PEMAT, a standardised tool for assessing educational materials.

Results: *The responses included the important aspects of blepharitis, yet the Flesch-Kincaid readability scores were below the suggested range of 60-70 for patient education materials. Gemini received a score of 38.75, whereas ChatGPT 3.5 earned 26.35, suggesting that the content might be too intricate for the target audience.*

Conclusion: *These findings suggest that while LLMs have the potential to be informative resources, their current readability levels may limit their effectiveness in providing accessible health information to patients. Further research is needed to explore methods for adapting LLM outputs to ensure clear and concise communication suitable for patient education.*

Key words: *Large Language Models (LLMs); Patient Education; Readability; Blepharitis; Natural Language Processing (NLP); Health Communication*

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Introduction

The human eye, a complex and delicate organ, is susceptible to various conditions that can significantly impact vision and overall well-being. Blepharitis, a chronic inflammatory condition affecting the eyelids, is a prevalent ocular disease with an estimated global prevalence ranging from 33% to 50% (1, 2). The primary manifestation of blepharitis is inflammation of the eyelid margins, often accompanied by symptoms like redness, irritation, stinging, burning, crusting, and even eyelash loss (3).

Blepharitis can be classified into two main types based on the location of the inflammation:

Anterior blepharitis affects the anterior eyelid structures, including the eyelid skin, base of the eyelashes, and the eyelash follicles. It can be further subcategorized as staphylococcal blepharitis, caused by an overgrowth of Staphylococcus bacteria, or seborrheic blepharitis, associated with seborrheic dermatitis, a condition that causes redness, scaling, and inflammation of the scalp and other oily areas of the body (4).

Posterior blepharitis, also known as meibomian gland dysfunction (MGD), affects the meibomian glands located within the eyelids. The International Workshop on Meibomian Gland Dysfunction defines MGD as a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion. MGD is considered to be the most common cause of evaporative dry eye disease, a condition in which the tears evaporate too quickly due to insufficient oil production by the meibomian glands. MGD can also occur in conjunction with anterior blepharitis (5, 6).

The Significance of Patient Education in Blepharitis Management

Effective blepharitis management relies on a multifaceted approach that includes proper lid hygiene, warm compresses, and sometimes topical medications or oral antibiotics (4). However, the cornerstone of successful treatment lies in patient education. Empowering patients with accurate and comprehensive knowledge about their condition equips them to actively participate in their own care and adhere to prescribed treatment regimens (7).

Limitations of Traditional Patient Education Methods

Traditionally, patient education on blepharitis has relied on methods such as brochures, websites, and in-person consultations with ophthalmologists. While these methods can provide valuable information, they often lack accessibility,

engagement, and personalization (8). Busy schedules, complex medical jargon, and information overload can prevent effective knowledge transfer. Brochures and websites may not be readily available to patients, particularly those in underserved communities or with limited technological access. Additionally, the information presented in these materials may be written in complex medical language that is difficult for patients to understand. In-person consultations, while offering the opportunity for personalized interaction, can be time-consuming for both patients and healthcare professionals, limiting the frequency and depth of education provided.

The Rise of Chatbots and their Potential for Patient Education

The emergence of chatbots, conversational AI (artificial intelligence) programs designed to simulate human conversation, presents a novel and potentially transformative approach to patient education. Chatbots can offer readily accessible, interactive, and on-demand information delivery, potentially overcoming some of the limitations of traditional methods (9).

Within the healthcare domain, chatbots hold immense promises for disseminating health information, promoting patient engagement, and even offering basic symptom assessment and triage. Studies have explored the application of chatbots in various areas. This list is not exhaustive, but it effectively highlights the diverse applications of chatbots in healthcare education and support (9, 10).

Research Gap and Rationale for the Study

While research has begun to explore the potential of chatbots in healthcare education, their application to educating patients about blepharitis remains relatively unexplored. Given the prevalence of blepharitis and the crucial role of patient education in its management, investigating the efficacy of chatbots in this context can be highly valuable.

This study aims to address this gap in knowledge by assessing the quality and reliability of information delivered by chatbots on blepharitis compared to a trusted source (the American Academy of Ophthalmology website). By evaluating chatbot responses using established scoring tools employed by ophthalmologists, this research will offer insights into the potential of chatbots to serve as a complementary tool for patients.

Materials and Methods

This study used a descriptive comparative design to evaluate the quality and reliability of information delivered by chatbots on blepharitis compared to a trusted source, the American Academy of Ophthalmology (AAO) website.

Selection of Frequently Asked Questions (FAQs) on Blepharitis

To ensure a comprehensive and representative sample of patient concerns, a two-step process was used to select the FAQs on blepharitis.

Step 1: The AAO website's "Eye Conditions" and “Ask an ophthalmologist” sections were visited. From this webpage, the twenty (20) most frequently asked questions (FAQs) were identified and documented. This initial selection ensures the chosen questions reflect the most common patient inquiries about blepharitis.

Step 2: Two ophthalmologists, independent of the study team, reviewed the twenty (20) initial FAQs.

This two-step approach ensures the selected FAQs represent a combination of the most commonly viewed questions on the AAO website and additional questions deemed crucial by ophthalmologists for comprehensive patient education.

Selection of Chatbots

Two large language models (LLMs) will be chosen for this study: Gemini and ChatGPT 3.5.

Gemini, developed by Google, is a generative AI that can generate text, answer questions, and perform tasks similar to ChatGPT. It’s known for its multimodal capabilities, allowing it to produce not only text but also images, video, audio, and code. Initially launched as Bard, it was later upgraded to the Gemini large language model and rebranded, offering various tiers for different user needs.

ChatGPT 3.5 is a conversational AI developed by OpenAI, capable of understanding and generating human-like text. It supports a wide range of languages and is fine-tuned for conversational applications, though it performs best in English. The model is built on a transformer architecture and can be used for various tasks, from answering questions to creative writing and code generation.

The data sources were responses to 20 frequently asked questions about blepharitis on the AAO website and outputs from ChatGPT 3.5 and Gemini to these questions as prompts.

As of March 3, 2024, we accessed the latest versions of chatbots on the websites of ChatGPT free version (which uses the GPT-3.5 engine) and Gemini of Google. The chat history and cache of each chatbot was cleared before the next question. This was done to ensure that each chatbot did not remember or use any previous information or conversation in answering the questions.

Expertise of Participating Ophthalmologists

Two ophthalmologists, board-certified in ophthalmology and with experience managing blepharitis, will be recruited to participate in this study. Their expertise in diagnosing and treating blepharitis is

crucial for evaluating the accuracy, comprehensiveness, and appropriateness of the information delivered by the chatbots.

Prior to commencing the evaluation, the ophthalmologists were briefed on the study objectives and methodology. They were provided with a standardized scoring sheet outlining the specific criteria for each assessment tool. The responses were blinded to evaluators before scoring.

Scoring Tools for Chatbot Response Evaluation

Three established scoring tools will be employed to evaluate the quality and reliability of the chatbot responses:

Patient Education Material Assessment Tool (PEMAT): The PEMAT is a standardized tool used to assess the understandability and actionability of educational materials for patients (11). It consists of two subscales:

PEMAT-U (Understandability) assesses factors like clarity, organization, layout, and use of language (17 items). Scores are calculated as a percentage (0-100%) with higher scores indicating better understandability for patients.

PEMAT-A (Actionability) assesses the specificity, practicability, and effectiveness of suggested actions (7 items). Scores are also calculated as a percentage (0-100%) with higher scores indicating clearer and more actionable information for patients.

SOLO Taxonomy (1-5): Developed by Biggs and Collis, the SOLO Taxonomy is a framework that categorizes the level of cognitive demand required to understand information (12). This tool will be used to assess the complexity and depth of knowledge conveyed in the chatbot responses. The SOLO Taxonomy categorizes learning outcomes into five levels:

Prestructural: Responses at this level demonstrate a lack of understanding of the question or task.

Unistructural: Responses focus on a single, isolated fact or aspect of the topic.

Multistructural: Responses include multiple facts or details but lack connection or integration.

Relational: Responses demonstrate a relational understanding by connecting different aspects of the topic or explaining cause-and-effect relationships.

Extended Abstract: Responses at this highest level demonstrate a deep and comprehensive understanding of the topic. They may involve applying knowledge to new situations, making generalizations, or drawing critical judgments.

By analysing the SOLO Taxonomy level of the chatbot responses, the ophthalmologists can assess whether the information provided is appropriate for patient education and fosters a deeper understanding of blepharitis.

