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T.C.Sağlık Bakanlığı Sağlık Bilimleri Üniversitesi, İstanbul Bağcılar Eğitim ve Araştırma Hastanesi adına Hastane Yöneticisi Doç. Dr. Ozan Beytemür. (Türkiye Cumhuriyeti Sağlık Bakanlığı Sağlık Bilimleri Üniversitesi, İstanbul Bağcılar Eğitim ve Araştırma Hastanesi, Ortopedi ve Travmatoloji Kliniği, İstanbul, Türkiye).

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The journal is published quarterly in March, June, September and December.

Original clinical and experimental articles,interesting case studies, and literature reviews made from relevant authors in their brancheswill be accepted for evaluation in BMB.

Bagcilar Medical Bulletin is indexed in **TÜBİTAK/ULAKBİM, EBSCO, Gale, Turk Medline, Turkey Citation Index, Index Copernicus, ProQuest, J-Gate** and **ScopeMed**.

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Derginin editöryal ve yayın süreçleri ile etik kuralları International Committee of Medical Journal Editors (ICMJE), World Association of Medical Editors (WAME), Council of Science Editors (CSE), Committee on Publication Ethics (COPE), European Association of Science Editors (EASE), ve National Information Standards Organization (NISO) gibi uluslararası kuruluşların kurallarına uygun olarak şekillenmektedir. Dergimiz, şeffaf olma ilkeleri ve "akademik yayıncılıkta en iyi uygulamalar ilkeleri" (doaj.org/bestpractice) ile uyum içindedir.

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Dergi Adı (İngilizce): Bagcilar Medical Bulletin

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in the section titled “declaration of interest” and should include the full name of the sponsor and grant number. Existence or lack of sponsorship of any kind as well as the type of sponsorship (consulting etc) has to be acknowledged, as well.

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All manuscripts submitted to the journal for publication are checked by Crossref Similarity Check powered by “iThenticate” software for plagiarism. If plagiarism is detected, relevant institutions may be notified. In this case, the authors might be asked to disclose their raw data to relevant institutions.

Language

The language of the Bagcilar Medical Bulletin is American English. In addition, abstracts of the articles are published in both English and Turkish, and abstracts in both languages are requested from the authour(s).

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All correspondence will be sent to the first-named author unless otherwise specified. Papers should be accompanied by a cover letter indicating that the paper is intended for publication and specifying for which section of the Journal it is being submitted (i.e., original research article,brief research article, review article, case report or letter to the editor). In addition, a Copyright Transfer Form, Author Contribution Form and ICJME Form for Disclosure of Potential Conflicts of Interest must be submitted. Authors will be notified of the receipt of their paper and the number assigned to it. The number should be included in all further correspondence. All parts of the manuscript, including case reports, quotations, references, and tables, must be double-spaced throughout. All four margins must be at least 2.5 cm. The manuscript should be arranged in the following order, with each item beginning a new page: 1) title page, 2) abstract, 3) text, 4) acknowledgement 5) references, and 6) tables and/or figures. All pages must be numbered consecutively.

Title Page

On the title page, include full names of authors, academic or professional affiliations, and complete address with phone, fax number(s) and e-mail address (es) of the corresponding author. Acknowledgments for personal and technical assistance should be indicated on the title page.

Abstract and Keywords

Title of the manuscript in English should be written in English abstract, and a Turkish title must be for Turkish abstract.. All articles should include abstract and keywords. For abstracts are most distinct parts of an article and take place on the electronic databases, author should be sure that abstract represents the content of the article accurately. Abstract should inform about the basis of the study and include the purpose, basic procedures (selection of cases and laboratory animals, observatory and analytical methods), key findings and conclusions. New and significant apects of the study or observations should be stated. Up to 3-10 key words in English and in Turkish should be in accordance with National Library of Medicine’s Medical Subjects Subheadings (MeSH).

Manuscript Types

Original Research

Original research articles report substantial and original scientific results within the journal scope. Original research articles comprised of Abstract, Key Words, Introduction, Material and Methods, Results, Discussion, Conclusion, References and Table/ Figures. The abstract should be structured as the following.

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Abstract

The abstract should be no longer than 500 words and structured as follows: objective, method, results, and conclusions. Objective -the primary purpose of the article; Material and Method(s) -data sources, design of the study, patients or participants, interventions, and main outcome measures; Results -key findings; Conclusions -including direct clinical applications.

Keywords

Up to 3-10 key words in English and in Turkish should be in accordance with National Library of Medicine's Medical Subjects Subheadings (MeSH).

Introduction

This section should contain a clear statement of the general and specific objectives as well as the hypotheses which the work is designed to test. It should also give a brief account of the reported literature. The last sentence should clearly state the primary and secondary purposes of the article. Only, the actual references related with the issues have to be indicated and data or findings related with the current study must not be included in this section.

Material and Methods

This section should contain explicit, concise descriptions of all procedures, materials and methods used in the investigation to enable the reader to judge their accuracy, reproducibility, etc. This section should include the known findings at the beginning of the study and the findings during the study must be reported in results section. Ethics Committee Approval of the research and written Informed Consent obtained from the participants should be indicated.

The selection and description of the participants

The election, source of population, inclusion and exclusion criteria of the people who participate to experimental or clinical study must be clearly defined in this section. The particular study sample must be explained by the authors (i.e., why the study is performed in a definite age, race or sex population, etc.)

Technical information

The methods, apparatus (the manufacturer's name and address in parentheses), and procedures in sufficient detail must be defined to allow others to reproduce the results. References to established methods, including statistical methods (see below) must be given and brief descriptions for methods that have been published but are not well-known must be provided; new or substantially modified methods must be described, the reasons for using them must be given, and their limitations of the methods must be evaluated. The all drugs and chemicals used, including generic name(s), dose(s), and route(s) of administration must be identified. Authors submitting review manuscripts should include a section describing the methods used for locating, selecting, extracting, and synthesizing data. These methods should also be summarized in the abstract.

Statistics

The statistical methods must be described with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results. If possible, findings should be quantified and presented with appropriate indicators of measurement error or uncertainty (such as confidence intervals). Relying solely on statistical hypothesis testing, such as P values, which fail to convey important information about effect size must be avoided. References for the design of the study and statistical methods should be to standard works when possible (with pages stated). Define statistical terms, abbreviations, and most symbols. The computer software used must be specified.

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Results

The results should be presented in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. The all the data in the tables or illustrations should not be repeated in the text; only the most important observations must be emphasized or summarized. Extra or supplementary materials and technical detail can be placed in an appendix where they will be accessible but will not interrupt the flow of the text, or they can be published solely in the electronic version of the journal.

Discussion

The findings of the study, the findings and results which support or do not support the hypothesis of the study should be discussed, results should be compared and contrasted with findings of other studies in the literature and the different findings from other studies should be explained. The new and important aspects of the study and the conclusions that follow from them should be emphasized. The data or other information given in the Introduction or the Results section should not be repeated in detail.

Conclusions

Conclusions derived from the study should be stated. For experimental studies, it is useful to begin the discussion by summarizing briefly the main findings, then explore possible mechanisms or explanations for these findings, compare and contrast the results with other relevant studies, state the limitations of the study, and explore the implications of the findings for future research and for clinical practice. The conclusions should be linked with the goals of the study but unqualified statements and conclusions not adequately supported by the data should be avoided. New hypotheses should be stated when warranted, but should be labeled clearly as such.

Tables, Graphics and Illustrations

Tables, graphics and illustrations should be numbered in Arabic numerals in the text. The places of the illustrations should be signed in the text. Detailed information is under the related heading in below.

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Brief researches are similar to original research in that they follow the same format and guidelines, but they consider small-scale research or research that is in early stages of development. These may include preliminary studies that has a simple research design or a small sample size and that have produced limited pilot data and initial findings that indicate need for further investigation. Brief researches are much shorter than manuscripts associated with a more advanced, larger-scale research project. They are not meant to be used for a short version of an article about research that would otherwise qualify for a full original research manuscript or for publishing material on research that lacks significance, is not rigorous or, if expanded, would not qualify for a full article or for research.

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Case reports consider new, interesting and intriguing case studies in detail. They should be unique and present methods to overcome any health challenge by use of novel tools and techniques and provide a learning source for the readers. Case reports comprise of: Abstract (unstructured summary), Key-words, Introduction, Case Report, Discussion, Reference, Tables and Figures. Written informed consent of the patient should be obtained and indicated in the manuscript.

Review

Review articles are written by individuals who have done substantial work on the subject or are considered experts in the field. The Journal invites authors to write articles describing, evaluating and discussing the current level of knowledge regarding a specific subject in the clinical practice.

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Use only standard abbreviations; use of nonstandard abbreviations can be confusing to readers. Avoid abbreviations in the title of the manuscript. The spelled-out abbreviation followed by the abbreviation in parenthesis should be used on first mention unless the abbreviation is a standard unit of measurement.

Acknowledgement(s)

All forms of support, including individual technical support or material support must be acknowledged in the author's footnote before references.

Case Reports and Word Limitation

Original papers and reviews have no specific word limitation. A case report must be strictly limited to 1000 words excluding abstract and have minimal figures, tables, and references. Letters to the Editor (maximum of 500 words, including references; no tables or figures) will be considered if they include the notation "for publication." A letter must be signed by all of its authors. Letters critical of an article published in the journal must be received within 12 weeks.

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The "Bagcilar Medical Bulletin'' follows the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals" (International Committee of Medical Journal Editors - http://www.icmje.org /). Upon submission of the manuscript, authors are to indicate the type of trial/research and provide the checklist of the following guidelines when appropriate:

CONSORT statement for randomized controlled trials (Moher D, Schultz KF, Altman D, for the CONSORT Group. The CONSORT statement revised recommendations for improving the quality of reports of parallel group randomized trials. JAMA 2001; 285: 1987-91) (http://www.consort-statement.org/),

PRISMA for preferred reporting items for systematic reviews and meta-analyses (Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009; 6(7): e1000097.) (http://www.prisma-statement.org/),

STARD checklist for the reporting of studies of diagnostic accuracy (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al, for the STARD Group. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Ann Intern Med 2003;138:40-4.) (http://www.stard-statement.org /),

STROBE statement-checklist of items that should be included in reports of observational studies (http://www.strobe-statement.org/),

MOOSE guidelines for meta-analysis and systemic reviews of observational studies (Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting Meta-analysis of observational Studies in Epidemiology (MOOSE) group. JAMA 2000; 283: 2008-12).

CARE guidelines are designed to increase the accuracy, transparency, and usefulness of case reports. (Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D; the CARE Group. The CARE Guidelines: Consensus-based Clinical Case Reporting Guideline Development.) (http://www.care-statement.org/

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Bağcılar Tıp Bülteni

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Although references to review articles can be an efficient way to guide readers to a body of literature, review articles do not always reflect original work accurately. Readers should therefore be provided with direct references to original research sources whenever possible. On the other hand, extensive lists of references to original work on a topic can use excessive space on the printed page. Small numbers of references to key original papers often serve as well as more exhaustive lists, particularly since references can now be added to the electronic version of published papers, and since electronic literature searching allows readers to retrieve published literature efficiently. Using abstracts as references should be avoided.

References to papers accepted but not yet published should be designated as “in press” or “forthcoming”; authors should obtain written permission to cite such papers as well as verification that they have been accepted for publication. Information from manuscripts submitted but not accepted should be cited in the text as “unpublished observations” with written permission from the source. Citing a “personal communication” should be avoided unless it provides essential information not available from a public source, in which case the name of the person and date of communication should be cited in parentheses in the text. For scientific articles, written permission and confirmation of accuracy from the source of a personal communication must be obtained.

Reference Style and Format

The Uniform Requirements style for references is based largely on an American National Standards Institute style adapted by the National Library of Medicine for its databases. Authors should consult NLM’s Citing Medicine (http://www.nlm.nih.gov/bsd/uniform_requirements.html) for information on its recommended formats for a variety of reference types. References should be numbered consecutively in the order in which they are first mentioned in the text. Identify references in text, tables, and legends by Arabic numerals in parentheses. References cited only in tables or figure legends should be numbered in accordance with the sequence established by the first identification in the text of the particular table or figure. The titles of journals should be abbreviated according to the style used in the list of Journals in National Library of Medicine sources. In addition the list should be obtained in the web address of http://www.nlm.nih.gov. Accuracy of citation is the author’s responsibility. All references should be cited in text. Type references in the style shown below. If there are more than 6 authors, list them followed by et al. Abbreviations of journal names should conform to the style used in National Library of Medicine. If a journal is not indexed in National Library of Medicine’s MEDLINE/PubMed, it should not be abbreviated.

Examples for References:

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For the published article from the journal which placed and abbreviated in MEDLINE:

Crow SJ, Peterson CB, Swanson SA, Raymond NC, Specker S, Eckert ED, et al. Increased mortality in bulimia nervosa and other eating disorders. Am J Psychiatry 2009;166(12):1342-1346.

For the published article from the journal which is not placed and is not abbreviated in MEDLINE:

Sevinçer GM, Konuk N. Emotional eating. Journal of Mood Disorders 2013;3:171-178.

2. For the supplement:

For the published article from the journal which placed and abbreviated in MEDLINE:

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For the published article from the journal which is not placed and is not abbreviated in MEDLINE:

Maner F. Yeme bozukluklarının tedavisi. Anadolu Psikiyatri Dergisi 2009;10(Ek 1):55-56.

3. For articles in press:

Cossrow N, Pawaskar M, Witt EA, Ming EE, Victor TW, Herman BK, et al. Estimating the prevalence of binge eating disorder in a community sample from the United States: comparing DSM-IV-TR and DSM-5 criteria. J Clin Psychiatry, 2016. (in press).

4. For the citations from books:

Books edited by one editor:

INSTRUCTIONS TO AUTHORS

McKnight TL. Obesity Management in Family Practice. 1st ed., NewYork: Springer, 2005:47-51.

For the citation from a section of book edited by editor(s):

Jebb S, Wells J. Measuring body composition in adults and children. In Clinical Obesity in Adults and Children, Copelman P, Caterson I, Dietz W (editors). 1st ed., London: Blackwell Publishing, 2005:12-18.

If the authors of the cited section are the editors of the book:

Eckel RH (editor). Treatment of obesity with drugs in the new millennium. In Obesity Mechanisms and Clinical Management. First ed., Philadelphia: Lippincott Williams & Wilkins, 2003:449-476.

For the citation from a translated book:

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5. For the citation from thesis:

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6. For the citation from posters:

Akbaş Öncel D, Akdemir A. Üniversite öğrencilerinde diyet, beden algısı ve kendilik algısı arasındaki ilişkiler. 47. Ulusal Psikiyatri Kongresi Özet Kitabı, 26-30 Ekim 2011, Antalya, 2011:102.

7. Online Article:

Kaul S, Diamond GA. Good enough: a primer on the analysis and interpretation of noninferiority trials. Ann Intern Med [Internet]. 2006 Jul 4 [cited 2007 Jan 4];145(1):62-9. Available from:http://www.annals.org/cgi/reprint/145/1/62.pdf

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It is hoped that this list will be useful during the final checking of an article prior to sending it to the journal’s editor for review. Please consult this Guide for Authors, for further details of any item.

Ensure that the following items are present:

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3. Statement that informed consent was obtained after the procedure(s) had been fully explained.
4. Indicating whether the institutional and national guide for the care and use of laboratory animals was followed as in “Guide for the Care and Use of Laboratory Animals”.
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Bağcılar Tıp Bülteni (Bagcilar Medical Bulletin), tıbbın her alanında araştırma makalelerini, güncel derleme yazılarını, olgu sunumlarını ve editöre mektupları İngilizce tam metin ve Türkçe özle yayınlayan hakemli bir dergidir. Dergi online olarak yılda 4 sayı yayınlanmaktadır. Tüm makaleler kabul edilir edilmez, online olarak pdf formatında bu web sitesinde, o dönemdeki sayının bir makalesi olarak yer alacaktır. Dergi Galenos Yayınevi tarafından yayımlanmaktadır.

Editoryal Politikalar ve Hakem Süreci

Yayın Politikası

Bağcılar Tıp Bülteni, yayınlanmak üzere gönderilen yazıları aşağıda belirtilen şekillerde kabul eder:

-Orijinal araştırmalar,

-Kısa araştırmalar,

-Olgu sunumları,

-Derlemeler,

-Editöre mektup

Dergi, Türkiye'de yapılan araştırmaların uluslararası bilim arenasına duyurulması, uluslararası bilim çevrelerince paylaşılması ve bu bağlamda Türkiye'nin tanıtılmasına katkıda bulunmayı misyon edindiğinden özellikle orijinal araştırma niteliğindeki yazıları yayınlamaya öncelik vermektedir. Dergide yayınlanacak derleme türündeki yazılar editör tarafından konu ile ilgili çalışan yetkin kişilere hazırlatılmaktadır.

Genel İlkeler

Daha önce yayınlanmamış ya da yayınlanmak üzere başka bir dergide halen değerlendirmede olmayan ve her bir yazar tarafından onaylanan makaleler dergide değerlendirilmek üzere kabul edilir. Yayın kurulu, yazarların iznini alarak yazıda değişiklikler yapabilir. Editör ve dil editörleri dil, imlâ ve kaynakların National Library of Medicine MEDLINE/PubMed Resources'da belirtildiği gibi yazılmasında ve ilgili konularda tam yetkilidir.

Eğer makalede daha önce yayınlanmış alıntı yazı, tablo, resim vs. mevcut ise makale yazarı, yayın hakkı sahibi ve yazarlarından yazılı izin almak ve bunu makalede belirtmek zorundadır. Gerekli izinlerin alınıp alınmadığından yazar(lar) sorumludur.

Bilimsel toplantılarda sunulan özet bildiriler, makalede belirtilmesi koşulu ile kaynak olarak kabul edilir. Editör, dergiye gönderilen makale biçimsel esaslara uygun ise, gelen yazıyı yurtiçinden ve/veya yurtdışından en az iki hakemin değerlendirmesinden geçirtir, hakemler gerek gördüğü takdirde yazıda istenen değişiklikler yazarlar tarafından yapıldıktan sonra yayınlanmasına onay verir. Makale yayınlanmak üzere dergiye gönderildikten sonra yazarlardan hiçbirinin ismi, tüm yazarların yazılı izni olmadan yazar listesinden silinemez ve yeni bir isim yazar olarak eklenemez ve yazar sırası değiştirilemez. Yayına kabul edilmeyen makale, resim ve fotoğraflar yazarlara geri gönderilmez.

Yazar Hakları

Makalelerinin telif haklarını dergiye devreden yazarlar, yayınladıkları yazıdaki yazılarını diğer çalışmalarında kısmen veya tamamen, herhangi bir revizyon veya değişiklik yapmadan kullanma ve uygun gördükleri takdirde kitap haline getirme hakkını saklı tutarlar. Dergideki, CC BY-NC-ND 4.0 Lisansında ve derginin Açık Erişim politikasında belirtildiği gibi açıkça yayınlanmalıdır. Makale, yazar tarafından bir kitap bölümü olarak veya bir koleksiyonda veya derlemede yeniden kullanılacaksa veya ticari amaçlarla bir kitap haline getirilecekse, atama veya feragat etme hakkını saklı tutan Dergi'den izin alınması gerekir. Bu yeniden kullanım için bedel ve dergide asıl yayına açıkça verilmek üzere uygun bir atıf yapılması gerekmektedir.

Yazarların Sorumluluğu

Makalelerin bilimsel ve etik kurallara uygunluğu yazarların sorumluluğundadır. Yazar makalenin orijinal olduğu, daha önce başka bir yerde yayınlanmadığı ve başka bir yerde, başka bir dilde yayınlanmak üzere değerlendirmede olmadığı konusunda teminat sağlamalıdır. Uygulamadaki telif kanunları ve anlaşmaları gözetilmelidir. Telife bağlı materyaller (örneğin tablolar, şekiller veya

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büyük alıntılar) gerekli izin ve teşekkürle kullanılmalıdır. Başka yazarların, katkıda bulunanların çalışmaları ya da yararlanılan kaynaklar uygun biçimde kullanılmalı ve referanslarda belirtilmelidir.

Gönderilen makalede tüm yazarların akademik ve bilimsel olarak doğrudan katkısı olmalıdır, bu bağlamda "yazar" yayınlanan bir araştırmanın kavramsallaştırılmasına ve desenine, verilerin elde edilmesine, analizine ya da yorumlanmasına belirgin katkı yapan; yazının yazılması ya da bunun içerik açısından eleştirel biçimde gözden geçirilmesinde görev yapan; yazının yayınlanmak üzere nihai halini onaylayan ve çalışmanın herhangi bir bölümünün doğruluğuna ya da bütünlüğüne ilişkin soruların uygun şekilde soruşturulduğunun ve çözümlendiğinin garantisini vermek amacıyla çalışmanın her yönünden sorumlu olmayı kabul eden kişi olarak görülür. Fon sağlanması, ya da araştırma grubunun genel süpervizyonu tek başına yazarlık hakkı kazandırmaz. Yazar olarak gösterilen tüm bireyler sayılan tüm ölçütleri karşılamalıdır ve yukarıdaki ölçütleri karşılayan her birey yazar olarak gösterilebilir. Çok merkezli çalışmalarda grubun tüm üyelerinin yukarıda belirtilen şartları karşılaması gereklidir. Yazarların isim sıralaması ortak verilen bir karar olmalıdır. Tüm yazarlar yazar sıralamasını Telif Hakkı Devir Formunda imzalı olarak belirtmek zorundadırlar. Yazarların tümünün ismi yazının başlığının altındaki bölümde yer almalıdır.

Yazarlık için yeterli ölçütleri karşılamayan ancak çalışmaya katkısı olan tüm bireyler teşekkür (acknowledgement) kısmında sıralanmalıdır. Bunlara örnek olarak ise sadece teknik destek sağlayan, yazıma yardımcı olan ya da sadece genel bir destek sağlayan kişiler verilebilir. Finansal ve materyal destekleri de belirtilmelidir.

Yazıya materyal olarak destek veren ancak yazarlık için gerekli ölçütleri karşılamayan kişiler "klinik araştırıcılar" ya da "yardımcı araştırıcılar" gibi başlıklar altında toplanmalı ve bunların işlevleri ya da katılımları "bilimsel danışmanlık yaptı", "çalışma önerisini gözden geçirdi", "veri topladı" ya da "çalışma hastalarının bakımını üstlendi" şeklinde belirtilmelidir. Teşekkür (acknowledgement) kısmında belirtilen bu ifadeler için bu bireylerden de yazılı izin alınması gerekmektedir.

Bütün yazarlar, araştırmanın sonuçlarını ya da bilimsel değerlendirmeyi etkileyebilme potansiyeli olan finansal ilişkiler, çıkar çatışması ve çıkar rekabetini beyan etmelidirler. Bir yazar kendi yayınlanmış yazısında belirgin bir hata ya da yanlışlık tespit ederse, bu yanlışlıklara ilişkin düzeltme ya da geri çekme için yayın yönetmeni ile hemen temasa geçme ve işbirliği yapma sorumluluğunu taşır. Yazarların katkısını belirten Yazar Katkı Formu ve çıkar çatışması olup olmadığını belirten ICMJE Potansiyel Çıkar Çatışması Beyan Formu makale ile birlikte gönderilmelidir. Yazarların görevleri ve sorumlulukları konusunda aşağıdaki kaynağa bakabilirsiniz; http://www.icmje.org/recommendations/browse/roles-and-responsibilities/

Editör ve Hakem Sorumlulukları ve Değerlendirme Süreci

Editörler, makaleleri, yazarların etnik kökeninden, cinsiyetinden, cinsel yöneliminden, uyruğundan, dini inancından ve siyasi felsefesinden bağımsız olarak değerlendirirler. Yayına gönderilen makalelerin adil bir şekilde çift taraflı kör hakem değerlendirmesinden geçmelerini sağlarlar. Gönderilen makalelere ilişkin tüm bilginin, makale yayınlanana kadar gizli kalacağını garanti ederler. Editörler içerik ve yayının toplam kalitesinden sorumludurlar. Gereğinde hata sayfası yayınlamalı ya da düzeltme yapmalıdırlar.

Genel Yayın Yönetmeni; yazarlar, editörler ve hakemler arasında çıkar çatışmasına izin vermez. Hakem atama konusunda tam yetkiye sahiptir ve Bağcılar Tıp Bülteni'nde yayınlanacak makalelerle ilgili nihai kararı vermekle yükümlüdür. Yayın etiği konusunda COPE kaynağına bakabilirsiniz. https://publicationethics.org/files/u7141/1999pdf13.pdf

Hakemler makaleleri, yazarların etnik kökeninden, cinsiyetinden, cinsel yöneliminden, uyruğundan, dini inancından ve siyasi felsefesinden bağımsız olarak değerlendirirler. Araştırmayla ilgili, yazarlarla ve/veya araştırmanın finansal destekçileriyle çıkar çatışmaları olmamalıdır. Değerlendirmelerinin sonucunda tarafsız bir yargıya varmalıdırlar. Hakemler yazarların atıfta bulunmadığı konuyla ilgili yayınlanmış çalışmaları tespit etmelidirler. Gönderilmiş yazılara ilişkin tüm bilginin gizli tutulmasını sağlamalı ve yazar tarafında herhangi bir telif hakkı ihlali ve intihal fark ederlerse Genel Yayın Yönetmeni`ne raporlamalıdırlar. Hakem, makale konusu hakkında kendini vasıflı hissetmiyor ya da zamanında geri dönüş sağlaması mümkün görünmüyorsa, Genel Yayın Yönetmeni`ne bu durumu bildirmeli ve hakem sürecine kendisini dahil etmemesini istemelidir.

Editör makalelerle ilgili bilgileri (makalenin alınması, içeriği, gözden geçirme sürecinin durumu, hakemlerin eleştirileri ya da varılan sonuç) yazarlar ya da hakemler dışında kimseyle paylaşmaz.

Değerlendirme sürecinde editör hakemlere gözden geçirme için gönderilen makalelerin, yazarların özel mülkü olduğunu ve bunun imtiyazlı bir iletişim olduğunu açıkça belirtir. Hakemler ve yayın kurulu üyeleri topluma açık bir şekilde makaleleri tartışamazlar. Hakemlerin kendileri için makalelerin kopyalarını çıkarmalarına izin verilmez ve editörün izni olmadan makaleleri başkasına

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veremezler. Hakemler gözden geçirmelerini bitirdikten sonra makalenin kopyalarını yok etmeli ya da editöre göndermelidirler. Dergimiz editörü de reddedilen ya da geri verilen makalelerin kopyalarını imha etmelidir.

Yazarın ve editörün izni olmadan hakemlerin gözden geçirmeleri basılamaz ve açıklanamaz. Hakemlerin kimliğinin gizli kalmasına özen gösterilmelidir. Bazı durumlarda editörün kararıyla, ilgili hakemlerin makaleye ait yorumları aynı makaleyi yorumlayan diğer hakemlere gönderilerek hakemlerin bu süreçte aydınlatılması sağlanabilir. Değerlendirme süreciyle ilgili olarak COPE kaynağına bakabilirsiniz: http://publicationethics.org/files/Peer review guidelines.pdf

Açık Erişim İlkesi

Açık erişimli bir yayın olan Bağcılar Tıp Bülteni dergisinin tüm içeriği okura ya da okurun dahil olduğu kuruma ücretsiz olarak sunulur. Okurlar, yayıncı ya da yazardan izin almadan dergi makalelerinin tam metnini okuyabilir, indirebilir, kopyalayabilir, dağıtabilir, basabilir, arayabilir ve link sağlayabilir.

Yayın Etiği

İlke ve Standartlar

Bağcılar Tıp Bülteni yayın etiğinde en yüksek standartlara bağlıdır ve Committee on Publication Ethics (COPE), Council of Science Editors (CSE), World Association of Medical Editors (WAME) ve International Committee of Medical Journals (ICJME) tarafından geliştirilen yayın etiği ilkelerini ve tavsiyelerini gözetir.

Gönderilen tüm makaleler orijinal, yayınlanmamış (konferans bildirilerindeki tam metinler de dahil) ve başka bir dergide değerlendirme sürecinde olmamalıdır. Her bir makale editörlerden biri ve en az iki hakem tarafından çift kör değerlendirmeden geçirilir. Gönderilen makaleleri intihal yazılımı ile denetleme hakkımız haklıdır. İntihal, veride hile ve tahrif (araştırma verisi, tabloları ya da imajlarının manipülasyonu ve asılsız üretimi), insan ve hayvanların araştırmada uygun olmayan kullanımı konuları denetimden geçmektedir. Bu standartlara uygun olmayan tüm makaleler yayından çıkarılır. Buna yayından sonra tespit edilen olası kuraldışı, uygunsuzluklar içeren makaleler de dahildir. Yayın etiği kurallarına bağlı olarak, intihal şüphesini ve duplikasyon durumlarını rapor edeceğimizi belirtiriz. Olası bilimsel hatalı davranışları ve yayın etiği ihlali vakalarını ele alırken COPE Ethics Flowcharts http://publicationethics.org/resources/flowcharts izlenir.

İnsan ve Hayvan Hakları, Bilgilendirilmiş Olur, Çıkar Çatışması

Bağcılar Tıp Bülteni, yayınladığı makalelerin ticarî kaygılardan uzak ve konu ile ilgili en iyi etik ve bilimsel standartlarda olması şartını gözetmektedir. Makalelerin etik kurallara uygunluğu yazarların sorumluluğundadır.

Bağcılar Tıp Bülteni, 1975 Helsinki Deklarasyonu'nun 2004 yılında revize edilen Ethical Principles for Medical Research Involving Human Subjects'e http://www.wma.net/en/30publications/10policies/b3/index.html ve 2006 yılında revize edilen WMA Statement on Animal Use in Biomedical Research'e http://www.wma.net/en/30publications/10policies/a18/uymayı prensip edinmiştir. Bu yüzden dergide yayınlanmak üzere gönderilen yazılarda, klinik deneylere katılan denekler ile ilgili olarak yukarıda belirtilen etik standartlara uyulduğunun mutlaka belirtilmesi gerekmektedir. Ayrıca deneyin türüne göre gerekli olan yerel veya ulusal etik komitelerden alınan onay yazıları yazı ile birlikte gönderilmelidir. Bununla birlikte deneye katılan kişi/hastalardan, hastalar eğer temyiz kudretine sahip değilse vâsilerinden yazılı bilgilendirilmiş onam alındığını belirten bir yazı ile beraber tüm yazarlar tarafından imzalanmış bir belgenin editöre gönderilmesi gerekmektedir.

Hastalardan izin alınmadan mahremiyet bozulamaz. Hastaların ismi, isimlerinin baş harfleri ya da hastane numaraları gibi tanımlayıcı bilgiler, fotoğraflar ve soy ağacı bilgileri vb. bilimsel amaçlar açısından çok gerekli olmadıkça ve hasta (ya da anne-baba, ya da vâsisi) yazılı bilgilendirilmiş onam vermedikçe basılmazlar. Özellikle olgu bildirimlerinde, çok gerekli olmadıkça hasta ile ilgili tanımlayıcı ayrıntılar çıkarılmalıdır. Örneğin, fotoğraflarda göz bölgesinin maskelenmesi kimliğin gizlenmesi için yeterli değildir. Eğer veriler kimliğin gizlenmesi için değiştirildiyse yazarlar bu değişikliklerin bilimsel anlamı etkilemediği konusunda güvence vermelidirler. Olgu sunumlarında yer verilen hastalardan bilgilendirilmiş onam alınmalıdır. Bilgilendirilmiş onam alındığı da makalede belirtilmelidir.

Bu tip çalışmaların varlığında yazarlar, makalenin YÖNTEM(LER) bölümünde bu prensiplere uygun olarak çalışmayı yaptıklarını, kurumlarının etik kurullarından ve çalışmaya katılmış insanlardan "bilgilendirilmiş onam" aldıklarını belirtmek zorundadırlar.

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Çalışmada "hayvan" kullanılmış ise yazarlar, makalenin YÖNTEM(LER) bölümünde "Guide for the Care and Use of Laboratory Animals" (www.nap.edu/catalog/5140.html) doğrultusunda çalışmalarında hayvan haklarını koruduklarını ve kurumlarının etik kurullarından onay aldıklarını belirtmek zorundadırlar. Hayvan deneyleri rapor edilirken yazarlar, laboratuvar hayvanlarının bakımı ve kullanımı ile ilgili kurumsal ve ulusal rehberlere uyup uymadıklarını yazılı olarak bildirmek zorundadırlar.

Editör ve yayıncı, reklâm amacı ile dergide yayınlanan ticari ürünlerin özellikleri ve açıklamaları konusunda hiçbir garanti vermemekte ve sorumluluk kabul etmemektedir. Eğer makalede doğrudan veya dolaylı ticarî bağlantı veya çalışma için maddî destek veren kurum mevcut ise yazarlar; kaynak sayfasında, kullanılan ticarî ürün, ilaç, ilaç firması vb. ile ticari hiçbir ilişkisinin olmadığını veya varsa nasıl bir ilişkisinin olduğunu (konsültan, diğer anlaşmalar) bildirmek zorundadır. Bağcılar Tıp Bülteni, WAME'nin çıkar çatışması tanımını benimser http://www.wame.org/about/wame-editorial-on-coi

Buna göre, yazar, hakem ya da editör sorumluluklarını aşırı düzeyde ve/veya haksızlığa yol açabilecek düzeyde etkileyebilecek ya da etkileyebileceği olası bir çıkar rekabeti içindeyse, çıkar çatışması söz konusudur ve bunun açıklanması gerekir. Açıklanması öngörülen çıkar çatışması tipleri, finansal bağlar, akademik taahhütler, kişisel ilişkiler, politik ya da dini inançlar, kurumsal bağlantılardır. Çıkar çatışması söz konusuysa bu makalede açıklanmalıdır.

Dergiye yayımlanmak üzere gönderilen tüm yazılar editör ve hakemlerin uzmanlığı ile Crossref Similarity Check powered by "iThenticate" programı ve internet üzerinden arama motorlarında taranarak, intihal kontrolünden geçmektedir. İntihal taraması sonucuna göre yazılar reddedilebilir. İntihal tespit edilmesi halinde, ilgili kurumlara yazarlar hakkında ihbar yapılabilir. Bu durumda yazarlar sorumlu kurumlara çalışmalarının ham sonuçlarını teslim etmek zorunda kalabilir.

Dil

Bağcılar Tıp Bülteni`nin yayın dili Amerikan İngilizcesi'dir, ayrıca makalelerin özleri hem İngilizce, hem Türkçe yayınlanır. Her iki dildeki özler yazarlardan istenir.

Yazıların Hazırlanması

Aksi belirtilmedikçe gönderilen yazılarla ilgili tüm yazışmalar ilk yazarla yapılacaktır. Gönderilen yazılar, yazının yayınlanmak üzere gönderildiğini ve Bağcılar Tıp Bülteni`nin hangi bölümü (Orijinal Araştırma, Kısa Araştırma, Olgu Sunumu, Derleme, Editöre Mektup) için başvurulduğunu belirten bir mektup, yazının elektronik formunu içeren Microsoft Word 2003 ve üzerindeki versiyonları ile yazılmış elektronik dosya ile tüm yazarların imzaladığı 'Telif Hakkı Devir Formu' , Yazar Katkı Formu ve ICMJE Potansiyel Çıkar Çatışması Beyan Formueklenerek gönderilmelidir. Yazıların alınmasının ardından yazarlara makalenin alındığı, bir makale numarası ile bildirilecektir. Tüm yazışmalarda bu makale numarası kullanılacaktır. Makaleler sayfanın her bir kenarından 2,5 cm kenar boşluğu bırakılarak ve çift satır aralıklı yazılmalıdır. Makalelerde aşağıdaki sıra takip edilmelidir ve her bölüm yeni bir sayfa ile başlamalıdır: 1) başlık sayfası, 2) öz, 3) metin, 4) teşekkür / 5) kaynaklar ve 6) tablo ve/veya şekiller. Tüm sayfalar sırayla numaralandırılmalıdır.

Başlık

Başlık sayfasında, yazarların adları, akademik ünvanları ve yazışılacak yazarın tam adres, telefon ve faks numaraları ile e-mail adresi mutlaka bulunmalıdır. Yazıların Türkçe özlerinde mutlaka Türkçe başlık da yer almalıdır.

Öz ve Anahtar Sözcükler

Makalenin İngilizce başlığı İngilizce özde, Türkçe başlığı da Türkçe özde yer almalıdır. Bütün makaleler öz ve anahtar kelime içermelidir. Özler bir makalenin birçok elektronik veri tabanında yer alan en belirgin kısmı olduğundan, yazarlar özün makalenin içeriğini doğru olarak yansıttığından emin olmalıdır. Öz çalışmanın temeliyle ilgili bilgi vermeli ve çalışmanın amacını, temel prosedürleri (olguların ya da laboratuvar hayvanlarının seçimi, gözlemsel ve analitik yöntemler), ana bulguları (mümkünse özgül etki büyüklüklerini ve istatistiksel anlamlılıklarını vererek) ve temel çıkarımları içermelidir. Çalışmanın ya da gözlemlerin yeni ve önemli yönleri belirtilmelidir. Anahtar sözcükler, her türlü yazıda Türkçe ve İngilizce özlerin altındaki sayfada 3-10 adet verilmelidir. Anahtar sözcük olarak National Library of Medicine'ın Tıbbi Konu Başlıkları'nda (Medical Subject Headings, MeSH) yer alan terimler kullanılmalıdır. MeSH'de yer alan terimlerin Türkçe karşılıklarına Türkiye Bilim Terimleri'nden http://www.bilimterimleri.com erişilebilir.

YAZARLARA BİLGİ

Makale Türleri

Orijinal Araştırma

Orijinal araştırma makaleleri derginin kapsamına uygun konularda önemli, özgün bilimsel sonuçlar sunan araştırmaları raporlayan yazılardır. Orijinal araştırma makaleleri, Öz, Anahtar Kelimeler, Giriş, Yöntem ve Gereçler, Bulgular, Tartışma, Sonuçlar, Kaynaklar bölümlerinden ve Tablo, Grafik ve Şekillerden oluşur. Öz bölümü araştırma yazılarında aşağıda belirtilen formatta yapılandırılmış olmalıdır.

Öz

Araştırma yazılarında Türkçe ve İngilizce özler en fazla 500 kelime olmalı ve şu şekilde yapılandırılmalıdır: Amaç/Objective: Yazının birincil ve asıl amacı; Yöntem ve Gereçler/Material and Method(s): Veri kaynakları, çalışmanın iskeleti, hastalar ya da çalışmaya katılanlar, görüşme/değerlendirmeler ve temel ölçümler; Bulgular/Results: Ana bulgular; Sonuç(lar)/Conclusion(s):Doğrudan klinik uygulamalar, çıkartılacak sonuçlar belirtilmelidir.

Anahtar Kelimeler

National Library of Medicine'ın Tıbbi Konu Başlıkları'nda (MedicalSubjectHeadings, MeSH) yer alan terimler kullanılmalıdır, en az üç anahtar kelime belirtilmelidir.

Giriş

Giriş/Introduction bölümünde konunun önemi, tarihçe ve bugüne kadar yapılmış çalışmalar, hipotez ve çalışmanın amacından söz edilmelidir. Hem ana hem de ikincil amaçlar açıkça belirtilmelidir. Sadece gerçekten ilişkili kaynaklar gösterilmeli ve çalışmaya ait veri ya da sonuçlardan söz edilmemelidir.

Yöntem ve Gereçler

Yöntem ve Gereçler/Material and Methods bölümünde, veri kaynakları, hastalar ya da çalışmaya katılanlar, ölçekler, görüşme/değerlendirmeler ve temel ölçümler, yapılan işlemler ve istatistiksel yöntemler yer almalıdır. Yöntem bölümü, sadece çalışmanın planı ya da protokolü yazılırken bilinen bilgileri içermelidir; çalışma sırasında elde edilen tüm bilgiler bulgular kısmında verilmelidir. Yöntem ve Gereçler bölümünde olguların seçimi ve tanımlanması hakkında bilgi, teknik bilgi ve istatistik hakkında bilgi yer almalıdır. Araştırmanın Etik Kurul Onayı ve katılımcılardan alınan yazılı Bilgilendirilmiş Onam belirtilmelidir.

Olguların Seçimi ve Tanımlanması

Gözlemsel ya da deneysel çalışmaya katılanların (hastalar, hayvanlar, kontroller) seçimi, kaynak popülasyon, çalışmaya alınma ve çalışmadan dışlanma ölçütleri açıkça tanımlanmalıdır. Yaş ve cinsiyet gibi değişkenlerin çalışmanın amacıyla olan ilişkisi her zaman açık olmadığından yazarlar çalışma raporundaki kullanımlarını açıklamalıdır; örneğin yazarlar niçin sadece belli bir yaş grubunun alındığını ya da neden kadınların çalışma dışında bırakıldığını açıklamalıdır. Çalışmanın niçin ve nasıl belli bir şekilde yapıldığı açık bir şekilde belirtilmelidir. Yazarlar etnisite ya da ırk gibi değişkenler kullandıklarında bu değişkenleri nasıl ölçtüklerini ve geçerliklerini açıklamalıdır.

Teknik Bilgi

Diğer çalışmacıların sonuçları yineleyebilmesi için yöntem ve kullanılan araçlar (üretici firma ve adres paragraf içinde belirtilerek) ayrıntılı bir şekilde belirtilmelidir. Önceden kullanılan bilinen yöntemler için (istatistiksel yöntemler dahildir) kaynak gösterilmeli, basılmış ama iyi bilinmeyen bir yöntem için kaynak verilmeli ve yöntem açıklanmalıdır. Aynı şekilde yeni ya da belirgin olarak modifiye edilmiş yöntemler tanımlanmalı ve kullanılma nedenleri belirtilip kısıtlılıkları değerlendirilmelidir. Kullanılan tüm ilaç ve kimyasallar doğru olarak tanımlanıp jenerik isimleri, dozları ve kullanım biçimleri belirtilmelidir. Gözden geçirme yazısı gönderen yazarlar veriyi bulma, seçme, ayırma ve sentezleme yöntemlerini belirtmelidir. Bu yöntemler aynı zamanda özde de yer almalıdır.

YAZARLARA BİLGİ

İstatistik

İstatistiksel yöntem, orijinal veriye erişebilecek bilgili bir okuyucunun rapor edilen sonuçları onaylayabileceği bir ayrıntıda belirtilmelidir. Mümkünse, bulgular niceliksel hale getirilmeli ve hata ölçümleri (güvenlik aralıkları gibi) sunulmalıdır. Etki büyüklüğünü vermeyen, p değerlerinin kullanımı gibi, salt istatistiksel hipotez sınamasına dayanılmamalıdır. Çalışma deseni ve istatistiksel yönteme dair kaynaklar sayfalar belirtilerek mümkün olduğu sürece standart kaynaklar olmalıdır. İstatistiksel terimler, kısaltmalar ve semboller tanımlanmalıdır. Kullanılan bilgisayar programı belirtilmelidir.

Bulgular

Ana bulgular istatistiksel verilerle desteklenmiş olarak eksiksiz verilmeli ve bu bulgular uygun tablo, grafik ve şekillerle görsel olarak da belirtilmelidir. Bulgular yazıda, tablolarda ve şekillerde mantıklı bir sırayla önce en önemli sonuçlar olacak şekilde verilmelidir. Tablo ve şekillerdeki tüm veriyi yazıda vermemeli, sadece önemli noktaları vurgulanmalıdır. Ekstra materyal ve teknik bilgi ek kısmında verilerek yazının akışının bozulmaması sağlanmalı, alternatif olarak bunlar sadece elektronik versiyonda yer almalıdır.

Tartışma

Tartışma/Discussion bölümünde o çalışmadan elde edilen veriler, kurulan hipotez doğrultusunda hipotezi destekleyen ve desteklemeyen bulgular ve sonuçlar irdelenmeli ve bu bulgu ve sonuçlar literatürde bulunan benzeri çalışmalarla kıyaslanmalı, farklılıklar varsa açıklanmalıdır. Çalışmanın yeni ve önemli yanları ve bunlardan çıkan sonuçları vurgulanmalıdır. Giriş ya da sonuçlar kısmında verilen bilgi ve veriler tekrarlanmamalıdır.

Sonuçlar

Sonuçlar/Conclusions bölümünde çalışmadan çıkarılan sonuçlar sıralanmalıdır. Deneysel çalışmalar için tartışmaya sonuçları kısaca özetleyerek başlamak, daha sonra olası mekanizmaları ya da açıklamaları incelemek ve bulguları önceki çalışmalarla karşılaştırmak, çalışmanın kısıtlılıklarını özetlemek, gelecekteki çalışmalar ve klinik pratik için uygulamalarını belirtmek faydalıdır. Varılan sonuçlar çalışmanın amacıyla karşılaştırılmalı, ancak elde edilen bulgular tarafından yeterince desteklenmeyen çıkarımlardan kaçınılmalıdır. Yazarlar, eğer elde ettikleri veriler ekonomik veri ve analizler içermiyorsa, ekonomik çıkar ya da faydalarla ilgili yorumlardan özellikle kaçınılmalıdır. Gerektiğinde yeni hipotezler ortaya konmalı, ancak bunların yeni hipotezler olduğu belirtilmelidir.

Tablo, Grafik ve Şekiller

Yazı içindeki grafik, şekil ve tablolar Arap sayıları ile numaralandırılmalıdır. Şekillerin metin içindeki yerleri belirtilmelidir. Ayrıntılı bilgi aşağıda ilgili başlık altında yer almaktadır.

Kısa Araştırma

Kısa Araştırma makaleleri tarz ve format açısından Orijinal Araştırma makaleleri gibidir; ancak daha küçük ölçekli araştırmaları ya da geliştirme çalışmasının erken aşamalarında olan araştırmaları ele alır. Basit araştırma tasarımı kullanan ön çalışmalar, sınırlı pilot veri sağlayan küçük örnek kitle ile yapılan çalışmalar, ileri araştırma gereksinimine işaret eden başlangıç bulguları bu tür araştırmalar kapsamında sayılabilir. Kısa Araştırma makaleleri, büyük ölçekli gelişkin araştırma projelerini konu alan Orijinal Araştırma makalelerinden daha kısadır. Ancak Kısa Araştırma, Orijinal Araştırma makalesi olabilecek kalitede bir araştırma makalesinin kısa versiyonu olarak anlaşılmamalıdır; önem derecesi düşük, titizlikle yapılmamış bir araştırma hakkında bir yayın malzemesi hazırlamak için kullanılmamalıdır ya da genişletildiğinde Orijinal Araştırma makalesi ya da araştırma niteliği kazanmayacak bir içeriği değerlendirecek bir makale türü olarak anlaşılmamalıdır.

Olgu Sunumu

Olgu sunumu makaleleri özgün vakaları rapor eden yazılardır. Derginin kapsamına giren konulara ilişkin bir problemin üstesinden gelen tedaviyle ilgili, yeni araçlar, teknikler ve metotlar göstererek okuyucular için bilgilendirme sağlamalıdır. Olgu sunumu yazıları

YAZARLARA BİLGİ

Öz (özün araştırma makalesinde olduğu gibi belli bir formatta yapılandırılmış olması gerekmiyor), Anahtar Kelimeler, Giriş, Olgu Sunumu, Tartışma, Referanslar, gerekirse Tablo ve açıklayıcı bilgilerden oluşur. Olgu sunumunda yazılı bilgilendirilmiş onam alınmalı ve makalede belirtilmelidir.

Derleme

Derleme makaleleri alanında zengin birikime ve atıf alan çalışmalara sahip uzman kişilerce yazılan yazılardır. Klinik pratiğe ilişkin bir konuda mevcut bilgiyi tanımlayan, değerlendiren ve tartışan; geleceğe ilişkin çalışmalara yol gösteren derleme yazıları yazmaları için dergi belirlediği yazarlara davet gönderir. Derleme makaleleri, Öz (özün, araştırma makalesinde olduğu gibi belli bir formatta yapılandırılmış olması gerekmiyor), Anahtar Kelimeler, Giriş, Sonuç bölümlerinden oluşur. Derleme makale gönderen yazarların, makalede kullandıkları verinin seçimi, alınması, sentezi için kullandıkları yöntemleri tanımlayan bir bölüme de makalede yer vermeleri gerekir. Bu yöntemler Öz bölümünde de belirtilmelidir.

Editöre Mektup

Editöre Mektup, kısa ve net görüş bildiren yazılardır. Dergide daha önce yayınlanmış olan makalelerle ilgili olarak ya da dergide ifade edilmiş görüşlerle ilgili olarak yazılmış olması tercih edilir. Editöre Mektup yazıları, daha sonra yeni bir yazı ile geçerlilik ispatı gerektirebilecek ön görüş bildiren yazılar olmamalıdır.

Tablolar

Tablolar bilgileri etkin bir şekilde gösterir ve ayrıca bilginin istenen tüm ayrıntı seviyelerinde verilmesini sağlar. Bilgileri metin yerine tablolarda vermek genelde metnin uzunluğunu kısaltır.

Her tablo ayrı bir sayfaya çift aralıklı olarak basılmalıdır. Tablolar metindeki sıralarına göre numaralanıp, her birine kısa bir başlık verilmelidir. MS Word 2003 ve üstü versiyonlarında otomatik tablo seçeneğinde "tablo klasik 1" ya da "tablo basit 1" seçeneklerine göre tablolar hazırlanmalıdır. Başlık satırı ve tablo alt üst satırları dışında tablonun içinde başka dikey ve yatay çizgiler kullanılmamalıdır. Her sütuna bir başlık verilmelidir. Yazarlar açıklamaları başlıkta değil, dipnotlarda yapmalıdır. Dipnotlarda standart olmayan tüm kısaltmalar açıklanmalıdır. Dipnotlar için sırasıyla şu semboller kullanılmalıdır: (*,†,‡,§,ǁ,¶,**,††,‡‡).

Varyasyonun standart sapma ya da standart hata gibi istatistiksel ölçümleri belirtilmelidir. Metin içinde her tabloya atıfta bulunulduğuna emin olunmalıdır. Eğer yayınlanmış ya da yayınlanmamış herhangi başka bir kaynaktan veri kullanılıyorsa izin alınmalı ve onlar tam olarak bilgilendirilmelidir. Çok fazla veri içeren tablolar, çok yer tutar ve sadece elektronik yayınlar için uygun olabilir ya da okuyuculara yazarlar tarafından doğrudan sağlanabilir. Böyle bir durumda uygun bir ifade metne eklenmelidir. Bu tip tablolar, hakem değerlendirmesinden geçmesi için makaleyle beraber gönderilmelidir.

Şekiller

Şekiller ya profesyonel olarak çizilmeli ve fotoğraflanmalı ya da fotoğraf kalitesinde dijital olarak gönderilmelidir. Şekillerin basıma uygun versiyonlarının yanı sıra JPEG ya da GIF gibi elektronik versiyonlarda yüksek çözünürlükte görüntü oluşturacak biçimlerde elektronik dosyaları gönderilmeli ve yazarlar göndermeden önce bu dosyaların görüntü kalitelerini bilgisayar ekranında kontrol etmelidir.

Röntgen, CT, MRI filmleri ve diğer tanısal görüntülemeler yüksek kalitede basılmış olarak gönderilmelidir. Bu nedenle şekillerin üzerindeki harfler, sayılar ve semboller açık ve tüm makalede eşit ve yayın için küçültüldüklerinde bile okunabilecek boyutlarda olmalıdır. Şekiller mümkün olduğunca tek başlarına anlaşılabilir olmalıdır. Fotomikrografik patoloji preparatları iç ölçekler içermelidir. Semboller, oklar ya da harfler fonla kontrast oluşturmalıdır. Eğer insan fotoğrafı kullanılacaksa, ya bu kişiler fotoğraftan tanınmamalıdır ya da yazılı izin alınmalıdır (Etik bölümüne bakınız).

Şekiller metinde geçiş sıralarına göre numaralandırılmalıdır. Eğer önceden yayınlanmış bir şekil kullanılacaksa, yayın hakkını elinde bulunduran bireyden izin alınmalıdır. Toplum alanındaki belgeler hariç yazarlığa ve yayıncıya bakılmadan bu izin gereklidir. Basılacak bölgeyi gösteren ek çizimler editörün işini kolaylaştırır. Renkli şekiller editör gerekli gördüğünde ya da sadece yazar ek masrafı karşılarsa basılır.

YAZARLARA BİLGİ

Şekillerin Dipnotları

Ayrı bir sayfadan başlayarak şekiller için tablo başlıkları ve dipnotları tek aralıklı olarak ve Arap sayıları ile hangi şekle karşı geldikleri belirtilerek yazılmalıdır. Semboller, oklar, sayılar ya da harfler şeklin parçalarını belirtmek için kullanıldığında, dipnotlarda her biri açıkça tanımlanmalıdır. Fotomikrografik patoloji preparatlarında iç ölçek ve boyama tekniği açıklanmalıdır.

Ölçüm Birimleri

Uzunluk, ağırlık ve hacim birimleri metrik (metre, kilogram, litre) sistemde ve bunların onlu katları şeklinde rapor edilmelidir. Sıcaklıklar Celsius derecesi, kan basıncı milimetre civa cinsinden olmalıdır. Ölçü birimlerinde hem lokal hem de Uluslararası Birim Sistemleri (International System of Units, SI) kullanılmalıdır. İlaç konsantrasyonları ya SI ya da kütle birimi olarak verilir, alternatif olarak parantez içinde de verilebilir.

Kısaltmalar ve Semboller

Sadece standart kısaltmaları kullanın, standart olmayan kısaltmalar okuyucu için çok kafa karıştırıcı olabilir. Başlıkta kısaltmadan kaçınılmalıdır. Standart bir ölçüm birimi olmadıkça kısaltmaların uzun hali ilk kullanılışlarında açık, kısaltılmış hali parantez içinde verilmelidir.

Teşekkür(ler)

Yazının sonunda kaynaklardan önce yer verilir. Bu bölümde kişisel, teknik ve materyal yardımı gibi nedenlerle yapılacak teşekkür ifadeleri yer alır.

Kelime Sayısı Sınırlandırması

Türkçe ve İngilizce özler en fazla 500 kelime olmalıdır. Orijinal makaleler ve derleme yazılarında özel bir kelime sayısı sınırlandırması yoktur. Olgu sunumları öz /abstract hariç 1000 kelime ile sınırlandırılmalı ve en az sayıda şekil, tablo ve kaynak içermelidir. Editöre mektuplar (en fazla 1000 kelime, tablosuz ve şekilsiz) olmalı ve mektup, tüm yazarlar tarafından imzalanmış olmalıdır. Bağcılar Tıp Bülteni`nde yayınlanmış olan bir yazı ile ilgili eleştiri ya da değerlendirme niteliğindeki mektuplar sözü edilen yazının yayınlanmasından sonraki 12 hafta içinde alınmış olmalıdır.

Makale Hazırlığı

"Bağcılar Tıp Bülteni", Tıp Dergilerinde Bilimsel Çalışmaların Yürütülmesi, Raporlanması, Düzenlenmesi ve Yayınlanmasına İlişkin yönergeleri takip eder "(Uluslararası Tıp Dergisi Editörleri Komitesi - http://www.icmje.org /). Makalenin sunulması üzerine, yazarlar deneme / araştırma türünü belirtmeli ve uygun olduğunda aşağıdaki kuralların kontrol listesini sağlamalıdır:

Randomize çalışmalar için CONSORT açıklaması (CONSORT Grubu için Moher D, Schultz KF, Altman D. CONSORT beyanı paralel grup randomize çalışmaların raporlarının kalitesini iyileştirmek için önerileri gözden geçirdi. JAMA 2001; 285: 1987-91) (http: // www.consort-statement.org /),

Sistematik gözden geçirmeler ve meta-analizler için tercih edilen raporlama maddeleri için PRISMA (Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Grubu. Sistematik İncelemeler ve Meta-Analizler için Tercih Edilen Raporlama Maddeleri: PRISMA Beyanı. PLoS Med 2009; 6 (7): e1000097.) (Http://www.prisma-statement.org /),

Tanısal doğruluk çalışmalarının raporlanması için STARD kontrol listesi (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, vd, STARD Grubu için. Teşhis doğruluğu çalışmalarının eksiksiz ve doğru raporlanmasına yönelik: STARD girişimi, Ann Intern Med 2003; 138: 40-4.) (http://www.stard-statement.org /),

STROBE gözlemsel çalışma raporlarında yer alması gereken maddelerin kontrol listesi (http://www.strobe-statement.org /),

Gözlemsel çalışmaların meta-analizi ve sistemik incelemeleri için MOOSE yönergeleri (Stroup DF, Berlin JA, Morton SC, vd.) Epidemiyolojideki gözlemsel çalışmaların meta-analizi: Epidemiyoloji (MOOSE) grubundaki gözlemsel çalışmaların Meta-analizini bildirme önerisi JAMA 2000; 283: 2008-12).

YAZARLARA BİLGİ

CARE kuralları, vaka raporlarının doğruluğunu, şeffaflığını ve kullanışlılığını artırmak için tasarlanmıştır. (Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D; CARE Grubu. CARE Yönergeleri: Konsensüs Tabanlı Klinik Vaka Raporlama Rehberinin Geliştirilmesi.) (Http://www.care-statement.org /

Kaynaklar

Kaynaklarla İlgili Genel Konular

Gözden geçirme yazıları okuyucular için bir konudaki kaynaklara ulaşmayı kolaylaştıran bir araç olsa da, her zaman orijinal çalışmayı doğru olarak yansıtmaz. Bu yüzden mümkün olduğunca yazarlar orijinal çalışmaları kaynak göstermelidir. Öte yandan, bir konuda çok fazla sayıda orijinal çalışmanın kaynak gösterilmesi yer israfına neden olabilir. Birkaç anahtar orijinal çalışmanın kaynak gösterilmesi genelde uzun listelerle aynı işi görür. Ayrıca günümüzde kaynaklar elektronik versiyonlara eklenebilmekte ve okuyucular elektronik literatür taramalarıyla yayınlara kolaylıkla ulaşabilmektedir.

Özler kaynak olarak gösterilmemelidir. Kabul edilmiş ancak yayınlanmamış makalelere atıflar "basımda" ya da "çıkacak" şeklinde verilmelidir; yazarlar bu makaleleri kaynak gösterebilmek için yazılı izin almalıdır ve makalelerin basımda olduğunu ispat edebilmelidir. Gönderilmiş ancak yayına kabul edilmemiş makaleler, "yayınlanmamış gözlemler" olarak gösterilmeli ve kaynak yazılı izinle kullanılmalıdır. Genel bir kaynaktan elde edilemeyecek temel bir konu olmadıkça "kişisel iletişimlere" atıfta bulunulmamalıdır. Eğer atıfta bulunulursa parantez içinde iletişim kurulan kişinin adı ve iletişimin tarihi belirtilmelidir. Bilimsel makaleler için yazarlar bu kaynaktan yazılı izin ve iletişimin doğruluğunu gösterir belge almalıdır.

Referans Stili ve Formatı

Tek tip kurallar esas olarak National Library of Medicine, tarafından uyarlanmış olan bir ANSI standart stilini kabul etmiştir. Kaynak atıfta bulunma örnekleri için yazarlar www.nlm.nih.gov/bsd/uniform_requirements.html sitesine başvurabilirler. Dergi isimleri National Library of Medicine kaynağında yer alan şekilleriyle kısaltılmalıdır. Kaynaklar yazının sonunda (Kaynaklar/References) başlığı altında metindeki geçiş sırasına göre numaralandırılıp dizilmelidir. Metin içinde ise parantez içinde belirtilmelidir. Kaynakların listesiyle metin içinde yer alış sırası arasında bir uyumsuzluk bulunmamalıdır.

Kaynaklar yazının sonunda (Kaynaklar/References) başlığı altında metindeki geçiş sırasına göre numaralandırılıp dizilmelidir. Metin içinde ise () şeklinde parantez içinde referans numarası belirtilmelidir. Kaynakların listesiyle metin içinde yer alış sırası arasında bir uyumsuzluk bulunmamalıdır.

Kaynakların doğruluğundan yazar(lar) sorumludur. Tüm kaynaklar metinde belirtilmelidir. Kaynaklar aşağıdaki örneklerdeki gibi gösterilmelidir. Altı yazardan fazla yazarı olan çalışmalarda ilk altı yazar belirtilmeli, sonrasında "ve ark." ya da "et al." ibaresi kullanılmalıdır. Kaynak dergi adlarının kısaltılması National Library of Medicine'de belirtilen kısaltmalara (https://www.ncbi.nlm.nih.gov/nlmcatalog/journals) uygun olmalıdır. National Library of Medicine'da indekslenmeyen bir dergi kısaltılmadan yazılmalıdır.

Kaynaklar için örnekler aşağıda belirtilmiştir:

1. Dergilerdeki makaleler için örnekler:

MEDLINE'da yer alan ve kısaltması MEDLINE'a göre yapılan dergi makalesi için: Crow SJ, Peterson CB, Swanson SA, Raymond NC, Specker S, Eckert ED, et al. Increased mortality in bulimia nervosa and other eating disorders. Am J Psychiatry 2009;166(12):1342-1346.

MEDLINE'da yer almayan ve kısaltması olmayan dergi makalesi için: Sevinçer GM, Konuk N. Emotional eating. Journal of Mood Disorders 2013;3:171-178.

2. Ek sayı için:

MEDLINE'da yer alan ve kısaltması MEDLINE'a göre yapılan dergi makalesi için: Sharan P, Sundar AS. Eating disorders in women. Indian J Psychiatry 2015:57(Suppl 2):286-295.

MEDLINE'da yer almayan ve kısaltması olmayan dergi makalesi için: Maner F. Yeme bozukluklarının tedavisi. Anadolu Psikiyatri Dergisi 2009;10(Ek 1):55-56.

YAZARLARA BİLGİ

3. Baskıdaki makale için:

Cossrow N, Pawaskar M, Witt EA, Ming EE, Victor TW, Herman BK, et al. Estimating the prevalence of binge eating disorder in a community sample from the United States: comparing DSM-IV-TR and DSM-5 criteria. J Clin Psychiatry, 2016. (in press).

4. Kitaptan alıntılar:

Tek yazarlı kitaptan alıntı için:

McKnight TL. Obesity Management in Family Practice. 1st ed., New York:Springer, 2005:47-51.

Kitaptan bir bölüm için, editör(ler) varsa:

Jebb S, Wells J. Measuring body composition in adults and children. In Clinical Obesity in Adults and Children, Copelman P, Caterson I, Dietz W (editors). 1st ed., London: Blackwell Publishing, 2005:12-18.

Editörler aynı zamanda kitabın içindeki metin ya da metinlerin yazarı ise: Önce alınan metin ve takiben kitabın ismi yine kelimeler büyük harfle başlatılarak yazılır.

Eckel RH (editor). Treatment of obesity with drugs in the new millennium. In Obesity Mechanisms and Clinical Management. 1st ed., Philadelphia: Lippincott Williams & Wilkins, 2003:449-476.

Çeviri Kitaptan Alıntı için:

McGuffin P, Owen MJ, Gottsman II. Psikiyatri Genetiği ve Genomiği. Abay E, Görgülü Y (translation editors) 1st ed., Istanbul: Nobel Tıp Kitabevleri, 2009:303-341.

5. Tezden alıntı için:

Keçeli F. Yeme bozukluğu hastalarında obsesif kompulsif bozukluk ve kişilik bozukluğu. Thesis, T.C. Sağlık Bakanlığı Bakırköy Prof. Dr. Mazhar Osman Ruh Sağlığı ve Sinir Hastalıkları Eğitim ve Araştırma Hastanesi, Istanbul:2006.

6. Kongre bildirileri için:

Akbaş Öncel D, Akdemir A. Üniversite öğrencilerinde diyet, beden algısı ve kendilik algısı arasındaki ilişkiler. 47. Ulusal Psikiyatri Kongresi Özet Kitabı, 26-30 Ekim 2011, Antalya, 2011:102.

7. Online Makale:

Kaul S, Diamond GA. Good enough: a primer on the analysis and interpretation of noninferiority trials. Ann Intern Med [Internet]. 4 Temmuz 2006 [Atıf tarihi:4 Ocak 2007];145(1):62-9. Erişim adresi:http://www.annals.org/cgi/reprint/145/1/62.pdf

Makalenin Dergiye Gönderilmesi

Çevrimiçi gönderim (online submission) ile birlikte Bağcılar Tıp Bülteni web sitesinin (www.ijfed.org) ilgili kısımlarındaki talimatlara uyarak makale gönderilebilmekte, hakem süreçleri de bu yolla yapılabilmektedir.

Makalelere eşlik eden ve aşağıdaki bilgileri içeren bir kapak mektubu olmalıdır.

1. Aynı ya da çok benzer çalışmadan elde edilen raporların daha önce yayına gönderilip gönderilmediği mutlaka belirtilmelidir. Böyle bir çalışmaya özgül olarak atıfta bulunulmalı ve ayrıca yeni makalede de eskisine atıfta bulunulmalıdır. Gönderilen makaleye bu tip materyalin kopyaları da eklenerek editöre karar vermesinde yardımcı olunmalıdır.

2. Eğer makalenin kendisinde ya da yazar formunda belirtilmemişse çıkar çatışmasına neden olabilecek mâli ya da diğer ilişkileri belirten bir ifade olmalıdır.

3. Makalenin tüm yazarlar tarafından okunup kabul edildiğini, önceden belirtilen şekilde yazarlık ölçütlerinin karşılandığını, her yazarın makalenin dürüst bir çalışmayı yansıttığına inandığını belirten bir ifade olmalıdır. Mektup editöre yardımcı olabilecek tüm diğer bilgileri içermelidir. Eğer makale önceden başka bir dergiye gönderilmişse önceki editörün ve hakemlerin yorumları ve yazarların bunlara verdiği cevapların gönderilmesi faydalıdır. Editör, önceki yazışmaların gönderilmesini hakem sürecini dolayısıyla yazının yayınlanma sürecini hızlandırabileceğinden istemektedir.

Yazarların makalelerini göndermeden önce bir eksiklik olmadığından emin olmalarını sağlamak için bir kontrol listesi bulunmaktadır. Yazarlar derginin kontrol listesini kullanıp gönderilerini kontrol etmeli ve makaleleri ile birlikte bu formu göndermelidirler.

YAZARLARA BİLGİ

SON KONTROL LİSTESİ

- Editöre sunum sayfası
- Makalenin kategorisi
- Başka bir dergiye gönderilmemiş olduğu bilgisi
- Sponsor veya ticari bir firma ile ilişkisi (varsa belirtiniz)
- İstatistik kontrolünün yapıldığı (araştırma makaleleri için)
- İngilizce yönünden kontrolünün yapıldığı

Telif Hakkı Devir Formu

Yazar Katkı Formu

ICMJE Potansiyel Çıkar Çatışması Beyan Formu

1. Daha önce basılmış materyal (yazı-resim-tablo) kullanılmış ise izin belgesi
2. İnsan öğesi bulunan çalışmalarda "gereç ve yöntemler" bölümünde Helsinki Deklarasyonu prensiplerine uygunluk, kendi kurumlarından alınan etik kurul onayının ve hastalardan "bilgilendirilmiş olur (rıza)" alındığının belirtilmesi
3. Hayvan öğesi kullanılmış ise "gereç ve yöntemler" bölümünde "Guide for the Care and Use of Laboratory Animals" prensiplerine uygunluğunun belirtilmesi
4. Kapak sayfası

- Makalenin Türkçe ve İngilizce başlığı (tercihen birer satır)
- Yazarlar ve kurumları
- Tüm yazarların yazışma adresi, iş telefonu, faks numarası, GSM, e-posta adresleri

1. Özler (400-500 kelime) (Türkçe ve İngilizce)
2. Anahtar Kelimeler: 3-10 arası (Türkçe ve İngilizce)
3. Tam metin makale
4. Teşekkür
5. Kaynaklar
6. Tablolar-Resimler, Şekiller

Yayınevi Yazışma Adresi

Galenos Yayınevi Tic. Ltd. Şti.
Adres: Molla Gürani Mah. Kaçamak Sk. No: 21, 34093 Fındıkzade-İstanbul-Türkiye
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YAZARLARA BİLGİ

Hakem Değerlendirmesi, Yayın Etiği ve Kötüye Kullanım

Hakem Değerlendirmesi

Makalelerin daha önce yayınlanmamış olması ve aynı anda başka bir yere gönderilmemiş olması koşuluyla başvuru kabul edilir; yazarlar, içeriği okuduğunu, onayladığını, tüm yazarların çıkar çatışmalarını beyan ettiğini, çalışmanın etik onaya uygun olduğunu ve uluslararası kabul görmüş etik standartlarda yürütüldüğünü kabul eder. Etik suistimalden şüphelenilmesi durumunda, Yayın Kurulu ilgili uluslararası yayın etiği kurallarına (COPE yönergelerine) uygun olarak hareket edecektir.

Derginin yayın politikaları, Bilim Konseyi Editörleri tarafından önerilen kurallarda belirtildiği gibi yürütülür ve Biyomedikal Dergilere Gönderilen Makaleler için Tekdüzen Gereklilikler: Biyomedikal Yayın için Yazma ve Düzenleme (http://www.icmje.org/)'da yansıtılır. Buna göre yazarlar, gözden geçirenler ve editörlerin bu bildirimde yer alan etik davranışa ilişkin en iyi uygulama kılavuzlarına uymaları beklenmektedir.

Gönderilen yazılar çift-kör hakem değerlendirmesine tabi tutulur. Dergide yayımlanacak yazıların seçimine rehberlik eden bilim kurulu, derginin seçilmiş uzmanlarından ve gerekirse ilgili araştırma alanında ulusal ve uluslararası uzmanlardan seçilmiş uzmanlardan oluşur. Tüm yazılar editör, bölüm yardımcı editörleri ve en az üç dahili ve harici uzman hakem tarafından incelenir. Tüm araştırma makaleleri de bir istatistik editörü tarafından yorumlanır.

İnsan ve Hayvan Araştırmaları

Deneysel, klinik, ilaç ve insan çalışmaları için, etik kurul onayı ve çalışma protokolünün uluslararası anlaşmalara uygunluğuna dair bir beyan (World Medical Association Association of Helsinki "Ethical Principles for Medical Research Involving Human Subjects," Ekim 2013, www.wma.net) gereklidir. Deneysel hayvan çalışmalarında yazarlar, izlenen prosedürlerin hayvan haklarına uygun olduğunu (Laboratuvar Hayvanlarının Bakım ve Kullanım Kılavuzu, www.nap.edu.catalog/5140.html) belirtmeli ve hayvan Etik Kurul Onayı almalıdır. Etik Kurul Onayı belgesi, makale ile birlikte Bağcılar Tıp Bülteni'ne gönderilmelidir.

Etik Kurul Onayı ile yukarıda belirtilen uluslararası kılavuzlara uyum ve hastanın aydınlatılmış onamının alındığına dair beyan "Materyal ve Yöntem" bölümünde belirtilmeli ve kullanılan veri/medyanın hastanın kimliğini ortaya çıkarabileceği durumlarda vaka raporları gerekmektedir. Yazarlar, kurumlar arasında çıkar çatışması beyanı, herhangi bir mali veya maddi desteğin kabulünün belirtilmesi makale gönderen yazarlar için zorunludur ve bu açıklama makalenin sonunda yer almalıdır. Hakemler, yazarlar veya kurumlar ile aralarında herhangi bir potansiyel çıkar çatışması varsa, bunu rapor etmelidir.

İntihal ve Etik Suistimal

Bağcılar Tıp Bülteni, tüm makaleleri yayınlanmadan önce "iThenticate" kullanarak intihal taramasına tabi tutar.

Yazarların aşağıda yazılanlar gibi her türlü intihal ve etik suistimalden kaçınmaları önemlidir:

İntihal: Başka bir yazarın yayınındaki bir içeriğin tamamını veya bir kısmını kaynak göstermeden yeniden yayınlamak.

Fabrikasyon (Uydurma): Var olmayan veri ve bulguları/sonuçları yayınlamak.

Çoğaltma: Bir makalenin farklı dillerde yeniden yayınlanmasını içeren başka bir yayından alınan verileri kullanmak.

Dilimleme (Salamizasyon): Bir çalışmanın sonuçlarını bölerek birden fazla yayın oluşturma.

Veri Manipülasyonu/Yanlışlığı: Yanlış bir izlenim vermek için araştırma verilerini manipüle etmek veya kasıtlı olarak çarpıtmak.

İntihal, fabrikasyon, çoğaltma, veri manipülasyonu ve dilimleme gibi etik olmayan uygulamaları ve yazarlık hediye etme, uygunsuz teşekkür ve COPE akış şemalarına uygun olmayan referanslar gibi uygulamalarla inceleme sürecini etkilemeye yönelik çabaları onaylamıyoruz.

Gönderilen yazılar ayrıca otomatik yazılım tarafından intihal ve yayın değerlendirmesine tabi tutulur. Yazarlar, çalışma sonuçlarını tamamen veya kısmen özet şeklinde yayınlayıp yayınlamadıklarını bildirmekle yükümlüdür.

YAZARLARA BİLGİ

A. YAYINCININ GÖREVLERİ:

Etik Olmayan Yayınlama Davranışının Ele Alınması

Yayıncı, iddia edilen veya kanıtlanmış bilimsel suistimal, hileli yayın veya intihal durumlarında, söz konusu makaleyi editörlerle yakın iş birliği içinde değiştirmek için tüm uygun önlemleri alacaktır. Bu, en ciddi durumda, etkilenen çalışmanın bir yanlışlık sonucu yayınlanmasını, ifşa edilmesini veya geri çekilmesini içerir. Yayıncı, editörlerle birlikte, araştırma suistimalinin meydana geldiği makalelerin yayınlanmasını tespit etmek ve önlemek için makul adımları atacak ve hiçbir koşulda bu tür kötüye kullanımın gerçekleşmesine teşvik etmeyecek veya bilerek izin vermeyecektir.

Editöryal Özerklik

Bağcılar Tıp Bülteni, herhangi birinin veya ticari ortakların etkisi olmaksızın editöryal kararların özerkliğini sağlamayı taahhüt eder.

Fikri Mülkiyet ve Telif Hakkı

Bağcılar Tıp Bülteni, dergide yayınlanan makalelerin mülkiyetini ve telif haklarını korur ve her makalenin yayınlanmış kaydını tutar. Dergi, yayınlanan her makalenin bütünlüğünü ve şeffaflığını sağlar.

Bilimsel Suistimal

Bağcılar Tıp Bülteni'nin yayıncısı, hileli yayın veya intihal ile ilgili gerekli tüm önlemleri almaktadır.

B. EDİTÖRLERİN GÖREVLERİ:

Yayın Kararı ve Sorumluluğu

Dergi editörü, dergideki her şeyi kontrol altında tutar, okuyucuların ve yazarların ihtiyaçlarını karşılamaya çalışır. Editör ayrıca dergiye gönderilen makalelerin hangilerinin yayınlanması gerektiğine karar vermekten ve hakaret, telif hakkı ihlali ve intihal ile ilgili yasal gerekliliklere tabi politikalar tarafından yönlendirilmekten sorumludur. Editör, yayın kararları verirken hakemlerle tartışabilir. Yayının içeriğinden ve genel kalitesinden editör sorumludur. Editör, adil ve uygun bir hakemlik süreci sağlamalıdır.

Nesnellik

Dergiye gönderilen makaleler her zaman önyargısız olarak değerlendirilir.

Gizlilik

Editör, gönderilen bir makaleyle ilgili herhangi bir bilgiyi, editör kadrosu, hakemler ve yayıncı dışında hiç kimseye açıklamamalıdır.

Çıkar Çatışmaları ve İfşa

Bağcılar Tıp Bülteni, yazarlar, hakemler ve editörler gibi taraflar arasında herhangi bir çıkar çatışmasına izin vermez. Gönderilen bir makaledeki yayınlanmamış materyaller, yazarın açık izni olmaksızın hiç kimse tarafından kullanılmamalıdır.

Yayımlanan Eserlerde Temel Hatalar

Yazarlar, yayınlanan çalışmada önemli hatalar veya yanlışlıklar tespit edilirse, derhal dergi editörlerini veya yayıncısını bilgilendirmek ve makaleyi düzeltmek veya geri çekmek üzere onlarla iletişim sağlamakla yükümlüdür. Editörler veya yayıncı, yayınlanan bir çalışmanın önemli bir hata veya yanlışlık içerdiğini üçüncü bir taraftan öğrenirse, yazarlar makaleyi derhal düzeltmeli, geri çekmeli veya dergi editörlerine makalenin doğruluğuna dair kanıt sağlamalıdır.

YAZARLARA BİLGİ

C. HAKEMLERİN GÖREVLERİ:

Değerlendirme

Hakemler, yazarların kökeni, cinsiyeti, cinsel yönelimi veya politik felsefesini gözetmeksizin yazıları değerlendirir. Hakemler ayrıca değerlendirme sırasında gönderilen yazılar için adil bir kör hakem incelemesi sağlar.

Gizlilik

Gönderilen makalelerle ilgili tüm bilgiler gizli tutulur. Hakemler, editör tarafından izin verilmedikçe başkalarıyla tartışılmamalıdır.

Çıkar Çatışmaları ve İfşa

Hakemlerin yazarlar, fon sağlayıcılar, editörler vb. taraflarla ilgili herhangi bir çıkar çatışması yoktur.

Editöre Katkı

Hakemler, editöre karar vermede ve makaleyi geliştirmede yardımcı olabilir.

Nesnellik

Daima objektif bir değerlendirme yapılır. Hakemler görüşlerini uygun destekleyici argümanlarla açıkça ifade eder.

Kaynakların Onaylanması

Hakemler, yazarların atıfta bulunmadığı ilgili yayınlanmış bir çalışmayı tanımlamalıdır. Hakemler ayrıca, makale ile kişisel bilgilerine sahip oldukları diğer yayınlanmış makaleler arasındaki önemli benzerlikleri veya örtüşmeleri editörün dikkatine sunarlar.

D. YAZARLARIN GÖREVLERİ:

Raporlama Standartları

Gönderilen bir makale orijinal olmalı ve yazarlar, makalenin daha önce herhangi bir dergide yayınlanmamış olmasını sağlamalıdır. Araştırmanın verileri makalede tam anlamıyla sunulmalıdır. Bir makale, başkalarının çalışmayı yeniden kopyalamasına izin vermek için gerekli ayrıntı ve referansları içermelidir.

Özgünlük

Çalışmalarını dergiye göndermek isteyen yazarlar, çalışmalarının tamamen özgün olduğundan emin olmalıdır. Literatürden alınan kelime ve cümleler uygun şekilde alıntılanmalıdır.

Çoklu Yayınlar

Yazarlar, aynı çalışmayı başka bir dergide yayınlanmak veya değerlendirilmek üzere göndermemiş olmalıdır. Aynı çalışmanın birden fazla dergiye aynı anda gönderilmesi kabul edilemez ve etik dışı bir davranış olarak nitelendirilir.

Kaynakların Belirtilmesi

Başkalarının çalışmalarının uygun bir şekilde alıntılanması gerekir. Yazarlar, çalışmayı belirlemede etkili olan yayınlara atıfta bulunmalıdır. Çalışmanın sürecini kapsayan tüm kaynaklar belirtilmelidir.

Makale Yazarlığı

Bir makalenin yazarlığı, çalışmaya kayda değer bir katkı yapmış olanlarla sınırlı olmalıdır. Başkaları araştırmaya katılmışsa, katkıda bulunanlar olarak listelenmelidir. Yazarlık aynı zamanda bir derginin editörü ile iletişim halinde olan bir sorumlu yazarı da içerir.

YAZARLARA BİLGİ

Sorumlu yazar, tüm uygun ortak yazarların bir makaleye dahil edilmesini sağlamalıdır.

Çıkar Çatışmaları ve İfşa

Tüm finansal destek kaynakları açıklanmalıdır. Tüm yazarlar, çalışmalarını oluşturma sürecinde (varsa) çıkar çatışmasını ifşa etmelidir. Gönderilen bir çalışma için bireylerden veya kurumlardan alınan mali yardımlar veya diğer destekler, Bağcılar Tıp Bülteni Yayın Kurulu'na açıklanmalıdır. ICMJE Potansiyel Çıkar Çatışması Bildirim Formu, olası bir çıkar çatışmasını açıklamak için katkıda bulunan tüm yazarlar tarafından doldurulmalı ve gönderilmelidir. Derginin Yayın Kurulu, editörler, yazarlar veya hakemler arasında olası bir çıkar çatışması durumlarında COPE ve ICMJE yönergeleri kapsamında hareket eder.

Mali veya şahsi fayda sağlayan koşullar, bir çıkar çatışması doğurur. Bu durum, bilimsel sürecin ve yayınlanan makalelerin güvenilirliği, bilimsel çalışmaların planlanması, uygulanması, yazılması, değerlendirilmesi, düzenlenmesi ve yayınlanması sırasında çıkar çatışmalarının objektif olarak ele alınması ile doğrudan ilişkilidir.

Finansal ilişkiler en kolay tespit edilen çıkar çatışmalarıdır ve derginin, yazarların ve bilimin güvenilirliğini zedelemesi kaçınılmazdır. Bu çatışmalara bireysel ilişkiler, akademik rekabet veya entelektüel yaklaşımlar neden olabilir. Yazarlar, çalışmanın tüm verilerine ulaşmalarını veya makalelerini analiz etme, yorumlama, hazırlama ve yayınlama olanaklarını kısıtlayan kâr veya başka bir avantaj elde etme düşüncesiyle sponsorlarla anlaşmalardan mümkün olduğunca kaçınmalıdır. Editörler, çalışmaları değerlendirirken aralarında ilişki olabilecek kişileri bir araya getirmekten kaçınmalıdır. Makaleler hakkında nihai kararı verecek olan editörlerin, karar verecekleri konulardan hiçbiriyle kişisel, mesleki veya mali bağı olmamalıdır. Yazarlar, makalelerinin bağımsız bir değerlendirme süreci ile etik ilkeler çerçevesinde değerlendirilmesini sağlamak için olası çıkar çatışmalarını yayın kuruluna bildirmelidir.

Editörlerden birinin herhangi bir yazıda yazar olması durumunda editör, makale değerlendirme sürecinden çıkarılır. Herhangi bir çıkar çatışmasını önlemek için makale değerlendirme süreci çift kör olarak yapılmaktadır. Çift kör değerlendirme sürecinden dolayı Baş Editör dışında hiçbir yayın kurulu üyesine, uluslararası danışma kurulu üyesine veya hakemlere, makalenin yazarları veya yazarların kurumları hakkında bilgi verilmemektedir.

Yayın ekibimiz tüm bu durumları göz önünde bulundurarak değerlendirme sürecinin tarafsız bir şekilde yürütülmesi için özveriyle çalışmaktadır.

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ORIGINAL RESEARCH

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Perineal and Abdominal Approaches in the Surgical Treatment of Rectal Prolapse: Our 10-year Clinical Experience

Rektal Prolapsus Cerrahi Tedavisinde Perineal ve Abdominal Yaklaşım: 10 Yıllık Klinik Deneyimimiz

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Abstract

Objective: Rectal prolapse is a rare condition characterized by protrusion of the rectum with all its layers from the anus. It is a disease that causes social and functional problems. In this study, it was aimed to investigate the abdominal and perineal approaches together with postoperative early and late results in our patients who underwent surgical treatment for rectal prolapse.

Method: The records of 39 patients who were operated on with the diagnosis of rectal prolapse between 2010 and 2020 in the Department of General Surgery, Dicle University Faculty of Medicine were evaluated retrospectively. Demographic and physical examination findings of the patients, surgical methods applied, early and late postoperative complications, recurrence and mortality rates were recorded.

Results: The most common complaints on admission to the hospital were gas control disorder, difficulty in defecating and getting wet with mucus. On physical examination, stage 1 rectal prolapse was found in 12.8% of the patients, and full-thickness prolapse was found in the other patients. The mean age of 39 patients included in the study was 36 (14-88) years. Of the patients included in the study, 14 (35.9%) were female and 25 (64.1%) were male. Surgery was performed with an abdominal and perineal approach in 53.8% of the patients, while laparoscopy was performed in 46.2%. The most frequently used abdominal surgical technique was Notaras (35.8%). The most common perineal approach technique was Altemeier (5.1%). Patients who underwent the perineal approach were older and had a shorter hospital stay, and it was often performed under regional anesthesia. Complications developed in the early postoperative period in 10.4% of the patients. The median hospital stay was 5 days (2-19) and the follow-up period was 13 months (9-19). Postoperative mortality did not occur in any of the patients. Hospital

Öz

Amaç: Rektal prolapsus, rektumun tüm katmanlarıyla birlikte anüsten çıkması ile karakterize nadir bir durumdur. Sosyal ve fonksiyonel sorunlara neden olan bir hastalıktır. Bu çalışmada, rektal prolapsus için laparoskopik ve açık cerrahi yöntemin postoperatif erken ve geç sonuçlarının araştırılması amaçlanmıştır.

Yöntem: Dicle Üniversitesi Tıp Fakültesi Genel Cerrahi Anabilim Dalı'nda 2010-2020 yılları arasında rektal prolapsus tanısıyla ameliyat edilen 39 hastanın kayıtları geriye dönük olarak değerlendirildi. Demografik ve fizik muayene bulguları, cerrahi yöntem, postoperatif erken ve geç komplikasyonlar, morbidite ve mortalite oranları kaydedildi.

Bulgular: Hastaneye başvuruda en sık başvuru şikayetleri gaz kontrol bozukluğu, dışkılamada güçlük ve mukusla ıslanma idi. Fizik muayenede hastaların %12,8'inde evre 1 rektal prolapsus, diğer hastalarda tam kat prolapsus saptandı. Çalışmaya alınan 39 hastanın yaş ortalaması 36 (14-88) idi. Çalışmaya alınan hastaların 14'ü (%35,9) kadın, 25'i (%64,1) erkekti. Hastaların %53,8'ine açık karın cerrahisi yapılırken, %46,8'ine laparoskopi yapıldı. En sık kullanılan abdominal cerrahi teknik Notaras (%35,8) idi. En yaygın perineal yaklaşım tekniği Altemeier (%5,1) idi. Perineal yaklaşım uygulanan hastalar daha yaşlıydı ve hastanede kalış süreleri daha kısaydı ve sıklıkla bölgesel anestezi altında uygulanıyordu. Hastaların %10,4'ünde erken postoperatif dönemde komplikasyon gelişti. Ortanca hastanede kalış süresi 5 gün (2-19), takip süresi 13 ay (9-19) idi. Hiçbir hastada postoperatif mortalite olmadı. Laparoskopik cerrahi uygulanan hastalarda hastanede kalış süresi anlamlı olarak daha kısaydı. Erken postoperatif komplikasyonlar ve nüks açısından istatistiksel olarak fark yoktu.