Flesch-Kincaid Readability Ease Score (0-100): The Flesch-Kincaid readability ease score is a metric used to assess the reading difficulty of a text. It is calculated based on the average number of words per sentence and the average number of syllables per word. Higher scores indicate easier readability, with scores ranging from 0 (most difficult) to 100 (easiest). A score of 60-70 corresponds to a typical eighth or ninth grade reading level, which is considered a suitable target for patient education materials (13). This ensures the information is comprehensible for a broad audience of patients with varying levels of education.

The Flesch-Kincaid score was used to evaluate the readability of the chatbot responses. Scores within the 60-70 range will be considered optimal for patient education materials on blepharitis.

Data Analysis

Following the scoring, the collected data was analysed using descriptive statistics. This involved calculating measures of central tendency (mean, median) and dispersion (standard deviation) for the scores obtained from each evaluation tool (PEMAT-U, PEMAT-A, SOLO Taxonomy, and Flesch-Kincaid).

Additionally, a comparative analysis (independent sample t-test or Mann Whitney U) was performed to assess any significant differences between the information quality provided by the two chatbots (Gemini and ChatGPT 3.5) and the information from the trusted source (AAO website).

Ethical Considerations

Since this project does not involve human subjects, approval from the Institutional Review Board was not required.

Results

The data presented in Table 1 allows for a comparative analysis of the information quality, reliability, and readability provided by the chatbots (Gemini and ChatGPT 3.5.)

Understandability (PEMAT-U): Both chatbots achieved scores exceeding 78% on the PEMAT-U understandability subscale, indicating that the information they delivered was generally clear and easy for patients to comprehend. A statistical analysis using an independent samples t-test revealed a trend towards higher scores for Gemini compared to ChatGPT 3.5. However, this difference did not reach statistical significance at the alpha level of 0.05 ($p=0.152$).

Table 1. Scores from Ophthalmologist Evaluations.

Scoring Tool	Chatbot	Ophthalmologist 1 (Mean)	Ophthalmologist 2 (Mean)	Mean Score (SD)
PEMAT-U (Understandability)	Gemini	82%	85%	83.5% (9.42)
	ChatGPT 3.5	78%	80%	79.0% (8.91)
PEMAT-A (Actionability)	Gemini	49%	50%	49.5% (10.21)
	ChatGPT 3.5	45%	48%	46.5% (8.89)
SOLO Taxonomy	Gemini	3.5	3.5	3.5 Relational (0.51)
	ChatGPT 3.5	3.5	3.4	3.45 Relational (0.6)
Flesch-Kincaid Readability*	Gemini			38.75 (8.3)
	ChatGPT 3.5			26.35 (8.73)

*p<0.001

Actionability (PEMAT-A): Scores on the PEMAT-A actionability subscale were lower than understandability scores for both chatbots. While the information provided was understandable, it could be further improved in terms of offering specific and actionable steps for patients to manage their blepharitis. Gemini again received slightly higher scores, indicating a relatively clearer presentation of recommended actions for patients. Mann Whitney U test analysis showed a non-significant difference between Gemini and ChatGPT 3.5 (p=0.28462).

Depth of Knowledge (SOLO Taxonomy): Both ophthalmologists categorized the responses from both chatbots as almost reaching the "Relational" level within the SOLO Taxonomy. This indicates that the chatbots were able to connect different aspects of blepharitis and explain cause-and-effect relationships, demonstrating a

more comprehensive understanding of the condition than isolated facts. Mann Whitney U test analysis showed a non-significant difference between Gemini and ChatGPT 3.5 (p=0.90448).

Readability (Flesch-Kincaid ease): The Flesch-Kincaid scores for both chatbots fell below the 60-70 range (Gemini:38.75, ChatGPT 3.5: 26.35), which is considered poor score for patient education materials. A statistically significant difference was found between the chatbots (t(2)=4.60, p=0.00004557). Gemini scored higher than ChatGPT 3.5 suggesting advantage in readability for Gemini's responses.

Table 2. Comparison of Information Depth (SOLO Taxonomy) of chatbots and the AAO website.

FAQ Topic	Chatbot Response (Level)	AAO Website FAQ (Level)
Symptoms of Blepharitis	Relational (Both Chatbots)	Relational
Causes of Blepharitis	Relational (Both Chatbots)	Extended Abstract
Treatment Options for Blepharitis	Multistructural (Both Chatbots)	Relational
Preventing Blepharitis	Multistructural (Both Chatbots)	Relational

Table 2 allows for a more granular comparison of how each FAQ topic is addressed by the chatbots and the AAO website.

It highlights that while the chatbots can demonstrate a relational understanding by connecting different aspects of blepharitis, the AAO website, likely due to its creation by medical professionals, may delve deeper into certain topics, reaching the "Extended Abstract" level.

Table 3. Inter-Rater Reliability for Ophthalmologist Evaluations.

Scoring Tool	Kappa Statistic
PEMAT-U (Understandability)	0.85
PEMAT-A (Actionability)	0.80
SOLO Taxonomy	0.75

Table 3 presents the Kappa statistic, a measure of inter-rater reliability between the two ophthalmologists who evaluated the chatbot responses. All Kappa values fall within the "substantial" agreement range according to benchmarks (14). This indicates a good level of consistency between the ophthalmologists in their scoring of the information provided by the chatbots using the PEMAT and SOLO Taxonomy tools. This strengthens confidence in the overall findings of the study.

Discussion

Leveraging Chatbots for Enhanced Patient Education in Ophthalmology

This study investigated the potential of chatbots as a tool for patient education on blepharitis. By analysing information quality, readability, and actionability, the research yielded valuable insights into both the strengths and weaknesses of this emerging technology in healthcare.

Strengths of Chatbot Information for Patient Education

The findings revealed that both Gemini and ChatGPT 3.5 delivered information on blepharitis that was generally clear and understandable (PEMAT-U scores exceeding 78%). This aligns with existing research highlighting the potential of chatbots to simplify complex medical topics for patients (15-17). Conversational agents, with their ability to access and process vast amounts of text data and generate human-like conversation, empowers patients by providing them with on-demand access to a wealth of medical knowledge (18).

Furthermore, both chatbots demonstrated a close to relational understanding of blepharitis, connecting various aspects of the condition and explaining cause-and-effect relationships (SOLO Taxonomy). This aligns with studies suggesting that chatbots can go beyond isolated facts, presenting a more comprehensive picture of

health topics (19, 20). This can be particularly beneficial for patients seeking to understand the underlying mechanisms of their condition and how their behaviours or lifestyle choices might influence it.

Beyond basic information delivery, the chatbots also offered some actionable recommendations, such as maintaining lid hygiene and using warm compresses. While there is room for improvement (lower PEMAT-A scores suggesting a need for more specific action steps), these initial steps could empower patients to take a more active role in managing their blepharitis. This aligns with the growing emphasis on patient-centred care and self-management of chronic conditions (21). However, it is important to acknowledge that, chatbots in their current form are not designed to provide definitive medical advice. Their reliance on training data, which may include outdated information, necessitates human oversight and fact-checking before delivering chatbot-generated content to patients.

Despite these strengths, the study also revealed areas for improvement in chatbot-delivered patient education. Analysis of readability scores revealed that the Flesch-Kincaid ease score for both chatbots fell below the recommended range for patient education materials (60-70). Specifically, the scores for Gemini and ChatGPT 3.5 were 38.75 and 26.35, respectively. This suggests that the information presented by the chatbots may be too complex for the intended audience of patients seeking health information.

One key limitation was the lack of in-depth information compared to the AAO website (SOLO Taxonomy). While chatbots reached close to relational level, the website potentially reached an extended abstract level, providing a more nuanced and detailed understanding. This highlights the current limitations of chatbots in replicating the comprehensiveness of established medical resources (22).

Chatbots medical knowledge bases could be enhanced by integrating with established databases and collaborating with ophthalmologists to curate information. This provides a more nuanced understanding of eye conditions, including potential variations and treatment considerations. Additionally, chatbots can personalize recommendations, empowering patients to take an active role in managing their condition by suggesting specific treatment approaches or medication use (23).

Another area for improvement is the provision of actionable recommendations. The chatbots primarily focused on general hygiene practices, and specific details regarding treatment options or medication use were often lacking. This could be due to limitations in the chatbot's programming or

the need for further development to tailor recommendations to individual patients' needs, as discussed earlier.