Sonuç: Rektal prolapsusu olan hastanın risk faktörleri göz önüne alındığında hem laparoskopik hem de açık cerrahi yaklaşımların sonuçları

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Abstract

stay was significantly shorter in patients who underwent laparoscopic surgery. There was no statistical difference in terms of early postoperative complications and recurrence.

Conclusion: Although more than a hundred surgical procedures have been described to date for the treatment of rectal prolapse, the ideal treatment method is still unclear. In terms of surgical treatment, the results of abdominal or perineal approaches to be applied are similar, considering the risk factors, patient findings and surgeon's experience.

Keywords: Abdominal and perineal surgery, notaras operation, rectal prolapse

Öz

benzerdir. Cerrahın deneyimine ve hastane olanaklarına göre cerrahi yöntemi seçmek gerekir.

Anahtar kelimeler: Abdominal ve perineal cerrahi, notaras operasyonu, rektal prolapsus

Introduction

Rectal prolapse (RP) is the protrusion of all or part of the rectum from the anatomical position of the rectum and protruding from the anus in all its layers (1). Although the actual frequency of the disease, which is accepted as a sliding hernia in various sources, is not known in the society, it is known that it is more common in the male population at an early age, while it is more common in women in adulthood. The generally accepted theory in its etiology is that an anatomical defect becomes evident for various predisposing reasons and causes the disease. Although so many surgical techniques have been described, there are still disagreements about the most ideal intervention method, due to the low frequency of the disease and the lack of large prospective randomized studies to prove the superiority of the surgical techniques applied to each other. Laparoscopy entered surgical practice about 20 years ago and has become widespread rapidly due to its advantages such as less pain, shorter hospital stay, earlier return to work, and better cosmetics. Laparoscopic procedures, which combine the functional results of open abdominal procedures with the advantages of minimally invasive surgery such as less pain, better cosmetics, and low perioperative morbidity, are recommended as the first treatment option in the treatment of RP (2). For this reason, the best surgical treatment for RP is still unknown and efforts to find an ideal intervention are still ongoing. However, the common goal of all described surgical interventions is to correct the deteriorated anatomical structure and to restore defecation mechanisms (3). In this study, it was aimed to investigate the abdominal and perineal approaches together with postoperative early and late results in our patients who underwent surgical treatment for RP.

Materials and Methods

The records of 39 patients who underwent surgical treatment with the diagnosis of RP between January 2010 and January 2020 in the Department of General Surgery, Dicle University Faculty of Medicine were evaluated retrospectively. Ethics committee approval for the study was obtained from Dicle University Faculty of Medicine, Health Sciences Non-Interventional Clinical Research Ethics Committee, with the decision dated 07.05.2020 and numbered 149. Patients' age, gender, symptoms at admission, duration of admission to the hospital, co-morbidities, physical examination findings, surgical methods applied, length of hospital stay, early and late postoperative complications, recurrence and mortality rates were recorded. Relapse cases, patients with inflammatory bowel disease and concomitant malignancy who had previously undergone surgical treatment with the diagnosis of RP were excluded from the study. Based on the physical examination findings of the patients, RP was classified according to the grading system made by Altemeier et al. (4) (Table 1). Concomitant diseases of the patients, including cardiovascular diseases (ischemic heart disease and/or heart failure, hypertension), respiratory diseases (chronic obstructive pulmonary disease and/or asthma) and diabetes, were considered. Due to technical shortcomings, anal manometry, electromyelography and endoanal ultrasonography,can not be analyzed, and preoperative and postoperative patient satisfaction was evaluated using the Boutsis-Ellis criteria (Table 2) (5).

All patients underwent bowel cleansing in the preoperative period and additional pathologies were investigated by performing rectosigmoidoscopy. The patients were

Table 1. Rating of rectal prolapse (4)

Stage 1: Mucosal prolapse
Stage 2: Intussusception of the rectum or rectosigmoid junction
Stage 3: True rectal prolapse

Table 2. Boutsis-Ellis criteria (5)

Stage 1: Normal control, rarely wetting with mucus
Stage 2: Gas control disorder, frequent mucus
Stage 3a: Frequent loss of control, wetting with feces in situations such as diarrhea
Stage 3b: Wetting with feces loss of total control

administered 2nd generation cephalosporin 1 gr/iv 30 minutes before the operation for prophylaxis. All surgical methods were performed under elective conditions, under general or spinal anesthesia, with abdominal or perineal approaches. The choice of the surgical method was carried out according to the experience and preference of the surgeon, taking into account the patient's age, general condition, accompanying pathologies and complaints. All patients were given a laxative agent and a high-fibrin diet postoperatively. Patients were followed up at 1, 6 and 12 months postoperatively, and after that, an annual check-up was recommended. The patients who did not come for the control were contacted by phone and questioned in terms of constipation, incontinence and the presence of recurrence.

Abdominal Surgical Procedures

Applied surgical procedures included posterior rectopexy (with and without prosthetic material) and rectopexy with sigmoid colon resection. In all abdominal methods, the rectum is completely liberated from the posterior wall of the proximal sacrum to the tip of the coccyx in the pelvis, and below the pouch of Douglas or cul-de-sac on the anterior and lateral walls. The lateral ligaments were cut in some cases and preserved in others. Posterior rectopexy was defined as the liberated rectum being pulled upwards from the pelvic floor and fixed to the presacral fascia of the sacrum. In the Ripstein technique, poly-propylene prosthetic material prepared in the form of a rectangle to encircle the rectum was fixed to the presacral fascia with non-absorbable sutures 5 cm below the promontorium (6). In the Notaras technique, the prosthetic material used was detected in the sacrum so that it covered the rectum 1/3-2/3 posteriorly (7). In patients with a long sigmoid colon, after mobilizing the rectum without cutting the lateral ligaments, posterior rectopexy (Goldberg-Frykman technique) was performed with sigmoid colon resection and colorectal anastomosis (8). In perineal proctosigmoidectomy (Altemeier technique), the rectum was cut in full thickness 2-3 cm proximal to the linea dentata in patients in whom the rectum protruded at least 5 cm. After the rectosigmoid colon was freed by opening the peritoneum, a colorectal anastomosis was performed by cutting from the proximal end of the overhanging part (9). In the Delorme technique, the rectal mucosa was excised in the form of a 3-4 cm ring from 1 cm proximal to the linea dentata, and an end-to-end anastomosis of the remaining mucosa was performed (10).

In the laparoscopic rectopexy technique, After the sigmoid colon meso was retracted laterally, the peritoneum was opened from the promontorium to the inferior mesenteric vessels and dissection was started from medial to lateral. Meanwhile, the hypogastic plexus, left ureter, and left gonadal vessels were visualized and the lateral ligaments were mobilized using Ligasure Atlas® (Vessel Sealing System, Tyco Healthcare Co., Ltd. USA). The sigmoid resection procedure was completed with an endoscopic linear stapler (Endo GIA 60, Tyco Healthcare Co, USA or Echelon, Ethicon Endosurgery, Cincinati, USA) to preserve the splenic flexion and lateral connections of the descending colon. The suprapubic trocar area (approximately 4 cm) was expanded and the sigmoid colon was removed from the abdomen. After intracorporeal anastomosis was performed with a transanally advanced circular stapler, it was fixed from the perirectal tissue 3 cm distal to the anastomosis to the presacral fascia at the level of the rectum promontorium.

Statistical Analysis

SPSS (Statistical Package for Social Sciences) Windows 11.5 program was used for statistical analysis in the evaluation of the findings obtained in the study. Descriptive statistics were used to evaluate the data. Quantitative data were expressed as median. The chi-square test was used to compare qualitative data. The Mann-Whitney U test was employed to compare non-parametric quantitative data. $p<0.05$ was considered statistically significant.

Results

Demographic and characteristic findings of the patients are shown in Table 3. The most common complaints were gas control, defecation problems, and often wetting with mucus. On physical examination, stage 1 RP was found in 12.8% of the patients, and full-thickness prolapse was found in the other patients. The mean age of 39 patients included in the study was 36 (14-88) years. Surgery was performed with an abdominal and perineal approach in 53.8% of the patients, while laparoscopy was performed in 46.2%. The most frequently used abdominal surgical technique was Notaras (35.8%). The most common perineal approach technique was Altemeier (5.1%). Complications developed in the early postoperative period in 10.4% of the patients. When patients who underwent

abdominal open surgery and patients who underwent laparoscopic surgery were compared, the length of hospital stay was statistically significant (p=0.021), but there was no significant difference when compared with other variables. When surgical approaches were compared, demographic and characteristic findings were similar except that the mean age was higher in open abdominal surgery. Although postoperative early and late complications were more common in patients who had open abdominal surgery, no statistical difference was found. Surgical treatments applied to patients with RP were classified (Table 4). No recurrence was observed in either group (Table 5). The median hospital stay was 5 days (2-19) and the follow-up period was 13 months (9-19). Postoperative mortality did not occur in any of the patients. Hospital stay was significantly shorter in patients who underwent laparoscopic surgery. There was no statistical difference in terms of early postoperative complications and recurrence. No postoperative mortality or complication requiring reexploration was observed. Patients were followed for a median of 19 months. Continence was achieved in all patients, except for 3 (0.7%) patients who had gas control disorders in late control examinations and no recurrence was observed. When the abdominal and perineal approaches applied to the patients were compared, demographic and characteristic findings were found to be similar, except that the mean age was more advanced in perineal approaches. Abdominal approaches were performed under general anesthesia, while perineal approaches were often performed under regional anesthesia. The hospital stay was shorter in perineal approaches. Although early postoperative complications were seen only in patients who underwent abdominal surgery, no statistical difference was found. No recurrence was observed in either group.

Table 3. Demographic and characteristic findings of patients who underwent surgery for rectal prolapse

Age* (year)	**36 (14-88)**
Gender	
Male, n (%)	25 (64.1)
Female, n (%)	14 (35.9)
Previous surgical history n (%)	
Abdominal surgery	2 (5.2)
Lateral internal sphincterectomy	1 (2.6)
Application complaints (Boutsis-Ellis criteria)	
Stage 1, n (%)	31 (79.4)
Stage 2, n (%)	4 (10.3)
Stage 3a, n (%)	3 (7.7)
Stage 3b, n (%)	1 (2.6)
Physical examination findings	
Full-thickness, n (%)	34 (87.2)
Mucosal, n (%)	5 (12.8)
Additional diseases in the patient ** n (%)	
Chronic diseases	10 (25.7)
Hypertension	5 (12.8)
Cancer	3 (7.7)
Psychiatric diseases	4 (10.3)
Hemorrhoids-fissure-other prolapse	5 (12.8)
Complications n (%)	
One year later, re-operation from inguinal hernia	1 (2.6)
Operate hemorrhoids after 6 months	1 (2.6)
Iatrogenic left ureter injury	1 (2.6)
Postop abdominal abscess and ileus	1 (2.6)
Hospital stay, day*	5 (2-19)
Follow-up time, month*	13 (9-19)

*Data are given as median (minimum-maximum), **There are more than one disease in some patients

Discussion

Numerous methods have been proposed for the treatment of RP, which can be done by perineal or abdominal route. Other factors such as the age and gender of the patient, the presence of constipation and incontinence, and the general condition of the patient, as well as the experience

Table 4. Surgical treatments applied to patients with rectal prolapse

Surgical methods	
Open surgery, n (%)	21 (53.8)
Laparoscopy, n (%)	18 (46.2)
Surgical methods applied	
Notaras, n (%)	14 (35.8)
Retropexy n (%)	15 (38.5)
Ribstein, n (%)	5 (12.8)
Goldberg-Frykman, n (%)	3 (7.7)
Altemeier n (%)	2 (5.1)

Table 5. Comparison of open abdominal and laparoscopic surgery patients due to rectal prolapse

	Open abdominal surgery	Laparoscopic abdominal surgery	p
Age	39 (16-88)	28 (14-68)	0.422
Gender n (%)			
Male	15 (33.3)	11 (38.9)	0.718
Female	7 (66.7)	6 (61.1)	
Previous surgical operation, n (%)			
No	19	17	0.643
Yes	2	1	

of the surgeon in this regard, are also effective in the choice of method (11). Since perineal procedures have a higher recurrence rate, they are generally preferred in elderly patients with comorbid factors or in men who do not accept the risk of sexual dysfunction, even if it is less (11). In the laparoscopic treatment of RP, rectopexy, resection, resection-rectopexy procedures were applied. In all studies, laparoscopic procedures were found to be as safe and effective as conventional surgery (2,12). The hospital stay is shorter and the operation time is longer in laparoscopy (13). Abdominal rectopexy, resection and resection-rectopexy procedures were performed and the last one was found to be superior in terms of functional results and recurrence when compared with other methods (14,15). The advantages of rectopexy alone are short hospital stay, early rehabilitation, excellent cosmetics, and low cost. Resection-rectopexy is a more invasive procedure compared to rectopexy alone. In addition to anastomotic leakage and pelvic sepsis, an incision of approximately 4 cm is required to remove the resected sigmoid colon. Abdominal incision problems such as infection, hematoma, and hernia formation may occur in this incision. On the other hand, functional results are better when resection is performed. Many issues are still being discussed, especially the limits of pelvic dissection in abdominal surgeries, whether or not to cut the lateral ligaments, whether or not to protect the superior rectal vessels in patients who have undergone resection, and how fixation should be done (patch, suture, tack). Speakman et al. (16) suggested that cutting the lateral ligaments caused constipation, and in other studies, with this idea, the lateral ligaments were not cut in order to protect the middle rectal vessels and accompanying nerves (17-19).

The clinical picture in RP depends on the type and degree of prolapse. Patients may have one or more of the complaints of tenesmus, urgent need to defecate, rectal bleeding, mucous discharge and incontinence (15). In the study of Çalıskan et al. (6), which included 68 patients, in the preoperative evaluation performed according to the Boutsis-Ellis criteria, stage 2 incontinence was found in 29 of the patients, stage 3a in 11, stage 3b in 7, and stage 3a and 16 in 2 after surgical treatment. They reported that stage 2 incontinence complaints continued during her period. In our study, 31 (79.4%) of the preoperative patients had stage 1, 4 (10.3%) stage 2, 3 (7.7%) stage 3a and 1 (2.6%) stage 3b incontinence. Complete continence was achieved in all patients, except for 2 (0.5%) patients whose stage 2 incontinence continued after surgical treatment. It has been reported that 70-90% of patients with RP have full thickness and 10% have mucosal prolapse (20). In the preoperative physical examination, 87.2% of our patients had full-thickness prolapse and 12.8% had mucosal prolapse. In the early period in the treatment of RP, although it has been reported that different conservative approaches such as prevention of straining during defecation, regulation of defecation method and time, elimination of constipation, perineal relaxing exercises, electronic stimulation, sclerosant injection, band ligation and infrared coagulation may be beneficial, many of these patients need an additional surgical method (21). While all abdominal approaches were performed under general anesthesia, 80% of perineal approaches were performed under regional anesthesia. Early postoperative complications were seen in 10.4% of our patients and all of them were in patients who underwent abdominal method. No early postoperative complications were observed in patients who underwent perineal method. The hospital stay was shorter in perineal approaches compared to abdominal approaches, since it is a less invasive procedure. High fiber diet and oral laxative use were recommended in our patient who underwent the Ripstein method because of the persistence of postoperative constipation. Postoperative incontinence complaint persisted at a rate of 0.5%, one patient from each group.

Mortality rates after RP surgery are reported to be between 0% and 2% (22). In our study, no mortality was observed in any patient who underwent surgical treatment.

Study Limitations

The limitation of our study is that the surgical technique chosen was determined by the experience of the patient and the surgeon, and we think that prospective, multicenter studies with large patient series are needed.

Conclusion

Considering the risk factors in terms of surgical treatment, patient's findings and the surgeon's experience, the results of the abdominal or perineal approaches to be preferred in patients who underwent both methods are similar, and RP can be treated surgically with low complications. However, laparoscopic resection-suture rectopexy is a safe and effective method in the treatment of RP. The method has the general advantages of minimally invasive surgery such as shorter hospital stay, better cosmetics, and less morbidity. Perineal approaches may be preferred in high-risk patients in terms of surgical treatment due to low complications and early positive results. In comparison of the long-term results of abdominal and perineal

approaches, studies with larger patient series and long follow-up periods are needed.

Ethics

Ethics Committee Approval: The records of 39 patients who underwent surgical treatment with the diagnosis of RP between January 2010 and January 2020 in the Department of General Surgery, Dicle University Faculty of Medicine were evaluated retrospectively. Ethics committee approval for the study was obtained from Dicle University Faculty of Medicine, Health Sciences Non-Interventional Clinical Research Ethics Committee, with the decision dated 07.05.2020 and numbered 149.

Informed Consent: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: Ö.B., F.V.A., G.Y., A.O., Desing: Ö.B., F.V.A., G.Y., Data Collection or Processing: Ö.B., F.V.A., G.Y., Analysis or Interpretation: Ö.B., H.B., G.Y., Drafting Manuscript: Ö.B., H.B., G.Y., Critical Revision of Manuscript: Ö.B., H.B., F.V.A., Final Approval and Accountability: Ö.B., H.B., G.Y., Supervision: H.B., Ö.B., A.O.

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL RESEARCH

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Association Between Bifurcation Angle and Coronary No-reflow Following Primary Percutaneous Coronary Intervention in Patients

Primer Perkutan Koroner Girişim Sonrası Hastalarda Bifurkasyon Açısı ile Koroner No-reflow Arasındaki İlişki

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Abstract

Objective: Percutaneous coronary intervention (PCI) has become the treatment method for patients presenting with ST elevation myocardial infarction (STEMI). One of the well-known complications of PCI is no-reflow. Studies demonstrated a relationship between endothelial dysfunction and disturbed vascular flow due to angulation of vascular tree. Although the relationship between hemodynamic alterations and coronary angulation is evident, there is a lack of detailed analysis in terms of hemodynamic changes between vascular geometry and coronary no-reflow. We aimed to elucidate the relationship between vascular geometry and coronary no-reflow.

Method: We reviewed PCI database of our hospital and enrolled a total of 120 patients with STEMI, who developed no-reflow following PCI, and sex and age matched 80 patients with normal flow. For each group, demographic and clinical characteristics, laboratory values and two dimensional quantitative coronary angiography measurements were evaluated.

Results: Patients with no-reflow had a higher prevalence of hypertension and diabetes mellitus. In addition, serum C-reactive protein levels were higher in patients with no-reflow compared to patients with normal flow (p<0.001). On the other hand, serum hemoglobin levels were significantly lower in patients with no-reflow compared to patients with normal flow (p<0.001). With respect to 3 dimensional coronary measurements, calculated bifurcation angle of left anterior descending artery (LAD) and

Öz

Amaç: Perkutan koroner girişim (PKG), ST yükselmeli miyokard enfarktüsü (STYMI) ile başvuran hastalarda tedavi yöntemidir. PKG'nin en iyi bilinen komplikasyonlarından biri, no-reflow'dur. Çalışmalar, endotel disfonksiyonu ile vasküler yapı angulasyonu nedeniyle bozulmuş vasküler akış arasındaki ilişkiyi göstermiştir. Hemodinamik değişiklikler ile koroner açılanma arasındaki ilişki hakkında bilgimiz olsa da, vasküler geometri ile koroner akım arasındaki hemodinamik değişiklikler açısından ayrıntılı bir analiz eksikliği vardır. Vasküler geometri ile koronerde no-reflow arasındaki ilişkiyi aydınlatmayı amaçladık.

Yöntem: Hastanemizin PKG veri tabanını gözden geçirdik ve PKG'yi takiben no-reflow gelişen ve buna ek olarak cinsiyet ve yaşı eşleşen 80 normal akım olan hastayı 120 STYMI hastasını kaydettik. Her grup için demografik ve klinik özellikler, laboratuvar değerleri ve iki boyutlu kantitatif koroner anjiyografi ölçümleri değerlendirildi.

Bulgular: No-reflow hastalarda daha yüksek hipertansiyon ve diabetes mellitus prevalansı vardı. Ek olarak, serum C-reaktif protein seviyeleri, normal akışa sahip hastalara kıyasla no-reflow gelişen hastalarda daha yüksekti (p<0,001). Öte yandan, serum hemoglobin seviyeleri, normal akışa sahip hastalara kıyasla, no-reflow gelişen hastalarda anlamlı olarak daha düşüktü (p<0,001). Üç boyutlu koroner ölçümlere göre, sol ön inen arter (LAD) ve sirkumfleks arterin (CX) hesaplanan çatallanma açısı, kontrol grubuna göre no-reflow grubunda anlamlı olarak daha genişti [110,9° (21,8°) vs. 85,9° (15,8°), p<0,001].

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Abstract

circumflex artery (CX) was significantly wider in the no-reflow group than in the control group [110.9° (21.8°) vs. 85.9° (15.8°), p<0.001].

Conclusion: Our data showed that a strong association existed between bifurcation angle of LAD-CX and no-reflow phenomenon in STEMI patients who underwent PCI.

Keywords: Bifurcation angle, no reflow, percutaneous coronary intervention

Öz

Sonuç: Verilerimiz, PKG uygulanan STYMI hastalarında LAD-CX'in bifurkasyon açısı ile no-reflow fenomeni arasında güçlü bir ilişki olduğunu gösterdi.

Anahtar kelimeler: Bifurkasyon açısı, no-reflow, perkutan koroner girişim

Introduction

Percutaneous coronary intervention (PCI) is the preferred method for revascularization in patients presenting with ST elevation myocardial infarction (STEMI) (1). Because of effective and immediate blood flow restoring in infarct related artery (IRA), its use has increased noteworthy over the past decades (2). However, PCI is not always associated with good clinical outcomes because of possible complications. One of the well-known complications of PCI is no-reflow phenomenon (3,4).

Previous studies have shown that incidence of no-reflow phenomenon ranged from 2% to 44% among patients who underwent primary or elective PCI and mortality rate ranged from 7.4 to 30.3% in these patient populations (4-12). The term ''no-reflow phenomenon'' is described as disturbance of myocardial perfusion throughout a specified segment of coronary circulation without any angiographic evidence of coronary artery obstruction, spasm, or dissection (4,9). Although this condition is generally diagnosed by using coronary angiography, myocardial contrast echocardiography is the gold standard method for the diagnosis of no-reflow phenomenon (10,11). Underlying factors contributing to the development of no-reflow phenomenon were described as distal atherothrombotic embolization, ischemic injury, reperfusion injury, and oxidative stress (13). This condition also is associated with adverse cardiac events including re-myocardial infarction, reduced left ventricular function, left ventricular remodeling, cardiac arrhythmias, and death (11). However, there is no definite treatment strategy for this phenomenon (14,15). Owing to afore-mentioned difficulties, it is essential to determine predictive risk factors for coronary no-reflow.

Laminar shear stress is the major pathophysiologic factor for progression, generation and destabilization on atherosclerotic plaques (16). Bifurcation sites of coronary arteries are more prone to the disruption of laminar blood flow and when laminar blood flow is disrupted, an atheroprone environment tends to occur. This pathophysiologic process have also been shown by recent studies that most of the atherosclerotic plaques form close to the bifurcation sites of the coronary arteries and strongly associated with vascular geometry (17,18). Although hemodynamic alterations due to various coronary artery angulations are strongly associated with atherosclerosis, there is a lack of detailed analysis in terms of hemodynamic changes in relation to vascular geometry and coronary no-reflow phenomenon.

Therefore, the aim of this study was to evaluate the relationship between vascular geometry and coronary no-reflow phenomenon.

Materials and Methods

Study Population

We reviewed the PCI database of our hospital and enrolled a total of 120 patients with acute STEMI, who developed no-reflow phenomenon following primary PCI between January 2019 and January 2020 and a total of age and sex matched 80 patients with acute STEMI in whom the no-reflow did not occur following primary PCI between November 2019 and January 2020. Acute STEMI was defined based on criteria by the European Society of Cardiology (19). All the patients were either presented with left anterior descending (LAD) or circumflex (CX) artery occlusion in the clinical aspect of STEMI and PCI was performed to the IRA. Demographic and clinical characteristics of patients and indication for the procedure were retrospectively analyzed. Patients with poor image quality, history of end-stage renal failure, liver failure, coagulopathy, malignancy, inflammatory disease, cardiogenic shock and pregnancy were excluded from the study. Patients who underwent primary PCI after 12 hours from the onset of symptoms and patients who underwent rescue PCI were also excluded. Informed consent was obtained from all patients in accordance with a protocol approved by local ethics committee.

Procedure

Coronary angiography was performed in 90 min following hospital admission. PCI procedures were performed via femoral or radial arterial access using 6 French (F) or 7 F sheaths. All patients were treated with dual antiplatelet therapy including loading dose of aspirin (162-325-mg orally) in addition to loading doses of clopidogrel (600 mg orally) or prasugrel (60 mg orally) or ticagrelor (180 mg orally) prior to the procedure. Intravenous heparin was administered to achieve an activated clotting time of 300s. Adjunctive pharmacotherapies, type of stent, use of pre-dilatation and post-dilatation were at the discretion of the interventional cardiologist. Epicardial coronary blood flow was quantified visually using the thrombolysis in myocardial infarction (TIMI) flow grade classification (20). Procedural success was defined as residual stenosis <20% and TIMI flow grade 3. Intracoronary injection of verapamil, adenosine and GP IIb/IIIa inhibitor were administered when no-reflow was observed. All patients underwent pre- and post-intervention electrocardiography and evaluated by cardiologist blinded to the assignment protocol.

Assessment of Coronary Angiograms

Initial TIMI flow was assessed at the beginning of the procedure prior to wire insertion and final TIMI flow was assessed at the end of the procedure. We also assessed coronary flow immediately before and after stent insertion by using myocardial blush grading (MBG) (21). According to our study, no reflow was defined as TIMI flow <3 (with any MBG grade) or TIMI flow 3 with MBG 0 or 1 at the end of the procedure in the absence of any coronary dissection or spasm. Depending on their final coronary flow status, patients were assigned to one of two groups; no-reflow occurred group (120 patients) and sex and age matched normal flow group (80 patients).

The bifurcation angles of the left main coronary artery (LMCA) - LAD, LMCA-CX and LAD-CX were measured by using three dimensional quantitative coronary angiography (QCA) analysis software named as medis suite XA/QAngio XA (Medis, Leiden, The Netherlands) (Figure 1). The software LMCA-LAD, LMCA-CX and LAD-CX bifurcation angles and these were measured at left anterior oblique -50° projection with 30° caudal angulation and right anterior oblique -30° projection with 20° caudal angulation. The mean values of three consecutive measurements were taken. All angiograms were interpreted by the consensus of two interventional cardiologists who were blinded to the patients' clinical and laboratory data. Intra-observer and inter-observer coefficients of variations for the measurement of bifurcation angle were found to be 1.2% and 1.7%, respectively.

Statistical Analysis

Data were analyzed with the IBM SPSS Statistics for Windows, Version 24.0 (IBM Corp., Armonk, NY, USA). In this study, data are expressed as mean (standard deviation) for continuous variables and as counts and percentages for categorical variables. The Kolmogorov-Smirnov's and Shapiro-Wilk test were used to evaluate the distribution of continuous variables. The χ^2 test and Fisher's Exact test were used to analyze categorical variables. The Student's t-test was used for continuous variables with normal distribution including LAD-CX bifurcation angle values and the values were presented as mean (standard deviation). Numerical variables not showing normal distribution were expressed as median (interquartile range), and categorical variables as percentages (%). Comparison of intergroup continuous variables without normal distribution was analyzed using the Mann-Whitney U test. The effect of various variables on no-reflow was calculated by univariate regression analysis. In these analyses, variables with unadjusted $p<0.05$ were identified as confounding factors and were included in multivariate regression analyses to determine the independent predictors of no-reflow. The predictive value for no-reflow related to bifurcation angle was estimated by using receiver operating characteristic curve (ROC) and Youden index [maximum (sensitivity + specificity -1)]. A 2-tailed p-value of <0.05 was considered statistically significant.

Results

Baseline demographic and clinical characteristics of patients with no-reflow and normal flow are shown in Table 1. The mean age of our study group was 64.2 (10.8) years and 161 (80.5%) patients of our study group were male. Patients with no-reflow had a higher prevalence of hypertension and diabetes mellitus (DM) compared to patients with normal flow (62.5% vs. 30.0% and 40.0% vs. 16.3%, $p<0.001$). In addition, serum C-reactive protein (CRP) levels were higher in the no-reflow group when compared to patients in the normal flow group (13.2 mg/dL vs. 3.3 mg/dL, $p<0.001$). On the other hand, serum hemoglobin levels were significantly lower in the no-reflow group when compared to the normal flow group [13.49 (2.06) g/dL vs. 14.50 (1.91) g/dL, $p<0.001$]. Other demographic and clinical variables were not significantly different between

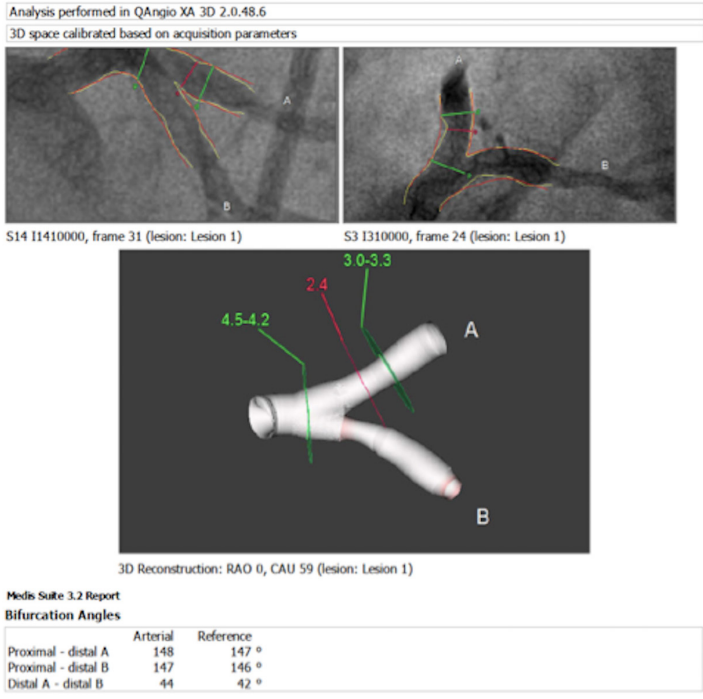

Figure 1. Figure shows an example of measurements for bifurcation angles in 3D software. Vessel B stands for left anterior descending artery and vessel A stands for circumflex artery. Proximal-distal A stands for angle between left main coronary artery and circumflex artery, proximal-distal B stands for angle between left main coronary artery and left anterior descending artery and distal A-distal B stands for angle between left anterior descending artery and circumflex artery

Table 1. Demographic, clinical and laboratory characteristics of the patients

	All patients (n=200)	No-reflow (-) (n=80)	No-reflow (+) (n=120)	p
Age, years	64.2 (10.8)	63.7 (9.3)	64.5 (11.7)	0.598
Male, n (%)	161 (80.5%)	68 (85.0%)	93 (77.5%)	0.190
LV ejection fraction, %	43.0 (9.5)	43.0 (10.0)	43.1 (9.3)	0.928
Smoking status, n (%)	87 (43.5%)	38 (47.5%)	49 (40.8%)	0.352
Hypertension, n (%)	99 (49.5%)	24 (30.0%)	75 (62.5%)	**<0.001**
Diabetes mellitus, n (%)	61 (30.5%)	13 (16.3%)	48 (40.0%)	**<0.001**
COPD, n (%)	15 (7.5%)	5 (6.3%)	10 (8.3%)	0.584
GFR, mL/min	86.6 (27.6)	85.8 (20.1)	87.3 (31.7)	0.707
Creatinine, mg/dL	0.90 (0.78-1.10)	0.94 (0.80-1.07)	0.90 (0.74-1.10)	0.353
C-reactive protein, mg/dL	4.5 (2.2-22.1)	3.3 (1.8-7.5)	13.2 (3.8-52.7)	**<0.001**
Total cholesterol, mg/dL	194 (41)	200 (35)	189 (45)	0.087
LDL, mg/dL	120 (36)	123 (33)	117 (38)	0.341
HDL, mg/dL	40.5 (10.5)	40.6 (9.2)	40.5 (11.4)	0.942
Triglyceride, mg/dL	140 (107-209)	161 (115-209)	129 (97-207)	0.054
White blood cells, 10^3/uL	11.10 (8.43-13.94)	11.15 (8.35-13.81)	10.94 (8.43-14.22)	0.842
Hemoglobin, g/dL	13.91 (2.05)	14.50 (1.91)	13.49 (2.06)	**0.001**
Platelet, 10^3/uL	263 (75)	267 (71)	261 (78)	0.540
Neutrophil, 10^3/uL	7.25 (4.93-11.15)	6.99 (4.72-8.94)	7.81 (5.11-11.52)	0.215
Lymphocyte, 10^3/uL	2.10 (1.44-2.89)	2.22 (1.50-3.32)	2.05 (1.43-2.80)	0.134

LV: Left ventricle, GFR: Glomerular filtration rate, COPD: Chronic obstructive pulmonary disease, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, MPV: Mean platelet volume

Table 2. Angiographic characteristics of the patients

	All patients (n=200)	No-reflow (-) (n=80)	No-reflow (+) (n=120)	p
LAD lesion, n (%)	155 (77.5%)	58 (72.5%)	97 (80.8%)	0.167
CX lesion, n (%)	45 (22.5%)	22 (27.5%)	23 (19.2%)	0.167
Pre TIMI score				0.259
0, n (%)	129 (64.5%)	50 (62.5%)	79 (65.8%)	
1, n (%)	36 (18.0%)	19 (23.8%)	17 (14.2%)	
2, n (%)	34 (17.0%)	11 (13.8%)	23 (19.2%)	
3, n (%)	1 (0.5%)	0 (0.0%)	1 (0.8%)	
Post TIMI score				**<0.001**
0, n (%)	48 (24.0%)	0 (0.0%)	48 (40.0%)	
1, n (%)	71 (35.5%)	0 (0.0%)	71 (59.2%)	
2, n (%)	1 (0.5%)	0 (0.0%)	1 (0.8%)	
3, n (%)	80 (40%)	80 (100%)	0 (0.0%)	
LMCA length, mm	14.4 (11.1-17.8)	14.0 (10.8-17.8)	14.9 (11.6-17.8)	0.507
LMCA-LAD bifurcation angle, °	123.0 (14.9)	124.8 (12.2)	121.7 (16.5)	0.147
LMCA-CX bifurcation angle, °	128.1 (17.7)	130.8 (18.1)	126.4 (17.2)	0.083
LAD-CX bifurcation angle, °	100.9 (23.1)	85.9 (15.8)	110.9 (21.8)	**<0.001**
Lesion length, mm	21.0 (3.5)	20.7 (3.3)	21.2 (3.6)	0.364
Reference vessel diameter, mm	2.94 (0.26)	2.96 (0.27)	2.93 (0.25)	0.478

LAD: Left anterior descending artery, CX: Circumflex artery, LMCA: Left main coronary artery

Table 3. Logistic regression analyses for investigation of independent correlates for no-reflow after PCI

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	**p**	**OR (95% CI)**	**p**
Hypertension	3.889 (2.125-7.117)	**<0.001**	7.268 (2.588-20.406)	**<0.001**
Diabetes mellitus	3.436 (1.711-6.900)	**0.001**	1.174 (0.377-3.654)	0.78
C-reactive protein	1.020 (1.007-1.032)	**0.002**	1.009 (0.993-1.025)	0.28
Hemoglobin	0.771 (0.660-0.900)	**0.001**	0.871 (0.667-1.138)	0.31
LAD-CX bifurcation angle	1.071 (1.049-1.093)	**<0.001**	1.082 (1.052-1.113)	**<0.001**

OR: Odds ratio, LAD: Left anterior descending artery, CX: Circumflex artery, CI: Confidence interval, PCI: Percutaneous coronary intervention

both groups. The angiographic characteristics are shown in Table 2. The no-reflow and normal flow groups were similar in terms of culprit vessels involved and total LMCA length. LAD lesions were dominant in both groups. Calculated bifurcation angle of the LAD-CX was significantly wider in the no-reflow group when compared to the normal flow group [110.9° (21.8°) vs. 85.9° (15.8°), p<0.001]. However, there was no significant difference between the groups in terms of reference vessel diameter and lesion length.

Univariate and multivariate regression analysis for no-reflow are shown in Table 3. Multivariate analyses showed that history of hypertension and LAD-CX bifurcation angle were significantly associated with no-reflow phenomenon (p<0.001) (Figure 2). Additionally, hemoglobin levels were analyzed according to gender in the study population (Table 4). In females, there was no significant difference in terms of hemoglobin levels and coronary no re-flow; however, in males, there was a significant difference in terms of hemoglobin levels and coronary no re-flow. Male patients who had coronary no re-flow had lower levels of hemoglobin when compared to the male patients without coronary no-reflow.

ROC analysis was performed to detect the optimal cut-off value for LAD-CX bifurcation angle in predicting the occurrence of no-reflow phenomenon. Bifurcation angle ≥98.1° predicted the occurrence of no-reflow phenomenon (Table 5, Figure 3). In the no-reflow group, 79.2% of the patients had LAD-CX bifurcation angle ≥98.1° and in contrast to that, 20.8% patients had LAD-CX bifurcation angle <98.1° (Figure 4). Additionally, CRP levels and hemoglobin levels were analyzed in ROC analysis to detect

Table 4. The relationship between coronary no-reflow and hemoglobin levels according to the gender

	Female			Male		
	No-reflow (-) (n=12)	No-reflow (+) (n=27)	p	No-reflow (-) (n=68)	No-reflow (+) (n=89)	p
Hemoglobin, g/dL	12.20±1.87	14.42±1.71	0.715	14.91±1.61	13.82±2.05	**<0.001**

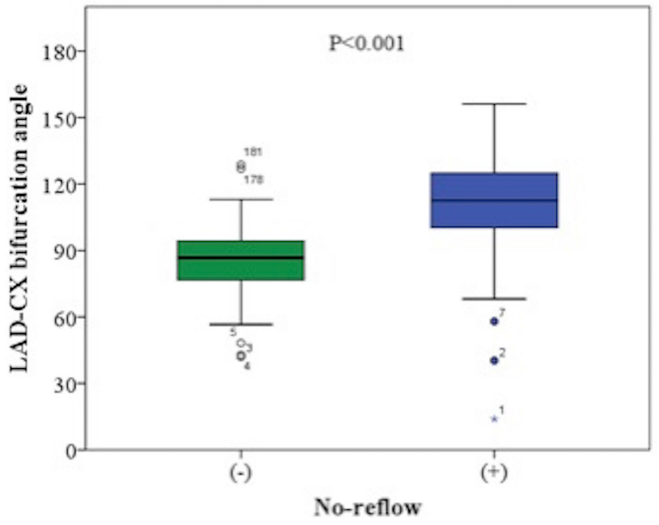

Figure 2. Figure shows the difference of left anterior descending artery-circumflex artery bifurcation angles between the two groups. The box plot provides the non-outlier minimum value, the first (25%) quarter, the median value, the third quarter (75%), and the non-outlier maximum value of the bifurcation angle. The dots indicate outliers

a cut-off value, and CRP level higher than 10.0 mg/dL and hemoglobin level less than 14.1 g/dL were found to be associated with no-reflow during PCI of STEMI patients.

Discussion

In the present study, we evaluated the association between bifurcation angle and development of no-reflow phenomenon in patients with STEMI treated with primary PCI. We found that bifurcation angle was a strong predictor for no-reflow phenomenon when compared to other parameters. To the best of our knowledge, this is the first study in literature, which evaluates the relationship between bifurcation angle and occurrence of no-reflow following primary PCI.

The no-reflow phenomenon is frequently observed during PCI and associated with various adverse cardiac events including left ventricular dysfunction, malignant arrhythmias, cardiogenic shock or death (11,13). According to a meta-analysis conducted by Fajar et al. (22), advanced age, male sex, family history of coronary artery disease, smoking, DM, hypertension, delayed reperfusion, higher Killip class at admission, elevated blood glucose, elevated creatinine, collateral flow, lesion length, multivessel disease, reference luminal diameter, initial TIMI flow, and high thrombus burden were proven to be associated with the development of no-reflow phenomenon following primary PCI. The underlying pathophysiologic mechanism, which contributes to the development of no-reflow, is mostly related to the association between parameters mentioned above and endothelial dysfunction and neurohumoral activation (22). Despite various known risk factors, it is still a challenge to predict the development of no-reflow in STEMI patients who underwent primary PCI. In our study, in contrast to previous studies, there was no significant difference between the groups in terms of lesion length, reference vessel diameter, advanced age, gender, and ejection fraction. On the other hand, DM, hypertension, higher serum CRP levels, lower serum hemoglobin levels and LAD-CX bifurcation angle were significantly associated with coronary no-reflow in univariate analysis. However, only hypertension and LAD-CX bifurcation angle were remained as independent predictors of no-reflow on multivariate analysis.

Recent studies in which investigated hemodynamics of coronary bifurcations by using computational fluid dynamics have demonstrated a close relationship between arterial hemodynamics and vascular geometry (23,24). Chiastra et al. (25) demonstrated that altered hemodynamics in all bifurcation regions led to a significant decrease in secondary flow of side branches. Not only vascular geometry of bifurcation site but also bifurcation angle resulted in recirculation and counter rotating helical flow. If the angle was wide, helical flows were found to be more evident. As a result of these alterations in fluid dynamics, decreased intravascular pressure and increased resistance in the arterial wall would be observed. Accordingly, this pressure-flow relationship was more pronounced when there was a significant side branch occlusion (25).

Studies also demonstrated a strong association between endothelial dysfunction and disturbed vascular flow due to wide angulation of vascular tree (26-28). Furthermore, it has been shown that shear stress in arterial wall and

Table 5. ROC analysis of bifurcation angle for no-reflow

	Sensitivity	Specificity	PPV	NPV	Accuracy
LAD-CX bifurcation angle ≥98.1	79.2%	81.2%	86.4%	72.2%	80.0%

PPV: Positive predictive value, NPV: Negative predictive value, LAD: Left anterior descending artery, CX: Circumflex artery, ROC: Receiver operating characteristic curve

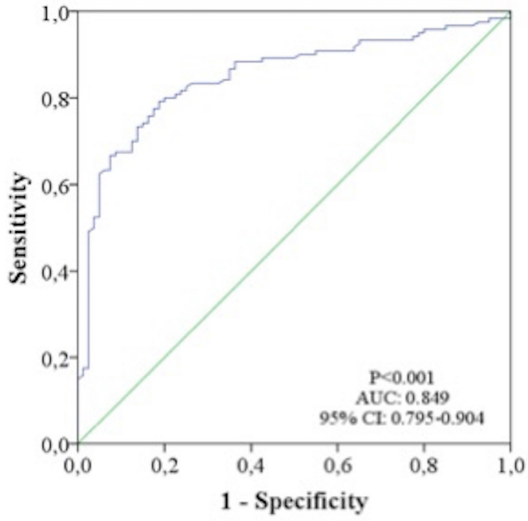

Figure 3. Receiver operating curve analysis showed the optimal cut-off value for left anterior descending artery-circumflex artery bifurcation angle in predicting no-reflow

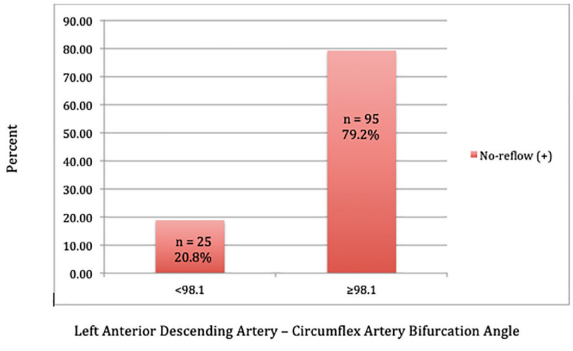

Figure 4. Figure shows, in the control group, 81.3% of the patients had left anterior descending artery-circumflex artery bifurcation angle <98.1 degrees and in the no-reflow (+) group, 79.2% of the patients had left anterior descending artery-circumflex artery bifurcation angle ≥98.1 degrees

disturbed blood flow in wide-angle bifurcations may contribute to the development of atherosclerosis as a result of endothelial dysfunction. Hemodynamic environment in the vascular tree is complicated because the geometric structure of vascular tree might be in different morphologies such as straight, curved, branched, converged and diverged. When a segment of an artery is straight, the hemodynamic flow pattern is typically laminar and wall shear stress is high and directed; however, in the curved, branched and diverged regions of arterial segments, the hemodynamic flow becomes disturbed with non-laminar and irregular distribution of low wall shear stress (18). Changes in hemodynamic forces might trigger complex and multiple signaling physiologic cascades that initiate mechanotransduction. This mechanotransduction process generates biochemical signals which results in changes in endothelial dysfunction and alterations in vascular behavior (29,30).

In our study, the estimated mean LAD-CX bifurcation angle was 85.9° (15.8°) in patients with normal flow which, was compatible with the outcomes of previous studies. According to a study conducted by Rodriguez-Granillo et al. (31), reported mean LAD-CX bifurcation angle was 88.5°. In another postmortem study, which consisted of 100 patients, Reig and Petit (32) reported a mean LAD-CX bifurcation angle of 86.7° (28.8°). Additionally, estimated LAD-CX bifurcation angle in patients with no-reflow phenomenon was 110.9° (21.8°). Our data suggested that bifurcation angle of LAD-CX showed a significant correlation with the development of no-reflow phenomenon. We hypothesize that the strong association between widely angulated left sided coronary artery bifurcations and low wall shear stress yields to disturbances of bloodstream, which contributes to the development of no reflow. We also speculate that this might be due to endothelial dysfunction that is a leading cause of coronary no-reflow.

Study Limitations

In this study, there are some limitations that should be acknowledged. First, the study design is retrospective and the number of cases who developed no-reflow following primary PCI is relatively small. Second, we only focused on bifurcation angles of the LMCA-LAD, LMCA-CX and LAD-CX in this study, while excluding other types of bifurcation subgroups including LAD- diagonal artery, CX-obtus marginalis and posterior descending artery-posterolateral artery. In addition, the results of this study need to be interpreted with caution with regard to diagnostic value of QCA measurements for evaluating bifurcation angles. Further studies with inclusion of more cases and all

subgroups of bifurcation angles by using more accurate techniques are desirable.

Conclusion

We conclude that measurement of bifurcation angles of LAD-CX could be a useful tool for predicting no-reflow phenomenon in STEMI patients who underwent primary PCI. This novel method not only allows earlier detection of STEMI patients with high risk of no-reflow but also helps to choose the best treatment. Since the causes of coronary no-reflow are multifactorial and there is lack of optimal treatment strategy for this phenomenon, it is mandatory to prevent the development of no-reflow. This study may provide a clinically useful approach in terms of investigating the predictive role of bifurcation angle for the development of coronary no-reflow.

Ethics

Ethics Committee Approval: Ethical approvement was retrieved from University of Health Sciences Turkey, İstanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital (date: 22.12.2020, no: 2020/82) Local Ethical Committee for the study.

Informed Consent: Informed consent was obtained.

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Authorship Contributions

Concept: Ö.T., R.G., M.D., Design: Ö.T., R.G., M.D., Data Acqusition: Ö.T., R.G., M.D., A.R.D., Data Analysis/Interpretation: Ö.T., A.A.Ş., A.R.D., Drafting Manuscript: A.A.Ş., Ö.T., M.D., Critical Revision of Manuscript: A.A.Ş., M.E., M.E.K., A.R.D., Final Approval and Accountability: A.A.Ş., Ö.T., M.E.K., M.E., Technical or Material Support: Ö.T., M.E., M.E.K., R.G.

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ORIGINAL RESEARCH

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Factors Affecting the Diagnostic Accuracy of Endometrial Pipelle® Biopsy

Pipelle® Biyopsinin Tanısal Doğruluğunu Etkileyen Faktörler

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Abstract

Objective: In this study, we aimed to compare the endometrial suction biopsy with Pipelle® and endometrial curettage (D&C) findings from patients with abnormal uterine bleeding and/or endometrial thickness to observe the possible influencing factors on ESB's diagnostic value.

Method: In Tekirdağ Community Hospital and Gynecology Clinic, data were retrospectively collected from hospital registry. 122 patients who had abnormal uterine bleeding and/or endometrial thickness were selected and from all cases, endometrial biopsies were taken with Pipelle® and D&C methods at the same time. In conclusion, pathologic results of two methods were compared.

Results: Pathology results were as follows: By Pipelle®, 44 patients (36.1%) were found with endometrial polyp, 26 patients (21.3%) with endometrial atrophy, 31 patients (25.4%) with proliferative endometrium, 11 patients (9%) with secretory endometrium, 4 patients (3.3%) with endometrial carcinoma, 1 patient (0.8%) with hyperplasia without atypia, 2 patients (1.6%) with inflammation; by D&C, 55 patients (45.1%) were found with polyp, 20 patients (16.4%) with endometrial atrophy, 34 patients (27.9%) with proliferative endometrium, 9 patients (7.4%) with secretory endometrium, 4 patients (3.3%) with endometrial carcinoma, 1 patient (0.8%) with hyperplasia without atypia, 2 patients (1.6%) with inflammation. Correlations between two methods were found as 97.6%, 95.3%, 91.7%, 98.3%, 100%, 100%, and 100% for proliferative endometrium, atrophy, polyp, secretory endometrium, endometrial cancer, hyperplasia without atypia and inflammation, respectively. Discorrelations between two diagnostic methods were more commonly seen in endometrial polyp pathology.

Conclusion: Our study findings revealed very high correlations between the pathology results of Pipelle® and D&C procedures. Pipelle®, with the advantages of being a simple outpatient procedure and having less complication rates, can be preferred over D&C reliably in most clinic situations. On the other hand, D&C method should be preferred in cases of endometrial polyp pathologies due to increased discorrelation rates and biopsy failures in Pipelle® biopsy.

Keywords: Dilatation and curettage, endometrial thickness, Pipelle® biopsy, uterine bleeding

Öz

Amaç: Anormal uterin kanama ve endometrial kalınlık artışı nedeniyle endometrial örnekleme yapılan hastaların Pipelle® biyopsi ve dilatasyon & küretaj (D&C) sonuçlarının karşılaştırılması ve Pipelle® biyopsinin tanısal doğruluğunu etkileyen faktörlerin araştırılması amaçlandı.

Yöntem: Tekirdağ Devlet Hastanesi, Kadın Hastalıkları ve Doğum Kliniği'ne anormal uterin kanama ve/veya endometrial kalınlık nedeniyle başvurup, aynı seansta Pipelle® D&C ile endometrial örnekleme yapılmış 122 olgunun retrospektif olarak dosya taraması ile sonuçları karşılaştırıldı.

Bulgular: Pipelle® yöntemi ile yapılan biyopsilerin sonuçlarında 44 (%36,1) polip, 26 (%21,3) atrofi, 34 (%27,9) proliferatif endometrium, 11 (%9,0) sekretuvar endometrium, 4 (%3,3) karsinom, 1 (%0,8) atipisiz hiperplazi, 2 (%1,6) enflamasyon bildirildi. D&C yöntemi ile yapılan biyopsilerde 55 (%45,1) polip, 20 (%16,4) atrofi, 31 (%25,4) proliferatif endometrium, 9 (%7,4) sekretuvar endometrium, 4 (%3,3) karsinom, 1 (%0,8) atipisiz hiperplazi, 2 (%1,6) enflamasyon saptandı. Her iki yöntemin uyum oranları proliferatif endometrium, atrofi, polip, sekretuar endometrium, endometrium kanseri, atipisiz hiperplazi ve enflamasyon için sırasıyla %97,6, %95,3, %91,7, %98,3, %100, %100 ve %100 olarak saptandı. İki tanısal yöntem arasında uyumsuzluk en fazla endometrial polip patolojisinde görüldü.

Sonuç: Sonuçlarımıza göre; Pipelle® biyopsi ve D&C prosedürü arasında patoloji sonuçları yönünden çok yüksek korelasyon olduğu görülmüştür. Pipelle® biyopsi; anestezi gerektirmemesi, ağrı miktarının az olması ve postoperatif komplikasyon riski azlığı nedeniyle endometrial patolojilerin teşhisi için D&C prosedürünün yerine güvenle tercih edilebilir. Diğer yandan, iki yöntem arasında en fazla uyumsuzluk görülen ve Pipelle® Biopside yetersizliğe yol açabilen endometrial polip olgularında D&C örneklemenin tercih edilmesi kanaatindeyiz.

Anahtar kelimeler: Dilatasyon ve küretaj, endometrial kalınlık, Pipelle® biyopsi, uterin kanama

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Introduction

Endometrial sampling is a valuable procedure in routine gynecology practice with its diverse advantages in differentiating malignant-premalignant lesions, excision of certain lesions, observing the cyclic hormonal effects and being simple feasible method. Sampling can be achieved by endometrial suction biopsy (ESB), dilatation and curettage (D&C) and hysteroscopic biopsies.

Ultrasonography and hysteroscopy are among valuable imaging methods for diagnosing uterine and endometrial pathologies. Endometrium, cervix, uterus and adnexa can easily be evaluated by transvaginal ultrasonography, which is a frequently preferred non-invasive method. On the other hand, the minimally invasive method, saline infusion sonography is superior to traditional ultrasonography in detecting small focal endometrial lesions (1).

Hysteroscopy is the gold standard method for visualizing focal intrauterine lesions. Diagnostic accuracy of endometrial biopsies is increased when performed during hysteroscopy (2). Not requiring anesthesia, diagnostic hysteroscopies became a practical and reliable outpatient office procedure.

Endometrial sampling is the gold standard diagnostic method for the most patients with abnormal uterine bleeding complaint (3). The most common such clinical scenarios are postmenopausal bleeding, postmenopausal endometrial thickening, and perimenopausal menometrorrhagia (>45 years of age). Endometrial polyps, atrophy, hormonal, inflammatory, premalignant and malignant differentiations are among the important pathological findings that can be reported. Dilatation and curettage (D&C) is an invaluable diagnostic method for endometrial pathologies. However, due to its need for anesthesia, risk for uterine perforation and post-procedure adhesions, ESB is commonly preferred over D&C in routine gynecology practice (4).

A diagnostic method's accuracy is measured by comparing its correct diagnoses by those of gold standard method, which sometimes can depend on different target group characteristics. In addition, practicality and cost-effectivity are important aspects of a diagnostic method on the way of being "gold standard". ESB by Pipelle® has been shown to be cost-effective in diagnosing endometrial cancer among patients with postmenopausal bleeding (5).

In this study, because it has been suggested as practical and cost-effective method, we aimed to evaluate diagnostic reliability of Pipelle® biopsy, and to further delineate the possible factors causing inconsistent results when compared to D&C method.

Materials and Methods

Prior to the study, Namık Kemal University Faculty of Medicine Clinical Research Ethical Board approval was obtained (Document number 2020.87.04.11, April 30th, 2020). One hundred and twenty-two patients' pathology reports of endometrial samplings done via concurrent Pipelle® biopsy and D&C methods were retrospectively collected from medical records of Department of Obstetrics and Gynecology at Namık Kemal Community Hospital.

Statistical Analysis

Statistical analyses were performed by using SPSS-20 software. Demographic characteristics and endometrial thickness values were analyzed. Categorical variables were given as numeric and percentages. By calculating consistency rates for sensitivity, specificity, negative and positive predictive values, Pipelle® biopsy's diagnostic accuracy was determined in this cohort.

Prior to the procedures, routine gynecologic evaluation by speculum, bimanual exam and transvaginal ultrasonography was completed. Also, complete blood count, liver and renal function tests, serum β-hCG, basic coagulation tests, and serum work-up for hepatitis B, C, and HIV were done. Inclusion criteria were postmenopausal bleeding, postmenopausal endometrial thickening (>5 mm), menorrhagia, metrorrhagia and focal endometrial lesion on a transvaginal ultrasonography. Exclusion criteria were history of previous hormonal therapy or intrauterine surgery. Since general anesthesia is not given in endometrial biopsy procedures in our clinic, in order to evaluate the pain tolerance and cervical stenosis condition during the procedure, it is a long-standing method in our clinic to perform the endometrial biopsy procedures with Pipelle® or a 4.5 mm 00 number sharp curette before the D&C procedure. Only cases whose Pipelle® biopsy and D&C samples were evaluated by the same gyneco-pathologist were included in this study. Pipelle® biopsy's competency was decided by comparing its results to that of standard D&C method.

Results

After applying the inclusion and exclusion criteria, the data from the cohort of 122 patients were reviewed. The median age was 48.3±8.7 years. There were 80 (65.6%) premenopausal and 42 (34.4%) postmenopausal patients.

The median values were 3.2±2.2 for gravida and 2.5±1.4 for parity. The mean body mass index (BMI) was calculated as 29.6±6.1 (Table 1). Pipelle® biopsy results were as follows: 44 cases with polyps (36.1%), 26 with atrophy (21.3%), 34 with proliferative endometrium (27.9%), 11 with secretory endometrium (9.0%), 4 with carcinoma (3.3%), 1 with hyperplasia without atypia (0.8%), and 2 with inflammation result (1.6%) (Table 2).

D&C results were as follows: 55 cases with polyps (45.1%), 20 with atrophy (16.4%), 31 with proliferative endometrium (25.4%), 9 with secretory endometrium (7.4%), 4 with carcinoma (3.3%), 1 with hyperplasia without atypia (0.8%), 2 with inflammation result (1.6%) (Table 2). Sensitivity, specificity, positive and negative predictive value of tests were measured, concordance rate was calculated for proliferative endometrium, atrophy, polyp, secretory endometrium, endometrial cancer, non-atypical hyperplasia and inflammation at the rates of 97.6%, 95.3%, 91.7%, 98.3%, 100%, 100%, and 100%, respectively (Table 3).

Table 1. Demographic characteristics of the patients (n=122)

Age (median ± SD)	48.3±8.7
Gravida (median ± SD)	3.2±2.2
Parity (median ± SD)	2.5±1.4
Endometrial thickness (median ± SD)	10.7±5.1
Menopause n (%)	42 (34.4)
Body mass index (median ± SD)	29.6±6.1

SD: Standard deviation

Table 2. Pipelle® EMB and D&C results

Pathology	D&C, n (%)	Pipelle® EMB, n (%)
Proliferative endometrium	31 (25.4)	34 (27.9)
Atrophy	20 (16.4)	26 (21.3)
Polyp	55 (45.1)	44 (36.1)
Secretory endometrium	9 (7.4)	11 (9.0)
Endometrial cancer	4 (3.3)	4 (3.3)
Hyperplasia without atypia	1 (0.8)	1 (0.8)
Inflammation	2 (1.6)	2 (1.6)

D&C: Dilatation and curettage

Discussion

In this study, our findings supported that, instead of D&C, a practical endometrial biopsy method Pipelle®s can be utilized in many clinical situations where uterine pathologies are searched for. In endometrial polyps and atrophies, acceptable inconsistency rates were observed while remarkably high consistency rates were found with the rest of the compared uterine pathologies.

Pipelle® biopsy is a valuable method that provides low false negative results especially in cases with endometrial cancer and atrophy (6). On the other hand, some factors can cause failures such as less than 4 mm endometrial thickness, inflammation, polyps, and submucous myomas (7). In some reports, hysteroscopic sampling was found to have lower sensitivity than Pipelle® biopsy and D&C methods, implying the leakage of endometrial cells along with hysteroscopic media (8).

D&C is the gold standard for diagnosing endometrial tissue pathologies (9). However, due the need for anesthesia, postoperative pain and relatively higher rate of complications, alternative diagnostic methods have been developed.

Pipelle® biopsy is an invaluable minimally invasive diagnostic method which provides sampling adequacy over 98% when endometrial thickness is over 5 mm (10). Interestingly none of our 12 cases with less than 5 mm endometrial thickness had result failure.

Piatek et al. (11) reported the sampling adequacy as 82.3% and 84.1% for Pipelle® biopsy and D&C methods, respectively. They observed that the highest sampling adequacy was in patients with abnormal uterine bleeding (88.8%) and lowest in patients with "abnormal endometrial imaging" indications (37%).

The most frequent factors associated with failure to report in D&C specimens were reported as menopausal status (25.4%) and BMI (11). At the same study, operator experience, whether performed by resident physician in training or by specialist in gynecology, was not associated with specimen adequacy. Although collection of all samples in this study by a single gynecologic oncologist was an advantage, limited number of patients could be considered as a disadvantage.

In endometrial sampling, both the diagnosis and exclusion of malignancy are important tasks. In this study, specimen inadequacy was not encountered whether specimens were obtained by Pipelle® biopsy or D&C in cases with endometrial hyperplasia or endometrial carcinoma. Regarding pathology results, diagnostic consistency of the two methods was 100% (Table 3). Amant et al. (12) reported that malignancy diagnosis was ruled out in 96% by using the postmenopausal endometrial thickness >4 mm as cut-off value.

However, in exclusion of malignancy, regularity of the entire endometrial cavity is an important factor. In 3 of our

Table 3. Diagnostic consistency rates between methods

Diagnosis	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Consistency rate
Proliferation	100%	96.8%	91.1%	100%	97.6%
Atrophy	100%	94.4%	76.9%	100%	95.3%
Polyp	83.3%	100%	100%	85.8%	91.7%
Secretory endometrium	100%	98.2%	81.8%	100%	98.3%
Endometrial cancer	100%	100%	100%	100%	100%
Hyperplasia without atypia	100%	100%	100%	100%	100%
Inflammation	100%	100%	100%	100%	100%

Table 4. Inconsistent results between Pipelle® EMB and D&C samplings

	Age	Gravida/ parity	BMI	Menopause duration	Endometrial thickness	Biopsy indication	Pipelle® EMB result	D&C result
Case 1	45	2/1	28.6	-	4 mm	Menorrhagia	Endometrial polyp	Atrophy
Case 2	56	3/2	31.25	8 yrs	6 mm	Endometrial thickness	Atrophy	Polyp
Case 3	67	2/2	33.09	20 yrs	9 mm	Endometrial thickness	Atrophy	Polyp
Case 4	44	2/2	19.5	-	10 mm	Intracavitary lesion	Atrophy	Polyp
Case 5	48	7/5	24.8	1 year	13 mm	Endometrial thickness	Proliferative endometrium	Polyp
Case 6	31	1/1	21.4	-	14 mm	Menorrhagia	Atrophy	Polyp
Case 7	49	1/1	24.2	1 year	3 mm	Postmenopausal bleeding	Secretory endometrium	Polyp
Case 8	42	3/3	26.5	-	22 mm	Endometrial thickness and Intracavitary lesion	Proliferative endometrium	Polyp
Case 9	54	2/2	32.1	4 yrs	14 mm	Endometrial thickness and bleeding	Atrophy	Proliferative endometrium
Case 10	53	0/0	29.2	2 yrs	10 mm	Endometrial thickness	Atrophy	Polyp
Case 11	60	3/2	28.5	15 yrs	9 mm	Endometrial thickness and bleeding	Atrophy	Polyp
Case 12	39	5/2	32.8	-	14 mm	Menorrhagia	Secretory endometrium	Polyp
Case 13	49	2/2	26.8	-	13 mm	Menorrhagia	Proliferative endometrium	Polyp
Case 14	51	10/5	27.1	-	14 mm	Menorrhagia	Polyp	Atrophy

BMI: Body mass index, D&C: Dilatation and curettage

endometrial carcinoma cases, endometrial irregularities were noticed as invasions into the myometrium. In this study, we diagnosed 3 endometrial cancers, these cases had >7 mm endometrial thickness. Behnamfar and Arshad (13) reported the sensitivity and specificity of Pipelle® biopsy as 94.1% and 100%, respectively. The one leiomyosarcoma case was diagnosed only with D&C method.

In a cohort of 1,535 cases, Machado et al. (14) Pipelle® biopsy's sensitivity and specificity in atypic hyperplasia and endometrial carcinoma diagnoses were reported as 84% and 99%, respectively. In another study, diagnostic accuracy for high grade endometrial cancer was higher than that of low-grade endometrial cancer by Pipelle® biopsy (15). Antoni et al. (16) observed 71% sensitivity

and 60% specificity in endometrial hyperplasia and endometrial cancer diagnoses. The latter percentages are lower than our findings. However, there was not any atypical hyperplasia case, which was a limitation in our study.

In this study of Pipelle® and D&C comparison in biopsy, very consistent results were observed except for endometrial polyp diagnosis. In detail, 13 inconsistent cases out of 14 (92.8%) had endometrial polyps (Table 4).

In their study, while Xie et al. (17) were able to diagnose all of the endometrial cancer cases by Pipelle® biopsy, the most common reasons for inconsistent results were endometrial polyp and atypical hyperplasia diagnoses. In diagnosing atypical hyperplasia and endometrial polyps, they reported the sensitivity and specificity of Pipelle® biopsy as 50% and 26.4%, respectively (17).

In their study, Dijkhuijen et al. (18) reported that in cases with endometrial polyps and endometritis, the sensitivity was 60% for Pipelle® biopsy and was 88.9% for D&C, with the accuracy rates of 98.6% and 99.3%, respectively. The possible reason for the relatively lower sensitivity of these two methods on certain diagnoses such as endometritis and polyps is inadequate sampling.

Chaudry and Javaid (19) observed high accuracy and consistency rates on histopathologic diagnosis results between Pipelle® biopsy and D&C, and they found Pipelle® biopsy method more advantageous since it is less invasive. However, Clark et al. (20), suggested that the Pipelle® biopsy accuracy rates might be lower and therefore additional diagnostic procedures would be recommended in cases with ongoing symptoms.

Several complications can be encountered during an endometrial sampling procedure, uterine perforation is the most bothersome. Seamark (21) reported 1% perforation rate during D&C procedures. In a study of Piatek et al. (11), D&C related uterine perforation rate was 0.5% and no complication was observed during Pipelle® biopsy procedures. In our current study, neither perforation nor other complications were occurred in either Pipelle® biopsy or in D&C groups.

Study Limitations

Finally, we mentioned some limitations and strengths of this study. Collection of all samples by experienced gynecologic oncologist and analysis of all samples by the same gyneco-pathologist were the strengths of the study, while presence of a single pathologist in analyzing process, absence of hysterectomy specimens as a definitive pathology results and low number of patients were among its limitations.

Conclusion

In this study, final pathology results were highly correlated between Pipelle® biopsy and D&C procedures. Pipelle®biopsy has lower complication rates, it is less painful and it does not require anesthesia. It can be reliably preferred over D&C in the diagnosis of endometrial pathologies with its comparable consistency rates. Future prospectively designed and larger studies would contribute more on this important subject.

Ethics

Ethics Committee Approval: Namık Kemal University Faculty of Medicine Clinical Research Ethical Board approval was obtained (document number 2020.87.04.11, April 30th, 2020).

Informed Consent: This study were designed as hospital data research retrospectively.

Peer-review: Externally peer-reviewed.

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ORIGINAL RESEARCH

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The Effect of First Trimester Smear Results on Pregnancy and Neonatal Outcomes in a Turkish Population

Birinci Trimester Smear Sonuçlarının Gebelik ve Yenidoğan Sonuçlarına Etkisi

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Abstract

Objective: We aimed to investigate the relationship between neonatal and pregnancy outcomes and cervicovaginal smear-determined reactive cellular changes and/or inflammation revealing an infectious agent in the first trimester of pregnant patients.

Method: A total of 153 pregnant women, who were in their first trimester period, were enrolled to the study. Records related to the pregnancy and neonates were identified and further analyzed.

Results: In terms of smear results, of 152 patients, 54 (35.5%) were reported as normal while 96 (63.2%) had reactive cellular changes and/or inflammation and 2 (1.3%) had atypical squamous cells of undetermined significance. In 117 patients (76.4%), no infectious agent was observed while 22 patients (14.5%) had fungus (candida), 8 had protozoon (trichomonas vaginalis), and 5 (3.3%) had bacterial vaginosis. There was no statistically significant difference observed for average pregnancy weeks, baby's birth weight, preterm birth and neonatal intensive care need between patients with reactive cellular changes and/or inflammation and those with normal smear results (p=0.72, p=26, p=0.44, p=0.52).

Conclusion: We found no association between inflammation or reactive cellular changes of smear results in the first trimester of pregnancy and adverse pregnancy or neonatal outcomes as being first research in our country.

Keywords: Neonatal outcome, pregnancy, smear, preterm birth, vaginal infections

Öz

Amaç: Çalışmamızda gebeliğin ilk trimesterinde başvuran gebe kadınların servikovajinal smear sonuçlarından elde edilen ve enfeksiyöz bir ajanın göstergesi olan reaktif selüler hücre ve enflamasyon bulgularının, gebelik ve neonatal sonuçlar üzerindeki etkisini araştırmayı amaçladık.

Yöntem: Gebeliğinin ilk trimesterinde olan 152 gebe kadın çalışmaya dahil edildi. Gebelik ve yenidoğan sonuçları kaydedilerek analiz edildi.

Bulgular: Gebeliğinin ilk trimesterinde olan 152 gebe kadının smear sonuçlarına bakıldığında 54'ünün (%35,5) sonucu normal, 96'sının (%63,2) sonucu reaktif selüler hücre ve/veya enflamasyon ve 2'sinin (%1,3) sonucunun ise ASCUS (önemi belirlenememiş atipik skuamöz hücreler) olduğu görüldü. Yüz on yedi hastada (%76,4) enfeksiyon ajanına rastlanmazken, 22 hastada (%14,5) mantar (kandida), 8 hastada protozoon (trichomonas vaginalis), 5 hastada ise (%3,3) bakteriyel vajinozis tespit edildi. Smear sonucu reaktif selüler hücre ve/veya enflamasyon ya da normal çıkanlar arasında ortalama gebelik haftası, bebek doğum kilosu, preterm doğum ve neonatal yoğun bakım ihtiyacı bakımından istatistiksel olarak anlamlı bir fark tespit edilemedi (p=0,72, p=26, p=0,44, p=0,52).

Sonuç: İlk trimesterde olan gebelerde, smear sonucunun reaktif selüler hücre ve/veya enflamasyon çıkması ile kötü gebelik ve yenidoğan sonuçları arasında anlamlı bir ilişki tespit edilememiştir ve bu çalışma ülkemizde bu konuyu araştıran ilk çalışmadır.

Anahtar kelimeler: Gebelik, neonatal sonuç, preterm doğum, smear, vajinal enfeksiyonlar

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Introduction

Pap smear provides us information about epithelial abnormalities as well as about some vaginal infections. In determining bacterial vaginosis (BV), Pap smear, and microbiological tests have a sensitivity of 43.1% and 77.8% and a specificity of 93.6% and 97.7%, respectively. In that case, despite not being as sensitive as microbiological tests, they are considered enough for the diagnosis of a BV due to its high specificity (1). BV is a common vaginal infection in pregnancy having a prevalence rate of 7-30% and instead of lactobacillus, there are increased number of *Gardnerella vaginalis*, *Prevotella bacteroides*, *Mycoplasma hominis*, and *Mobiluncus* (2). Many doctors treat symptomatic BV due to its known association with preterm birth, miscarriage, postpartum endometritis, and lower birth weight. In addition, it is recommended to scan for asymptomatic BV in pregnancy (3). If there is a vaginal infection in pregnant woman originated from aerobic bacteria, it should be treated to improve perinatal results (4). In some publications, authors have reported an association between human papilloma virus (HPV) infection and BV and concluded that HPV-high risk (HPV-HR) may be present in case of BV presence (5).

In terms of candidal infections, during a Pap smear evaluation, candidal mycelium and conidium may show a specificity of 99.83% and 99.62% and a sensitivity of 92.18% and 94.53%, respectively (6). Additionally, vaginal candidiasis is observed with a rate of 31.4% among pregnant women, while its rate is 19.9% among non-pregnant women. Asymptomatic candidiasis is observed with a rate of 45.6% among pregnant women, while its rate is 16% among non-pregnant women. The negative effect of vaginal candidal colonization on perinatal results is not as clear as BV and the efficiency of scanning in pregnancy should be researched (7).

In communities not having got accustomed to periodical control visit, like in our country, visiting doctor for routine control during pregnancy provides a good opportunity to scan neoplastic changes and infectious agents of cervix. Previous studies have showed that one of each 100 cervix cancer patients was pregnant at the time of diagnosis (8). Pap smear test during pregnancy, different results between pregnancy outcomes and cervical inflammation, and HPV infection were reported. The cervical inflammation and HPV infection were associated with negative obstetric outcomes such as preterm birth, preeclampsia, cervical incompetence, and neonatal sepsis. There has been no reported exact association with adverse obstetrical outcomes and newborn outcomes with infectious agents apart from BV in recent reports (9).

In our study, we aimed to investigate the association between the smear results of the women in first trimester and pregnancy or neonatal outcomes.

Materials and Methods

The study was retrospectively conducted in between March 2018 and May 2019, with the pregnant women in their first trimester visit to University of Health Sciences Turkey, Gaziosmanpaşa Training and Research Hospital, in which smear results and risk factors were evaluated. Ethical approval was obtained from Ethics Committee of University of Health Sciences Turkey, İstanbul Gaziosmanpaşa Training and Research Hospital (no: 91,02.06.2020). Patients' socio-demographical information such as age, smoking status, parity, number of partners, pregnancy week, first sexual activity age, contraception method, and birth styles were recorded. After the required informed consents were obtained, smear results were recorded. One hundred-four pregnant women's hospital records who gave birth in University of Health Sciences Turkey, İstanbul Gaziosmanpaşa Training and Research Hospital, as well as birth and neonatal records of 48 pregnant women who gave birth in another hospital, were obtained by communicating via telephone.

For smear test process in pregnant women, after providing the related information and getting the consent, cervix was visualized in lithotomy position via sterile single-use speculum and swap sample was taken from cervix with Ayre spatula, then pap-smear samples taken as liquid-based samples were evaluated with Bethesda system in pathology laboratory. Same swap samples were investigated for HPV types, chlamydia, and gonorrhea with real time polymerase chain reaction (PCR) system. Reactive cellular changes were defined as increase of nuclear volume, binucleation, cytoplasmic vacuolization, and polychromasia (10). Intense leukocyte presence in smear was defined as inflammation. Gestational age was determined based on last mensuration dates of patients or based on initial ultrasound measurements if measurements were not conforming with the last mensuration date. Gestational week was recorded in the time of smear test and all of them were less than 14 weeks of gestation. Gestational week of birth was recorded along with birth weight. The babies whose cardiac activities stopped before 20 weeks were defined as miscarriage.

Statistical Analysis

Data analysis was done with SPSS 23th version (IBM Corp, Armork, USA). Variables were stated as average ± standard deviation or median (minimum-maximum). Parametric variables' conformity with normal distribution was evaluated with the Kolmogrov-Smirnov test. In comparison of the variables, the Student-t test or Mann-Whitney U test was used. In comparison of nominal data, the chi-square test was used. $p<0.05$ value was accepted as statistically significant.

Results

One hundred-fifty three pregnant women between 18 and 41 years old visited for first trimester control and performed vaginal smear for presence of infectious agents during the study period were included into the study. One patient was excluded due to that her newborn data were not accessible. The study was conducted with 152 pregnant women and newborn results. Patients' socio-demographic data are shown in Table 1. Age range was between 18 and 41 years and the average age was 28±5.9 years in our study. The average pregnancy week was 11 weeks. In terms of smear results, among 152 patients, 54 (35.5%) were reported as normal, while 96 (63.2%) had reactive cellular changes and/or inflammation, and 2 (1.3%) had atypical squamous cells of undetermined significance (ASCUS). Comparisons were performed between the groups having normal and inflammation and/or reactive cellular results. Considering infectious agent findings obtained from smear results of the population, 117 patients (76.4%) had no infectious agent while 22 patients (14.5%) had fungus (candida), 8 had protozoon (trichomonas vaginalis), and 5 (3.3%) had BV (Table 2).

After excluding 2 patients with ASCUS, demographical data of remained patients were compared according to the groups having normal smear result and having reactive cellular changes and/or inflammation and results were summarized in Table 3. In terms of the patients' age, smoking status, pregnancy, parity and average pregnancy weeks, there were no difference among the groups. In patients having inflammation in smear result, pelvic inflammatory disease history was meaningfully higher, and first coitus age was also younger [(p=0.03), (p=0.03)] (Table 3). Chlamydia and gonorrhea tests in all patients were resulted as negative. In terms of HPV, 2 pregnant women, having ASCUS results, had negative HPV results. Among the remained 150 patients, in the group having 54 pregnant women with normal smear results, 2 patients had HPV 16 positive and 1 patient had HPV HR positive. In the other group including 96 patients reported to have smear results with inflammation or reactive cellular changes, 1 patient had HPV 16 positive and 2 patients had HPV HR positive. No HPV 18 positivity was observed in each group (Table 4).

Table 1. Demographic characteristics of the patients

Total number of the patients: 152	
Age	28±5.9 (18-44)
Gravida	2.5 (1-8)
Parity	1 (0-3)
Gestational week	11 (5-13)
Smear result	
Normal	54 (35.5%)
Reactive cellular	96 (63.2%)
ASCUS	2 (1.3%)

ASCUS: Atypical squamous cells of which significance were not determined

Table 2. Infectious agents obtained from the smear results

Infectious agent	Number of cases	Percentage
Bacterial vaginosis	5	3.3%
Fungal infection (candida)	22	14.5%
Protozoon (trichomonas)	8	5.8%
None	117	76.4%

Considering groups' pregnancy and neonatal outcomes, no statistically significant difference was observed regarding the average pregnancy weeks, baby's birth weight, preterm birth, and neonatal intensive care need (Table 5). One patient having a smear result reported as reactive cellular changes had in-utero-mort-fetus in the 28th week.

Discussion

In the retrospective study we conducted, no statistically significant difference was observed between the groups having smear results as normal and the ones with inflammation and/or reactive cellular changes in terms of pregnancy and neonatal outcomes. In the group having a smear result with inflammation, first sexual intercourse age was determined earlier and the rate of patients with PID history was higher (p=0.03, p=0.03). In a retrospective and community-oriented study by Nimrodi et al. (11), pregnancy and neonatal outcomes of pregnant women having HPV infection or inflammation in Pap smear result were compared and the results were discussed in terms of preterm birth, cervical incompetence, and low birth weight. When the group having HPV positivity or

Table 3. Comparison of the demographic properties of the groups

150 patients	Smear normal (n=54)	Smear inflammation and/or reactive cellular changes (n=96)	p
Age	26.9±6.5	28.6±5.5	0.08[a]
Smoker women	6 (11.1%)	14 (14.6%)	0.54[d]
Gravida	2 (1-6)	3 (1-8)	0.99[b]
Parity	1 (0-3)	1 (0-1)	0.37[b]
Multipartnerity	1 (1.9%)	2 (2.1%)	0.99[d]
Gestational week	9.6±2.6	10.1±2.5	0.21[a]
First coitus age	22.4±4.5	20.6±3.8	0.03[a]
History of cesarean section	8 (14.8%)	26 (27.1%)	0.08[c]
History of pelvic inflammatory disease	1 (1.9%)	12 (12.5%)	0.03[d]
Intrauterine device usage	5 (9.3%)	10 (10.4%)	0.82[c]

[a] Student's t-test, [b] Mann-Whitney U test, [c] chi-square test, [d] Fisher's exact test

Table 4. HPV types of the patients

Smear result	Normal	Inflammation and/or reactive cellular changes
HPV negative	51 (94.4%)	93 (96.9%)
HPV 16 positive	2 (3.7%)	1 (1%)
HPV-HR positive	1 (1.9%)	2 (2.1%)

HPV-HR: Human papillomavirus-high risk

Table 5. Comparison of pregnancy outcomes of the patients

150 patients	Smear, normal	Inflammation and/or reactive cellular changes	p
Term delivery	38.4±2.0	38.3±1.8	0.72[a]
Preterm delivery	7 (14%)	7 (8%)	0.26[b]
Birth weight (gr)	3304±500	3239±464	0.44[a]
Neonatal intensive care unit administration (number, %)	9 (16.7%)	11 (11.5%)	0.51

[a] Student's t-test, [b] chi-square test, one patient who had reactive cellular changes in her smear result was diagnosed with in utero mort fetus in the 28th week of gestation

inflammation in Pap smear was compared with the group having no anomaly, it was concluded that there was no statistically significant difference between obstetric or neonatal outcomes (11). In our study, we observed that HPV positivity was very low, so it was not possible to evaluate risk statistically but we neither determined a meaningful difference in comparison of newborn results of the group having a smear result with inflammation or reactive cellular changes, and the group having a normal smear result. In another community-oriented study by Buchmayer et al. (12), finding of coccobacillus or trichomonas in Pap smear samples taken from pregnant women was evaluated as risky in terms of fetal development, and if this positive result was within 4 weeks prior to the birth, it was associated with 4 times more risk of preterm birth. In our study, trichomonas vaginalis was determined in 8 cases and bacterial agent in 5 cases. Neonatal outcomes of these patients were not negative. In a cohort study by Jacobsson et al. (13), even not being statistically significant, 2 times more preterm delivery was observed in pregnant women having a pap smear result with BV within first trimester, and also a threefold increase was determined in these patients' postpartum endometriosis frequency. In our study, we investigated Pap smear in pregnant women within first trimester and the percentage of smears with bacterial agent was 3.3%, and there was no negativeness observed in these patients' neonatal outcomes.

In a study by Quinlivan et al. (14) including pregnant women younger than 17 years old, 27% of the participants had chlamydia positivity and 38% had abnormal smear findings. It is especially stated that scanning and treating chlamydia is important in terms of reducing newborn febrile morbidity (14). In our study, there was no adolescent pregnant, and all chlamydia results were negative, in this respect we believe that the chlamydia is not a threatening agent for our region.

In smear samples taken by Helou et al. (15) from pregnant women within 15-20 weeks, BV was determined in 15% of the patients and it was concluded that this rate was not associated with preterm birth. Pregnant women who are in their first trimester (<14th weeks of gestation) were included in our study and BV frequency was 3.3%. The difference in BV rate may be resulted from the patient group being within different gestational weeks but still, the preterm delivery was not associated with BV in both studies. In a study by Svare et al. (16), including pregnant women within second trimester, BV was determined in 16% of cervical smear samples and it was concluded that this condition constituted an independent risk for lower birth weight, preterm birth and chorioamnionitis. The study of Svare et al. (16) was conducted on pregnant women before 20 weeks within second trimester, in this respect the obtained results might be associated with the selected patient group.

In a study by Smith et al. (17), HPV positivity rate in pregnant women within first trimester was determined as 0.8%. In our study, this rate was determined as 1.3% and, also 2 patients having a smear test with ASCUS had a negative HPV result. In the remaining patients, no statistically significant difference was determined between the group having a normal smear result and the group having a smear result with inflammation or reactive cellular changes in terms of HPV positivity (17).

There are few studies related to this condition in our country. İvit et al. (18) determined BV in 16% of patients, candida in 10% and trichomonas in 5%, and this study only reveals the frequency of infectious agents in first trimester. The most frequent vaginal infection in our study was fungus (candida) with a rate of 14.5%. BV rate was 3.3%, while trichomonas rate was 5.8%. Apart from BV frequency, both studies had similar results. In our country, cervical smear studies on pregnant women are rather related to the reliability of smear on pregnant women and almost all concluded that it is a good scan during pregnancy (19-21).

Study Limitations

During the study, we had some limitations. The most important limitations were the sample size and the low frequency of infectious agents detected in Pap smear; therefore, statistical analysis was not too strong for the infected cases.

Conclusion

We found no association between inflammation and/or reactive cellular changes of smear results in the first trimester of pregnancy and adverse pregnancy or neonatal outcomes. This is the first study investigating the relationship between first trimester smear results on pregnancy and neonatal outcomes in our country. For revealing this relation better, studies having a broader sample size are needed.

Ethics

Ethics Committee Approval: The ethical approval was obtained from Ethics Committee of University of Health Sciences Turkey, İstanbul Gaziosmanpaşa Training and Research Hospital (no: 91, 02.06.2020).

Informed Consent: Informed consent was obtained from all the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: F.K.G., S.Y., S.K., Design: F.K.G., S.Y., S.K., Data Collection or Processing: F.K.G., S.Y., Ö.S., Statistical Analysis or Interpretation: S.Y., Drafting Manuscript: F.K.G., Critical Revision of Manuscript: S.Y., S.K., Final Approval and Accountability: F.K.G., S.Y., S.K., Ö.S., Technical or Material Support: F.K.G., S.K., Ö.S., Supervision: S.Y., S.K.

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Mean Platelet Volume, Neutrophil Lymphocyte Ratio and Platelet Lymphocyte Ratio to Predict Complications During Postoperative Recovery of High Risk Surgical Patients

Postoperatif Yoğun Bakım Ünitesinde Takip Edilen Olgularda Komplikasyon Gelişimi ile Kan Parametreleri Arasındaki İlişkinin Değerlendirilmesi

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Abstract

Objective: This study sought to define the correlation between the occurrence of the complications and certain blood parameters in high risk surgical patients who were monitored for 24 hours in the intensive care unit postoperatively.

Method: Two hundred-fifty seven cases (126 females 131 males; mean age 42.18±8.54 years; range 19-73 years) who were operated on in our hospital and followed up in the intensive care unit for 24 hours were included in this study. The files of all cases included demographic characteristics, erythrocyte count (RBC), leukocyte count (WBC), platelet count (PLT), mean platelet volume (MPV), neutrophil, lymphocyte, neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), serum blood urea nitrogen (BUN) and creatinine values. Group A consisted of cases that did not develop complications in the first 24 hours, and group B consisted of cases that developed complications in the first 24 hours postoperatively. The blood hemogram parameters RBC, WBC, PLT, MPV, NLO, PLO, and the biochemistry parameters BUN and creatinine were compared between the groups.