Developing chatbots with multilingual functionalities can improve accessibility for patients with diverse linguistic backgrounds. This is crucial for ensuring equitable access to health information and empowering patients from all communities to actively participate in their healthcare (24). Imagine a chatbot that can seamlessly switch between languages based on the patient's preference, ensuring they receive clear and accurate information regardless of their native tongue (25).

Ethical Considerations and Human Oversight

Furthermore, the role of human oversight and ethical considerations should remain paramount in the development and implementation of chatbots for patient education. Integrating chatbots into ophthalmic care should be done in a way that complements, not replaces, the expertise of healthcare professionals. Chatbots can act as a first point of contact, providing basic information and education while directing patients to seek professional medical advice for diagnosis and treatment decisions. Additionally, ensuring data privacy and security is crucial when collecting and storing patient information through chatbots (26).

The current study acknowledges several limitations. Firstly, it focused on evaluating only two large language models (Gemini and ChatGPT 3.5). The evolving landscape of chatbot development suggests that a wider range of chatbots with potentially different functionalities and information delivery approaches might yield varying results. Future research should explore a more diverse selection of chatbots to provide a more comprehensive understanding of their capabilities in patient education.

Secondly, using convenience sampling method, the study evaluated a limited set of FAQs on blepharitis. While these FAQs covered core aspects of the condition, a broader range of topics could reveal additional strengths or weaknesses in the chatbots' information delivery. Additionally, the information provided by the AAO website, used as a benchmark, might not encompass the full spectrum of details a medical professional would address during a consultation. Expanding the scope of evaluated topics and incorporating consultations with ophthalmologists as a reference point could provide a more holistic understanding of how chatbots compare to traditional patient education methods.

Conclusion

The findings of this study suggest that chatbots hold promise as valuable tools for patient education on blepharitis. They can deliver clear, understandable, and relatable information, potentially empowering patients and improving their health literacy. However, there is room for improvement in terms of comprehensiveness, personalization of recommendations, and interactivity. Future research should explore these areas while emphasizing the importance of human oversight, ethical considerations, and data privacy. As chatbot technology continues to evolve, ophthalmologists and healthcare professionals have the opportunity to leverage these advancements to enhance patient education, promote self-management of eye conditions, and ultimately improve patient care outcomes.

Acknowledgements

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author(s) used QuillBot tool to improve language and readability, with caution. After using this tool/service, the author(s) reviewed and edited the content as needed and took full responsibility for the content of the publication.

Conflict of Interest

The authors declare no conflict of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Eberhardt M, Rammohan G. Blepharitis. In: StatPearls. Treasure Island (FL): StatPearls Publishing; January 23, 2023.
2. Trattler W, Karpecki P, Rapoport Y, et al. The Prevalence of Demodex Blepharitis in US Eye Care Clinic Patients as Determined by Collarettes: A Pathognomonic Sign. Clinical Ophthalmology 2022;16; doi: 10.2147/OPTH.S354692.
3. Pflugfelder SC, Karpecki PM, Perez VL. Treatment of blepharitis: Recent clinical trials. Ocular Surface 2014;12(4):273–284; doi: 10.1016/j.jtos.2014.05.005.
4. Duncan K, Jeng BH. Medical Management of Blepharitis. Curr Opin Ophthalmol 2015;26(4); doi: 10.1097/ICU.0000000000000164.
5. Shah PP, Stein RL, Perry HD. Update on the Management of Demodex Blepharitis. Cornea 2022;41(8); doi: 10.1097/ICO.0000000000002911.
6. Nichols KK, Foulks GN, Bron AJ, et al. The International Workshop on Meibomian Gland Dysfunction: Executive Summary. Investigative Opthalmology & Visual Science 2011;52(4):1922; doi: 10.1167/iovs.10-6997a.
7. Rhodes L, Huisingh C, McGwin G, et al. Eye Care Quality and Accessibility Improvement in the Community (EQUALITY): impact of an eye health education program on patient knowledge about glaucoma and attitudes about eye care. Patient Relat Outcome Meas 2016; doi: 10.2147/prom.s98686.
8. Görtz M, Baumgärtner K, Schmid T, et al. An artificial intelligence-based chatbot for prostate cancer education: Design and patient evaluation study. Digit Health 2023;9. doi: 10.1177/20552076231173304.

9. Frangoudes F, Hadjiaros M, Schiza EC, et al. An Overview of the Use of Chatbots in Medical and Healthcare Education. Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics) 2021;12785 LNCS:170–184; doi: 10.1007/978-3-030-77943-6_11/cover.
10. Chaix B, Bibault JE, Pienkowski A, et al. When chatbots meet patients: One-year prospective study of conversations between patients with breast cancer and a chatbot. JMIR Cancer 2019;5(1); doi: 10.2196/12856.
11. PEMAT for Printable Materials (PEMAT-P) | Agency for Healthcare Research and Quality. Available from: https://www.ahrq.gov/health-literacy/patient-education/pemat-p.html.
12. Biggs J, Collis K. Evaluating the Quality of Learning: The SOLO Taxonomy (Structure of the Observed Learning Outcome). 2014.
13. Kincaid PJ. Derivation of New Readability Formulas. Naval Technical Training Command Millington TN Research Branch 1975;(February).
14. Cohen J. A Coefficient of Agreement for Nominal Scales. Educ Psychol Meas 1960;20(1); doi: 10.1177/001316446002000104.
15. Sallam M. ChatGPT Utility in Healthcare Education, Research, and Practice: Systematic Review on the Promising Perspectives and Valid Concerns. Healthcare (Switzerland) 2023;11(6); doi: 10.3390/healthcare11060887.
16. Zheng Y, Wang L, Feng B, et al. Innovating Healthcare: The Role of ChatGPT in Streamlining Hospital Workflow in the Future. Ann Biomed Eng 2023; doi: 10.1007/S10439-023-03323-W.
17. Cascella M, Montomoli J, Bellini V, et al. Evaluating the Feasibility of ChatGPT in Healthcare: An Analysis of Multiple Clinical and Research Scenarios. J Med Syst 2023;47(1); doi: 10.1007/S10916-023-01925-4.
18. Laranjo L, Dunn AG, Tong HL, et al. Conversational agents in healthcare: A systematic review. Journal of the American Medical Informatics Association 2018;25(9):1248–1258; doi: 10.1093/jamia/ocy072.
19. Car LT, Dhinagaran DA, Kyaw BM, et al. Conversational agents in health care: Scoping review and conceptual analysis. J Med Internet Res 2020;22(8); doi: 10.2196/17158.
20. Ayers JW, Zhu Z, Poliak A, et al. Evaluating Artificial Intelligence Responses to Public Health Questions. JAMA Netw Open 2023;6(6); doi: 10.1001/jamanetworkopen.2023.17517.
21. Wu Q, Jiang S. The Effects of Patient-Centered Communication on Emotional Health: Examining the Roles of Self-Efficacy, Information Seeking Frustration, and Social Media Use. J Health Commun 2023;28(6):349–359; doi: 10.1080/10810730.2023.2208537.
22. Bhirud N, Tatale S, Randive S, et al. A Literature Review On Chatbots In Healthcare Domain. 2019.
23. Lin J, Joseph T, Parga-Belinkie JJ, et al. Development of a practical training method for a healthcare artificial intelligence (AI) chatbot. BMJ Innov 2021;7(2):441–444; doi: 10.1136/bmjinnov-2020-000530.
24. Multilingualism and WHO. n.d. Available from: https://www.who.int/about/policies/multilingualism.
25. Crossing the Quality Chasm: A New Health System for the 21st Century. 2001; doi: 10.17226/10027.
26. Li H, Moon JT, Purkayastha S, et al. Ethics of large language models in medicine and medical research. Lancet Digit Health 2023;5(6):e333–e335; doi: 10.1016/S2589-7500(23)00083-3.

Experimental and Applied Medical Science, 5, 3: 150-159, 2024. DOI: 10.46871/eams.1463163

Reliability of Thyroid Imaging Reporting and Data Systems' Scoring in the Evaluation of Thyroid Nodules

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Abstract

It is known that Thyroid Ultrasonography (US), guided by Fine Needle Aspiration (FNA), is a cost-effective and safe diagnostic method for evaluating thyroid nodules. Our purpose in the present study is to determine the reliability of the Thyroid Imaging Reporting and Data Systems (TIRADS) Scoring System for the evaluation of thyroid nodules. A total of 724 patients who were followed up in our endocrinology and general surgery clinic and operated on with the diagnosis of multinodular and nodular goiter were included in the study. The malignancy risk rate of all TIRADS categories was analyzed according to postoperative pathology results. Among the 724 patients, who were included in the study, preoperative FNA results were as 11.04% (n=80) benign, follicular, Hurthle cell neoplasia or suspected 8.83% (n=64), malignancy suspected 40.33% (n=292) and malignant 39.77% (n=288). We determined in the study that the malignancy was 72.15% (n=228) in TR-4 nodules and 97.1% (n=336) in TR-5 nodules. No correlations were detected between anti-TPO, anti-TG, TSH level, and malignancy. TIRADS Scoring System was successful in predicting malignancy rates in the present study.