Öz

Amaç: Bu çalışmada, elektif şartlarda opere edilen ve postoperatif 24 saat boyunca yoğun bakım ünitesinde takip edilen olgularda komplikasyon gelişimi ile kan parametreleri arasındaki ilişki araştırıldı.

Yöntem: Bu çalışmaya, hastanemizde ameliyat edilip, 24 saat postoperatif yoğun bakımda takip edilen 257 olgu (126 kadın 131 erkek; ortalama yaş 42,18±8,54 yıl; aralık 19-73 yıl) dahil edildi. Tüm olguların dosyaları demografik özellikleri, eritrosit sayısı (RBC), lökosit sayısı (WBC), trombosit sayısı (PLT), ortalama trombosit hacmi (MPV), nötrofil, lenfosit, nötrofil/lenfosit oranı (NLO), trombosit/lenfosit oranı (PLO), serum kan üre azotu (BUN) ve kreatinin değerleri açısından değerlendirildi. Grup A postoperatif ilk 24 saatte komplikasyon gelişmeyen olgulardan, grup B postoperatif ilk 24 saatte komplikasyon gelişen olgulardan oluşmakta idi. Gruplar arasında kan hemogram parametrelerinden RBC, WBC, PLT, MPV, NLO, PLO, biyokimya parametrelerinden BUN ve kreatinin değerleri karşılaştırıldı.

Bulgular: Grup B'de preoperatif MPV değeri ve postoperatif MPV değeri grup A'dan anlamlı olarak daha yüksekti (p-değerleri sırasıyla 0,038 ve

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Abstract

Results: Preoperative MPV value and postoperative MPV value were significantly higher in group B than group A (p-values 0.038 and 0.045, respectively). In groups A and B, the postoperative MPV value increased significantly compared to the preoperative period (p=0.032, p=0.000, respectively). Preoperative PLR and postoperative PLR values did not differ significantly in groups A and B (p=0.101 and p=0.458, respectively). The postoperative PLR value increased significantly in groups A and B compared to the preoperative period (p=0.000 and p=0.047, respectively) Preoperative and postoperative NLR values in group B were significantly higher than group A (p=0.006 and p=0.025 respectively). In groups A and B, the postoperative NLR value increased significantly compared to the preoperative period (p=0.000 and p=0.006, respectively).

Conclusion: In this study, the cases that developed complications had more significant increases in their MPV, NLR, and PLR values during the postoperative period than their counterparts who experienced no complications.

Keywords: ASA-3 cases, complication, intensive care, mean platelet volume, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio

Öz

0,045). Grup A ve B'de postoperatif MPV değeri preoperatif döneme göre anlamlı artış göstermiştir (sırasıyla p=0,032, p=0,000). Grup A ve B'de preoperatif PLO değeri ve postoperatif PLO değeri anlamlı farklılık göstermemiştir (sırasıyla p=0,101 ve p=0,458). Grup A ve B'de postoperatif PLO değeri preoperatif döneme göre anlamlı artış göstermiştir (sırasıyla p=0,000 ve p=0,047) grup B'de preoperatif ve postoperatif NLO değeri grup A'dan anlamlı olarak daha yüksekti (sırasıyla p=0,006 ve p=0,025). Grup A ve B'de postoperatif NLO değeri preoperatif döneme göre anlamlı artış göstermiştir (sırasıyla p=0,000 ve p=0,006).

Sonuç: Bu çalışmada, komplikasyon gelişen olgularda MPV, NLO ve PLO değerlerinin postoperatif dönemde daha fazla arttığı izlendi. MPV, NLO ve PLO gibi basit, hızlı ve ucuz bir teknikle yoğun bakım ünitesinde takip edilen olgularda gelişebilecek komplikasyonlar hakkında öngörü sağlanması, şüphesiz mortalite oranını azaltacaktır.

Anahtar kelimeler: ASA-3 hastalar, komplikasyon, nötrofil/lenfosit oranı, ortalama trombosit hacmi, trombosit/lenfosit oranı, yoğun bakım

Introduction

Intensive care units (ICU) are capable of administering treatments, where patients are applied close observation and rapid monitoring for life-threatening organ failure that may occur after surgery (1). It is recommended that cases with cardiac, respiratory, and neurological risk factors are monitored in ICUs even if complications do not occur postoperatively (2). Both the increased need for ICU beds and the rising population pose a significant healthcare problem worldwide. The relatively low number of beds and increasing demands have made the more effective use of ICU space necessary (3). Therefore, a rapid and cost-effective screening method for patients at higher risk of complications is needed to make the best use of ICU availability.

Technological and scientific advancements have contributed to the implementation of minimally invasive surgical methods. Despite this progress in alternative ways for major surgical operations, the complications of these surgeries continue to be significant. Although complication rates are impacted by both endogenous and exogenous factors, such as advanced age, gender, smoking, hypercholesterolemia, diabetes mellitus, and hypertension, the complications from these factors only explain a portion of the total complications observed (4,5). Various risk factors have been investigated to aid in predicting the probability of complications linked to surgical procedures. Current research indicates that any variation in specific blood parameters impacts the complication occurrence and mortality of various diseases. Many studies in the literature have evaluated the correlation between mortality and blood parameters of cases monitored in the ICU (5-8). However, few have assessed the relationship between the occurrence of complications and changes in blood parameters for patients followed in the ICU. Therefore, this study sought to define the correlation between occurrence of the complications and certain blood parameters in high risk surgical patients who had undergone elective surgery and were monitored for 24 hours in the ICU postoperatively.

Materials and Methods

Approval for the study was granted by the Hospital Ethics Committee (University of Health Sciences Turkey, İstanbul Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committee no: 2017-154). A list was drawn up in the preoperative assessment of all patients classified as American Society of Anesthesiologists classification 3-4, who might require postoperative intensive care. They were then admitted and followed up in the ICU after elective otolaryngology, general surgery, orthopedic, thoracic, brain, and urology operations between June 2016 and June 2017. This study was completed under the Declaration of Helsinki principles and best clinical practice guidelines. A retrospective review was made of collected data of the patients who underwent elective surgery and were treated at least for 24 hours in the ICU. The medical

charts for all these patients were reviewed. Data were collected by a researcher using a standardized case report form, including the hemogram and biochemistry values checked in the preoperative anesthesia outpatient clinic (or preoperatively if the anesthesia outpatient clinic duration has been prolonged) and the day after the postoperative surgery, since there were elective cases. The data recorded included hemodynamics heart rate, systolic blood pressure, diastolic blood pressure, and mean blood pressure, oxygen saturation measured via pulse oximetry, duration of mechanical ventilation, and length of stay in the ICU.

The demographic information of the patients was retrieved from the hospital records system.

The study included cases aged ≥18 years, operated on under elective conditions, were monitored for 24 hours or more in the ICU postoperatively and were discharged while being stable.

Considering the exclusion criteria, cases aged <18 years, those who died, underwent emergency surgery, had a history of operation, and had any hematological disease were excluded from the study.

The files of all cases were assessed in terms of demographic characteristics, erythrocyte count (RBC), leukocyte count (WBC), platelet count (PLT), mean platelet volume (MPV), neutrophil count, lymphocyte count, neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), BUN and serum creatinine values. The values were recorded preoperatively and 24 hours after surgery for all the cases in the study.

The cases were separated into two groups considering the occurrence of complications in the first 24 hours postoperatively. Group A comprised of cases who did not have any complications, and group B involved cases that developed complications in the first 24 hours postoperatively.

Postoperative complications that were accepted were as follows;

• Cardiac complications; ventricular tachycardia, angina, atrial fibrillation (AF), myocardial infarction (MI),

• Pulmonary complications; pneumonia, pneumothorax, pulmonary embolism, pleural effusion

• Neurological complications; stroke, cerebrovascular ischemia, hemorrhage, transient ischemic attack

• Renal complications; acute renal failure (accepted as serum creatinine values >2.0 mg/dL or 50% increase compared to preoperative values) and electrolyte disorder require hemodialysis.

• Infection complications; sepsis, systemic inflammatory response syndrome, deep or superficial sternal tissue infections.

The groups were compared in terms of the blood parameters of RBC, WBC, PLT, MPV, NLR, PLR, BUN, and creatinine values.

Statistical Analysis

Data obtained in the study were analyzed statistically using NCSS 2007 software (Number Cruncher Statistical System, Kaysville, Utah, USA). Descriptive statistics were stated as mean, standard deviation, median, minimum and maximum values, or frequency and percentage. Independent quantitative data were analyzed with the Independent Samples t-test and Mann-Whitney U test. Dependent quantitative data were analyzed using the Friedman test and Wilcoxon test. In the analysis of independent qualitative data, the chi-square test was applied. A value of $p<0.05$ was accepted as statistically significant.

Results

Patient characteristics: This study included 257 cases (126 female, 131 male) followed up after elective surgeries for 48 hours in the ICU. The demographic characteristics of the cases included in the study are given in Table 1. Surgery types and anesthesia data are summarized in Table 2.

Clinical outcomes: In group B (46 patients), the preoperative and postoperative RBC values were significantly lower compared to those of group A (211 patients) ($p=0.006$, $p=0.002$, respectively). There was a significant fall in postoperative RBC values in both groups compared to the preoperative values (group A: $p=0.000$, group B: $p=0.000$).

Table 1. Demographic data of the patients

	Group A (n=211)	Group B (n=46)
Age (years)	40.46±12.40 (19-68)	46.28±15.18 (30-73)
Male (n)	118 (55.92%)	24 (52.18%)
Female (n)	93 (44.08%)	22 (47.82%)
Complications	None	Cardiac: 17 (36.96%) Infection: 11 (23.91%) Pulmonary: 11 (23.91%) Neurological: 6 (13.04%) Renal: 1 (2.18%)

Table 2. Surgery types and anesthesia data of patients

Otolaryngological operations (n=63)	**General surgery operations (n=56)**
- Transoral robotic surgery for obstructive sleep apnea syndrome (16)	- Colorectal surgeries (26)
- Uvulopalatopharyngoplasty (21)	- Total thyroidectomy (8)
- Superficial parotidectomy (11)	- Bariatric surgery (22)
- Total parotidectomy (9)	
- Tympanomastoidectomy (5)	
Urology operations (n=38)	**Orthopedic operations (n=35)**
- Transurethral resection of the prostate (18)	- Knee, elbow, hip, shoulder, foot and ankle (10)
- Robotic prostatectomy (12)	- Multipl injuries (25)
- Partial nephrectomy (8)	
Thoracic surgery (n=27)	**Brain operations (n=37)**
- Lung cancer surgery (13)	- Brain tumors (22)
- Surgery for chest wall tumors (6)	- Subarachnoid hemorrhage (15)
- Surgery for lung and respiratory infection (8)	

There were no significant differences in preoperative and postoperative WBC values in groups A and B (p>0.05). The postoperative WBC amount was significantly increased compared to the preoperative values in group A and B (p=0.000, p=0.030, respectively).

In groups A and B, there was no significant difference in preoperative and postoperative PLT values (p>0.05). The postoperative PLT values in group A and B were significantly lower compared to the preoperative value (p=0.000, p=0.005, respectively).

The preoperative and postoperative MPV values in group B were significantly higher than those of group A (p=0.038, p=0.045, respectively). In group B, the postoperative MPV value was significantly increased compared to the preoperative value (p=0.032). The postoperative MPV value in group A was also significantly increased compared to the preoperative value (p=0.000).

In group B, the preoperative neutrophil value was significantly higher than that of group A (p=0.020). In groups A and B, the postoperative neutrophil values were not significantly different (p>0.005). The postoperative neutrophil values in groups A and B were significantly increased compared to the preoperative values (p=0.000 for both).

In group B, the preoperative lymphocyte and postoperative lymphocyte values were significantly lower than those of group A (p=0.005, p=0.018, respectively). The postoperative lymphocyte values in groups A and B fell significantly compared to the preoperative values (p<0.05 for both).

In groups A and B, the preoperative BUN values did not significantly differ (p>0.005). In group B, the postoperative BUN value was significantly higher than that of group A (p=0.006). The postoperative BUN value in group B was not significantly different from the preoperative value (p>0.005). The postoperative BUN value in group A was significantly increased compared to the preoperative value (p=0.012).

In groups A and B, the preoperative creatinine values were not significantly different (p>0.005). The postoperative creatinine value in group B was significantly higher compared to that of group A (p=0.026). In group B, the postoperative creatinine value showed a significant increase compared to the preoperative value (p=0.047). The postoperative creatinine value in group A was not significantly increased than the preoperative value (p>0.005).

No significant differences were determined between groups A and B regarding preoperative and postoperative PLR values (p=0.101 and p=0.458, respectively). The postoperative PLR values in groups A and B were significantly increased compared to the preoperative values (p=0.000 and p=0.047, respectively).

In group B, the preoperative and postoperative NLR values were significantly higher compared to those of group A (p=0.006 and p=0.025, respectively). The postoperative NLR values in groups A and B were significantly increased compared to the preoperative values (p=0.000 and p=0.006, respectively) (Table 3).

Discussion

In this retrospective study, the correlation was evaluated between complication occurrence and blood parameters of high risk patients operated under elective conditions and monitored for 24 hours postoperatively in the ICU.

Table 3. Comparison of preoperative and postoperative blood values in the groups

	Group A		Group B		p	
	Mean ± SD	**Median**	**Mean ± SD**	**Median**		
RBC (10^6/μL)						
Preoperative	4.4±0.9	4.6	4.1±0.7	4.2	**0.006**	m
Postoperative	3.9±0.8	3.9	3.5±0.7	3.6	**0.002**	m
Variation p	**0.000**	w	**0.000**	w		
WBC (10^3/μL)						
Preoperative	9.9±4.4	9.0	11.8±6.5	10.5	0.111	m
Postoperative	12.5±5.0	12.3	14.4±9.1	12.2	0.487	m
Variation p	**0.000**	w	**0.030**	w		
PLT (10^3/μL)						
Preoperative	244.9±99.1	234.4	241.7±134.8	216.1	0.207	m
Postoperative	215.7±95.4	206.4	214.3±140.9	187.0	0.169	m
Variation p	**0.000**	w	**0.005**	w		
MPV (fL)						
Preoperative	8.0±1.5	7.7	8.5±1.6	8.2	**0.038**	m
Postoperative	8.3±1.7	8.0	8.8±1.7	8.6	**0.045**	m
Variation p	**0.000**	w	**0.032**	w		
Neutrophil (%)						
Preoperative	66.4±15.5	66.3	72.1±14.2	73.4	0.020	m
Postoperative	80.2±11.6	82.9	83.2±6.7	84.1	0.186	m
Variation p	**0.000**	w	**0.000**	w		
Lymphocyte (%)						
Preoperative	22.5±12.8	22.3	16.7±11.1	15.3	**0.005**	m
Postoperative	11.6±9.0	9.6	10.0±11.1	7.2	**0.018**	m
Variation p	**0.000**	w	**0.001**	w		
BUN (mg/dL)						
Preoperative	42.8±30.2	34.0	50.1±33.9	38.5	0.122	m
Postoperative	42.7±29.9	34.0	58.7±37.7	45.0	**0.006**	m
Variation p	0.550	w	**0.012**	w		
Creatinine (mg/dL)						
Preoperative	1.1±1.0	0.9	1.1±0.6	1.0	0.402	m
Postoperative	1.3±1.4	0.8	1.4±1.0	1.0	**0.026**	m
Variation p	0.412	w	**0.047**	w		
PLT/lymphocyte (%)						
Preoperative	18.8±21.8	10.5	28.6±37.3	12.1	0.101	m
Postoperative	27.9±29.7	20.7	36.4±42.3	23.5	0.458	m
Variation p	**0.000**	w	**0.047**	w		
Neutrophil/lymphocyte (%)						
Preoperative	5.8±7.9	2.9	8.8±8.8	4.4	**0.006**	m
Postoperative	10.7±8.7	8.6	13.3±9.3	11.9	**0.025**	m
Variation p	**0.000**		**0.006**			

SD: Standard deviation, BUN: Blood urea nitrogen, PLT: Platelet count, MPV: Mean platelet volume, WBC: Leukocyte count, RBC: Erythrocyte count
Statistically significant values were shown as bold characters

In the cases with complications, the blood parameters of MPV, NLR, and PLR were higher in the postoperative period. The elevation of MPV, NLR, and PLR, especially in cases with complications, showed the role of the inflammatory response in the occurrence of complications.

ICUs are the units where cases are closely monitored for surgical complications. Knowing the factors that affect the occurrence of complications is very important for clinicians working in ICUs to comprehend the seriousness of the situation. An estimation of complications beforehand and taking necessary precautions will both reduce mortality and prevent long hospital stays. Identifying and preventing complications before they occur is clear, considering that patient care in ICUs is costly and creates a greater economic burden.

Current researches have focused on high mortality in ICUs, and cause-effect studies have an important place in the literature. There are very few studies in the literature on the prediction of complications in ICUs. The current study researched whether the blood parameters of MPV, NLR, and PLR primarily had predictive value for the occurrence of complications in cases monitored in the postoperative ICU. To the best of our knowledge, this is the first study related to this topic in the literature. The study included cases operated under elective conditions and monitored in the ICU. Cases were separated into two groups as those who had and did not have complications, and the correlation with blood parameters was assessed.

The chemical and physical properties of platelets are related to size. The increase in MPV is a new parameter used as a cardiovascular risk factor. MPV is an important parameter showing the activation and function of platelets, and activated platelets are known to play an important role in systemic inflammatory response syndrome the pathogenesis of atherothrombosis. Studies have shown that in the occurrence of atherothrombosis, not only the platelet content but also the material released from platelets plays an effective role in the induction of inflammation (5).

In vitro studies have shown that parameters such as p-selectin, active glycoprotein 2b/3a, platelet factor 4, and beta-thromboglobulin play a role in platelet activation and functions. However, these parameters are not studied in routine applications because of the need for detailed equipment and expertise and the relatively higher expense, so they are not used to assess platelet activation and functions. Examining MPV is a simple, inexpensive, straight forward process. While MPV levels show a correlation with platelet activation and functions, increased MPV values are related to short hemorrhage time and increased plasma thromboxane A2 level (4). In this study, the MPV was used to assess platelet functions in all cases. The *in vitro* parameters of p-selectin, active glycoprotein 2b/3a, platelet factor 4 and beta-thromboglobulin could not be evaluated for platelet activation and function as the study was retrospective and routine use of these parameters is very expensive.

A study by Taglieri et al. (9) reported that increased MPV levels were related to the repeated MI risk within one year. Bath et al. (10) also stated that increased MPV levels were a predictive factor for a new attack in cases with cerebrovascular disease or transient ischemic attack. The MPV level was determined to be an important biomarker for prognosis in cases with cardiovascular disease. Another study by Dogan et al. (11) reported that increased MPV values in non-ST elevation MI cases were associated with cardiac death, recurrent angina, or prolonged hospital stay. Topuz et al. (12) reported that MPV levels were higher in cases with paroxysmal AF. A study by Choudhury et al. (13) found that platelet activation and MPV levels were higher in cases with AF compared to cases with normal sinus rhythm. Ha et al. (14) also identified higher MPV values in AF cases. Erdem et al. (15) reported that preoperative MPV values were related to the risk of AF occurrence after coronary bypass. Many studies in the literature have investigated the correlation of MPV with mortality in ICU patients. Altun et al. (16) reported no correlation between MPV and mortality. A meta-analysis by Tajarernmuang et al. (17) stated no correlation between the MPV value at the time of admission to ICU and mortality. Yarkıcı et al. (18) found a significant correlation between increased MPV and mortality in intensive care. However, no previous study has evaluated the correlation between the occurrence of complications in cases monitored in the ICU and MPV. The results of the current study showed that the preoperative and postoperative MPV values in group B were significantly higher than those of group A. In group B, the postoperative MPV value was significantly increased compared to the preoperative value. The postoperative MPV value in group A was significantly increased compared to the preoperative value (Table 3).

In recent years, NLR has started to measure the severity of inflammation in a variety of diseases such as cardiovascular diseases, malignancy, and diabetes. The ratios of neutrophil and platelet counts to lymphocyte count have been shown to be possible markers of systemic inflammation and to be

associated with prognosis in many cardiovascular diseases, malignancies, and chronic inflammatory diseases (19-22). Even though NLR is a marker of inflammatory conditions, it may also be responsible for renal endothelial damage and impaired microcirculation as a consequence of the inflammatory process arising from neutrophil infiltration, activated endothelium, lymphocytes, and platelets (23,24). PLR has been used to predict patients' prognosis with different inflammatory and ischemic events (25). Temiz et al. (26) observed that elevated PLR was correlated with hospital mortality. In the current study, no significant differences were determined between groups A and B in respect of the preoperative and postoperative PLR values. The postoperative PLR values in groups A and B were significantly increased compared to the preoperative values. In group B, the preoperative and postoperative NLR values were significantly higher compared to those of group A. The postoperative NLR values in groups A and B were significantly increased compared to the preoperative values (Table 3).

Although blood parameters are now used as predictive values for many diseases and malignancies, their effect on the occurrence of complications in cases monitored in ICUs is unknown. In this study, the cases monitored in ICU were separated into two groups according to whether complications were observed or not. The blood parameters of MPV, BUN, creatinine, WBC, RBC, PLT, NLR, and PLR were evaluated and compared. In the cases with complications, the blood parameters of MPV, NLR, and PLR were observed to be higher in the postoperative period. The elevation of MPV, NLR, and PLR, especially in cases with complications, shows the role of the inflammatory response for complications. This study is important in assessing the effect of the MPV, NLR, and PLR values on postoperative complications. When the results of this study are considered, the widespread increase in MPV, NLR, and PLR values in the postoperative period may be an indicator of complications. When all cases are re-evaluated in terms of complications, taking precautions against possible complications will reduce mortality and the duration of hospital stay.

Study Limitations

Although this study provides valuable information, there are some limitations, primarily its retrospective design. Other limiting factors include the relatively low number of cases included in the study, the lack of randomization, not knowing which factors affecting blood parameters were present in cases, not knowing if cases had sudden temperature loss affecting blood parameters previously and not knowing if cases had diseases such as congenital platelet diseases. There is a need for further, randomized controlled studies with higher patient numbers to extend this topic's knowledge.

Conclusion

The occurrence of complications while cases are monitored in ICUs remains a significant problem. The prediction of complications that may occur in cases monitored in ICUs and taking rapid and effective precautions against these complications will significantly reduce mortality rates. The MPV, NLR, and PLR values of patients who had complications were observed to increase in the postoperative period. Therefore, the use of simple, rapid, and inexpensive techniques such as MPV, NLR, and PLR for the prediction of potential complications in cases monitored in ICUs will undoubtedly reduce mortality rates. statistical analysis.

Ethics

Ethics Committee Approval: Approval for the study was granted by the Hospital Ethics Committee (University of Health Sciences Turkey, İstanbul Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committee no: 2017-154).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: B.B., M.Ç., D.Y., G.O.H., Design: B.B., M.Ç., D.A., B.T.Ç., G.O.H., Data Collection or Processing: B.B., M.Ç., D.Y., D.A., G.O.H., B.T.Ç., Analysis or Interpretation: D.A., D.Y., B.T.Ç., G.O.H., Literature Search: B.B., M.Ç., D.A., G.O.H., Writing: B.B., M.Ç, D.A., G.O.H., Manuscript Review and Revisation: B.B., M.Ç., D.A., D.Y.

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ORIGINAL RESEARCH

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Assessment of Lateral Epicondylitis Videos on YouTube

YouTube'da Lateral Epikondilit Videolarının Değerlendirilmesi

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Abstract

Objective: The aim of the present study was to assess the quality, reliability and educational value of health-related information videos about lateral epicondylitis on YouTube.

Method: The study conducted a search on YouTube on April 1, 2021 using the search term "lateral epicondylitis". Based on relevance to this keyword, the first 50 videos were recorded for assessment. The videos were assessed by two orthopedic surgeons. Video length in seconds, view counts, number of likes, number of dislikes, video category (animation or not), video content, days since upload, and source of upload (uploader) were recorded. All videos were analyzed for length, view counts, number of likes and source of upload. Quality of the videos was assessed using the global quality score (GQS) (score range: 0-4), Journal of the American Medical Association (JAMA) score (0-5), and DISCERN (15-75) score. The data were statistically analyzed according to these scoring systems.

Results: Like rate had no significant correlation with GQS, DISCERN, and JAMA scores. There was a significant positive correlation between view rate and GQS scores (p=0.038). View rate had no significant correlation with DISCERN (p=0.453) and JAMA scores (p=0.946). There was a significant positive correlation between video power index and GQS scores (p=0.036). Video power index had no significant correlation with DISCERN (p=0.442) and JAMA scores (p=0.938). According to the source of upload, there was a significant difference in JAMA and DISCERN scores between physicians and non-physicians. GQS did not significantly differ (p=0.15) according to the source of upload.

Conclusion: The analysis of the first 50 videos relevant to lateral epicondylitis on YouTube revealed that videos were uploaded mainly by healthcare professionals. Overall, the 50 videos had an average level of adequacy.

Keywords: Lateral epicondylitis, social media, YouTube

Öz

Amaç: Bu çalışmanın amacı YouTube'da lateral epikondilit ile ilgili sağlık ve bilgilendirme videolarının kalitesini, güvenilirliğini ve eğiticilik düzeyini değerlendirmektir.

Yöntem: Çalışmada YouTube üzerinde arama kelimesi "lateral epikondilit" yazılarak, 1 Nisan 2021 tarihli arama yapıldı. İlk 50 video bu anahtar terime göre en alakalı sıralama ile değerlendirme için kaydedildi. Videolar iki ortopedik cerrah tarafından değerlendirildi. Videoların saniye olarak uzunluğu, izlenme sayısı, beğenme sayısı, beğenmeme sayısı, animasyon olup olmadığı, içeriği, yüklenme gün sayısı ve video kaynağı kaydedildi. Tüm videolar uzunluk, izlenme sayısı, beğenme sayısı ve videonun kaynağı bilgileri ile analiz edildiler. Videoların kalitesini değerlendirmek için global kalite skoru (GQS) (score range: 0-4), Journal of the American Medical Association (JAMA) (0-5) ve DISCERN (15-75) skorlama sistemleri kullanıldı. Elde edilen veriler bu skorlama sistemlerine göre istatistiksel olarak analiz edildiler.

Bulgular: Beğenme oranı ile GQS, DISCERN ve JAMA arasında anlamlı bir ilişki yoktur. İzlenme oranı ile GQS (p=0,038) arasında pozitif yönlü anlamlı bir ilişki vardır. İzlenme oranı ile DISCERN (p=0,453) ve JAMA (p=0,946) arasında anlamlı bir ilişki yoktur. Video güç indeksi ile GQS (p=0,036) arasında pozitif yönlü anlamlı bir ilişki vardır. Video güç indeksi ile DISCERN (p=0,442) ve JAMA (p=0,938) arasında anlamlı bir ilişki yoktur. Yüklenme kaynaklarına göre JAMA ve DISCERN skorlarında doktor ve doktor olmayanlar arasında anlamlı fark vardır. Yüklenme kaynağı açısından GQS düzeyinde (p=0,15) anlamlı bir farklılık yoktur.

Sonuç: YouTube'da lateral epicondilit ile en alakalı ilk 50 video analiz edildiğinde ağırlıklı olarak sağlık profesyonelleri tarafından videoların yüklenmiş olduğu görüldü. Genel olarak, 50 video analiz edildiğinde ortalama düzeyde yeterliliğe sahiptir.

Anahtar kelimeler: Lateral epikondilit, sosyal medya, YouTube

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Introduction

The Internet has become the most practical and quickest way to access information in the last three decades. In parallel with the popularity of the Internet, many people utilize the Internet or social media as the first source of information especially before medical procedures to be performed during the pandemic or to learn the details of their diseases. The video-sharing site most commonly used to explain medical conditions and medical procedures is YouTube.

There are currently over 2 billion active YouTube users. Almost 70% of video viewers watch videos on mobile devices (1). Patients often try to gather information about their diseases by watching YouTube videos (2-4). These patients also include those with extremity disorders. In particular, patients with lateral epicondylitis, which is resistant to medical and conservative therapy, go through a more comprehensive search over time. Patients can increase their anxiety levels by constantly thinking about the worst and referring to the most negative examples based on the videos they watch.

Kunst et al. (5) concluded in their study, conducted in 2002, that health-related websites had not been improved enough and had inadequate information. In order for patients to access accurate information, videos need to have a high-quality content about health-related information. However, although accessed by everyone, the utility and accuracy of the information obtained over the Internet is controversial (5).

Since being founded in 2005, YouTube has 30 million daily and 2 billion monthly active users (6). From this point of view, YouTube is a site with visual browsing on almost every topic, including health-related subjects. However, YouTube is a video site established for entertainment or social purposes rather than educational or academic videos.

Although patients utilize the Internet or YouTube to search their medical conditions, only 18% discuss this online search with their clinicians (7). In addition, 75% of chronic patients make online search to reach a final decision just before treatment (8). Despite all, the Internet still does not have an effective control mechanism for health education.

Lateral epicondylitis is a common medical condition seen in orthopedics and physical therapy outpatient clinics. We conducted this study to establish the extent of accurate information obtained by our patients about this condition through online search. Lateral epicondylitis patients, particularly those who work in the heavy industry, are under significant stress to maintain their active work lives. In the literature, orthopedic and physical therapy studies evaluating the quality and specificity of YouTube videos are limited in number. These studies are about scoliosis, bone tumors, arthritis of the hip, and anterior cruciate ligament tear in particular (3,9-12). There is a lack of studies on lateral epicondylitis.

The aim of the present study was to assess the quality, reliability and educational value of health-related information videos about lateral epicondylitis on YouTube.

Materials and Methods

YouTube search

In this study, a search was performed on YouTube on April 1, 2021, using the search term ''lateral epicondylitis''. Based on the relevance to this keyword, the first 50 videos were recorded for assessment (Table 1). This was considered an appropriate method for video selection because this was an accepted assessment method in other peer-reviewed literature on orthopedic surgery (9). Only videos in English language were included in the study. Videos with information unrelated to lateral epicondylitis, those in non-English languages, those for advertising purposes, and those with only audio were excluded. This study does not contain any human or animal resources, ethical approval was not needed for this study. Patient information was not used in the study. Therefore, the patient consent document was not obtained.

The videos were watched independently by two orthopedists. Video length in seconds, view counts, number of likes, number of dislikes, video category (animation or not), video content, days since upload, and source of upload (uploader) were recorded. The source of upload was classified as patient experience, physician, physiotherapist and health website. The video content was categorized as surgical technique, disease-specific assessment, exercise training, and advertisement. For each video, a video power index (VPI) (like ratio × view ratio/100), a view ratio (number of views/days), and a like ratio [like×100/(like + dislike)] were calculated. We used these measurements in our study since they were used in previous studies published in previous peer-reviewed journals (13).

Assessment of video reliability and educational content

Videos were independently scored by two orthopedists according to content, global quality score (GQS), Journal of the American Medical Association (JAMA) score, and DISCERN score (14-16). The videos were watched separately

Table 1. Links of videos sorted by relevance in the search for lateral epicondylitis on YouTube (first 50 videos)

N	Video source link
Video 1	https://www.youtube.com/watch?v=4vk3i22z3Ko
Video 2	https://www.youtube.com/watch?v=r_A84ox9JRM
Video 3	https://www.youtube.com/watch?v=qn2VT7Df7no
Video 4	https://www.youtube.com/watch?v=qdbC9Ic3qCg
Video 5	https://www.youtube.com/watch?v=Lf695_IJO8g
Video 6	https://www.youtube.com/watch?v=8K7jzDIUpLI
Video 7	https://www.youtube.com/watch?v=kAy8q7yJAHM
Video 8	https://www.youtube.com/watch?v=92FXZlXZaf0
Video 9	https://www.youtube.com/watch?v=X2BrySMybtI
Video 10	https://www.youtube.com/watch?v=xoj-L_UlbEw
Video 11	https://www.youtube.com/watch?v=NExFfXSe2Mc
Video 12	https://www.youtube.com/watch?v=uFNhlBR-Ae0
Video 13	https://www.youtube.com/watch?v=iAlFqxkYz_o
Video 14	https://www.youtube.com/watch?v=DgwQSPQv_Zo
Video 15	https://www.youtube.com/watch?v=w-uLcHXO2b4
Video 16	https://www.youtube.com/watch?v=BXAzcjxIHMg
Video 17	https://www.youtube.com/watch?v=r_A84ox9JRM
Video 18	https://www.youtube.com/watch?v=txB_JsCGaBo
Video 19	https://www.youtube.com/watch?v=ltjqrllSxDk
Video 20	https://www.youtube.com/watch?v=bW2jpzl1FSY
Video 21	https://www.youtube.com/watch?v=Wk6ZNJ8MVk4
Video 22	https://www.youtube.com/watch?v=XK9tqcQnykE
Video 23	https://www.youtube.com/watch?v=Z50T8J5mQEE
Video 24	https://www.youtube.com/watch?v=MghCqfcqJHI
Video 25	https://www.youtube.com/watch?v=w-uLcHXO2b4
Video 26	https://www.youtube.com/watch?v=thUlPbCX4fU
Video 27	https://www.youtube.com/watch?v=BXAzcjxIHMg
Video 28	https://www.youtube.com/watch?v=slf_42AhFzU
Video 29	https://www.youtube.com/watch?v=uY-oy4h2YnI
Video 30	https://www.youtube.com/watch?v=GOwqNDP40TQ
Video 31	https://www.youtube.com/watch?v=uSHNPJQEs4Q
Video 32	https://www.youtube.com/watch?v=NTs9q8WdTbY
Video 33	https://www.youtube.com/watch?v=4bgELYdFavs
Video 34	https://www.youtube.com/watch?v=LttMqFJI2WM
Video 35	https://www.youtube.com/watch?v=yKjVcdD1dig
Video 36	https://www.youtube.com/watch?v=ofKRUmAaqy4
Video 37	https://www.youtube.com/watch?v=7xMn9RRsmAs
Video 38	https://www.youtube.com/watch?v=8ls_H4vHfOM
Video 39	https://www.youtube.com/watch?v=PdGuk6RSGh4
Video 40	https://www.youtube.com/watch?v=8k-mqAqGnGA
Video 41	https://www.youtube.com/watch?v=IjUrBZC8KwE
Video 42	https://www.youtube.com/watch?v=OT7jVNF8wvw
Video 43	https://www.youtube.com/watch?v=ayCJYZ47SJo
Video 44	https://www.youtube.com/watch?v=UpZKU677pqQ

Table 1. Continued

N	Video source link
Video 45	https://www.youtube.com/watch?v=rRlGA9cerhs
Video 46	https://www.youtube.com/watch?v=FiQF6QLv4Y0
Video 47	https://www.youtube.com/watch?v=jxbTNT_ZdL8
Video 48	https://www.youtube.com/watch?v=EsZcJRttJPo
Video 49	https://www.youtube.com/watch?v=qTjDq3_D-FU
Video 50	https://www.youtube.com/watch?v=sWiLrHy9ky8

by two orthopedists and then their scores were added up and divided by two, yielding the average GQS, DISCERN, and JAMA scores (Figure 1).

The JAMA scoring system is a non-specific and objective tool for online videos and resources. It consists of 4 individual criteria. Each criterion is scored 1 point and the total score ranges from 0 to 4 points. A score of 4 indicates high reliability and accuracy for the online source, while a score of 0 indicates poor source reliability and accuracy (Table 2).

Non-specific educational content quality was assessed using the GQS. The GQS assesses the educational value of video content based on 5 criteria. The source is given 1 point for each of the present criteria. A score of 5 indicates the highest quality of education (Table 3).

The DISCERN score generally assesses the video content for integrity, purpose and relevance, objectivity, accuracy of therapeutic options, and the availability of alternative therapeutic options. It is a test consisting of 15 items. Each item is scored from 1 to 5. A score of 63-75 is considered as excellent, 51-62 as good, 39-50 as fair, 28-38 as poor, and <28 as very poor (Table 4).

In the study, the VPI, view ratio and like ratio were calculated using respective formulas. The formula used to calculate the view ratio and like ratio were as follows: (number of

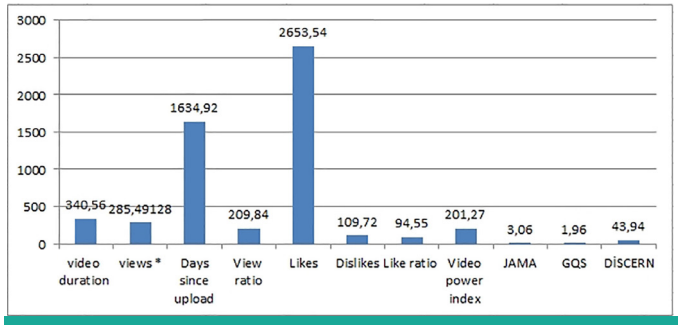

Figure 1. Representation of the variables used in the study on the scatterplot

** Value×10³, JAMA: Journal of the American Medical Association, GQS: Global quality score*

Table 2. JAMA scoring system

Criteria	Description
Authorship	Author and contributor credentials and their affiliations should be provided.
Attribution	Clearly lists all copyright information and states references and sources for content.
Currency	Initial date of posted content and subsequent updates to content should be provided.
Disclosure	Conflicts of interest, funding, sponsorship, advertising, support, and video ownership should be fully disclosed.

JAMA: Journal of the American Medical Association

Table 3. Global quality score criteria

Score	Description of quality
1	Poor quality; is unlikely of be to use for patient education.
2	Poor quality; is of limited use to patients because only some information is present.
3	Suboptimal quality and flow; is somewhat useful to patients; important topics are missing, some information is present.
4	Good quality and flow; useful to patients because most important topics are covered.
5	Excellent quality and flow; is highly useful to patients.

Table 4. DISCERN scoring system, each item is scored from 1 to 5 and then added up

Section 1 **Is the publication reliable?**
1. Are the aims clear?
2. Does it achieve its aims?
3. Is it relevant?
4. Is it clear what sources of information were used to compile the publication (other than the author or producer)?
5. Is it clear when the information used or reported in the publication was produced?
6. Is it balanced and unbiased?
7. Does it provide details of additional sources of support and information?
8. Does it refer to areas of uncertainty?
Section 2 **How good is the quality of information on treatment choices?**
9. Does it describe how each treatment works?
10.Does it describe the benefits of each treatment?
11. Does it describe the risks of each treatment?
12. Does it describe what would happen if no treatment is used?
13. Does it describe how the treatment choices affect overall quality of life?
14. Is it clear that there may be more than one possible treatment choice?
15. Does it provide support for shared decision-making?

views/days) and [likex100/(like + dislike)], respectively. The formula used to calculate the VPI was as follows: (like ratio*view ratio/100) (9,13).

Statistical Analysis

Statistical analysis was performed using SPSS 25.0 for Windows 10 software. The independent samples t-test was used to analyze the difference in mean scores between two groups. Correlations among continuous variables were examined using the Pearson's correlation test. The study was conducted at 95% confidence interval.

Results

All results are summarized in Tables 5-7. All analyzed data, mean values, standard deviation and ranges are explained in Table 5. Three (6%) videos included animation, 22 (44%) videos physicians, 10 (20%) videos health websites, 13 (26%) videos physiotherapists, 1 (2%) video commercial product company, 3 (6%) videos academic content, and 1 (2%) video included a patient's own experience. Regarding video contents, there were 22 (44%) clinical (disease-related) videos, 11 exercise (22%) training videos, 2 (4%) advertisement videos, 11 (22%) disease-specific information videos, 3 (6%) surgical technique and approach videos, and 1 (2%) patient experience video.

According to the Pearson's correlation test, like ratio was not statistically significantly correlated with GQS (p=0.772), DISCERN (p=0.713), and JAMA (p=0.486) scores. There was a significant positive correlation between view ratio and GQS scores (p=0.038). View ratio had no significant correlation with DISCERN (p=0.453) and JAMA scores (p=0.946). There was a significant positive correlation between view ratio and GQS scores (p=0.036). View ratio had no significant correlation with DISCERN (p=0.442) and JAMA scores (p=0.938).

When sources of upload were classified as physician and non-physician (academic content, commercial product companies, medical content and animation, physiotherapist, physical training or athletic trainer (non-physiotherapist), patient), there was a significant difference in JAMA and DISCERN scores between physicians and non-physicians. GQS did not significantly differ (p=0.15) according to the source of upload. According to this result, the GQS score did not differ between physician and non-physician uploaders. There was a significant difference in JAMA scores ($p<0.05$) between the sources of upload. There was a significant difference in JAMA scores in favor of physicians between videos uploaded by physicians and by non-physicians. There was a significant difference in

DISCERN scores (p<0.05) between the sources of upload. There was a significant difference in DISCERN scores in favor of physicians between videos uploaded by physicians and by non-physicians (Table 7).

There was no significant difference in view ratios (p>0.05) between the sources of upload (physicians and non-physicians). According to this result, the view ratios did not differ between physician and non-physician uploaders. There was no significant difference in like ratios (p>0.05) between the sources of upload (physicians and non-physicians). According to this result, the like ratios did not differ between physician and non-physician uploaders (Table 7).

Discussion

This is the first study to focus on lateral epicondylitis and provide information on the effects of video content quality on patients. The first focus of the study was to discuss how well lateral epicondylitis was explained on YouTube and the quality of video content.

Most of the videos were produced by healthcare professionals in our study. Although the literature review showed that video uploads by patients were not to be underestimated, our study found that videos were mainly uploaded by healthcare professionals.

The mean video length was 5.67 min in our study, while previous studies reported a length of 6.17-16.18 min (3-9-17-18).

Table 5. Video characteristics of the YouTube videos

Characteristic	Mean	SD	Minumum	Maximum
Video duration (sec)	340.56	244.16	23	1234
Views	285491.28	496753.60	119	2180469
Days since upload	1634.92	1130.91	27	4369
View ratio[α]	209.84	351.74	0.5	1274.84
Likes	2653.54	5658.88	6	24000
Dislikes	109.72	268.24	1600	0
Like ratio[β]	94.55	4.76	78.18	100
Video power index[ı]	201.27	338.08	0.48	1217.29
JAMA*	3.06	0.91	1	4
GQS*	1.96	0.75	1	5
DİSCERN*	43.94	43.94	15.5	71.4

*Average of the scores given by two orthopedists watching the videos, [α]View ratio; number of views/days, [β]Like ratio; like×100/(like+dislike), [ı]VPI: Video power index; like ratio × view ratio, SD: Standard deviation, JAMA: Journal of the American Medical Association, GQS: Global quality score

The statistical assessments did not reveal any statistically significant relationship among like ratios and GQS, DISCERN and JAMA scores. This finding suggests that video likes by video viewers are not related to video content quality and originality. However, GQS scores were found to have a significant positive correlation with view ratio and VPI (Table 6). The GQS assesses non-specific educational content quality. Obviously, view ratio increases with increasing content, specific information and quality useful for patients. However, DISCERN and JAMA scores were not correlated with like ratio, view ratio and VPI. DISCERN and JAMA scores, which provide more academic and professional information flow, did not attract the attention of video viewers. However, other studies established more likes in low quality videos (19,20).

Our study established statistically significant differences between physician and non-physician uploaders. No significant difference was found in GQS scores and like

Table 6. Statistical relationship among like ratio, view ratio, video power index and GQS, DISCERN and JAMA scores

	GQS	DISCERN	JAMA
Like ratio (p-value[α])*	0.772 (r=0.04)	0.713 (r=0.05)	0.486 (r=-0.10)
View ratio (p-value[α])*	0.038 (r=0.30)	0.453 (r=0.11)	0.946 (r=-0.01)
Video power index (p-value[α])*	0.036 (r=0.29)	0.442 (r=0.11)	0.938 (r=-0.01)

[α]Pearson correlation test, *Correlation is significant at the 0.05 level (2-tailed), SD: Standard deviation, JAMA: Journal of the American Medical Association, GQS: Global quality score

Table 7. Relationship between doctor and other video uploaders by video source

Scoring system	Video source	N	Median score	SD	p
GQS	Doctor	22	2.13	0.77	0.15
	Others*	28	1.82	0.72	
JAMA	Doctor	22	3.81	1.18	0.01
	Others*	28	2.92	1.15	
DISCERN	Doctor	22	52.09	13.27	<0.001
	Others*	28	37.54	12.35	
Like ratio	Doctor	22	93.45	5.40	0.15
	Others*	28	95.41	4.09	
View ratio	Doctor	22	225.99	403.53	0.78
	Others*	28	197.15	312.25	

* Academic content, commercial product companies, medical content and animation, physiotherapist, physical training or athletic trainer (non-physiotherapist), patient (uploaded for individual experience), p: Independent samples t-test, SD: Standard deviation, JAMA: Journal of the American Medical Association, GQS: Global quality score

ratios between physician and non-physician uploaders; however, there was a significant difference in JAMA and DISCERN scores between physician and non-physician uploaders in favor of physicians. Physician uploaders were more successful in describing the current medical condition, explaining the treatments and complications in detail, and questioning the reliability of their resources. However, there was no difference in the like and view ratios, which are the causes of trends on YouTube, between videos uploaded by physicians and non-physicians. However, the review of literature did not identify any significant correlation between videos by uploaders and video quality (20,21).

In their study on bone tumors and YouTube contents, Sezgin and Erman (9) reported the mean GQS, JAMA and DISCERN scores as 2.22 (1-4), 2.12 (1-3), and 33.48 (17-66), respectively. In this study, the average JAMA, GQS and DISCERN scores, which were used to assess various aspects of the videos such as content, appropriateness of treatment, quality, accuracy and reliability, were 3.06, 1.96, and 43.94, respectively. Considering these findings, the video quality in our study was average.

The most important limitation of the study was that the first 50 videos were watched and assessed. However, previous studies were also found to conduct a similar assessment (22,23). Another limitation of the study was that the assessment was made by two orthopedists. Another limitation is that YouTube search ranking varies across countries. However, we found that the most relevant video ranking remained same when the country was changed using proxy networks. Another limitation of the study is that lateral epicondylitis is also referred to as tennis elbow at the same time. In the study, lateral epicondylitis was used instead of tennis elbow as a search word. Tennis elbow search term is a disease that is mostly used by the public. However, lateral epicondylitis is a more scientific and medical term than tennis elbow. However, when the literature is searched, YouTube reviews with the search term tennis elbow have not been done before. Moreover, the search term of tennis elbow and YouTube videos have not been examined in the literature before.

Conclusion

In conclusion, the Internet and YouTube are the first sources that people refer to about health as is every topic in the 21st century. The analysis of the first 50 videos relevant to lateral epicondylitis on YouTube revealed that videos were uploaded mainly by healthcare professionals. Overall, the 50 videos had an average level of adequacy in terms of quality and content. We believe that this study revealed the extent of accurate information obtained on YouTube videos by patients with lateral epicondylitis and the quality standards of the videos watched from the perspective of healthcare professionals.

Ethics

Ethics Committee Approval: This study does not contain any human or animal resources, ethical approval was not needed for this study.

Informed Consent: Patient information was not used in the study. Therefore, the patient consent document was not obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.A., A.M., Design: M.A., A.M., Data Collection or Processing: M.A., A.M., Analysis or Interpretation: M.A., A.M., Writing: M.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL RESEARCH

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Does Vitamin D Level Affect Beta Cell Activity?

D Vitamini Seviyesi Beta Hücre Aktivitesini Etkiler mi?

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Abstract

Objective: The prevalence of vitamin D deficiency is ever-increasing throughout the world. Vitamin D deficiency is associated with disorders such as diabetes, insulin resistance, obesity, dyslipidemia, and hypertension. This research study was carried out to assess serum vitamin D levels of patients with type 2 diabetes, insulin resistance, obesity, and impaired fasting glucose.

Method: This study was carried out on 504 patients, who were newly diagnosed and did not receive medication before, aged 18 to 80 years, and who had type 2 diabetes, insulin resistance, obesity, and impaired fasting glucose. Their fasting glucose, fasting insulin, total cholesterol, high-density lipoprotein (HDL)-cholesterol, low-density lipoprotein-cholesterol, triglyceride, 25(OH)D concentration, height and body weight measurements were analyzed retrospectively. Body mass index, homeostatic model assessment (HOMA) for insulin resistance and HOMA beta (B) values of the patients were calculated.

Results: It was found that 89.9% of the patients with type 2 diabetes, 90.6% of the insulin resistance patients, 91.7% of the obesity patients and 94.1% of the impaired fast glucose patients had less than 30 ng/mL of serum 25(OH)D concentration. It was seen that the serum 25(OH)D concentrations of the patients were negatively correlated with their fasting insulin concentrations and HOMA B values, and positively correlated with their HDL-cholesterol levels.

Conclusion: Based on this study, vitamin D deficiency was found to be common in the patients with type 2 diabetes, insulin resistance, obesity, and impaired fasting glucose. Serum 25(OH)D concentrations were correlated with the levels of fasting insulin, HDL-cholesterol, and beta-cell function.

Keywords: HOMA B, HOMA-IR, insulin resistance, obesity, type 2 diabetes, vitamin D

Öz

Amaç: D vitamini yetersizliği tüm dünyada giderek artmaktadır. D vitamini yetersizliği diyabet, insülin direnci, obezite, dislipidemi ve hipertansiyon gibi düzensizlikler ile ilişkilidir. Bu araştırma tip 2 diyabet, insülin direnci, obezite ve bozulmuş açlık glikozu olan hastaların serum D vitamini düzeylerini değerlendirmek amacıyla yapılmıştır.

Yöntem: Bu araştırma, 18-80 yaş arası yeni tanı konulmuş ve daha önce ilaç tedavisi almamış, tip 2 diyabet, insülin direnci, obezite ve bozulmuş açlık glikozu olan 504 bireyin bulguları incelenerek yapılmıştır. Hastaların açlık glikoz, açlık insülin, total kolesterol, yüksek yoğunluklu lipoprotein (HDL)-kolesterol, düşük yoğunluklu lipoprotein-kolesterol, trigliserit, 25(OH)D konsantrasyonları, boy ve vücut ağırlığı ölçümleri retrospektif olarak analiz edilmiştir. Hastaların vücut kütle indeksi, insülin direncinin homeostatik modeli değerlendirmesi (HOMA) ve HOMA beta (B) değerleri hesaplanmıştır.

Bulgular: Tip 2 diyabetli hastaların %89,9'unun, insülin direnci hastalarının %90,6'sının, obezite hastalarının %91,7'sinin ve bozulmuş açlık glikozu hastalarının %94,1'inin serum 25(OH)D konsantrasyonlarının 30 mg/mL'nin altında olduğu bulunmuştur. Serum 25(OH)D konsantrasyonu ile açlık insülin konsantrasyonu ve HOMA B değerleri arasında negatif korelasyon, HDL-kolesterol seviyesi ile pozitif korelasyon olduğu görülmüştür.

Sonuç: Bu çalışmada tip 2 diyabet, insülin direnci, obezite ve bozulmuş glikoz toleransı hastalarında D vitamini yetersizliği sık görülmüştür. Serum 25(OH)D konsantrasyonu açlık insülin, HDL-kolesterol ve beta hücre fonksiyonu ile ilişkili bulunmuştur.

Anahtar kelimeler: HOMA B, HOMA-IR, insülin direnci, obezite, tip 2 diyabet, vitamin D

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Introduction

Vitamin D is a fat-soluble vitamin. It is stored in adipose tissue and released when needed (1). Vitamin D deficiency is quite common across the world (2). It is thought that vitamin D deficiency is linked to cardiometabolic risk factors including low levels of chronic inflammation, dyslipidemia, hypertension, insulin resistance, and obesity (3).

Serum 25(OH)D concentration is checked in order to assess the status of vitamin D in the body. How it is classified is given in Table 1 (4).

Obesity is negatively correlated with the status of vitamin D in the body (1). Possible causes of low vitamin D levels in obesity include the fact that obese people do not sufficiently take vitamin D, they get less sunlight, and thus their vitamin D synthesis through the skin is decreased (3). Vitamin D storage increases and the bioavailability of the vitamin decreases in the adipose tissue, which increases with obesity. This mechanism is effective in reducing serum vitamin D levels in obesity. Vitamin D deficiency leads to an increase in the release of the parathyroid hormone. The parathyroid hormone stimulates the transport of calcium into adipocytes and increases lipogenesis (2).

Obesity and low vitamin D levels seem to synergistically affect the risk of insulin resistance (1). There is a relationship between vitamin D deficiency and insulin resistance (2,3). There is a negative correlation between serum vitamin D concentrations and fasting insulin levels (3).

Vitamin D deficiency is associated with metabolic syndrome and type 2 diabetes (4). A change in vitamin D balance plays an important role in the development of type 2 diabetes and insulin resistance (5). Vitamin D deficiency is common in diabetes. Low serum 25(OH)D levels, which are indicative of vitamin D status in general, are negatively correlated with type 2 diabetes and impaired fasting glucose (6). The effect of vitamin D on insulin resistance can mediate the relationship between type 2 diabetes and serum vitamin D concentrations (7). People with a low serum 25(OH)D level are more prone to develop diabetes than those with a high serum 25(OH)D level (8). Among the reasons for this close relationship are the facts that vitamin D affects peripheral insulin sensitivity, that it provides cytokine activation associated with insulin resistance and that it plays an important role in maintaining pancreatic beta-cell function (9,10).

Vitamin D has an important role in glucose and insulin metabolism. Vitamin D affects pancreatic islet cells via receptors and increases insulin secretion. Vitamin D also has anti-inflammatory and immune regulatory effects. It can lead to an increase in insulin release and a decrease in insulin resistance by regulating the immune system (11).

Table 1. Classification of serum 25(OH)D concentration levels

Serum 25(OH)D concentration	
0-9.9 ng/mL	Severe insufficiency
10-19.9 ng/mL	Insufficiency
20-29.9 ng/mL	Deficiency
30-100 ng/mL	Optimal concentration
>100 ng/mL	Risk of toxicity

Homeostatic model assessment (HOMA) is a method used to evaluate insulin resistance and beta cell function. While calculating HOMA, serum fasting glucose and insulin values are used (12). HOMA of insulin resistance (HOMA-IR) is the main method used in the assessment of insulin resistance (13). HOMA-IR is calculated using HOMA-IR= [glucose (fasting) (mg/dL) × insulin (fasting) (μIU/mL)]/405 (14). HOMA beta (HOMA B) is useful for determining beta cell function (12). HOMA B is calculated using HOMA B= [insulin (fasting) (μIU/mL) × 360]/[(glucose (fasting) (mg/dL)-63] (14).

This research study was carried out to assess serum vitamin D levels of patients with type 2 diabetes, insulin resistance, obesity, and impaired fasting glucose.

Materials and Methods

This study was carried out on 504 patients aged 18 to 80 years, who had type 2 diabetes, insulin resistance, obesity and impaired fasting glucose, and who were referred by the internal medicine clinic of a hospital to the diet polyclinic. The patients included in the study were newly diagnosed and did not receive medication for their diagnosis before. Certain biochemical findings and anthropometric measurements of the patients were examined retrospectively.

The study included the patients who did not have any systemic diseases other than type 2 diabetes, insulin resistance and obesity, whose body length and weight were measured, and whose serum 25(OH)D fasting glucose, fasting insulin, total cholesterol, HDL-cholesterol, LDL-cholesterol, and triglyceride concentrations were checked.

A total of 3.220 patients' hospital files were examined during the research period. Among these patients, the number

of those who had type 2 diabetes or insulin resistance or obesity and also serum 25(OH)D concentrations recorded in files were 504 and they were included in the study. The remaining patients were not included in the study because they did not have the diseases that constituted the subject of the study, or because they also had diseases that did not constitute the subject of the study, or because they did not undergo the necessary biochemical measurements.

Body mass indexes (BMIs) of the patients referred from the internal medicine polyclinic to the diet polyclinic were calculated using their body length and weight measurements. Body mass indices were calculated using the following formula (15).

BMI=Body weight (kg)/[height (m)]^2

All biochemical measurements were made at the Central Laboratory of İstanbul Anatolian North Public Hospitals Association.

Blood glucose levels were measured by using a Roche Hitachi Modular DPP device and determined by enzymatic colorimetric measurements. Blood insulin levels were measured by using a Beckman Coulter Unicel DXI 800 device. Determination of insulin is an immunoenzymatic measurement.

Blood total cholesterol, triglyceride, and HDL-cholesterol levels were measured using a Roche Hitachi Modular DPP device. Total cholesterol and triglyceride concentrations were measured by using an enzymatic colorimetric test. HDL-cholesterol levels were measured by using a homogeneous enzymatic colorimetric assay. Finally, LDL-cholesterol levels were calculated by using the formula below (16).

LDL-cholesterol=Cholesterol-(HDL-cholesterol+triglycerides/5)

Serum 25(OH)D levels of the patients were measured by drawing blood samples on an empty stomach. Serum 25(OH)D concentrations were measured by using an Abbott/architect device and the chemiluminescent microparticle immunoassay method at the Central Laboratory of İstanbul Anatolian North Public Hospitals Association.

HOMA-IR and HOMA B values were calculated by using the fasting glucose and fasting insulin values of the patients. HOMA-IR and HOMA B were calculated by using the following formulas (14).

HOMA-IR=[glucose (fasting) (mg/dL) × insulin (fasting) (µIU/mL)]/405

HOMA B=[insulin (fasting) (µIU/mL) × 360]/[(glucose (fasting) (mg/dL)-63]

Statistical Analysis

IBM SPSS Statistics Version 22 package program was used in order to analyze the data. The mean and standard deviation values of age, height, body weight, BMI, and serum 25(OH)D concentration levels were calculated. The means and standard deviations of serum fasting glucose, fasting insulin, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, 25(OH)D concentrations, and HOMA-IR and HOMA B values were also calculated separately for the patient groups. One-Way analyses of variance were carried out to determine whether there were notable differences between the groups. Distributions of the patients according to the disease groups and serum 25(OH)D levels were determined by using calculations based on percentages. Pearson correlation analyses were carried out to determine whether the fasting glucose, fasting insulin, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglyceride, HOMA-IR, and HOMA B values of the patients were related to their ages, body weights, BMIs, and serum 25(OH)D values.

This research was evaluated and approved by the İstanbul Medipol University Non-Interventional Clinical Research Ethics Committee. Moreover, it is registered in the Chinese Clinical Trial system, which is one of the international clinical trial registry systems. Chinese Clinical Trial Registration Number: ChiCTR1900027133.

Results

This study included 504 patients with type 2 diabetes, insulin resistance or obesity. Of the patients, 385 (76.4%) were female, and 119 (23.6%) were male. The mean age of the patients was 46.02±13.7 years, their height was 162.19±8.51 cm, body weight was 88.25±16.74 kg, the average BMI was 33.65±6.22 kg/m^2, and serum 25(OH)D concentration was 16.7±10.1 ng/mL.

Table 2. Distribution of patients according to serum vitamin D levels

Level of vitamin D		N	%
0-9.9 ng/mL	Severe insufficiency	143	28.4
10-19.9 ng/mL	Insufficiency	204	40.5
20-29.9 ng/mL	Deficiency	112	22.2
≥30 ng/mL	Normal	45	8.9
Total		504	100.0

Distribution of the patients according to serum vitamin D levels is given in Table 2. Of the patients, 143 (28.4%) were found to have 0-9.9 ng/mL of serum 25(OH)D concentration, 204 (40.5%) had 10-19.9 ng/mL, 112 (22.2%) had 20-29.9 ng/mL, and 45 (8.9%) had 30 ng/mL or more serum 25(OH)D concentration.

In Table 3, the patients' mean biochemical findings are given according to their diagnoses. The mean serum 25(OH) D concentrations of all groups were at the level of 10-19.9 ng/mL, which is the insufficient level. The mean HOMA-IR value in obese patients was 1.7±0.4. The mean HOMA B value was 168.8±83.8 in patients with insulin resistance, 113.8±73.5 among obese patients. The differences between the mean fasting glucose (p=0.000), fasting insulin (p=0.000), total cholesterol (p=0.022), HDL-cholesterol (p=0.002), triglyceride (p=0.000), HOMA-IR (p=0.000) and HOMA B (p=0.000) were found to be extremely significant among the patients with type 2 diabetes, insulin resistance, obesity and impaired fasting glucose. Nevertheless, no major difference was observed between the groups in terms of the mean LDL-cholesterol (p=0.166) and mean 25(OH)D concentration (p=0.965).

Table 4 shows the distribution of the patients according to the disease groups and serum 25(OH)D levels. Serum 25(OH)D concentration of 89.9% (n=133) of patients with type 2 diabetes mellitus, 90.6% (n=135) of patients with insulin resistance, 91.7% (n=143) of obese patients and 94.1% (n=48) of patients with impaired fasting glucose were below 30 ng/mL.

Table 5 shows the results on the relationship between the biochemical findings of the patients and their age, body weight, BMI and serum 25(OH)D values. It was found that the patients' ages were positively but poorly correlated with their fasting glucose and triglyceride concentration, positively and moderately correlated with their total cholesterol and LDL-cholesterol, and negatively but moderately correlated with their fasting insulin concentration. The patients' body weights were found to be positively but poorly correlated with their HOMA-IR (Graph 1) and HOMA B values (Graph 2), moderately correlated with their fasting insulin, and negatively but poorly correlated with their total cholesterol, HDL-cholesterol and LDL cholesterol. The patients' BMIs were found to be positively but poorly correlated with their fasting insulin and HOMA-IR values (Graph 3). No

Table 3. Patients' average biochemical findings according to their diagnoses

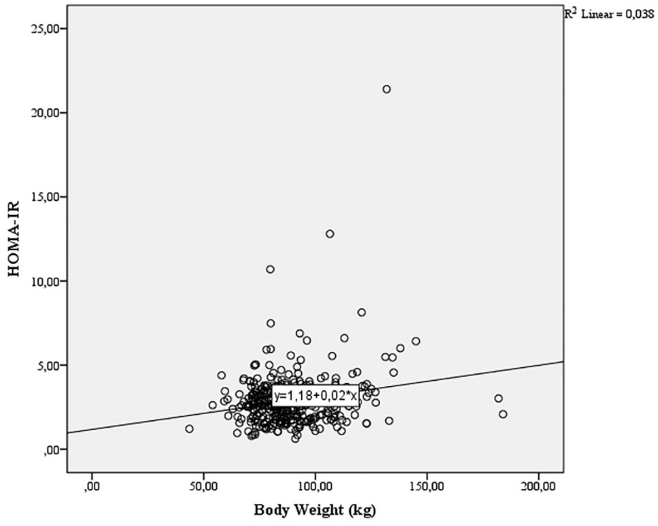
Biochemical findings	Diagnosis				
	Type 2 diabetes Mean ± SD	Insulin resistance Mean ± SD	Obesity Mean ± SD	Impaired fasting glucose Mean ± SD	p
Fasting glucose (mg/dL)	161.0±65.4	96.3±6.9	95.3±64.0	110.0±5.3	0.000*
Fasting insulin (μIU/mL)	10.7±5.3	14.4±4.3	7.9±2.7	12.6±7.1	0.000*
Total cholesterol (mg/dL)	215.0±40.9	208.7±43.3	208.9±41.0	229.0±47.9	0.022*
HDL-cholesterol (mg/dL)	44.6±11.0	47.0±12.0	49.9±11.3	46.0±11.9	0.002*
LDL-cholesterol (mg/dL)	140.8±34.5	135.6±37.0	135.6±36.7	148.0±43.4	0.166
Triglycerides (mg/dL)	162.5±80.8	138.5±97.5	121.1±62.9	165.4±66.2	0.000*
25(OH)D (ng/mL)	16.9±11.2	16.7±10.2	16.7±9.7	16.0±8.2	0.965
HOMA-IR	4.0±3.5	3.4±0.9	1.7±0.4	3.4±2.0	0.000*
HOMA B	63.5±45.4	168.8±83.8	113.8±73.5	92.8±53.8	0.000*

*One-Way ANOVA (p<0.05), SD: Standard deviation, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, HOMA-IR: Homeostatic model assessment for insulin resistance, Homa B: Homeostatic model assessment beta

Table 4. Diagnosis and distribution of patients according to serum 25(OH)D levels

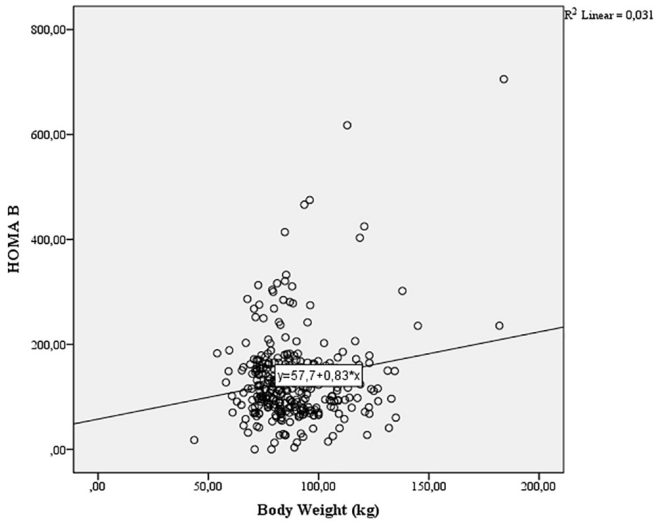
	Serum 25(OH)D								TOTAL	
	0-9.9 ng/mL		10-19.9 ng/mL		20-29.9 ng/mL		≥30 ng/mL			
Diagnosis	N	%	N	%	N	%	N	%	N	%
Type 2 diabetes mellitus	42	28.4	61	41.2	30	20.3	15	10.1	148	100.0
Insulin resistance	41	27.5	63	42.3	31	20.8	14	9.4	149	100.0
Obesity	46	29.5	58	37.2	39	25.0	13	8.3	156	100.0
Impaired fasting glucose	14	27.5	22	43.1	12	23.5	3	5.9	51	100.0

statistically significant correlation was found between the body mass indexes of the patients and their HOMA B values (Table 5) (Graph 4). A positive but weak correlation was found between the patients' serum 25(OH)D values and their HDL-cholesterol values, and a negative but weak correlation was found between their serum 25(OH)D values and their fasting insulin and HOMA B values. Serum 25(OH)D concentrations were found to be not correlated with fasting glucose concentrations (Graph 5).



Graph 1. Scatterplot for the relationship between patients' body weights and HOMA-IR values

HOMA-IR: Homeostatic model assessment for insulin resistance



Graph 2. Scatterplot for the relationship between patients' body weights and HOMA B values

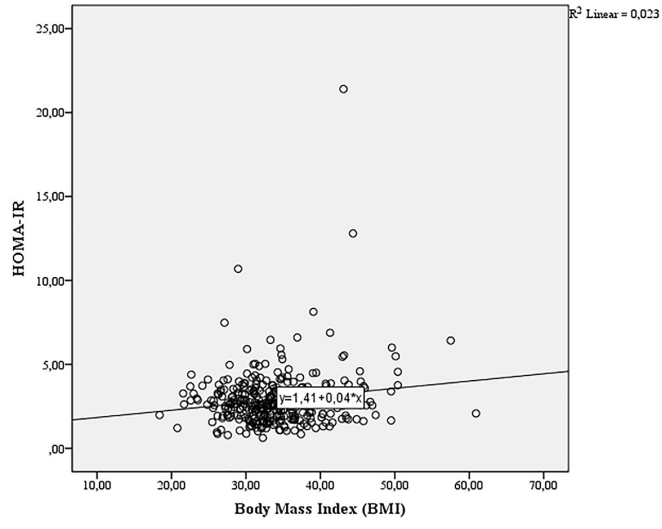
HOMA B: Homeostatic model assessment beta

Discussion

Vitamin D is thought to be a complex steroid hormonal system that regulates calcium balance and gets involved in autocrine, paracrine and endocrine processes (17). Vitamin D levels in the body are determined by measuring plasma 25(OH)D levels (3).

Vitamin D deficiency is a global social health problem and is mainly associated with various chronic diseases (3,17). In a study carried out by Schmitt et al. (18), 463 post-menopausal women were divided into 3 groups according to their serum vitamin D levels. It was found that 151 of the women (32.6%) suffered deficiency, and 164 (35.4%) were included in the group of insufficiency. In a study carried out by Diaz et al. (19), serum 25(OH)D levels of 712 people with metabolic syndrome were categorized. In this study, vitamin D deficiency was found in the majority of patients with type 2 diabetes mellitus, insulin resistance, obesity, and impaired fasting glucose. This result clearly supports previous studies in which vitamin D deficiency is highly common among such patients (4).

It is indisputable that obesity is closely related to vitamin D deficiency (3,20). Serum 25(OH)D levels of 89 overweight and obese people were analyzed in a study carried out by Kaseb et al. (21). Based on their findings, 93.2% of the overweight and obese people participating in the study were found to have serum 25(OH)D concentrations below 30 ng/mL. The mean serum 25(OH)D concentration of the people was found to be 13.8±11.36 ng/mL. In this



Graph 3. Scatterplot for the relationship between patients' body mass indexes and HOMA-IR values

HOMA-IR: Homeostatic model assessment for insulin resistance

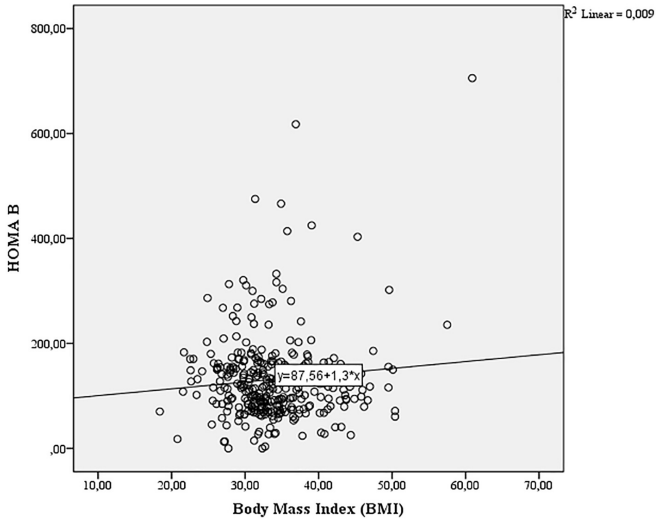
present study, the mean serum 25(OH)D concentration of the obese people was found to be 16.7±9.7 ng/mL (Table 3). Moreover, 91.7% (n=143) of the obese people had serum 25(OH)D concentration below 30 ng/mL (Table 4). Less exposure to the sun light and more covered clothing of obese individuals reduce vitamin D synthesis (3). In addition, vitamin D is stored in adipose tissue and as a result, its amount in circulation decreases (2). The causes of the negative correlation between the status of vitamin D and obesity include volumetric dilution, storage, and inactivation (1). For this reason, it is important to note that vitamin D supplementation has positive effects on body weight management (22).

There is a negative correlation between vitamin D levels in the body and insulin resistance. Low vitamin D levels increase insulin resistance (23,24). In the present study, the mean serum 25(OH)D concentration of the patients with insulin resistance was 16.7±10.2 ng/mL (Table 3). Of the patients, 27.5% (n=41) had 0-9.9 ng/mL of serum 25(OH)D concentration, 42.3% (n=63) had 10-19.9 ng/mL, 20.8% (n=31) had 20-29.9 ng/mL, and 9.4% (n=14) had 30 ng/mL or more serum 25(OH)D concentration (Table 4). In this study, it was concluded that 90.6% (n=135) of the patients with insulin resistance had vitamin D deficiency. This result supports the relationship between vitamin D deficiency and insulin resistance. Low serum 25(OH)D concentration contributes to insulin resistance and the development of diabetes through death of beta cells. Vitamin D plays an important role in reducing inflammation, which is

Table 5. Results on the relationship between the biochemical findings of the patients and their age, body weight, BMI and serum 25(OH)D values

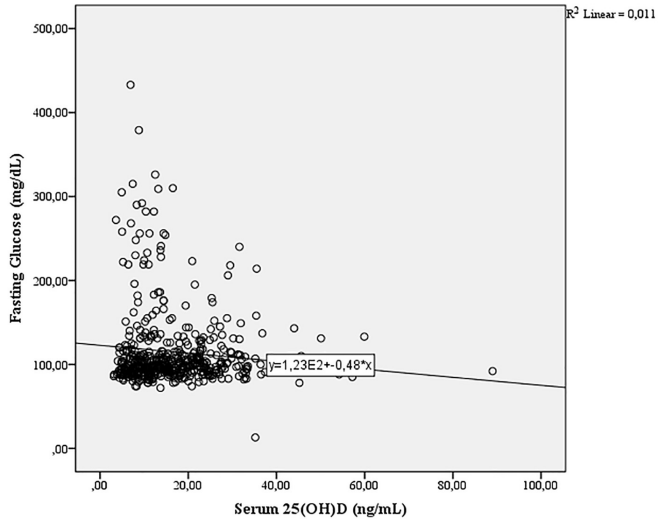
Biochemical findings	Age		Body weight		BMI		Serum 25(OH)D	
	r	p	r	p	r	p	r	p
Fasting glucose	0.153**	0.001	-0.035	0.431	-0.059	0.185	-0.080	0.073
Fasting insulin	-0.211**	0.000	0.210**	0.000	0.147**	0.008	-0.146**	0.008
Total cholesterol	0.336**	0.000	-0.133**	0.005	-0.035	0.458	0.037	0.435
HDL-cholesterol	0.066	0.169	-0.171**	0.000	-0.064	0.179	0.097*	0.042
LDL-cholesterol	0.320**	0.000	-0.110*	0.022	-0.025	0.600	0.016	0.738
Triglycerides	0.131**	0.005	0.069	0.145	-0.039	0.410	-0.026	0.585
HOMA-IR	-0.065	0.241	0.196**	0.000	0.152**	0.006	-0.101	0.068
HOMA B	-0.342	0.000	0.177**	0.001	0.094	0.089	-0.155**	0.005

BMI: Body mass index, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, HOMA-IR: Homeostatic model assessment for insulin resistance, HOMA B: Homeostatic model assessment beta, *Pearson correlation analysis correlation significant at the 0.05 level, ** Correlation significant at the 0.01 level



Graph 4. Scatterplot for the relationship between patients' body mass indexes and HOMA B values

HOMA B: Homeostatic model assessment beta

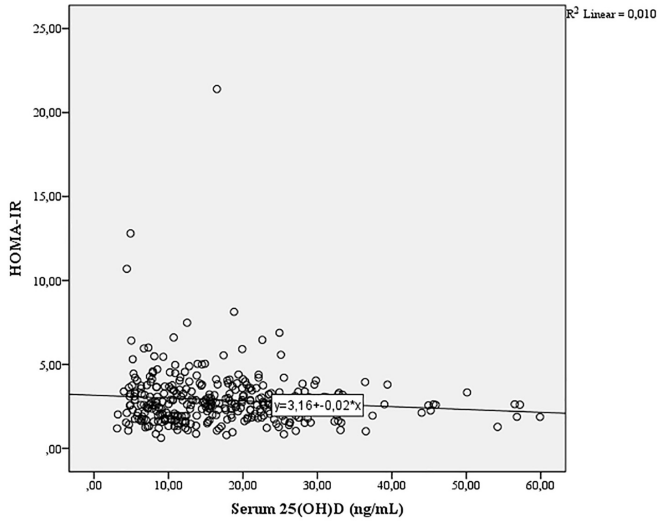


Graph 5. Scatterplot for the relationship between serum 25(OH)D values and fasting glucose values of patients

an important process in the development of insulin resistance (25). Research has associated low plasma concentration of 25(OH)D with increased serum fasting glucose concentration, increased insulin resistance and increased insulin release (23,26). A study by Sun et al. (5) has shown that vitamin D supplementation may reduce insulin resistance. In a study carried out by Gupta et al. (27), 25 patients with polycystic ovary were supplemented with 60,000 IU/week vitamin D for 12 weeks. It was found that fasting insulin, fasting glucose and insulin resistance decreased and insulin sensitivity increased at the end of the supplementation period. In a study carried out by Wang et al. (24), it was found that serum 25(OH)D concentration was negatively correlated with serum insulin levels (r=-0.209, p=0.012) and HOMA-IR (r=-0.273, p=0.001). Serum 25(OH)D concentrations of 92 healthy and overweight people were analyzed in a study carried out by Wallace et al. (28). It was found that the difference between fasting insulin values of the people with sufficient and insufficient serum vitamin D levels was not statistically significant (p>0.05). It was concluded that there was no correlation between serum 25(OH)D levels and insulin resistance. In a study of 1,514 adult people without diabetes carried out by Li et al. (29), it was determined that there was a negative correlation between serum 25(OH)D concentrations and HOMA-IR. A study conducted by Schmitt et al. (18) showed that women with low serum 25(OH)D levels had high levels of insulin and HOMA-IR (p<0.05). In a study carried out by Han et al. (30), although there was a negative correlation between serum 25(OH)D levels and HOMA-IR in men (r=-0.055, p=0.028), there was no significant correlation between these two parameters in women (r=-0.005, p=0.798). In a study carried out by Yoon et al. (31), serum vitamin D concentrations of non-diabetic people were found not to have a significant correlation with their HOMA-IR values, but to have a negative correlation with their HOMA B values. It was concluded that vitamin D was not correlated with insulin resistance, but with beta-cell function. In a study conducted, the difference between HOMA-IR and HOMA B values in diabetic patients was found to be significant in terms of serum 25(OH)D levels (p<0.05), and it was seen that there was a positive correlation between serum 25(OH) D levels and beta-cell function (32). In this study, serum 25(OH)D concentration was found not to be correlated with HOMA-IR (r=-0.101, p=0.068) (Graph 6), but to be negatively correlated with HOMA B (r=-0.155, p=0.005) (Table 5) (Graph 7).

Vitamin D deficiency is associated with insulin resistance and decreased beta-cell function (33). In a study conducted by Pan et al. (34), patients with metabolic syndrome and people without metabolic syndrome were compared in terms of serum 25(OH)D concentration levels. It was found that the serum 25(OH)D concentration of the patients with metabolic syndrome was 21.74±7.43 ng/mL, and that of the people without metabolic syndrome was 24.96±8.76 ng/mL. It was concluded that the concentration of vitamin D in serum was lower in the patients with metabolic syndrome. In a study carried out by Haidari et al. (35) the mean serum 25(OH)D concentration of the type 2 diabetes patients was found to be 11.01±5.55 ng/mL. In this present study, the mean serum 25(OH)D concentration of the patients with type 2 diabetes was found to be 16.9±11.2 ng/mL. This study supports previous research. Vitamin D deficiency or insufficiency was found in almost all of the patients with Type 2 diabetes mellitus included in this study. It was concluded that vitamin D deficiency was widespread in the patients with type 2 diabetes. Vitamin D has anti-inflammatory and insulin sensitivity support effects. Vitamin D deficiency promotes inflammation and insulin resistance, which contributes to the formation of type 2 diabetes mellitus, and as a result, the risk of developing type 2 diabetes mellitus increases (9,10).

In a study conducted by Haidari et al. (35), the relationship between serum 25(OD)D levels of patients with type 2

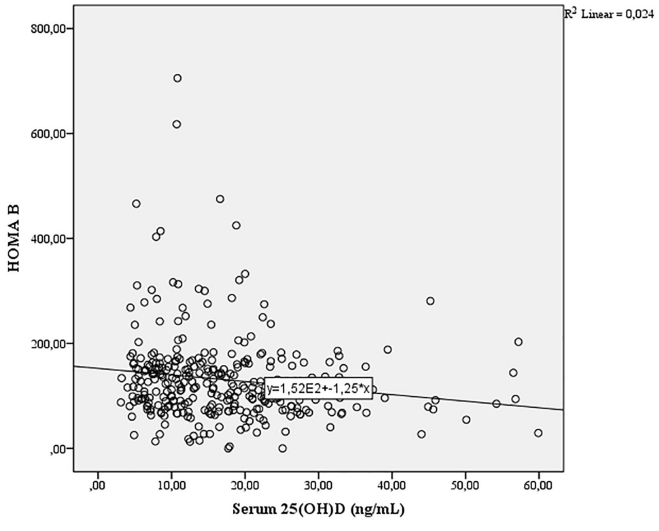


Graph 6. Scatterplot for the relationship between serum 25(OH)D values and HOMA-IR values of patients

HOMA-IR: Homeostatic model assessment for insulin resistance

diabetes and their fasting glucose, fasting insulin and HOMA-IR was examined. It was determined that vitamin D levels were negatively correlated with fasting glucose concentrations, but not significantly with HOMA-IR. In their study, Kwon and Lim (36) grouped people with prediabetes according to their serum vitamin D concentrations. No correlation was found between the mean serum fasting glucose, fasting insulin and HOMA-IR levels of the people and their serum 25(OH)D levels. In a study carried out by Srimani et al. (37), serum 25(OH)D levels and blood glucose levels were found to be negatively and significantly correlated. In this present study, the relationship between fasting glucose, fasting insulin concentrations and serum 25(OH)D concentrations was examined. Serum 25(OH)D concentrations were found to be not correlated with fasting glucose concentrations (r=-0.080, p=0.073), but negatively correlated with fasting insulin concentrations (r=-0.146, p=0.008) (Table 5). This study supports some of the results found in previous research.

Vitamin D deficiency is correlated with decreased high-density lipoprotein (HDL) levels, increased triglyceride levels, and hypercholesterolemia. Vitamin D levels can be low in people with hypercholesterolemia (3). It has been concluded in a study carried out by de Courten et al. (23) that decreased plasma 25(OH)D concentration is associated with increased triglyceride levels and decreased HDL-cholesterol levels. In a study conducted by Yang et al. (32), 97 patients with type 2 diabetes were assigned into two groups: Serum 25(OH)D concentrations below 37.5 nmol/L (n=61) and above (n=36). As a result of the study, the difference between the groups was significant in total cholesterol and HDL-cholesterol concentrations (p<0.05). In this study, a positive correlation was found between serum 25(OH)D concentration and HDL-cholesterol concentration. This may be due to the effect of vitamin D on increasing lipoprotein lipase activity, regulating calcium metabolism and decreasing parathyroid hormone activity (38).



Graph 7. Scatterplot for the relationship between serum 25(OH)D values and HOMA B values of patients

HOMA B: Homeostatic model assessment beta

Conclusion

Vitamin D is a fat-soluble vitamin and has certain functions other than regulating calcium metabolism. Vitamin D deficiency is common in society. There is a strong correlation between vitamin D deficiency and metabolic syndrome risk factors. In this study, it was seen that vitamin D deficiency was found in almost all patients with type 2 diabetes, insulin resistance, obesity and impaired fasting glucose. There was no significant difference between serum 25(OH)D concentrations of the patients with type 2 diabetes, insulin resistance, obesity and impaired fasting glucose. Serum 25(OH)D concentrations were found to be negatively correlated with serum fasting insulin concentrations and positively correlated with serum HDL cholesterol concentrations. It was determined that HOMA B, which shows beta-cell function, was negatively correlated with serum 25(OH)D concentrations. In conclusion, vitamin D deficiency was found to be common in the patients with type 2 diabetes, insulin resistance, obesity and impaired fasting glucose. Examining serum 25(OH) D concentrations of patients with type 2 diabetes, insulin resistance, obesity and impaired fasting glucose, and giving them supplementations may positively contribute to the treatment process.

Ethics

Ethics Committee Approval: This research was evaluated and approved by the İstanbul Medipol University Non-Interventional Clinical Research Ethics Committee. Moreover, it is registered in the Chinese Clinical Trial system, which is one of the international clinical trial registry systems. Chinese Clinical Trial Registration Number: ChiCTR1900027133.

Informed Consent: This study was conducted retrospectively by using the routine values of the patients.

Peer-review: Externally peer-reviewed.

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ORIGINAL RESEARCH

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Bowel Pathologies Caused by the Use of Electrocautery Knife in Spinal Surgery with Facet Denervation: The First Experimental Study

Faset Denervasyonu Olan Omurga Cerrahisinde Elektrokoter Bıçağı Kullanımının Neden Olduğu Bağırsak Patolojileri: İlk Deneysel Çalışma

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Abstract

Objective: Monopolar electrocautery (MEC) or bipolar electrocautery (BEC) are surgical instruments commonly used in spinal surgery. Our study aimed to determine the bowel end pathologies induced by sacral parasympathetic network degeneration due to the use of MEC or BEC in spinal surgery.

Method: Twenty male hybrid rabbits were used in the study, including 5 in the control group, 7 in the BEC group, and 8 in the MEC group. We used the thoracic vertebra 11-lumbar vertebra 2 (T11-L2) spinal laminectomy for the operation technique. After one week, the animals' abdominal organs were examined on computerized tomography, and then the animals were sacrificed. The descending colon and Onuf's nucleus/S4 spinal ganglia were histopathologically examined. The colonic degeneration scores were numbered as follows: Normal (0P), vasospasm (1P), endothelial injury (2P), thrombus (3P), colonic wall injury (4P), inflammation (5P), colonic mucosal degeneration (6P), Auerbach myenteric ganglion degeneration (7P), and necrosis (8P). The groups were scored according to 36 points, and the results were compared with the number of degenerated pudendal ganglion neurons.

Results: The mean numbers of normal neurons/degenerated neurons were 22.610±962/5±2, 21.617±890/103±21, and 16.692±641/345±62 in the control, BEC, and MEC groups, respectively. The colonic degeneration score was <8 points in the control group, 9-30 points in the BEC group, and >31 points in the MEC group. Our results were statistically significant ($p<0.05$ for all).

Conclusion: In this study, we have found that high-voltage electrical devices such as MEC/BEC may cause bowel pathologies due to their harmful effects on the Adamkiewicz artery/sacral parasympathetic network and should not be used in spinal surgery unless necessary.

Keywords: Electrocauterization, facet denervation, neuronal injury, rabbit, spinal surgery

Öz

Amaç: Monopolar elektrokoter (MEC) veya bipolar elektrokoter (BEC), spinal cerrahide yaygın olarak kullanılan cerrahi aletlerdir. Çalışmamızda spinal cerrahide MEC veya BEC kullanımına bağlı sakral parasempatik ağ dejenerasyonunun neden olduğu bağırsak patolojilerini belirlemeyi amaçladık.