Key words: *FNA biopsy, Risk assessment, Risk factors, TIRADS, Ultrasonography*

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Introduction

It is known that Thyroid Ultrasonography (US) guided by Fine Needle Aspiration (FNA) is a cost-effective and safe diagnostic method for evaluating thyroid nodules (1). It was shown that Thyroid FNA has a sensitivity of 65-99%, and a specificity of 72-100%, with a high positive predictive value (97-99%). However, with FNA, 10-42% of cases are detected as non-diagnostic in nodules and follicular lesions with unknown importance at 3-18% (2, 3). Despite these known limitations of FNA, the optimal management of these nodules has not yet been fully identified. Thyroid cancer has no typical sonographic model. Previous sonographic criteria were suggested to estimate malignancy risk in thyroid nodules (4). Thyroid Imaging Reporting and Data Systems (TIRADS) scoring methods (EU-TIRADS, ACR TI-RADS, and Kwak-TIRADS) based on nodule models by thyroid ultrasonography were published for risk classification of thyroid nodules (5-7). This scoring system identifies the thyroid nodule risk level according to appearance in ultrasonography. The risk of cancer in thyroid nodules is collected under five categories from TIRADS 1 to TIRADS 5. FNA and follow-up are recommended according to this risk status (8).

The present study aimed to determine ultrasonographic findings' diagnostic performance and reliability over TIRADS methods.

Methods

Ethics Committee Approval: This study was conducted in accordance with the ethical rules with the approval of Medicana International Samsun Hospital's clinical research ethics committee (Date: 20.04.2021, decision no: 7129).

Study Design: Patients were included in the study who operated on and followed up in our endocrinology and general surgery clinic with the diagnosis of multinodular and/or nodular goiter between September 2015 and April 2021. Among these patients, 724 individuals (456 females, 268 males) with complete detailed thyroid ultrasound scan reports, FNA cytology, and histopathology reports were included in the study. Patients with incomplete data were excluded. The demographic characteristics of the patients, preoperative thyroid ultrasound findings, FNA cytology reports, and histopathological analysis results were collected from the patient files and electronic records.

Data Collection: EU-TIRADS categories are evaluated in 5 main categories as EU-TIRADS 1: normal, EU-TIRADS 2: benign, EU-TIRADS 3: low risk, EU-TIRADS 4: intermediate risk and EU-

TIRADS 5: high risk (15). In our study, EU-TIRADS category 2, 3, 4 and 5 (TR 2, TR 3, TR 4 and TR 5), FNA reports and histopathologic distribution of thyroid cancers data were collected. FNA is performed through EU-TIRADS suggestions. The patients with follicular neoplasia, suspected malignancy, and positive malignancy findings in the FNA cytology report were operated on. Some patients with benign findings in the FNA cytology report presenting indications for aesthetic appearance and compression findings were also operated on. Benign and malignant rates of thyroid nodules were determined according to TIRADS classification, and the diffusion of the thyroid cancer was determined according to histopathology reports. Cases whose EU-TIRADS score was determined by criteria such as echogenicity, microlobulation, irregular edges, microcalcifications, pure cystic feature, spongy appearance, oval, or not in the preoperative thyroid US report made by an experienced endocrinologist were selected and included in the study.

In addition, intranodular rough calcifications, intermittent calcifications on the nodule wall, a nodule with intense blood supply, and solid nodules detected by Elastsonography are classified as TR-4 except four ultrasonographic characteristics which are highly suspicious for malignancy were classified as TR-4 (Figure 1).

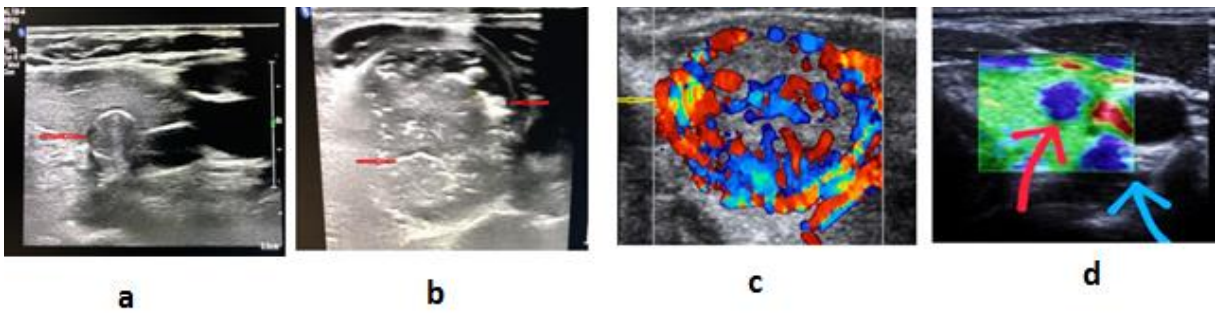

Figure 1. Intermittent calcifications in the thyroid nodule wall. **a**: coarse intranodal calcifications; **b**: intensely bloody nodule; **c**: and hard nodules on elastsonography; **d**: in TIRADS 4 categories.

The Ultrasound Scan (USS) reports of thyroid patients are recorded electronically in files of the endocrinology clinic of our hospital. Thyroid USS is performed in our endocrinology clinic during pre- and postoperative follow-ups in our hospital. Thyroid Ultrasonography was performed with high-resolution apparatus equipped with eL18-4 MHz broadband linear array probe (The Philips Affinity 70 ultrasound; Philips North America Corporation, 3000 Minuteman Road M/S 109 Andover, MA 01810, USA). All the procedures were performed by an experienced person.

Statistical Analyses: The SPSS 22.0 (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis. Categorical variables were expressed as frequency and percentage values, continious variables as arithmetic mean and standard deviation. Statistical significance level was taken as $p<0.05$

Results

Of the 724 patients included in the study, 456 were female and 268 were male. The mean age of the patients was 48.15±11.7. Demographic data and thyroid function fold test parameter values of the patients are shown in Table 1.

Table 1. Demographic data and thyroid function fold test parameter values of the patients.

Parameters		**n/mean±standard deviation**
Gender	Female	456
	Male	268
Age (Years) SD		48.15±11.7
TSH, mIU/L		2.82±1.4
Anti-TPO, IU/mL		135.3±38.7
Anti-TG, IU/mL		91.5±13.7

TPOAb: Anti-thyroperoxidase autoantibodies; TgAb: Anti-thyroglobulin antibody.

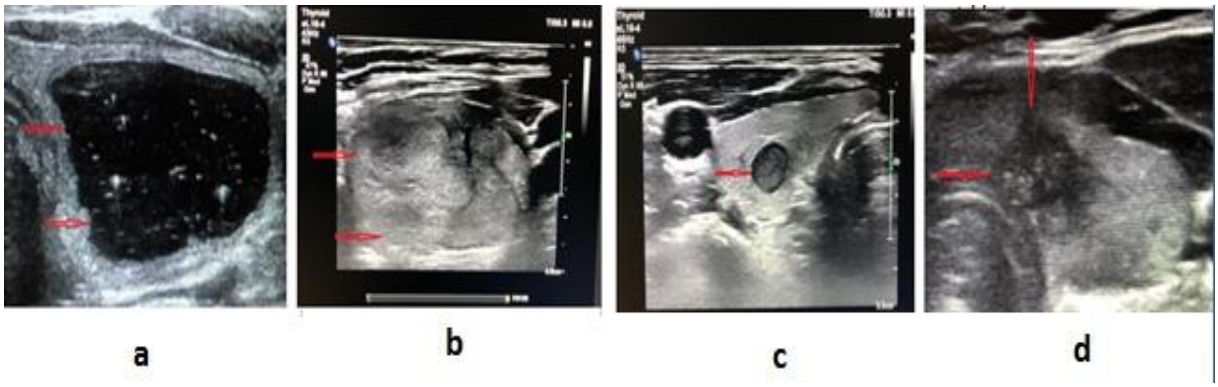

Figure 2. TIRADS categories and risk of malignancy.

TR-2, **a:** TR-3, ovoid, smooth, isoechoic or hyperechoic, no features of high suspicion, malignancy risk, 2-4%; **b:** TR-4, ovoid, smooth, mildly hypoechoic, no features of high suspicion, malignancy risk, ~6-17%; **c:** TR-5, at least 1 of the following features of high suspicion; **d:** Irregular shape, irregular margins, microcalcifications, marked hypoechogenicity (and solid), malignancy risk, 26-87%.

TIRADS categories and malignancy risk are shown in figure 2. Of 80 benign FNA patients, 20 (25.0%) were TR-2, 41 (51.2%) were TR-3, 14 (17.5%) were TR-4 and 5 (6.25%) were TR-5. Distribution of the cases according to TI-RADS Classification, FNA reports and histopathologic distribution of thyroid cancers were given Table 2. All of these patients were operated on within the scope of the indication. The FNA analysis result of 724 patients who have been operated on was as follows: benign by 11.04% (n=80), follicular, hurtle cell neoplasia or suspected hurtle cell neoplasia by 8.83% (n=64), suspected malignancy by 40.33% (n=292), malignancy by 39.77% (n=288).

The histopathological analysis results were nodular goiter, benign by 21.27% (n=154), malignancy by 77.9% (n=564), and lesion with unknown malignancy potential by 0.82% (n=6). Histopathological distribution of these cancers was papillary cancer at % 90.42 (n=510), follicular cancer at 7.44% (n=42), and medullary cancer at 2.12% (n=12) (Table 2). Intermittent calcifications in the thyroid nodule wall are shown in Figure 2. We detected the sensitivity and specificity of TIRADS classification as 100% and 67.5%, respectively. The positive and negative predictive values were 88.5% and 97%, respectively. These findings are shown in Table 3.

Table 2. Distribution of the cases according to TI-RADS Classification, FNA reports and histopathologic distribution of thyroid cancers.

Parameters	**TR-2 n (%)**	**TR-3 n (%)**	**TR-4 n (%)**	**TR-5 n (%)**
FNA benign, n=80	20 (100)	41 (97.6)	14 (4.4)	5 (1.4)
FNA follicular, Hurthle Cell neoplasia or suspicion, n=64	-	1 (2.3)	48 (15.1)	15 (4.3)
FNA malignity suspicion, n=292	-	-	153 (48.4)	139 (40.1)
FNA malignant, n=288	-	-	101 (31.9)	187 (5.4)
Histopathologically benign, n=154	20 (100)	**41 (97.6)**	85 (26.8)	8 (2.3)
Histopathologically malignant, n=564	-	-	228 (72.1)	336 (97.1)
Histopathological malignity potential unclear, n=6	-	1 (2.3)	3 (0.9)	2 (0.5)

FNA: Fine Needle Aspiration; TR: Thyroid Imaging Reporting and Data Systems (TIRADS).

Table 3. Diagnostic performances of TIRADS.

Parameter	Malignant	Benign	SE (%)	SP (%)	PPV (%)	NPV (%)
TIRADS 2-3	1	61	100	67.5	88.5	97
TIRADS 4-5	643	19				

TIRADS 2-3: According to the Thyroid Imaging Reporting and Data Systems category, not suspicious-mildly suspicious; TIRADS 4-3: According to the Thyroid Imaging Reporting and Data Systems category, moderately suspicious-highly suspicious; SE: Sensitivity; SP: Specificity; PPV: Positive predictive value; NPV: Negative predictive value.

Discussion

There are various guidelines recommended for the evaluation of thyroid nodules. Among these manuals, the risk factors determined by thyroid US in the evolution of thyroid nodules proposed by the Thyroid Association of America and British Thyroid Association and the revisions of these manuals are more common (7, 8). These guidelines focused on sonographic patterns rather than the size of the thyroid nodules as the primary determinant factor for biopsy. TIRADS classification predicts the malignant risks according to US characteristics of nodules. Complying with the risk classification system may result in a decreased number of unnecessary biopsies at significant levels (9, 10). Our study found that using TIRADS Scoring System increased the diagnostic performance of the thyroid nodules' evolution. Suppose cytologically non-diagnostic, atypical or follicular uncertainty is present in the nodules classified as TIRADS 1-3. In that case, the evolution of the nodule and/or cancer diagnosis may be inadequate because it is not operated on yet (11, 12). Our study showed that FNA increased the development of thyroid nodules through the reliability and diagnostic performance of ultrasonographic features. We determined that intranodular rough calcifications, intermittent calcifications on the nodule wall, the nodule with intense blood supply, and solid nodules detected by Elastsonography increase the risk of cancer from the other US features that are not classified in TIRADS. The risk of cancer was reported as ~0% in TIRADS 2 and 2-4% in TIRADS 3. In many previous studies, malignancy was not detected in any of the nodules with a score of TIRADS 1-3 (13, 14). We identified in our study that FNA biopsy was benign (20/20) in TI-RADS 2 nodules, FNA biopsy was benign in (41/42) FNA follicular, Hurthle cell neoplasia or suspected in 2.3% (1/42) in TI-RADS 3 nodules. Nodular goiter was detected in TIRADS 2, benign (20/20), nodular goiter in TIRADS 3, benign (41/42), and malignancy potential unclear in 2.3% (1/42) in postoperative tissue histopathology.

TIRADS classification system seems to have significant clinical value in determining benign and malignant thyroid nodules. Performing biopsy for nodules with high risk in line with TIRADS recommendations is considered as a rational approach.

It was shown that TIRADS 4 nodules have a 6-17% cancer risk (15). In other studies, cancer risk in TIRADS 4 nodules was 3.3-72.2% (6) and 5.9-12.8% (16). The cytology report result of TIRADS 4 nodules revealed the following result in our study: FNA benign by 4.43% (14/316), follicular, hurtle cell neoplasia or suspected hurtle cell neoplasia by 15.18% (48/316), suspected malignancy by 48.41% (153/316), and malignancy by 31.96% (101/316). Postoperative histopathological report results were as follows: nodular goiter, benign by 26.89% (85/316), thyroid cancer by 72.15% (228/316), lesion with unknown malignancy potential by 0.94% (3/316). When the present research was compared with the literature data, the cancer rate was much higher in TR-4 nodules. The inclusion of intranodular rough calcifications may explain such a higher rate, nodules with intense blood supply, solid nodules detected by elastsonography in TR-4 class along with highly suspected malignant lesion in EU-TIRADS (non-oval or round shape, irregular margins, microcalcifications, and a marked hypoechogenicity) and five ultrasound findings in ACR-TIRADS (composition, echogenicity, shape, margin, and echogenic foci). These US features appear to increase the risk of cancer. In this context, we think that these features should be included in the EU-TIRADS and ACR-TIRADS classification.

Cancer risk in TIRADS 5 nodules was 26-87% (5). This risk was reported to be 85.7% (18), 87.5% (7), 91% (19), and 100% in other studies (20). In our study, FNA biopsy benign was 1.44% (5/346) in TIRADS 5 nodules, FNA follicular, Hurthle cell neoplasia or suspicion was 4.33% (15/346), malignancy suspicion was 40.17% (139/346), and malignancy was 54.04% (187/346). In the postoperative tissue histopathology, we identified that nodular goiter was benign in TIRADS 5 at 1.73% (8/346), thyroid cancer at 97.10% (336/346), and malignancy potential unclear at 0.57% (2/346). In line with these findings, TIRADS 5 in our study was similar to the literature data in which thyroid nodules are at higher risk. TIRADS provides effective malignancy risk identification in the evolution of thyroid nodules. It appears to be beneficial in the decision of an FNA biopsy.

It is known that the prevalence of histological subtypes of thyroid tumors is 69.6% papillary thyroid carcinoma, 17.5% thyroid follicular carcinoma, 7.9% hurthle cell carcinoma, and 2.8% medullar thyroid

carcinoma (21). Papillary and follicular cancers constitute most thyroid cancers (>90%) (22, 23). In the present study, the histopathological distribution of thyroid cancers was found to be 89.47% papillary thyroid carcinoma, 7.36% thyroid follicular carcinoma, 2.1% medullary thyroid carcinoma, and 1.05% with uncertain malignancy potential. Our study results are similar to the frequency of differential thyroid and medullary cancers in line with the literature (21-23). In our study, the evaluation of thyroid nodules guided by the TIRADS classification presented a significantly higher sensitivity and moderate specificity, a higher negative predictive value to rule out malignancy, and a higher positive predictive value to detect malignancy.