Yöntem: Çalışmada, kontrol grubunda 5, BEC grubunda 7 ve MEC grubunda 8 olmak üzere toplam 20 erkek hibrid tavşan kullanıldı. Ameliyat tekniği olarak torasik vertebra 11-Lomber vertebra 2 (T11-L2) spinal laminektomi uygulandı. Bir hafta sonrasında, hayvanların karın organları bilgisayarlı tomografi ile incelendi ve ardından hayvanlar sakrifiye edildi. İnen kolon ve Onuf çekirdeği/S4 spinal gangliyonları histopatolojik olarak incelendi. Kolonik dejenerasyon skorları: Normal (0P), vazospazm (1P), endotelyal hasar (2P), trombüs (3P), kolonik duvar hasarı (4P), inflamasyon (5P), kolonik mukozal dejenerasyon (6P), Auerbach miyenterik ganglion dejenerasyonu (7P) ve nekroz (8P) olarak skorlandı. Gruplar toplamda 36 puana göre puanlandı ve sonuçlar dejenere olmuş pudendal ganglion nöronlarının sayısı ile karşılaştırıldı.

Bulgular: Kontrol, BEC, MEC gruplarında sırasıyla ortalama normal nöron/dejenere nöron sayıları 22,610±962/5±2, 21,617±890/103±21 ve 16,692±641/345±62 idi. Kolonik dejenerasyon skoru kontrol grubunda <8 puan, BEC grubunda 9-30 puan ve MEC grubunda >31 puandı. Sonuçlarımız istatistiksel olarak anlamlıydı.

Sonuç: Bu çalışmada, MEC/BEC gibi yüksek voltajlı elektrikli cihazların Adamkiewicz arter/sakral parasempatik ağ üzerindeki zararlı etkileri nedeniyle bağırsak patolojilerine neden olabileceği ve gerekli olmadıkça omurga cerrahisinde kullanılmaması gerektiği sonucuna ulaştık.

Anahtar kelimeler: Elektokoterizasyon, faset denervasyonu, nöronal hasar, spinal cerrahi, tavşan

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Introduction

Parasympathetic innervation of the bowels is maintained by the lumbosacral plexus and blood supply provided by the Adamkiewicz artery (AKA), which was first described in 1882 by Adamkiewicz (1). Onuf's nucleus is a small group of neurons in the sacral spinal cord's ventral horns that provide parasympathetic innervation to the bowel, centralized in the sacral parasympathetic network (2). AKA provides the arterial circulation of the lower spinal cord; as a result, the arterial nutrition of the Onuf's nucleus and dorsal root ganglia (DRG) is also provided by AKA. DRG contains pseudounipolar neurons that convey sensory information from the colon to the spinal cord (3). DRG neurons innervate the large intestines of rats (4).

Bilateral segmental occlusion of AKA causes spinal cord ischemia-related dysfunctions of the lower extremities (5). Spinal subarachnoid hemorrhage may cause vasospasm in AKA (6). AKA vasospasm leads to degenerations in Onuf's nucleus/pudendal ganglia induced by urinary retention (7). Intestinal distension may occur secondary to DRG degeneration due to AKA spasm during SAH (8). These studies showed the importance of AKA in the functions of the abdominopelvic organs.

Electrical energy can cause nerve damage due to its thermal properties (9). The electric current's direction, location, and application time contribute to the amount of damage (10). A low-voltage electrical injury can cause arterial thrombosis, while a higher voltage electrical current can cause tetraplegia (11). Electrical injury results in vascular impairment, histological and electrophysiological changes in peripheral nerves (12).

Although electrical energy is known to cause tissue damage, it is frequently used in surgical applications. Especially in spinal surgery, monopolar electrocoagulation (MEC) or bipolar electrocoagulation (BEC) is preferred.

We aimed to reveal the neurovascular damage and adverse events caused by MEC and BEC, used mainly at high voltages in spinal surgery in the intestine, by conducting an experimental study.

Materials and Methods

Twenty male hybrid rabbits (age: 2 years; mean ± standard deviation weight: 3.5±0.4 kg) were used. The experiments were conducted with the approval by the Ethics Committee of Atatürk University (06.01.2004, no:17, number: B30.2.ATA.0.01.00/2). Rabbits are frequently used in such studies because they are suitable for experimental analyses. The effects of AKA-insult-related intestinal pathologies after MEC/BEC have not been studied yet in an experimental model.

In our study, five animals were assigned to the control group to estimate the normal neuron density in Onuf's nucleus/S4 spinal ganglia and colonic degeneration score. In the remaining animals, general anesthesia was induced with 25-mg/kg ketamine hydrochloride, 15-mg/kg lidocaine hydrochloride, and 1-mg/kg acepromazine. After the required surgical cleaning of the operation site, we cut the skin and subcutaneous tissue with a median skin incision adequate for the thoracic vertebra 10-lumbar vertebra 3 in the animals. The paraspinal muscles were removed subperiosteally from the spinous processes, laminae, and facet joints of the vertebrae by using a scalpel in the control group. We used MEC and BEC in the other groups for this purpose. Then, thoracic 11-lumbar two vertebrae (T11-L2) laminectomy was performed, and the facets were denervated with BEC (n=7) and MEC (n=8) using electrocoagulation using 220 V and 50 Hz. Fascia and skin were sutured with 3-0 cotton sutures. The animals were postoperatively followed up in their cages for 7 days without antibiotic/analgesic treatment. All the animals were subjected to multislice computed tomography (CT) to observe the abdominopelvic organs and then sacrificed. The S4 DRG ganglia neuron density, volumes of the descending colon sections, and colonic degeneration scores were determined. The colonic intestinal degeneration criteria we developed are as follows: Normal (0P), vasospasm (1P), endothelial injury (2P), thrombus (3P), colonic wall injury (4P), inflammation (5P), colonic mucosal degeneration (6P), Auerbach myenteric ganglion degeneration (7P), and necrosis (8P). The groups were scored according to 36 points, and the results were compared with the number of degenerate pudendal ganglion neurons. The tissues were preserved in paraffin blocks, and sections were stained with hematoxylin and eosin, aldehyde fuchsin, vanGieson, and terminal deoxynucleotidyl transferase UTP nick-end labeling. To estimate the numbers of degenerated neurons of the S4 ganglia, the physical dissector method was used as described by Yolas et al. (7).

The accepted neuronal degeneration criteria are cellular angulations, peri-cytoplasmic halo formation, cytoplasmic condensation, and nuclear shrinkage. Our former method to estimate the degenerated neuron density of the S4 ganglia (13) and the AKA degeneration criteria were used (6).

Statistical Analysis

Statistical analysis was performed in the SPSS 11.0 software for Windows. The volumetric changes of the colon and

the numbers of alive and degenerated neurons of S4 DRG were compared between the groups using a two-tailed t-test. Non-parametric relationships were examined with the Mann-Whitney U tests. For the analyses in which non-parametric tests were used, the differences between the groups were evaluated with the Tukey HSD post-hoc test. A p-value <0.05 was considered significant.

Results

Two animals with MEC and one animal with BEC showed wound problems at the thoracic operation level. The distended abdomen was detected in most animals in the MEC group (n=5) and a few in the BEC group (n=3). The animals showed defecation problems with cardiorespiratory disturbances secondary to abdominal swelling.

Radiological examination determined segmentary colonic dilatation, excessive intraluminal gas collection, and diaphragmatic elevation. It was found in the morphological examination that perivertebral duro-ligamentary adhesions, fibrosis, vascular congestion, and scar formation were more prominent in the MEC group than in the BEC group. Colonic examination revealed colonic dilatation, wall edema, hemorrhage, and scattered necrosis.

Mononuclear infiltration, neurovascular disarrangements, perineural capsule thickening, venous dilatations, arterial thinning, ligamentous rigidity, laminary burning scars, and spinal canal narrowing by intracanalicular tissues were more severe in the MEC group, moderately severe in the BEC group and absent in the control group. The spinal cord, nerve roots, evacuated intervertebral disk space, and denervated facets were visualized during the operation. After the operation, peridural adhesions and fibrotic tissue development were found in the denervated rabbits. Angulation, cytoplasmic condensations, flattening, elongations, vascular wall degeneration with atrophy/necrosis, and thrombus with intimal infiltrations in the AKA or branches were moderately severe in the BEC group and most severe in the MEC group.

An enlarged gaseous descending colon was detected in the multi-slice CT evaluation in the MEC group, and a necrotic descending colon was found in the macroscopic pathological evaluation (Figure 1). We detected the histopathological appearance of the degenerated/scaled endothelium and muscles, AKA, and dorsal root ganglion in an animal undergoing MEC (Figure 2). The S4 dorsal root ganglion and spinal cord degenerated or lost axons, and apoptotic neurons of the S4 roots in a MEC-treated animal were histopathologically evaluated (Figure 3). In an animal treated with MEC, the secretory cells, myenteric ganglia, and the histopathological appearance of the intestine and degenerated part of the intestine were detected (Figure 4). Histopathological appearance of colonic mesenteric artery branches is seen in control, with moderate BEC, and severe degenerated/desquamated endotheliums and muscles are seen in a MEC applied animal (Figure 5). The damaged intestinal wall was detected in the dilated segment of the MEC-treated animal (Figure 6).

The numbers of normal and degenerated neurons, and the colonic degeneration scores are given in Table 1. The mean number of the alive/normal and degenerated neurons were 22,610±962/5±2, 21,617±890, and 16,692±641/345±62 in the control, BEC, and MEC groups, respectively. There were significant differences among the groups (p<0.001). The values in the MEC group were significantly lower than in the other two groups (p<0.001 for both).

The mean colonic degeneration scores were <8, 9-30, and >31 in the controls, BEC, and MEC groups. The score in the

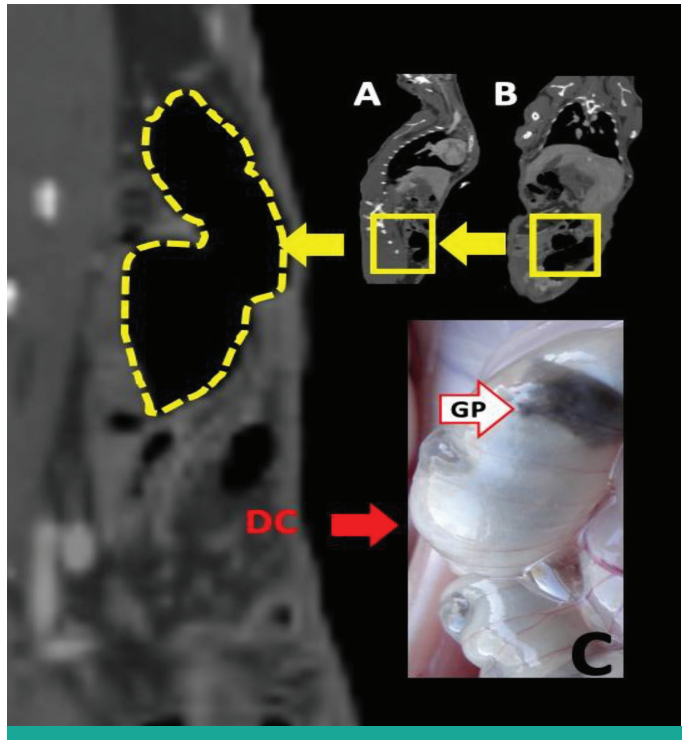

Figure 1. Multislice computed tomography image of a rabbit's abdomen in the sagittal (A) and coronary planes (B), showing an enlarged gaseous descending colon (yellow sguaresin A and B) and the anatomical appearances of the descending colon (DC) and gangrenous necrotic colon part (GP) (C) in a rabbit treated with monopolar electrocautery

MEC group was statistically higher than in the other groups (Table 1).

Discussion

Although MEC/BEC has hazardous effects on neurovascular tissues, it is used mainly in spinal surgery (13). Vascular deformities, myoendothelial degeneration, and thrombus in most spinal radicular arteries and the AKA were most severe in the MEC group and moderately severe in the BEC group (14).

The sacral parasympathetic fibers originating from Onuf's nucleus innervate the distal colon, and peripheral axons of the DRG travels through the pudendal, pelvic, and hypogastric nerves (15). Peripheral axons originating from sacral cord ganglion cells, named "pudendal nerves,'' course into the urethra and distal colon (16). The sacral parasympathetic nucleus originates from fibers innervating the contractor smooth muscle of the bladder, colon descendants, and rectum (17). With the activation of Onuf's nucleus, the pelvic floor sphincters relax during micturition or defecation, or sexual activity (18). The DRG contains pseudounipolar neurons that convey sensory information from the colon to the spinal cord and central nervous system. DRG or nerve root compression is an essential factor causing intestinal problems due to neuronal insensitivity to ectopic discharges of target organs (19). As a result, the sacral parasympathetic network provides parasympathetic innervation of the lower abdominal and pelvic organs.

Facet denervation may be related to the higher incidence of postoperative complications after the spinal surgery (14). We may think that the intestinal complications are related to the harmful effects on the sacral parasympathetic in facet denervation animals. We did not analyze its effect on the development of intestinal pathologies due to the lack of animals without facet denervation. So, future

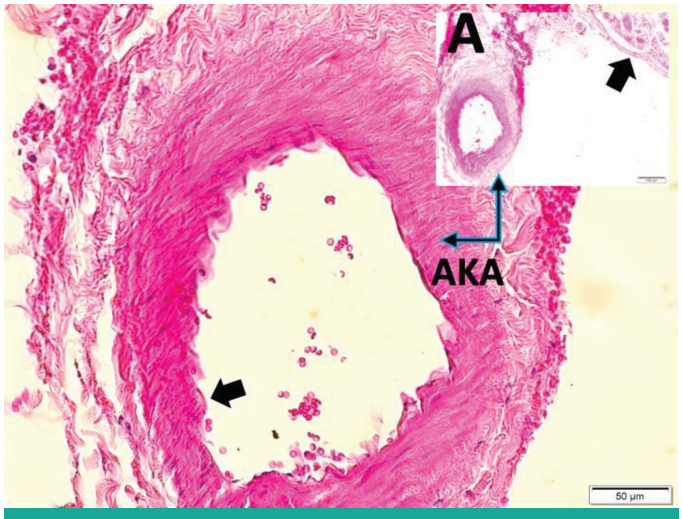

Figure 2. Histopathological appearance of the Adamkiewicz artery (AKA) and dorsal root ganglion [black arrow/light microscopy (LM), hematoxylin&eosin (H&E) staining, original magnification' 4/A] and magnified form of the AKA with degenerated/desquamated endothelium and muscles in a monopolar electrocautery-treated rabbit (LM; H&E, original magnification '20/base)

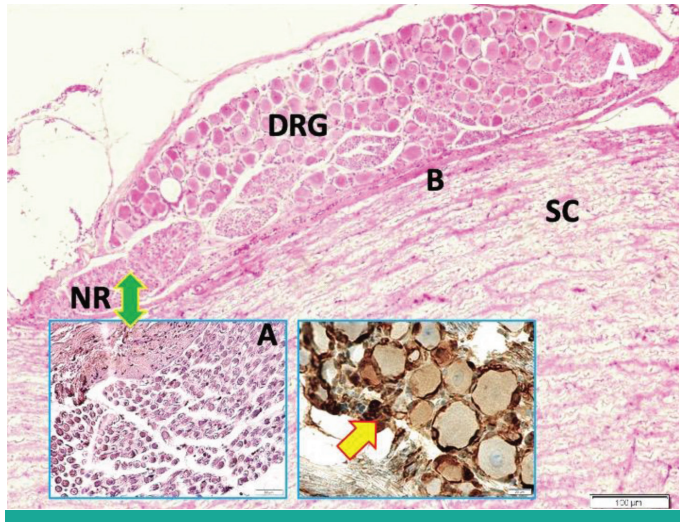

Figure 3. Histopathological appearance of the L4 dorsal root ganglion, nerve root (NR), and spinal cord [SC; light microscopy (LM), hematoxylin and eosin staining, original magnification '10/base]. Degenerated or lost axons (Pale) and apoptotic neurons of the L4 roots can be observed in a monopolar electrocautery-treated rabbit (LM; terminal deoxynucleotidyl transferase dUTP nick-end labeling, original magnification '10/B)

Table 1. NND/DND of S4 ganglia (n/mm^3) and CDS

	Control (n=5)	BEC (n=7)	MEC (n=8)	p1	p2	p3
NND †	22.610±962	21.617±890	16.692±641	0.125	<0.001	<0.001
DND †	5±2	103±21	345±62	0.003	<0.001	<0.001
CDS ‡	<8	9-30	>31	<0.05	<0.001	<0.001

†: Mean ± standard deviation, †: n, (min-max)

p1: Between control and BEC, p2: Between control and MEC, p3: Between BEC and MEC. NND: Normal neuron densities, DND: Degenerated neuron densities, CDS: Colonic degeneration scores, BEC: Bipolar electrocautery, MEC: Monopolar electrocautery

experimental studies are needed to evaluate the impact of facet denervation and sacral parasympathetic injuries.

The effect of MEC on the number of degenerated neurons after experimental spinal surgery has been studied previously. Aydin et al. (13) found that MEC application caused significantly higher numbers of degenerated neurons. They concluded that neuronal degeneration was directly related to the impact of the electric current. Our study is the first to use both MEC and BEC applications in experimental spinal injuries. The present findings may be regarded as evidence for the harmful effects of MEC applications on the neurovascular tissues.

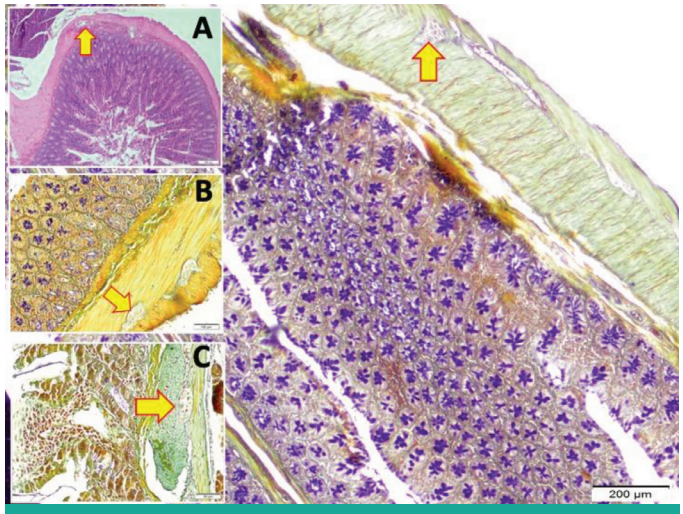

Figure 4. Histopathological appearance of the bowel with normal [light microscopy (LM), hematoxylin and eosin staining, original magnification '4/A] secretory cells and myenteric ganglia (LM, aldehyde fuchsin, original magnification' 4/base; magnified form, original magnification '10/B), and degenerated part of the bowel is a monopolar electrocautery-treated rabbit (LM, aldehyde fuchsin, original magnification '10/C)

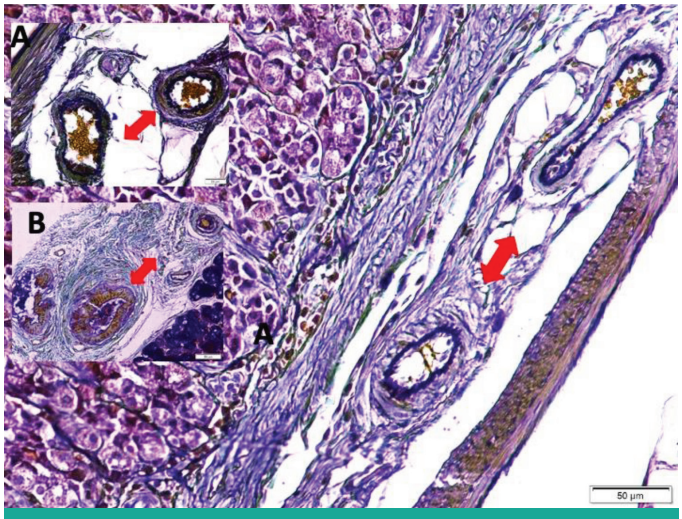

Figure 5. Histopathological appearance of colonic mesenteric artery branches (arrows) are seen in control (LM, Aldeyde fuchsine, x20/base), with moderate (LM, Aldeyde fuchsine, x20/A) in BEC and severe degenerated/desquamated endotels and muscles (LM, Aldeyde fuchsine, x20/B) are seen in a MEC applied animal

The association of electricity and neurovascular injury is another speculated issue. Longer contact time and higher voltage cause severe injuries than brief contact with low voltages (13,14). The non-thermal mechanisms can be questioned, leading to the reversible cell damages in such injuries. Besides, electrical burn also causes arterial injuries and consequently the development of thrombosis (14). Therefore, even in direct contact with the neuronal tissues, an electric current may be hazardous if used in spinal surgery incautiously.

Our study experimentally determined that the AKA could be seriously damaged by high-voltage electrocautery applications, which can cause sacral parasympathetic network dysfunction and bowel paralysis. Although we investigated bowel involvement due to parasympathetic damage in our study, parasympathetic damage will cause changes in much lower abdominal and pelvic organs. Ozturk et al. (8) showed that AKA vasospasm was seen after spinal subarachnoid hemorrhage secondary to the neurodegeneration of the dorsal root ganglion. They also reported the coexistence of bowel dilatation with subarachnoid hemorrhage in association with AKA vasospasm. Our study provides a better understanding of the mechanism of abdominopelvic complications of unknown causes after a safe spinal surgery. The effects on other abdominopelvic organs can also be investigated.

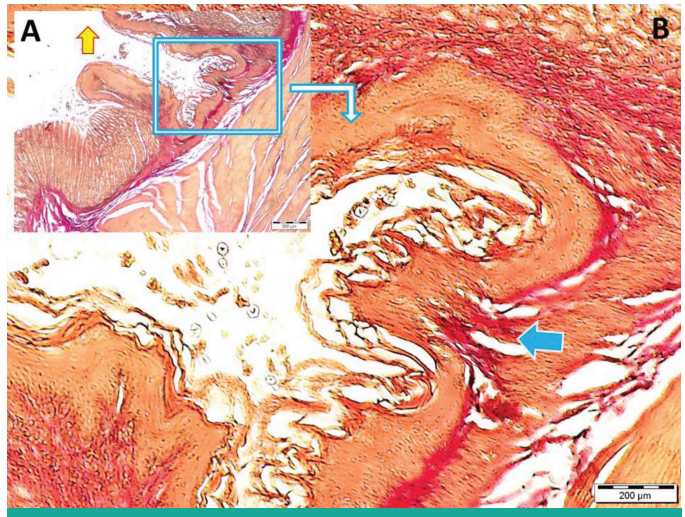

Figure 6. Histopathological appearance of destructed bowel wall at the dilated segment in Figure 1C of a MEC applied animal (LM, Van Gieson, xx4/A; x10 B)

In this sense, it will also benefit clinicians. We think that better results will be obtained with angiography and electrophysiological examinations.

Conclusion

The lack of experimental groups without facet degeneration and functional motor testing of the urinary bladder were the major limitations of the present study.

Our results show that electrocautery knives such as BEC/MEC should not be used in spinal surgery, unless necessary, to avoid neurovascular tissue damage.

Ethics

Ethics Committee Approval: The experiments were conducted with the approval by the ethics committee of Atatürk University (06.01.2004, no:17, number: B30.2.ATA.0.01.00/2).

Informed Consent: It is an experimental study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.K.K., A.Y., A.A., Design: M.K.K., A.Y., A.A., Data Collection or Processing: M.K.K., A.Y., M.D.A., Analysis or Interpretation: M.K.K., A.Y., M.D.A., A.A., Critical Review of the Manuscript: M.D.A., A.Y., A.A., Final Approval: M.K.K., A.A., A.Y., M.D.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL RESEARCH

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Single-center Experiences of Ovarian Sex Cord Stromal Tumors

Ovaryan Seks Kord Stromal Tümörlerin Tek Merkez Deneyimleri

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Abstract

Objective: The aim of this study is to examine the sex cord stromal tumors of the ovary operated in our clinic in the last 4 years and to contribute to the literature on this rare tumor.

Method: The clinical and laboratory findings of 34 patients with pathological diagnosis of ovarian sex cord stromal tumor, who were operated in our obstetrics and gynecology clinic between 2016 and 2020, were evaluated retrospectively. Pathological diagnoses were classified and other accompanying pathologies and complaints were evaluated for each type.

Results: Ovarian sex cord stromal tumors usually attract attention with the peripheral effects of the hormones produced by the tumor tissue. They rarely come to very large sizes. They are mostly benign. When the hormone estrogen is produced, accompanying endometrial pathologies should not be overlooked. Hormonal complaints in patients improve dramatically after surgery both clinically and laboratory. Oncological follow-up is required following diagnosis in some malignant types.

Conclusion: If ovarian sex cord stromal tumor is suspected, preoperative blood androgen levels, inhibin A, and alpha feto protein (AFP) should be evaluated. In addition, ultrasonographic and, if necessary, endometrial histopathological evaluations are important for patient follow-up as well as diagnosis. The patient's fertility desire and age should be considered during treatment.

Keywords: Endocrinologic changes, ovarian mass, sex cord stromal ovarian tumors

Öz

Amaç: Bu çalışmanın amacı kliniğimizde son 4 yılda ameliyat edilen overin seks kord stromal tümörlerini incelemek ve nadir görülen bu tümör ile ilgili literatüre katkı sağlamaktır.

Yöntem: 2016-2020 yılları arasında kadın hastalıkları ve doğum kliniğimizde opere edilen ve patolojik tanısı ovaryan seks kord stromal tümör olan 34 hastanın klinik, laboratuvar bulguları geriye dönük olarak değerlendirildi. Patolojik tanılar sınıflandırıldı ve eşlik eden diğer patolojiler ve şikayetleri her tip için değerlendirildi.

Bulgular: Ovaryan seks kord stromal tümörleri çoğunlukla tümör dokusunun ürettiği hormonların periferik etkileri ile dikkat çeker. Çok büyük boyutlara nadir gelirler. Çoğunlukla iyi huyludurlar. Üretilen hormon östrojen olunca hastada eşlik eden endometrial patolojiler gözden kaçırılmamalıdır. Hastalardaki hormonal şikayetler klinik ve laboratuvar olarak ameliyat sonrası dramatik olarak düzelir. Bazı malign tiplerde tanıyı takiben onkolojik takip gereklidir.

Sonuç: Ovaryan seks kord stromal tümörü şüphesi halinde preoperatif kan androjen seviyeleri, inhibin A, alfa fetoprotein değerlendirilmelidir. Ayrıca ultrasonografik ve gerektiği taktirde endometrial histopatolojik değerlendirme tanının yanı sıra hasta takibi için önemlidir. Hastanın fertilite isteği ve yaşı tedavi esnasında önemsenmelidir.

Anahtar kelimeler: Endokrin değişiklikler, ovaryan kitle, ovaryan seks kord stromal tümörleri

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Introduction

Sex cord-stromal tumors of the ovary (SCST) are rare tumors arising from stromal cells outside the follicular tissue of the ovary and can be benign or malignant. Ovarian SCSTs are almost always unilateral, but 1.5% are bilateral. Ovarian SCST is less common than epithelial or germ cell origins, benign ovarian SCSTs account for 4% of benign neoplasms of the ovary, malignant forms are less than 8% of malignant neoplasms of the ovary (1).

Malignant forms of SCSTs are rarely encountered and if there is a malignant SCST, it is generally diagnosed at early stages because of the clinical effects of hormones that are produced by the tumor itself. Most of the malignant forms have a histologically low grade and good prognosis (2).

SCSTs are divided into 3 categories: Pure stromal tumors, mixed cord tumors, mixed-sex cord-stromal tumors. SCSTs are observed in a wide range of ages and they often produce steroid hormones [especially androgens, estrogens (E), cortisone] with symptoms varying up to hormones related (3). Whenever androgen levels are above normal, menstrual irregularity (especially oligomenorrhea/amenorrhea), hirsutism, and even virilization may occur.

Estrogen elevation can lead to abnormal uterine bleeding, endometrial hyperplasia, postmenopausal bleeding, and puberty praecox in children. The patient can complain of abdominal and pelvic pain. In some cases, it can be noticed during a gynecological examination.

In this study, we aimed to share our single-center experiences about SCST over the past four years.

Materials and Methods

Documents of 34 patients with pathological diagnoses of ovarian SCST were reviewed retrospectively. The patients, who applied to our gynecology and obstetrics outpatient clinic from January 2016 to January 2020, were diagnosed with an ovarian mass, underwent surgical treatment, and had a pathological diagnosis of ovarian SCST, were included in our study. This retrospective study was initiated following the decision of the Ethics Committee of İstanbul Medipol University, Non-Interventional Clinical Research, dated 20.05.2021 and numbered 484. The patients' age, parity, clinical complaints, ultrasonographic findings, menstrual patterns, results of additional diagnostic methods, and hormone test results were recorded. Signs and symptoms such as abdominal pain, dyspareunia, bloating, constipation, hairiness, clitoromegaly, voice change, and pain were evaluated retrospectively. Type of the tumor, its largest diameter, number of pathological masses, and the type of surgery performed with the menstrual pattern in menstruating patients and its duration were recorded. Pathological diagnoses of all patients were grouped. The clinical changes and complaints during the postoperative period were also questioned.

Statistical Analysis

As a statistical calculation, only the percentage was calculated, that is, no special test was used.

Results

Between the years of 2016 and 2020, 34 female patients were diagnosed with pathological ovarian SCST. The clinical and laboratory findings of the patients before the operation are summarized in Table 1, 2. The ovaries of the patients were evaluated by ultrasonography, and their size and appearance were recorded. There was no significant increase in preoperative CA12-5, CA19-9, AFP, and human corionic gonadotropin (hCG) levels.

The age of patients varied between 15 and 78 years. The median age was calculated as 55 years. While the 15-year-old patient with granulosa cell tumor (GCT) had never been pregnant, the maximum number of parity was 13 in all groups and the median parity count was 3. One of the patients with Leydig cell tumor was also infertile.

Eighteen patients were in the menopause period. Among 16 premenopausal patients, 6 of them were normally menstruating patients, while 4 patients were complaining from polymenorrhea, 3 patients (8.82%) were oligomenorheaic and remaining 3 (8.82%) were amenorheic.

Among 34 patients, 6 patients (17.65%) had hirsutism (Ferriman-Gallwey score >8 points) and 2 patients (5.88%) had hyperandrogenemia findings except for hirsutism (oligomenorrhea, amenorrhea, clitoromegaly, voice change). Patients without hormonal findings were suffering from mild abdominal pain and bloating.

Androgen hormone levels were measured in 8 patients with hyperandrogenemic symptoms (such as oligomenorrhea, amenorrhoea, clitoromegaly, voice change, hirsutism) and were found above the normal range in 2 of them. In the patient with Leydig cell tumor, whose preoperative serum testosterone (T) level was 9 ng/mL, postoperative value decreased to 2 ng/mL on the first following day.

Table 1. The age range distribution according to tumor types, the parity of the patients and the largest size of the mass measured on ultrasonography

TM type		Age	Parity	Tm diameter
Fibroma	N	5	5	5
	Mean	53.2	3.8	6.5
	SD	13.81	2.05	3.74
	Median	54	4	5
	Minimum	31	2	3
	Maximum	67	7	11
Fibrothecoma	N	12	12	12
	Mean	57.83	5.33	8.79
	SD	13.08	3.94	4.77
	Median	58	4.5	8.5
	Minimum	33	1	3
	Maximum	78	13	16
Tecomata	N	1	1	1
	Mean	51	3	7
	SD	.	.	.
	Median	51	3	7
	Minimum	51	3	7
	Maximum	51	3	7
Steroid HC tm	N	1	1	1
	Mean	63	10	4
	SD	.	.	.
	Median	63	10	4
	Minimum	63	10	4
	Maximum	63	10	4
Granulosa	N	10	10	10
	Mean	43.5	2.6	8.3
	SD	20.38	2.22	5.22
	Median	46.5	2	7.5
	Minimum	15	0	2
	Maximum	71	7	19
Sex cord with annuler tubules	N	1	1	1
	Mean	42	3	17
	SD	.	.	.
	Median	42	3	17
	Minimum	42	3	17
	Maximum	42	3	17
Fibroma with minor sex cord elements	N	1	1	1
	Mean	34	1	13
	SD	.	.	.
	Median	34	1	13
	Minimum	34	1	13
	Maximum	34	1	13
Sclerosing stromal tm	N	1	1	1
	Mean	39	3	7
	SD	.	.	.
	Median	39	3	7
	Minimum	39	3	7
	Maximum	39	3	7
Sex cord stromal tm	N	1	1	1
	Mean	63	7	5
	SD	.	.	.
	Median	63	7	5
	Minimum	63	7	5
	Maximum	63	7	5
Leydig HC tm	N	1	1	1
	Mean	37	0	5
	SD	.	.	.
	Median	37	0	5
	Minimum	37	0	5
	Maximum	37	0	5
All patient groups	N	34	34	34
	Mean	50.71	4	8.21
	SD	16.07	3.24	4.64
	Median	55	3	7
	Minimum	15	0	2
	Maximum	78	13	19

SD: Standard deviation

In the study group, the most frequent pathology was fibrothecoma, which was diagnosed in 12 patients (35.29%), and the second common one was GCT in 10 patients (29.41%).

Sclerosing cell tumor and fibrothecoma were detected as multiple foci, while other cases were diagnosed as a single mass. Polymenorrhea, which may be a sign of hyperestrogenemia, was observed in patients with GCTs, thecoma, and fibrothecoma.

The diameter of the masses was evaluated by ultrasonography (using the General Electric Logiq C3 Premium device). The detected range of masses was from 2 to 19 cm, and the median value was calculated as 7 cm. All SCSTs were unilateral except for 2 patients.

All patients underwent surgical treatment. Hysterectomy (laparoscopic or by laparotomy) and bilateral salpingo-oophorectomy were performed in 16 (47.6%), oophorectomy in 12 (35.29%), and cystectomy in 6 patients (17.65%).

Table 2. The numerical classification of tumors and clinical complaints and types of surgery (hyperandrogenism only shows patients with high laboratory value)

		n	%
TM type	**Fibroma**	5	14.71
	Fibrothecoma	12	35.29
	Tecomata	1	2.94
	Steroid HC tm	1	2.94
	Granulosa	10	29.41
	Sex cord with annular tubules	1	2.94
	Fibroma with minor sex cord elements	1	2.94
	Sclerosing stromal tm	1	2.94
	Sex cord stromal tm	1	2.94
	Leydig hc tm	1	2.94
Menstrual pattern	**Menopause**	18	52.94
	Oligomenorrhea	3	8.82
	Polymenorrhea	4	11.76
	Amenorrhea	3	8.82
	Normal	6	17.65
Hyperandrogenism	**None**	32	94.12
	Yes	2	5.88
Hirsutism	**None**	28	82.35
	Yes	6	17.65
TM number	**Single**	32	94.12
	Multiple	2	5.88
Surgical type	**Cystectomy**	6	17.65
	Oophorectomy	12	35.29
	Hysterectomy+oophorectomy	16	47.06

No recurrence was observed in any patient. Chemotherapy was given only to 1 patient with a pathological diagnosis of GCT.

We detected endometrial pathology accompanying ovarian SCST in 7 patients. These endometrial pathologies were seen as early-stage endometrial cancer in 2 patients, endometrial hyperplasia with atypia in 1 patients, endometrial hyperplasia without atypia in 2 patients, and endometrial polyp in 2 patients. Both endometrial cancer cases were stage 1A FIGO grade 2 endometrioid cancer and one of them had AGCT and the other had fibrothecoma. A squamous cell component was also detected in the endometrial specimen in the case of fibrothecoma and endometrial cancer.

One of the patients with endometrial polyp was accompanied by ovarian thecoma and the other by GCT. Fibrothecoma in one case and AGCT in the other were detected in the ovary of the cases with endometrial hyperplasia without atypia. Ovarian AGCT was observed in the patient who had hyperplasia with atypia.

Discussion

Ovarian SCSTs are rare tumors and in the literature, there are not many studies with large patient groups on this subject. We aimed to classify our patients with a definite diagnosis of postoperative pathology in terms of their preoperative findings and to reveal the symptoms that should be kept in mind in the preliminary diagnosis. Most patients with SCSTs need to be operated regardless of tumor size due to endocrine complaints.

The important thing is to choose the most appropriate treatment for the patient. Considering that it is frequently seen in patients at the end of the reproductive age, it may be good to postpone the operation that will affect the ovarian reserve or to plan the operation early for the treatment of infertility in women of reproductive age.

Since SCSTs are rarely seen, publications on postoperative long-term follow-up are also limited.

When SCSTs are evaluated together with an adnexal mass, accompanying hormonal clinical findings, and some laboratory features, diagnosis becomes easier. In laboratory examination, blood levels of reproductive hormones such as estrogen and testosterone, and blood levels of tumor markers such as inhibin A and B and AFP may be useful (4). AFP, E2, inhibin (A and B), T, A4, DHEAS, and CA 125 generally do not elevate in Sertoli Leydig cell tumors (5).

Polymenorrhea, which may be a sign of hyperestrogenism, has been observed in GCTs, thecoma, and fibrothecoma.

In the literature, the rates of endometrial hyperplasia and endometrial cancer associated with E produced from ovarian mass in the presence of ovarian GCT were found to be 50% and 10%, respectively (6). In our patients' group, we found endometrial pathologies accompanying adult-type granulosa cell tumor (AGCT), thecoma and fibrothecoma. In our study group, endometrial cancer in fibroma case, hyperplasia without endometrial atypia in fibrothecoma case, and endometrial polyp in our thecoma patient were seen. If there is a mass in the ovary, it should be kept in mind that the tumor type may be SCST in premenopausal women with abnormal uterine bleeding and in women with menopausal bleeding complaints.

Preoperative endometrial sampling should be performed in the presence of endometrial thickness more than 5 mm on ultrasonography in a postmenopausal woman with uterine

bleeding and presence of irregular and thick endometrium, breakthrough bleeding, and irregular bleeding in a premenopausal woman for the screening of endometrial pathologies.

Fibrothecoma is a rare tumor in all ovarian tumors. In our study, the most common tumor was fibrothecoma, with a rate of 35.29% (12 cases). The absence of exact criteria in the pathological diagnosis of fibrothecoma may have changed the frequency of diagnosis. GCT was seen in second place with 29.41% (10 cases). In the literature, 2-5% of all ovarian cancers are GCT (6).

SCSTs are mostly seen over the age of 50 years (7). In our study, menopausal patients were in the majority and this is consistent with the literature (52.94%). In the study group, there was no significant difference among the tumor groups in terms of menstrual pattern, and there were even patients with normal menstrual cycles.

Some types of SCST present with endocrine symptoms rather than mass effects. In our study group, we mostly have not seen the clinical signs of hyperandrogenemia.

SCSTs are mostly unilateral and not very large masses, rarely reaching 10-15 cm. Two (5.88%) of 34 patients had multiple masses, and the remaining 32 ones (94.12%) had a single mass. Some SCST types present with endocrine symptoms rather than mass effects.

Nowadays, SCSTs are treated in the same way as ovarian germ cell tumors and epithelial tumors. Only genetic mutation existence should be considered during treatment (4).

The most malignant form of SCSTs is AGCT, which may closely resemble the surface epithelial tumors. It may even be confused with endometrioid ovarian carcinoma on microscopic examination (8).

In the pathological examination, SCSTs may be cystic with solid components, lobulated, soft, and fragile. These masses may present with functional findings without the effect of intra-abdominal mass such as abdominal distension and constipation. Hyperandrogenism up to virilization has been reported in the literature, and especially in hirsutism that starts suddenly and increases rapidly, androgenic hormones and tumor markers should be checked in addition to the examination with trans vaginal ultrasonography of the ovaries. Women with breast tightness, bleeding abnormalities should be screened for SCST in detail. Any existing GCT should be operated without delay because of its malignant potential. In the presence of hormonal findings accompanying a solid mass in the ovary in adolescent patients, the patient's future fertility should be considered, and tumor markers should be followed up preoperatively and after treatment. In addition, genetic consultation should be done in terms of genetic mutations and other family members should be warned. There is no correlation between virilization level and serum androgen levels, but it should be remembered that cell type and tumor size correlate with clinical findings (8).

In our study, other gynecological cancers that might accompany ovarian SCSTs caught our attention. However, the limited patient count prevents us from explaining the relationship between SCST and cancer. Therefore, studies with larger case numbers are needed.

The small number of patients in the study is the most important limiting factor, and the presence of rare pathological types is insufficient to explain the relationship between tumor type and clinical picture. Due to the low prevalence of these tumors, even a small number of case groups are valuable to have an idea about their clinical picture.

Conclusion

In this study, we wanted to emphasize the necessity of evaluating the clinical findings of women with solid ovarian masses and to contribute to the literature by measuring preoperative blood androgen levels and tumor markers such as inhibin A and AFP that may be useful in postoperative patient follow-up.

Ethics

Ethics Committee Approval: This retrospective study was initiated following the decision of the Ethics Committee of İstanbul Medipol University, Non-Interventional Clinical Research, dated 20.05.2021 and numbered 484.

Informed Consent: Consent was obtained from the patients participating in the study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: Ö.K.A., G.T., T.Ş., Design: Ö.K.A., G.T., T.Ş., Data Collection or Processing: Ö.K.A., E.E.K., Y.C., G.T., M.U., Analysis or Interpretation: Ö.K.A., Y.C., T.Ş., M.U., E.E.K., Drafting Manuscript: Ö.K.A., E.E.K., Y.C., G.T., M.U., T.Ş., Critical Revision of Manuscript: Ö.K.A., E.E.K., Y.C., T.Ş., G.T., Final Approval and Accountability: Ö.K.A., E.E.K., Y.C., T.Ş.

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ORIGINAL RESEARCH

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Evaluation of Transverse Acetabular Ligament Assessment due to Acetabular Labral Tear in Patients Undergoing Magnetic Resonance Arthrography

Manyetik Rezonans Artrografisi Yapılan Hastalarda Asetabular Labral Yırtığa Bağlı Transvers Asetabular Ligamanın Değerlendirilmesi

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Abstract

Objective: In this study, we investigated the relationship between labral tear with its stage and transverse acetabular ligament (TAL) morphology in patients who underwent magnetic resonance arthrography (MRA) examination for acetabular labral tear.

Method: Radiological images of 55 patients who applied to our hospital with MRA for acetabular labral pathology were evaluated. Labral lesions were classified as post-traumatic (1A, 2A and 3A) and dysplastic (1B, 2B and 3B) according to the Czerny staging system. The widest contact surface and TAL area with the TAL femoral head were measured in MRAs of patients. In the statistical analysis, the widest contact surface of TAL with the femoral head and TAL area were compared to the right and left sides and according to the Czerny classification.

Results: When labral pathologies were evaluated according to the Czerny classification, the widest contact surface of TAL with the femoral head and TAL area, left and right sides, and double groups (1-2,1-3,2-3) in Czerny 1-2-3 classification were compared as post-traumatic (1A, 2A and 3A) and dysplastic (1B, 2B and 3B) lesions of the labrum. As a result, no statistically significant difference was observed (p>0.05).