Similar to EU-TIRADS, our findings showed that the risk of malignancy was associated with the composition, echogenicity, shape, marginal irregularities of the nodules, microlobulation, microcalcification, and echogenic foci. In addition, it was determined by the TR-4 classification that ultrasound features not included in EU-TIRADS increased the risk of thyroid cancer. In addition, there was no relationship between Anti-TPO, Anti-TG, TSH levels and malignancy.

Conclusion

In conclusion, in our study, the TIRADS scoring system successfully predicted the malignancy rate. In line with our findings, we support using the TIRADS scoring system for evaluating thyroid nodules, the risk of malignancy, and the classification of nodules. Since the risk of malignancy in TIRADS 2-3 thyroid nodules is very low, it can be followed in experienced clinics without a biopsy. Other ultrasound scan features (i.e., intranodular rough calcifications, nodules with intense blood supply, and solid nodules detected by elastosonography) were first evaluated within the TIRADS classification in our study. Clarified suggestions could be made for the approach to the nodules which are out of the classification as further studies support such findings. Biopsy must be performed for TIRADS 4 and 5 nodules. FNA biopsy must be performed in line with TIRADS Scoring System to avoid unnecessary biopsies until new methods are developed to detect cancer. These tumors are small and silent, and care must be paid to excessive biopsy recommendations for excessive diagnosis.

Conflict of Interest

No conflict of interest was declared by the authors.

Acknowledgement

All researches contributed equally to the study.

Ethics Committee Approval

This study was conducted by the ethical rules with the approval of Medicana International Samsun Hospital's clinical research ethics committee (Date: 20.04.2021, decision no: 7129,).

Author Contributions

Concept – ZE, HE, ÖKO; Supervision – ZE, HE, ÖKO; Materials – ZE, HE, ÖKO; Data Collection and/or Processing – ZE, HE, ÖKO; Analysis and/or Interpretation – ZE, HE, ÖKO; Writing – ZE, HE, ÖKO.

References

1. Jeong EJ, Chung SR, Baek JH, et al. A Comparison of Ultrasound-Guided Fine Needle Aspiration versus Core Needle Biopsy for Thyroid Nodules: Pain, Tolerability, and Complications. Endocrinol Metab (Seoul). 2018;33(1):114-120.
2. Rossi ED, Adeniran AJ, Faquin WC. Pitfalls in Thyroid Cytopathology. Surg Pathol Clin. 2019;12(4):865-881.
3. Lee YH, Baek JH, Jung SL, et al. Ultrasound-guided fine needle aspiration of thyroid nodules: a consensus statement by the korean society of thyroid radiology. Korean J Radiol. 2015;16(2):391-401.
4. Middleton WD, Teefey SA, Reading CC, et al. Multiinstitutional analysis of thyroid nodule risk stratification using the American College of Radiology Thyroid Imaging Reporting and Data System. American Journal of Roentgenology. 2017;208(6):1331-1341.
5. Tessler FN, Middleton WD, Grant EG. Thyroid Imaging Reporting and Data System (TI-RADS): A User's Guide. Radiology. 2018;287(1):29-36.
6. Yoon JH, Lee HS, Kim EK, et al. Malignancy risk stratification of thyroid nodules: comparison between the thyroid imaging reporting and data system and the 2014 American Thyroid Association management guidelines. Radiology. 2016;278(3):917-924.
7. Perros P, Boelaert K, Colley S, et al. British Thyroid Association. Guidelines for the management of thyroid cancer. Clin Endocrinol (Oxf) 2014;81(1):1-122.
8. Tappouni RR, Itri JN, McQueen TS, Lalwani N, Ou JJ. ACR TI-RADS: Pitfalls, Solutions, and Future Directions. Radiographics. 2019;39(7):2040-2052.
9. Moon HJ, Kim EK, Yoon JH, et al. Malignancy risk stratification in thyroid nodules with non-diagnostic results at cytologic examination: combination of thyroid imaging reporting and data system and the Bethesda System. Radiology 2015;274(1):287-295.
10. Zheng Y, Xu S, Kang H, et al. A Single-Center Retrospective Validation Study of the American College of Radiology Thyroid Imaging Reporting and Data System. Ultrasound Q. 2018;34(2):77-83.
11. Wei X, Li Y, Zhang S, et al. Meta-analysis of thyroid imaging reporting and data system in the ultrasonographic diagnosis of 10,437 thyroid nodules. Head Neck. 2016;38(2):309-15.
12. Barbosa TLM, Junior COM, Graf H, ve ark. ACR TI-RADS and ATA US scores are helpful for the management of thyroid nodules with indeterminate cytology. BMC Endocr Disord. 201929;19(1):112-115.
13. Jabar ASS, Koteshwara P, Andrade J. Diagnostic reliability of the Thyroid Imaging Reporting and Data System (TI-RADS) in routine practice. Pol J Radiol. 2019;10(2);274-280.
14. Weiss VL, Andreotti RF, Ely KA. Use of the thyroid imaging, reporting, and data system (TI-RADS) scoring system for the evaluation of subcentimeter thyroid nodules. Cancer Cytopathol. 2018;126(8):518-524.
15. Russ G, Bonnema SJ, Erdogan MF, et al. European thyroid association guidelines for ultrasound malignancy risk stratification of thyroid nodules in adults: The EU-TIRADS. Eur Thyroid J. 2017;6(5):225-237.
16. Tessler FN, Middleton WD, Grant EG, et al. ACR Thyroid Imaging, Reporting and Data System (TI-RADS): White Paper of the ACR TI-RADS Committee. J Am Coll Radiol. 2017;14(5):587-595.
17. Lauria Pantano A, Maddaloni E, Briganti SI, et al. Differences between ATA, AACE/ACE/AME and ACR TI-RADS ultrasound classifications performance in identifying cytological high-risk thyroid nodules. Eur J Endocrinol. 2018;178(6):595-603.
18. Lassoued MB, Souissi B, Hammami K, et al. The Thyroid Imaging Reporting and Data System (TIRADS) for ultrasound of the thyroid: a pratical approach. European Congress of Radiology-ECR 2015.
19. Chandramohan A, Khurana A, Pushpa BT, et al. Is TIRADS a practical and accurate system for use in daily clinical practice? Indian J Radiol Imaging. 2016;26(1):145-52.

20. Srinivas MN, Amogh VN, Gautam MS, et al. A Prospective Study to Evaluate the Reliability of Thyroid Imaging Reporting and Data System in Differentiation between Benign and Malignant Thyroid Lesions. J Clin Imaging Sci. 2016;69(2):5-15.
21. Al-Qurayshi Z, Foggia MJ, Pagedar N, et al. Thyroid cancer histological subtypes based on tumor size: National perspective. Head Neck. 2020;42(9):2257-2266.
22. Baloch ZW, LiVolsi VA. Special types of thyroid carcinoma. Histopathology. 2018;72(1):40-52.
23. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association Management Guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid. 2016;26(1):1-133.

Experimental and Applied Medical Science, 5, 3: 160-167, 2024. DOI: 10.46871/eams.1489388

The Relationship between Posture and Muscle Stiffness with Blood Flow in Cervicogenic Headache

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Abstract

Purpose: *The aim of this study was to investigate the relationship between head-shoulder posture, and head-neck muscle stiffness, with blood flow in cervicogenic headache (CH).*
Methods: *A total of 37 patients who met the inclusion criteria participated in this study. Head-shoulder posture was assessed with PostureScreen application, suboccipital, upper trapezius (UT) and sternecleidomastoid (SCM) muscle stiffness with the Myoton Pro device, internal carotid (ICA), vertebral artery (VA) blood flow with Doppler US.*
Results: *Head-shoulder posture deviations increased with increasing right and left suboccipital muscle stiffness (p=0.002, p=0.004, p=0.043, p=0.011) and head posture deviations increased with increasing left SCM muscle stiffness (p=0.004). As the UT muscle stiffness increased, VA blood flow (p=0.047, p=0.049) and as the left SCM muscle stiffness increased, ICA-VA blood flow decreased (p=0.009, p=0.002). As head posture deviation increased, ICA-VA blood flow decreased (p=0.002, p=0.011).*
Conclusion: *In conclusion, muscle stiffness and head-shoulder posture deviations negatively affect blood flow in CH.*

Key words: *Blood flow, Cervicogenic Headache, Neck, Stiffness, Posture*

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Introduction

Cervicogenic headache (CH) is a secondary headache type with a unilateral compressive and sometimes throbbing character spreading from the back of the head and neck to the ear and zygomatic region. The pain may be triggered after mechanical maneuvers and may last for weeks, starting from a few days, and may have a serious negative effect on the quality of life (1). Although the prevalence and incidence of CH vary according to societies, its prevalence was reported to be 0.1-4.1% in a recent study considering the accepted diagnostic criteria (2). It constitutes 15-20% of chronic headaches (3).

There is an increasing number of studies investigating the relationship between CH and musculoskeletal disorders. The convergence of the primary afferent inputs of the trigeminal and upper cervical nerves in the spinal trigeminal nucleus and the convergence of the head-face nociceptive sensory inputs from the upper cervical structures in the trigeminal nucleus may cause the pain signal in one region to spread to the other region, increase sensitivity to pain, and cause a pain response to nonpainful stimuli (4,5). Thus, it is thought that nociceptive input from cervical structures may cause headaches or that headache may spread to the cervical region. Current studies investigating the relationship between the cervical musculoskeletal system and CH are rather inadequate.

There are also studies that report the presence of a forward head posture in CH (6,7). The presence of tension and tenderness in the muscles of the neck due to this postural deviation has been reported in several studies (8,9). There are also studies reporting that cervical and thoracic posture deviations and suboccipital, upper trapezius (UT) muscle stiffness are higher in CH compared to healthy individuals (10).

In a study in which vertebral artery (VA) blood flow parameters were evaluated in individuals with CH, changes in VA blood flow were observed with cervical rotation movement. It has been reported that changes in blood flow may be the main pathogenetic mechanism in the development of pain (11). There are several studies investigating changes in head-neck blood flow, mostly in primary headache types. Studies on head-neck blood flow changes in CH are insufficient. Studies investigating changes in posture and neck-shoulder muscle stiffness with head-neck blood flow in CH are limited. No studies have investigated the relationship between postural deviations, muscle stiffness, and head-neck blood flow in CH. In this respect, our study contributes to the literature. The aim of our study was to investigate the relationship between neck-shoulder posture

deviations, neck-shoulder muscle stiffness, and head-neck blood flow in individuals with CH.

Material and Methods

The study was approved by the Clinical Research Ethics Committee of SANKO University in accordance with the Declaration of Helsinki (Session No: 2020/04, Decision No: 03). Patients who presented to the Neurology Outpatient Clinic of Sani Konukoğlu Practice and Research Hospital and were diagnosed with CH by a specialist were included in the study. Patients with CH who signed the voluntary consent form. The inclusion criteria were as follows: diagnosed with CHA, an adult between 18 and 65 years of age, and not having received medical treatment (excluding analgesics) or physiotherapy for CHA in the previous months. The exclusion criteria were as follows: history of headache surgery, history of serious heart disease or surgery, history of current or previous malignancy, and diagnosis of epilepsy.

First, the demographic data of individuals such as gender, age, body weight (kg), height (m), body mass index (kg/m2), and disease duration (years) were also recorded. The PostureScreen Mobile® (PSM) application was used for posture evaluation. This is a valid and reliable application developed to evaluate posture (12). Head and shoulder angulation and translation values measured via the application were recorded as lateral posture analyses.

The suboccipital, UT, and sternocleidomastoid (SCM) muscle stiffness of the patients was evaluated bilaterally with a myotonometer (Myoton AS, Tallinn, Estonia). Myotonometers are valid and reliable methods for assessing stiffness (13). In muscle stiffness evaluations, suboccipital was evaluated in the prone position, UT in the sitting position, and SCM in the supine position. The measurement was repeated 3 times for the right-left sides. The average of the measurements was taken and recorded in N/m units (14,15).

A Siemens Acuson S2000 (Siemens, Erlangen, Germany) device was used to evaluate the patients' internal carotid artery (ICA)-VA blood flow. Measurements were recorded for the right and left sides (16). The average of the right-left sides of blood flow was taken. While the ICA and VA blood flow evaluations were carried out by a radiologist with 20 years of experience, all other evaluations were performed face-to-face by the same physiotherapist under the same conditions.

Statistical Analysis

All analyses were conducted using SPSS software version 25. The normality and homogeneity of the data were evaluated

with the Shapiro Wilk test. Mean and standard deviation were given for continuous variables determined by measurement, and frequency and percentage were given for qualitative variables in descriptive statistics. Since the data were not normally distributed, the correlation between the data was analyzed using the Spearman test.

Results

The study was completed with a total of 37 individuals, 28 females and 9 males, who fulfilled the inclusion criteria. In descriptive statistics; mean age of the study participants was 32.30±9.171, and the mean BMI was 22.29±5.64. Also, the mean presence of headache was 2.97±1.83 years (Table 1).

Table 1. Demographics and presence of headache

	X ± SD
Age (years)	32.30±9.171
BMI (kg/m^2)	22.29±5.64
Presence of headache (years)	2.97±1.83
Gender	n (%)
Famale	28(75.67%)
Male	9(24.32%)

X:Mean; SD:Standard deviation; BMI:Body mass index; n:number of patients; %:percentage

When the relationship between muscle stiffness and posture was analyzed, a moderate correlation was found between right suboccipital muscle stiffness and head translation, shoulder angulation, and translation (p=0.002, p=0.005, p=0.004), between left suboccipital muscle stiffness and head translation and shoulder angulation (p=0.043, p=0.011) and between left SCM muscle stiffness and head angulation (p=0.004). The relationship between muscle stiffness and posture is shown in Table 2.

Table 2. Relationship between muscle stiffness and posture

	Head translation		Head angulation		Shoulder translation		Shoulder angulation	
	r	p	r	p	r	p	r	p
R suboccipital	**0.483***	0.002	0.254	0.129	**0.448***	0.005	**0.456 ***	0.004
L suboccipital	**0.334***	0.043	0.236	0.160	0.321	0.053	**0.413***	0.011
R UT	0.231	0.169	0.110	0.518	0.087	0.609	0.206	0.221
L UT	0.261	0.119	0.051	0.762	0.092	0.586	0.019	0.909
R SCM	0.171	0.311	0.312	0.060	0.185	0.274	0.047	0.783
L SCM	0.034	0.842	0.**460***	0.004	0.027	0.876	0.041	0.811

Spearman Test, r* correlation coefficient; p <0.05; R:right; L:left; UT:upper trapez; SCM:sternocleidomastoideus

When the relationship between posture and blood flow was analyzed, a negative moderate correlation was found between head translation and ICA PS and between ED and VS PS (p=0.002, p=0.022, p=0.011). The relationship between posture and blood flow is shown in Table 3.

Table 3. Relationship between posture and blood flow

	ICA PS		ICA ED		VA PS		VA ED	
	r	p	r	p	r	p	r	p
Head translation	-0.181	0.284	-0.222	0.186	0.009	0.957	0.127	0.453
Head angulation	**-0.490***	0.002	**-0.377***	0.022	**-0.412***	0.011	-0.276	0.098
Shoulder translation	-0.156	0.356	-0.271	0.105	-0.036	0.832	0.103	0.543
Shoulder angulation	-0.097	0.570	-0.322	0.052	-0.189	0.264	-0.051	0.763

Spearman Test, r*:correlation coefficient; p <0.05; ICA:internal carotid artery; VA: vertebral artery; Ps:peak sistoloc; ED:end diastolic

When the relationship between muscle stiffness and blood flow was analyzed, a negative low-level correlation was found between right and left UT muscle stiffness and VA ED (p=0.047, p=0.049), and a negative moderate-level correlation was found between left SCM and ICA PS and VA ED (p=0.009, p=0.002). The relationship between muscle stiffness and blood flow is shown in Table 4.

Table 4. Relationship between muscle stiffness and blood flow

	ICA PS		ICA ED		VS PS		VA ED	
	r	p	r	p	r	p	r	p
R suboccipital	0.089	0.600	0.115	0.499	0.196	0.245	0.035	0.839
L suboccipital	0.087	0.611	0.093	0.584	0.181	0.283	0.093	0.585
R UT	-0.004	0.982	-0.076	0.656	-0.188	0.266	**-0.329***	0.047
L UT	-0.062	0.714	-0.047	0.781	-0.127	0.455	**-0.326***	0.049
R SCM	-0.083	0.627	-0.215	0.201	-0.004	0.982	-0.322	0.052
L SCM	-0.**423***	0.009	-0.318	0.055	-0.240	0.153	**-0.502***	0.002

Spearman Test, r* correlation coefficient; p <0.05; R: right; L:left; UT:upper trapez; SCM:sternocleidomastoideus; ICA:internal carotid artery; VS:vertebral artery; PS:peak sistoloc; ED:end diastolic

Discussion

This study investigated the relationship between head-shoulder posture and neck-shoulder muscle stiffness with head-neck blood flow in CH. It was observed that head translation, shoulder translation, and angulation increased with increasing suboccipital muscle stiffness. In addition, it was observed that posture affects negatively blood flow. Also, VA blood flow decreased as UT and SCM muscle stiffness increased, and ICA-VA blood flow decreased as head translation increased.

Farmer et al. compared the cervical lordosis of patients with CH with the control group by radyographic methods. It is reported that

cervical lordosis is higher in individuals with CH compared to the healthy group. However, the results of the study cannot provide information about whether this deviation in cervical posture causes CH (17). Yoon evaluated the neck tilt angle and T1 slope angle in a study to contribute to the diagnostic criteria and clinical evaluation in CH. They found a significant difference in posture in CH compared to healthy individuals (10). Moustafa et al. investigated 3D spinal alignment in CH and found that there was much more thoracolumbar deviation compared to healthy individuals (18). Studies in the literature have generally shown that postural deviations may be associated with CH. This study similarly analyzed postural deviations but reported that head and shoulder posture may be related to muscle stiffness and blood flow.

The mechanical properties of the cervical muscles were investigated in CH. No significant difference was found in the elasticity of the suboccipital and UT muscles compared with healthy subjects, but a significant difference was found in cervical muscle stiffness (11). Lin et al. reported increased stiffness in superficial neck extensor muscles in cervicogenic headache. They concluded that increased muscle stiffness, especially on the side of the headache, may be significant for the diagnosis of CH. A systematic review showed that manual therapy approaches to reduce the tension of the muscles in the neck region may be effective in the treatment of CH (19). All these studies reported that muscle stiffness is a symptom to be considered in individuals with CH. In parallel with the literature, our study reported that posture deviations may be associated with neck muscle stiffness. In addition, the results that increased cervical muscle stiffness may adversely affect head and neck blood flow contribute to the literature.

Kaur et al. study with a large population showed that factors that would cause compression of the VBA may be associated with CH (20). Research suggests that low blood flow velocity and high resistance in the transverse cervical artery may be closely related to the underlying pathogenesis of cervical and upper back stiffness (21). Abdullaiev R Ya et al. compared the VA blood flow of patients with CHA and healthy individuals and reported that blood flow decreased, especially in head rotation (11).

In the literature, head-neck blood flow relationships related to headache have generally been examined. Another study showed that VA blood flow increased after acupuncture application in individuals with tension-type headache (22). Similarly, there are studies showing that blood flow may be affected by headache after various

interventions. Based on the literature, we examined the factors that may be associated with VA and ICA blood flow in a cervicogenic headache in our study. We reported that VA-ICA blood flow may be significantly related to posture and neck stiffness. In the literature, most of the studies on postural deviations, muscle stiffness, and head and neck blood flow have been conducted in relation to the diagnosis of CH. The relationship between these symptoms in CH has not been studied. Our study is one that will contribute to the literature in this aspect.

The main limitation of our study is that we were able to reach a limited number of individuals diagnosed with CH since our study was conducted in a single center. We recommend that the relationship between neck-shoulder postural deviations, muscle stiffness, and blood flow in individuals with CH be examined in larger population studies. We also think that examining the relationship between not only neck-shoulder posture but also postural deviations of the entire spine and muscle stiffness will bring a different perspective to the literature. Our study contains results that may give clinicians insight into the treatment approaches of individuals with CH.

Conclusion

This study showed that neck-shoulder postural deviations and suboccipital and UT muscle stiffness with VA and ICA blood flow may be related in individuals with CH. Postural deviations, muscle stiffness, and blood flow should be taken into account during the evaluations made in patients with CH. Additionally, posture correction and muscle relaxation methods can be added to treatment programs to increase blood flow.

Conflict of interest: No potential conflict of interest was reported by the author(s)

References

1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018;38:1-211.
2. Antonaci F, Inan LE. Headache and neck. Cephalalgia. 2021;41(4):438-442.
3. Nilsson N. The prevalence of cervicogenic headache in a random population sample of 20-59 year olds. Spine (Phila Pa 1976). 1995;20(17):1884-1888.
4. Liang Z, Galea O, Thomas L, et al. Cervical musculoskeletal impairments in migraine and tension type headache: A systematic review and meta-analysis. Musculoskeletal Science & Practice. 2019;42:67-83.
5. Bogduk N. The neck and headaches. Neurologic Clinics. 2014;32:471-487.
6. Zito G, Jull G, Story I. Clinical tests of musculoskeletal dysfunction in the diagnosis of cervicogenic headache. Manuel Therapy. 2006;11:118-129.
7. Farmer PK, Snodgrass SJ, Buxton AJ, et al. An investigation of cervical spinal posture in cervicogenic headache. Physical Therapy Rehabilitation Journal. 2015;95:212-222.
8. Olivier B, Pramod A, Maleka D. Trigger Point Sensitivity Is a Differentiating Factor between Cervicogenic and Non-Cervicogenic Headaches: A Cross-Sectional, Descriptive Study. Physiotherapy Canada. 2018;1–7.
9. Hall T, Briffa K, Hopper D, Robinson K. Reliability of manual examination and

frequency of symptomatic cervical motion segment dysfunction in cervicogenic headache. Manual Therapy. 2010;15(6):542–546.
10. Yoon JH, An Convergence Analysis of Muscle Characteristics, Muscle Activity and Posture in Patients with Cervicogenic Headache. Journal of Digital Convergence. 2021;19(6):265-271.
11. Abdullaiev RY, Kalashnikov VI, Voronzhev IA, et al. Dopplerographic Assessment of Blood Flow Parameters of Vertebral Arteries in Patients with Cervicogenic Headache Due to Arthrosis and Instability of Atlanto-Axial Junction, Trends in Technical & Scientific Research. 2018;1(5).
12. Hopkins BB, Vehrs PR, Fellingham GW, et al. Validity and Reliability of Standing Posture Measurements Using a Mobile Application. Journal of Manipulative and Physiological Therapeutics. 2019;42(2):132-140.
13. Pruyn EC, Watsford ML Murphy AJ. Validity and reliability of three methods of stiffness assessment. Journal of Sport and Health Science. 2016;5(4):476–483.
14. Park SK, Yang DJ, Kim JH, et al. Analysis of mechanical properties of cervical muscles in patients with cervicogenic headache. Journal of Physical Therapy Science. 2017;29(2):332–335.
15. Taş S, Yaşar Ü, Kaynak BA. Interrater and Intrarater Reliability of a Handheld Myotonometer in Measuring Mechanical Properties of the Neck and Orofacial Muscles. Journal of Manipulative and Physiological Therapeutics. 2021:44(1):42-48.
16. Kocabey B, Coşkunsu DK, Güven K. Effects of Manual Versus Instrumental Spinal Manipulation on Blood Flow of the Vertebral and Internal Carotid Arteries in Participants with Chronic Nonspecific Neck Pain: A Single-Blind, Randomized Study. Journal of Chiropiractic Medicine. 2023;22(1):1–10.
17. Farmer PK, Snodgrass SJ, Buxton AJ, et al. An Investigation of Cervical Spinal Posture in Cervicogenic Headache. Physical Therapy and Rehabilitation Journal. 2015;95(2):212-22.
18. Moustafa IM, Shousha TM, Harrison DE. An investigation of 3D spinal alignment in cervicogenic headache. Musculoskeletal Science and Practice. 2021;51:102284
19. Núñez-Cabaleiro P, Leirós-Rodríguez R. Effectiveness of manual therapy in the treatment of cervicogenic headache: A systematic review. Headache. 2022;62(3):271–283.
20. Kaur A, Rakesh N, Sujatha SR, et al. Association Between Vertebrobasilar Insufficiency and Cervicogenic Headache: Hypothetical Approach Towards Etiopathogenesis of Headache. Journal of Oral Medicine and Pain. 2020;45(4):97-109.
21. Aikawa R, Kishino T, Shibasaki S, et al. Relationship between trapezius muscle hardness and transverse cervical artery flow in association with neck and upper-back stiffness. Clinical Physiology and Functional Imaging. 2020;40:385–389.
22. Park KH, Kim HJ, Baek SY. Effect of Acupuncture on Blood Flow Velocity and Volume in Common Carotid and Vertebral Arteries in Migraine Patients. Medical Acupuncture. 2009;21(1):47-54.