Conclusion: There was no significant relationship between the staging of acetabular labral pathologies and TAL morphology, suggesting that TAL cannot be shown as a predisposing factor in terms of acetabular labral tear.

Keywords: Acetabular labrum, Czerny classification, labral tear, magnetic resonance arthrography, transverse acetabular ligament

Öz

Amaç: Bu çalışmada amacımız, asetabuler labral yırtık nedeniyle manyetik rezonans artrografi (MRA) tetkiki yapılan hastalarda labral yırtığın evresi ile transvers asetabular bağ (TAL) morfolojisi arasındaki ilişkiyi araştırmaktı.

Yöntem: Asetabular labral patoloji nedeniyle MRA ile hastanemize başvuran 55 hastanın radyolojik görüntüleri değerlendirildi. Labral lezyonlar Czerny evreleme sistemine göre travma sonrası (1A, 2A ve 3A) ve displastik (1B, 2B ve 3B) olarak sınıflandırıldı. Hastaların MRA'sında TAL femur başı ile en geniş temas yüzeyi ve TAL alanı ölçüldü. İstatistiksel analizde TAL'nin femur başı ile en geniş temas yüzeyi ve TAL alanı sağ ve sol taraflarla ve Czerny sınıflamasına göre karşılaştırıldı.

Bulgular: Czerny sınıflamasına göre labral patolojiler değerlendirildiğinde, Czerny'de TAL'nin femur başı ile en geniş temas yüzeyi ve TAL alanı, sol ve sağ taraflar ve ikili gruplar (1-2,1-3,2-3) 1-2-3 sınıflandırması labrumun travma sonrası (1A, 2A ve 3A) ve displastik (1B, 2B ve 3B) lezyonları olarak karşılaştırıldı. Sonuç olarak, istatistiksel olarak anlamlı bir fark gözlenmedi (p>0,05).

Sonuç: Asetabular labral patolojilerin evrelemesi ile TAL morfolojisi arasında anlamlı bir ilişki bulunmamıştır, bu da TAL'nin asetabular yırtık açısından predispozan bir faktör olarak gösterilemeyeceğini düşündürmektedir.

Anahtar kelimeler: Asetabular labrum, Czerny sınıflandırması, labral yırtık, manyetik rezonans artrografi, transvers asetabular ligaman

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Introduction

The acetabular labrum seals the joint cavity by deepening the acetabular fossa in the hip joint, providing coxofemoral joint stability, lubrication and articular support (1). In labral tears, this support diminishes and chronic hip, as well as groin pain, occurs. Labral tears result in a significant decrease in the productivity of work and social life in the young and middle age groups. At this point, the prevention of labral tears and preemptive application of preventive medicine come to use. Trauma, degenerative processes, congenital dysplasia, femoroacetabular impingement (FAI), ligamentous laxity, and hypermobility are the etiological factors considered in labral tears. In the study of Ranavat and Kelly (2) that included 300 cases, FAI prevails in etiology with a rate of 55%, while degenerative processes (48.6%) stand out in the study of Lage et al. (3). The most common accompanying disease was developmental hip dysplasia in studies performed in Turkey (4). These results indicate that the etiology of labrum pathologies are variable, and studies with larger patient cohorts are needed. Identification of clear and definitive results can eliminate the preventable causes before rupture occurs. This is possible only if the anatomy of the acetabular labrum and adjacent structures are fully understood, where MR arthrography is an excellent imaging modality that shows the labral anatomy clearly. Czerny et al. (5) classified the labral pathologies on MRA according to the Lage's arthroscopic classification. The evaluations made according to the Czerny classification with MRA are largely in agreement with the arthroscopy results. While the sensitivity and specificity of conventional MRI in detecting labral pathologies are 30% and 36%, these values increase to 90-91%, respectively, with MRA (5).

The acetabular labrum is a fibrocartilage structure composed of collagen fibers that adhere circumferentially to the edge. In the superior part of the acetabulum, the load becomes thinner towards the bearing surface and acetabular labrum increases its depth (6). The acetabulum socket is defective in the inferomedial region in the form of a notch. TAL attaches to the edges of this notch and turns it into a hole. The vessels and nerves, travelling to the joint, pass through this anatomical structure. Acetabular labrum and TAL form 22% of the hip joint surface and increase the acetabulum volume by 33%. They increase the stability of the hip joint by creating a negative pressure against the displacement of the hip. It was shown that TAL submitted to tension due to natural incongruity (7).

Acetabular labrum tears are one of the most common causes of hip pain presenting with mechanical symptoms. Labral tears can occur from the anterior, posterior and superior due to different factors such as trauma, ligamentous laxity, hypermobility, femoracetabular impingement, developmental hip dysplasia, and degenerative osteoarthritis. Although tears often occur anteriorly, posterior labral tears are more common in young people with hip dislocation or hip dysplasia (8).

To the best of our knowledge, there is no prior study investigating the changes seen in TAL related to ALT. In this study, we evaluated whether there is a relationship between acetabular labral pathologies and TAL morphology on MRA.

Materials and Methods

Study population

Patients who underwent MRA examination with a pre-diagnosis of acetabular pathology at the musculoskeletal imaging center of our hospital between the dates of January 2011 and January 2015 were included in the study. Patients with a history of previous labral surgery, with a tear in the posterior part of the labrum, and with congenital or genetic diseases disrupting normal anatomy in the musculoskeletal system were excluded from the study. The study protocol was approved by İstanbul University Cerrahpaşa-Cerrahpaşa Faculty of Medicine Ethics Committee (date: 09.07.2015, no: 02-218671).

MRA technique

3D MRA images were taken in the supine position after 20 mL of gadolinium compound (diluted 1/200) was administered to the coxofemoral joint space under ultrasonography with a 20 G spinal needle. All MRA examinations were performed with a 1.5 T MR device (Magnetom Avanto Siemens Medical Solution). The gradient power of the device was 45 m/m, and an 8-channeled intraabdominal specific flex coil was used. The MRA protocol was fat-suppressed T1-weighted (T1W) turbo spin echo (TSE), coronal fat-suppressed proton density (FSPD) TSE and transverse T1 VIBE 3D sequences in sagittal, coronal and axial planes. Detailed parameters of the sequences are reported in the supplementary tool (Spll tool).

MRA imaging analysis and measurements

Imaging assessment was performed in three stages in MRA. First, labrum pathologies were evaluated on transverse T1A VIBE and TSE sequences according to the Czerny classification (Czerny 1A, 1B, 2A, 2B, 3A, 3B) (Figure 1) (5). Taking into account the degree of anteversion of the femoral neck in coronal FSPD TSE images, the widest

contact surface of the transverse ligament with the femoral head was measured in parallel sections (Figure 2). In the transverse T1W VIBE sequence, the TAL area was measured in the transverse section taken parallel to the collodiaphyseal angle in the coronal section in 3D images (Figure 3). All images were evaluated retrospectively at the PACS-archive system and measurements were calculated digitally using special software programs in Siemens, Syngo via Workstation.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Science (SPSS, version 20.0) package program. The significance (p-value) was determined with the Mann-Whitney U test used for non-parametric variables. A p-value less than 0.05 was considered as statistically significant.

Results

The study included a total of 55 patients. 35% of patients were male (n=19), and 65% were female (n=36), with an average age of 40 (15-67) years. Right acetabular labral pathology was found in 54.5% (n=30) of patients and left acetabular labral pathology was detected in 45.5% (n=25) of the patients. In patients with acetabular labral pathology, the widest contact surface of the femoral head and TAL and the TAL area were measured. The results were then compared between left and right sides, among 1-2-3 groups according to the Czerny classification (1-2, 1-3 and 2-3), and as post-traumatic (1A, 2A, and 3A) and dysplastic (1B, 2B and 3B) lesions. There was no statistically significant difference between these parameters (p>0.05). Statistical data of the study are shown in Table 1-3.

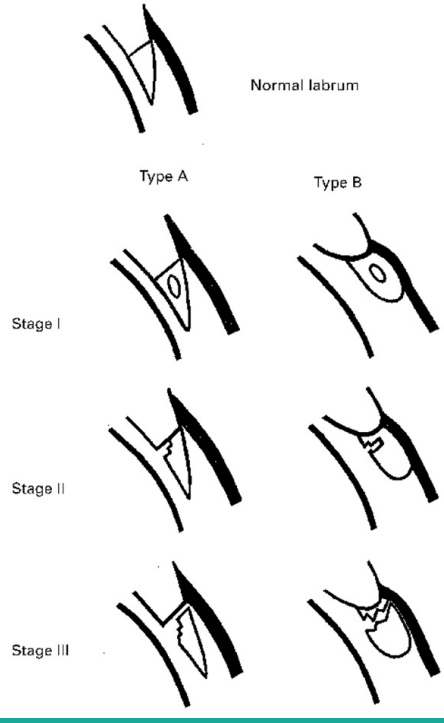

Figure 1. Schematic representation of acetabular labral tears according to the Czerny classification

Discussion

ALT causes the joint cartilage to remain unprotected by causing the labrum to separate from the cartilage. As a result, cartilage lesions occur with repetitive collisions of the femoral head and acetabulum, leading to the onset of degenerative joint disease (9). For this reason, the diagnosis and treatment of labral pathologies gain importance in the prevention of both disability and secondary early-onset degenerative processes, especially in young and middle-aged patients. In the study conducted by Burnett et al. (10), despite the high sensitivity and specificity of MRA, the average time between the onset of patients' complaints and the diagnosis was found to be 21 months (5). Farjo et al. (11)

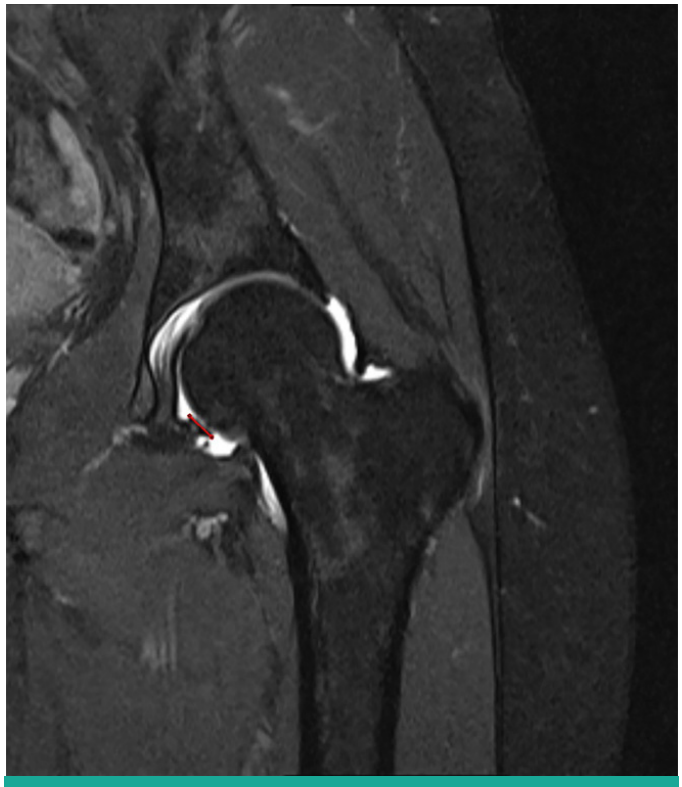

Figure 2. TAL-femoral head widest contact surface measurement on coronal FSPD TSE images

TAL: Transverse acetabular ligament, FSPD: Fat-suppressed proton density, TSE: Turbo spin echo

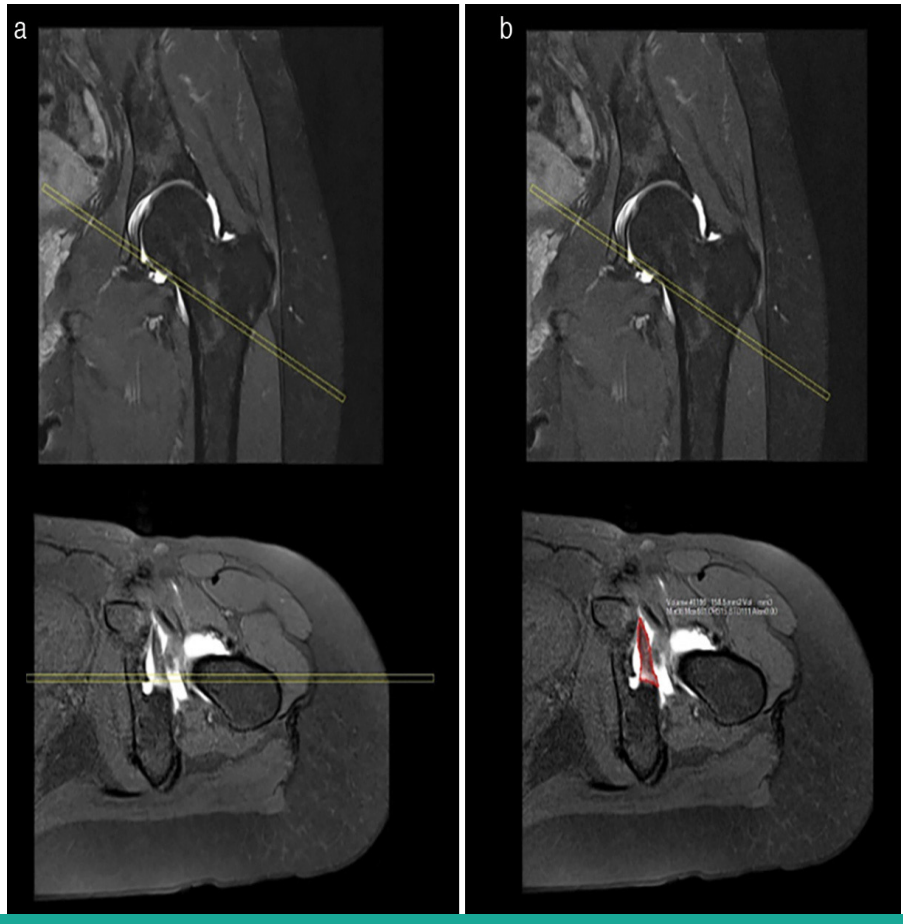

Figure 3. a) The appearance of TAL in the transverse section taken parallel to the collodiaphyseal angle determined in the coronal section in the 3D images in the transverse T1W VIBE sequence, the area measurement is shown in Figure 3b

TAL: Transverse acetabular ligament, T1W: T1-weighted

obtained similar results for this period. The length of this period may be due to the late presentation of patients to the healthcare institution, as well as insufficient physical examination, incomplete use of diagnostic radiology, misdiagnosis and ineffective treatment. It is essential to reach a diagnosis with increased awareness among the physicians, taking detailed patient history, and completing a thorough physical examination.

TAL is a short fibrous band that acts as a bridge between the two ends of the acetabular notch and is the continuation of the acetabular labrum posteroinferiorly. Biomechanical studies have revealed that during load transport, the acetabular lunate joint face limits the degree to which lunate horns move apart. Thus, the increase in the compressive force applied to the femoral head is prevented by stretching TAL (12,13). The role of acetabular labrum and TAL in hip joint load transfer has been the subject of study for many researchers. However, there is no consensus among researchers on this issue.

Löhe et al. (7) and Vandenbussche et al. (14) have emphasized that TAL plays an important role against the compression of the hip joint, which occurs during the load bearing and which moves the lunate horns away from each other due to native disharmony in the joint. In the immunohistological study conducted by Milz et al. (12) on 8 cadavers, they showed that TAL allowed the fibrocartilage cell layer to withstand the compression that occurred during load transport, both on the inner surface of the femoral head and at both bone junction points (11). However, the fact that these studies were conducted with fixed specimens taken from cadavers makes it impossible to consider the effect of the dense muscle layer surrounding the hip joint on load transfer. Konrath et al. (15) removed the TAL in eight of the hip specimens taken from 17 cadavers and the acetabular labrum in nine of the specimens. They then measured the changes in the contact surface area and pressure distribution between the acetabulum and the femoral head in the samples from which both labrum

Table 1. Gender distribution according to Czerny classification, transverse ligament-femoral head largest contact surface, transverse ligament area (mean ± SD) and (min-max) values

	In all patients Mean ± SD (min-max)	Pathology in the right acetabular labrum	Pathology in the left acetabular labrum	Czerny 1A Mean ± SD (min-max)	Czerny 1B Mean ± SD (min-max)	Czerny 2A Mean ± SD (min-max)	Czerny 2B Mean ± SD (min-max)	Czerny 3A Mean ± SD (min-max)	Czerny 3B Mean ± SD (min-max)
Female	36	16	13	7	-	10	12	1	6
Male	19	14	12	2	1	9	5	-	2
Transverse ligament-femoral head largest contact surface	8.04±1.78 (4.3-12)	7.79±1.67 (5.1-11.8)	8.33±1.89 (4.3-12)	7.4±2.28 (4.3-11.3)	6.1 (6.1-6.1)	8.3±2.11 (5.3-12)	8.08±1.44 (5.4-10.4)	8.4 (8.4-8.4)	8.16±1.08 (6.8-10)
Transverse ligament area	2.06±0.55 (1.16-3.37)	1.97±0.49 (1.16-3.37)	2.18±0.60 (1.16-3.25)	1.98±0.69 (1.16-3.23)	1.64 (1.64-1.64)	2.05±0.46 (1.18-3.14)	2.22±0.66 (1.16-3.37)	1.18 (1.18-1.18)	1.91±0.25 (1.6-2.3)

SD: Standard deviation

Table 2. (Mean ± SD) and (min-max) values of patients with ALT of Czerny type A (1-2-3) and Czerny type B (1-2-3)

	Czerny A Mean ± SD (min-max)	Czerny B Mean ± SD (min-max)	p
Transverse ligament-femoral head largest contact surface	8.05±2.12 (4.3-12)	8.03±1.34 (5.4-10.4)	0.80
Transverse ligament area	2.02±0.53 (1.16-3.2)	2.12±0.58 (1.16-3.37)	0.65

SD: Standard deviation, ALT: Acetabular labral tear

Table 3. Representation of the statistical relationship between the mean ± SD and min-max values of the patients with ALT according to the Czerny (1-2-3) classification and in pairs in groups

	Czerny 1 Mean ± SD (min-max)	Czerny 2 Mean ± SD (min-max)	Czerny 3 Mean ± SD (min-max)	Czerny 1-2 p	Czerny 1-3 p	Czerny 2-3 p
Transverse ligament-femoral head largest contact surface	7.33±2.19 (4.3-11.3)	8.2±1.80 (5.3-12)	8.1±1.01 (6.8-10)	0.16	0.20	0.91
Transverse ligament area	1.94±0.66 (1.16-3.23)	2.14±0.57 (1.16-3.37)	1.90±0.23 (1.67-2.38)	0.22	0.87	0.24

SD: Standard deviation, ALT: Acetabular labral tear, Mann-Whitney U; $p<0.05$

and TAL were removed (15). As a result, acetabulum and femoral head contact surface area decreased only in the group in which TAL was removed, while no significant difference was found in samples where the labrum or both were removed. There was no difference in the pressure distribution between acetabulum and femoral head in all three groups. These findings led Konrath et al. (15) to state that acetabular labrectomy or TAL removal was not one of the causes of premature osteoarthrosis.

In the study of Löhe et al. (7), it was emphasized that TAL was effective in eliminating the instability caused by the native incompatibility between the acetabulum and the femoral head in the hip joint. It was suggested that TAL played an effective role in carrying the tensile stress that occurred especially during physical activities such as walking (13). Various anatomical and physiological studies have noted a clear stress on TAL; however, no study is available demonstrating the changes of TAL in patients

with acetabular labral tear. Our study showed that there was no gross morphological change at TAL on MRA in patients with acetabular labral tear.

Another area where TAL gains importance is its use for orientation in total hip replacement operations. According to Kalteis et al. (16), when TAL and posterior labrum were used for soft tissue orientation in the placement of the acetabular component, it was shown that it provided less malposition rate compared to traditional methods. In a study published recently by Harris et al. (17), the role of TAL in terms of treatment and recovery in acetabular pathologies has also been emphasized by showing that the healing rates of labral tears that cannot be repaired with the labral reconstruction method including the transverse acetabular ligament are favorable.

Until now, there has been no study in the literature evaluating the widest contact surface of TAL with the femoral head and TAL area in patients with acetabular labral pathology. In this study, we compared the mean values of these two parameters with respect to the right and left sides. However, we could not find any significant difference in these values. In the parameters measured in ALTs which were evaluated according to the Czerny classification, no significant difference was found between the Czerny 1-2-3 groups in the comparisons made in pairs. In addition, the widest contact surface and area of TAL with the femoral head were measured between post-traumatic (1A, 2A and 3A) and dysplastic (1B, 2B and 3B) lesions of the labrum, and no significant difference was found.

Study Limitations

Our study has a number of limitations. The most important limitation is that the arthroscopic response of labrum pathologies described with MRA is not investigated. Arthroscopy is still the gold standard in the diagnosis of acetabular labral pathologies. According to Chan et al. (18), the sensitivity of MRA is 100%, while the accuracy rate is 94%. This rate is due to false-positive results. Another limitation is the exclusion of posterior labral pathologies from the study. TAL is the continuation of the posterior labrum and there are significant changes in TAL morphology in its pathologies; it is necessary to evaluate the anterior-superior and posterior lesions in separate groups. This area may serve as a starting point for further studies in the future. In addition, in a small number of patients evaluated in the study, the TAL orientation was not taken into account. Lack of knowledge on presenting complaints and clinical findings of acetabular labrum pathologies is among other limitations.

Conclusion

We found no significant relationship between Czerny staging of acetabular labral pathologies and transverse acetabular ligament morphology. This result suggests that transverse acetabular ligament morphology cannot be indicated among the predisposing factors in acetabular labral pathologies. Considering that TAL, which has an important role in acetabulum and labrum mechanics, may theoretically be associated with these pathologies, more detailed studies will be required in the future to prove this relationship.

Ethics

Ethics Committee Approval: The study protocol was approved by İstanbul University Cerrahpaşa-Cerrahpaşa Faculty of Medicine Ethics Committee (date: 09.07.2015, no: 02-218671).

Informed Consent: Written informed consent was not necessary because no patient data has been included in the manuscript.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: F.U., D.E.T.Ş., F.K., Design: F.U., D.E.T.Ş., F.K., Data Collection or Processing: F.U., D.E.T.Ş., E.E., Analysis or Interpretation: D.E.T.Ş., F.K., Drafting Manuscript: F.U., D.E.T.Ş., E.E., Critical Revision of Manuscript: F.K., D.E.T.Ş., E.E., Final Approval and Accountability: F.K., F.U., D.E.T.Ş., E.E.

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ORIGINAL RESEARCH

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BhCG as a Rupture Marker in Ectopic Pregnancy: A Retrospective Study

Ektopik Gebelikte Rüptür Belirteci Olarak BhCG: Retrospektif Bir Çalışma

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Abstract

Objective: To find effective criteria in determining the risk of ectopic pregnancy rupture in patients with ectopic pregnancy.

Method: The data of 101 patients who were hospitalized with the diagnosis of ectopic pregnancy in the tertiary center between January 2018 and January 2021 were analyzed retrospectively. Demographic data of the patients, the month of admission, the patients' beta-human corionic gonadotropin (BhCG) values at the time of admission, blood type, endometrial thickness measured with transvaginal ultrasound, presence of adnexal mass suggestive of ectopic pregnancy and treatments applied to the patients were recorded. These data were compared between patients who had surgery for ectopic pregnancy rupture and those whose treatment was completed without it.

Results: In the statistical analysis of the data, ectopic pregnancy rupture was found significantly more frequent for a threshold value of BhCG >4000 IU/L. Other data were not statistically significant.

Conclusion: In cases of ectopic pregnancy, if the BhCG value at the time of admission exceeds the threshold value, the possibility of surgical approach increases. Medical treatment may be more successful at lower BhCG levels.

Keywords: BHcg, ectopic pregnancy, rupture prediction, tubal rupture

Öz

Amaç: Ektopik gebelik saptanmış hastalarda rüptür riskinin belirlenmesinde etkili kriterleri bulmaktır.

Yöntem: Ocak 2018-Ocak 2021 tarihleri arasında üçüncü basamak merkezde ektopik gebelik tanısı ile yatırılan 101 hastanın verileri retrospektif olarak incelendi. Hastaların demografik verileri, başvuru ayı, hastanın başvuru anındaki BhCG değeri, kan grubu, transvaginal ultrasonografi ile endometrial kalınlık, ektopik gebelik odağı varlığı ve hastalara uygulanan tedaviler kaydedildi. Bu veriler, ektopik gebelik rüptürü nedeniyle ameliyat olan ve ameliyat olmadan tedavisi tamamlanan hastalar arasında karşılaştırıldı.

Bulgular: Verilerin istatistiksel analizinde BhCG >4000 IU/L için sadece rüptür grubunda anlamlı olarak daha sık bulundu. Diğer veriler istatistiksel olarak anlamlı değildi.

Sonuç: Ektopik gebelik olgularında giriş anındaki BhCG değeri eşik değerini aşarsa ameliyat olma olasılığı artar. Düşük BhCG düzeylerinde tıbbi tedavi daha başarılı olabilir.

Anahtar kelimeler: BHcg, ektopik gebelik, rüptür öngörüsü, tubal rüptür

Introduction

Ectopic pregnancy is the pregnancy outside the uterine cavity and accounts for 1-2% of all pregnancies (1). It is an important emergency disease of the reproductive age, which can show a fatal course. The mortality rate of ectopic pregnancies ranges around 3-4% (2).

Today, pregnancies are being detected in very early weeks with sensitive pregnancy tests, high-resolution ultrasonography, Doppler ultrasonography, and magnetic resonance imaging (MRI) when necessary (3,4).

Methotrexate (Mtx) treatment was first applied in ectopic pregnancy cases by Stovall et al. (5). According to current

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data, approximately one third of ectopic pregnancy cases are suitable for medical treatment (6).

While the primary treatment protocol was laparoscopic salpingostomy in unruptured tubal ectopic pregnancies until 1997, medical treatment started to be accepted as a reliable treatment method with the randomized controlled study of Hajenius et al. (7).

There are many studies in the literature to find the most appropriate treatment method for ectopic pregnancies. In this study, we wanted to set approaches that might reduce the risk of ectopic pregnancy ruptures and therefore the mortality and morbidity rates of the cases by using the clinical features, examination findings and laboratory values of the patients, and contribute to the literature by determining a threshold BhCG value.

Materials and Methods

In this retrospective study, following the permission of the Non-Interventional Clinical Research and Ethics Committee of İstanbul Medipol University, dated 20.05.2021 and numbered 483,101 patients with inpatient follow-up and diagnosis of ectopic pregnancy in a tertiary health center in İstanbul for a period of 3 years between January 2018 and January 2021 were included. We used the algorithm created by Stovall and Ling (8) in 1993 for the diagnosis of ectopic pregnancy.

The month of admission, age, gravida, parity, blood type, history of previous pelvic surgery, and menstrual cycle of the last 6 months were recorded. Endometrial thickness measured with transvaginal ultrasound, BhCG value (d0BhCG) at the time of admission, presence of an adnexal mass suggestive of ectopic pregnancy, and size of the adnexal mass if present were recorded in all patients.

In cases when urgent surgical approach was not required, patients with BhCG value >1000 IU/L received medical treatment while patients with BhCG value <1000 IU/L were followed with expectant management. Mtx (single-multidose) was administered intramuscularly to the patients as medical treatment. Mtx was calculated as 50 mg/m^2 and BhCG value was measured on the 4th and 7th days when given as a single dose. Accepting that 15% decrease in serum BhCG value between the 4th and 7th days is a very good indicator of the possible success of Mtx, a second dose of Mtx was administered to the patients whose BhCG values did not decrease adequately (9). Surgery was not applied unless an acute abdomen developed. Laparoscopic salpingectomy was performed in patients requiring surgical intervention.

Before starting Mtx treatment, liver function tests, complete blood count, renal function tests, and blood group determination were performed in order to determine the general health status of the patients and to understand whether there were contraindications for Mtx treatment. Patients with breastfeeding, intrauterine pregnancy, acute peptic ulcer, impaired immune system, unclear diagnosis, active pulmonary disease, renal disease, and unexplained blood disorder and patients who were not hospitalized or able to be followed up during the treatment period were excluded from the study group.

BhCG values were recorded from 101 patients at the time of hospitalization, and the patients were divided into two groups as patients who did not require surgery (medical treatment or expectant management) and patients who underwent surgery. The patients who underwent surgery were called the primary surgery group if no medical treatment was applied priorly. The patients who were operated due to the development of acute abdomen while taking Mtx or during spontaneous follow-up were called the secondary surgery group. The pathological material of the operated patients was preserved for pathological analysis and postoperative BhCG values were not followed up in the patients who underwent surgery.

The BhCG value was studied in the hospital laboratory using the Beckman counter UniCel DxI 800 immunoassay system device with the total chemiluminescent immunoassay method and the results were recorded as IU/L.

Statistical Analysis

With the Pearson chi-square test and Fisher's Exact test, statistically significant variables were evaluated between patients having and not having surgery. The threshold value for predicting rupture was determined for the d0BHcg value by ROC analysis.

Results

Of all the patients in the study group, 60.4% of the patients did not undergo surgery while 39.6% of them required surgical intervention. Of the 39 patients who underwent surgery, 28 of them (71.80%) were operated without receiving medical treatment (primary surgery group) and 11 of them (28.20%) were operated while having Mtx treatment (secondary surgery group).

In the distribution of patients according to the month of admission, the highest number of patients who underwent surgery was admitted in September (18.8%) and the lowest number of patients who underwent surgery was admitted in May and August (2.0%).

Among the patients who underwent surgery, patients with blood groups of A rH+ (35.6%) and 0 rH+ (25.7%) were seen most frequently. Patients with blood group of AB rH- were rarest among the patients who required surgery (1.0%).

We did not find a significant difference in age between the groups with and without ectopic pregnancy rupture during the ectopic pregnancy treatment course.

Of 101 patients who were hospitalized for ectopic pregnancy, 16 (15.84%) were nulliparous and 85 (84.16%) were multiparous. We found that the risk was higher in patients with lower gravida who needed surgery. Four nulliparous patients (25%) and 36 multiparous patients (42.4%) needed surgical intervention. However, gravida was not a statistically significant factor in terms of operation necessity.

We observed adnexal mass suggestive of ectopic pregnancy by transvaginal ultrasound in 61 patients (60.40%) and 25 of them (41.0%) needed surgical intervention. In 40 patients, (39.60%) transvaginal ultrasonography of adnexa was normal and 15 of them (37.5%) needed surgical approach. In our study, we could not find any statistically significant difference between the patients with and without an adnexal mass suggestive of ectopic pregnancy with regard to the necessity of surgery.

In their first examination with transvaginal ultrasound, 15 (31.9%) of 47 patients with an endometrial thickness measurement less than 7 mm, 15 (45.5%) of 33 patients with an endometrial thickness of 7-12 mm and 10 (47.6%) of 21 patients with endometrial thickness greater than 12 mm were operated. We did not find any significant relevance between endometrial thickness and the necessity of surgery.

A single dose of Mtx was given to 51 (72.86%) of 70 patients who received medical treatment, and multidose of Mtx was given to 19 (27.14%) of them. Eight patients (15.69%) who received a single dose of Mtx and 3 patients (15.78%) who received multidose of Mtx were operated. Statistically, we could not find any significant difference between patients using single dose and multidose Mtx in terms of operation frequency.

Of the 70 patients who received Mtx, 11 of them (15.70%) were operated.

One of the 3 patients who was followed with expectant management required surgery. This patient's BhCG value was 454 IU/L (Figure 1).

In the ROC analysis, predictive BhCG value was determined as 4177 IU/L in terms of surgical approach (sensitivity: 60%, specificity: 88.52%, positive predictive value: 76.7, negative predictive value: 78.3). AUC was 0.786, and the data were considered reliable. According to the binary-logistic analysis based on the aforementioned threshold BhCG value of 4.177 IU/L, it was found that requirement of surgical intervention was 4.8 times (OR) more likely ($p<0.001$). When all the variables are included in the model, and in the same binary logistic regression model, when we take the need for surgery as the dependent variable and the threshold value of BhCG exceeds, it is OR=4.8 ($p<0.001$) times more likely that surgery is required. The d0BhCG value is higher in those requiring surgery.

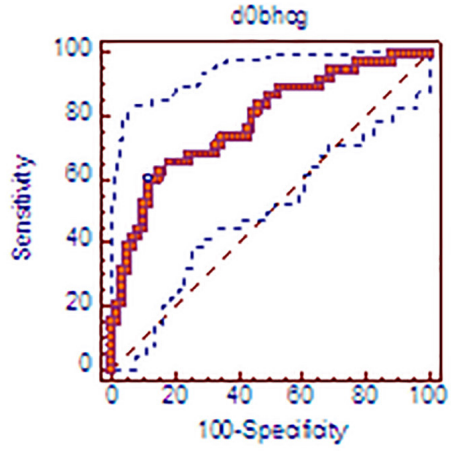

Figure 1. ROC analysis table: According to d0 BhCG, in the classification made according to the threshold value as a result of the ROC analysis, the rate of those who needed surgery was significantly higher than the threshold value.

ROC: Receiver operating characteristic

Discussion

Ectopic pregnancy is an urgent gynecological condition, which may have catastrophic consequences and is seen in women of reproductive age. Ectopic pregnancies are located in fallopian tubes in 95% of cases. Rupture of the ectopic pregnancy, tubal abortion or spontaneous regression may occur in tubal ectopic pregnancies. 10-15% of maternal deaths are due to complications related to ectopic pregnancy (10). In the literature, the rate of ectopic pregnancy rupture is 32% in ectopic pregnancy patients, and it is the main cause of ectopic pregnancy-related mortality (11). Therefore, surgery is essential in ruptured ectopic pregnancy. The surgical method may be salpingectomy or salpingostomy. Criteria such as the patient's desire for fertility, the patient's general condition and hemodynamic changes may be effective in determining the surgical

method. The surgery can be executed with laparotomic or laparoscopic approach. Mtx is used for medical treatment. Mtx treatment scheme for medical treatment is based on a 2007 study (9).

In this study, we could not find any definitive criterion to predict ectopic pregnancy rupture. We only found that patients with a BhCG value of 4177 IU/L had an increased risk of rupture. There was no statistically significant relevance between operation requirement and patients' age, endometrial thickness, gravida, presence of an adnexal mass suggestive of ectopic pregnancy, blood type, and the month of admission.

Although BhCG shows the presence of pregnancy in the patients, an adnexal mass suggestive of ectopic pregnancy may not be detected by ultrasonography. In this case, considering the possible intrauterine pregnancy and the side effects of Mtx treatment, 48-72 hours of expectant management may be considered in the hemodynamically stable patient. If BhCG value is <2000 IU/L or the BhCG value decreases spontaneously, expectant management is suitabl (12). In our study, there were 3 patients who were eligible for expectant management. Among them, a patient with BhCG value of 454 IU/L was operated because of the development of acute abdomen and hemodynamic instability.

Although it was published in 2009 by Col-Madendag et al. (13) that endometrial thickness was a significant evaluation criterion when BhCG level was below 1000 IU/L, it was not explained how many millimeters were statistically significant. According to the publication in 2009 by Knafel et al. (14), endometrial thickness is not significant in the prediction of tubal ectopic pregnancy rupture. In our study, endometrial thickness, blood type, and admission month of the patient did not have any differential effect between patients with and without ectopic pregnancy rupture.

In the literature, there are studies that are conflicted with each other in terms of the predictive value of BhCG for ectopic pregnancy ruptures. Despite previous publications showing that BhCG level is not significant in predicting the risk of rupture, a population-based study by Job-Spira et al. (15) reported that ectopic pregnancy rupture was 3 times more common in cases with β-hCG ≥10,000 IU/L. Latchaw et al. (16) calculated BhCG threshold value 5000 IU/L in 2005. Fukami et al. (17) determined a threshold value of 3000 IU/L in 2016. While BhCG threshold value was calculated 5000 IU/mL in some publications, it was determined as 10000 IU/L in some others (18-20). In our study, we found that the need of surgical approach increased 4.8 times (OR) over the threshold value of BhCG 4177 IU/L ($p<0.001$).

The lack of patients followed by expectant management, who could have been considered as another control group, limited our study in terms of observing the course of untreated follow-up. One of three patients on expectant management had acute abdomen and salpingectomy was performed.

Patient complaints, laboratory tests and examination findings cannot fully predict ectopic pregnancy rupture and despite all advances, ectopic pregnancy rupture is still a significant cause of maternal death. Although the risk of rupture decreases by 2.5% each passing day after the first 48 hours of diagnosis, the presence of symptoms always poses risk for ectopic pregnancy rupture (11). Mtx treatment is 89% successful in the early period in ectopic pregnancy cases (20). It is known that the lower the BhCG value upon the diagnosis of ectopic pregnancy, the more successful the medical treatment can be.

Conclusion

It cannot be guaranteed that ectopic pregnancy rupture will not occur in any case, and we could not find any predictive parameter for ectopic pregnancy rupture other than BhCG in our study. Therefore, close follow-up and studies with larger patient series are required.

Ethics

Ethics Committee Approval: In this retrospective study, following the permission of the Non-Interventional Clinical Research and Ethics Committee of İstanbul Medipol University, dated 20.05.2021 and numbered 483,101.

Informed Consent: Consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: Ö.K.A., E.E.K., Design: Ö.K.A., E.E.K., Data Collection or Processing: Ö.K.A., T.Ç., Analysis or Interpretation: Ö.K.A., H.G., Drafting Manuscript: Ö.K.A., E.E.K., T.Ç., Critical Revision of Manuscript: H.G., Ö.K.A., Final Approval and Accountability: Ö.K.A., H.G., E.E.K., T.Ç.

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ORIGINAL RESEARCH

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Deltoid Ligament Repair in Addition to Syndesmotic Fixation in Distal Fibula Fractures is Associated with Better Clinical Results in Mid- and- Long-term Follow-up: A Comparative Study

Distal Fibula Kırıklarında Sindesmotik Fiksasyona Deltoid Ligament Tamirinin Eklenmesi Orta-uzun Dönem Takipte Daha İyi Klinik Sonuçlarla İlişkilidir: Karşılaştırmalı Bir Çalışma

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Abstract

Objective: To evaluate mid to long term effects of adding deltoid ligament repair (DLR) to syndesmotic screw fixation (SSF) in the treatment of distal fibula fractures -in terms of functional and radiographic results and quality of life.

Method: Seventy-eight patients who underwent SSF or SSF+DLR with the diagnosis of distal fibula fracture in the Maltepe University Hospital, Department of Orthopedics and Traumatology were included in the study retrospectively.

Results: 71.8% of the cases were male. The mean age was 39.24±11.95 years. The radiographic and functional results and quality of life were better in the SSF+DLR group compared to the SSF group. Additionally, the operation time was longer in the SSF+DLR group.

Conclusion: Performing DLR in appropriate cases of distal fibula fracture may contribute to better clinical outcomes in the mid to long term.

Keywords: Ankle, deltoid ligament repair, distal fibula fractures, syndesmosis

Öz

Amaç: Distal fibula kırıklarının tedavisinde sindesmotik vida fiksasyonuna (SSF) deltoid ligament tamirinin (DLR) eklenmesinin fonksiyonel ve radyografik sonuçlar ve yaşam kalitesi üzerindeki orta-uzun vadeli etkisini değerlendirmektir.

Yöntem: Maltepe Üniversite Hastanesi Ortopedi ve Travmatoloji Anabilim Dalı'nda distal fibula kırığı tanısı ile SSF veya SSF+DLR yapılan 78 hasta geriye dönük olarak çalışmaya dahil edildi.

Bulgular: Olguların %71,8'i erkekti. Ortalama yaş 39,24±11,95 yıldı. SSF grubu ile karşılaştırıldığında SSF+DLR grubunda radyografik, fonksiyonel sonuçlar ve yaşam kalitesi daha iyiydi. Ek olarak, SSF+DLR grubunda operasyon süresi daha uzundu.

Sonuç: Distal fibula kırıklarında uygun olgularda DLR yapılması orta-uzun vadede daha iyi klinik sonuçlara katkıda bulunabilir.

Anahtar kelimeler: Ayak bileği, deltoid ligament tamiri, distal fibula kırıkları, sindesmoz

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Introduction

Fibula fractures are common ankle fractures and rarely require surgical stabilization. In some of these fractures, the syndesmosis, which contributes to the stability of the ankle, is also injured. Syndesmosis creates a mortise in the talotibial joint by tightly connecting the tibia and fibula (1,2). Besides, the deltoid ligament plays an important role in talar stability and its injury may accompany ankle fractures (3).

The deltoid ligament is the strongest ligament of the ankle and is a thick, triangular band of tissue that arises from the medial malleolus. Eversion forces can cause deltoid ligament injury, and deltoid ligament sprains typically require longer rehabilitation compared to anterior talofibular and calcaneofibular ligament sprains (4). In mild traumas of the foot and ankle, treatment may consist of medical options and immobilization with a splint/cast, while severe cases may require surgical intervention. Usually, treatment consists of a combination of these options. Many studies have investigated the benefits of deltoid ligament repair (DLR) for deltoid ligament injuries. The necessity of adding DLR to surgical treatment in ankle fractures is still not clear. While recent comprehensive studies evaluating ankle fractures have shown positive effects of DLR in terms of radiographic, functional, or quality of life findings (5-10), other studies have suggested that it has no beneficial effect (4,11-15).

Inadequately treated fractures and injuries can lead to instability, syndesmosis widening, and talar shift. Functional results are often poor in cases that do not undergo proper anatomic reduction and adequate fixation. When previous studies on this subject are reviewed, it is evident that there are very few studies reporting long-term results. In this study, it was aimed to evaluate the mid to long term effects of adding DLR to syndesmotic screw fixation (SSF) for the treatment of distal fibula fractures. Evaluations were based on functional and radiographic results and quality of life.

Materials and Methods

Patients who underwent SSF with a diagnosis of distal fibula fracture at Maltepe University Hospital, Department of Orthopedics and Traumatology between July 1, 2008 and December 31, 2015 were included in the study retrospectively. Ethical approval was obtained from Maltepe University.

Patients

Patients with distal fibula fractures who had syndesmosis injury, deltoid ligament rupture, more than 4 mm separation in the fracture line and had undergone SSF or SSF+DLR were included in the study, given that they were older than 18 years of age. All subjects included in the study had deltoid ligament rupture. The files of 118 patients who were operated for distal fibula fractures on the relevant dates were reviewed.

Exclusion criteria:

- Being younger than 18 years old,
- Having undergone different surgical procedures,
- Having additional fractures,
- Having additional health conditions affecting fracture healing (such as severe diabetes mellitus, malignancy, use of cortisone),
- Lost to follow-up.

Finally, 78 cases meeting the inclusion/exclusion criteria were included in the study. 71.8% of the cases were male. The mean age was 39.24±11.95 years, and the mean follow-up time was 66.90±6.11 weeks.

In our clinic, DLR was not performed between 2008 and 2012, while DLR was performed between 2013 and 2016. The cases were divided into two groups according to the surgical procedure. The cases in which plate and syndesmotic screw were applied to the fibula were defined as the “SSF group” (n=46), and cases that additionally underwent DLR were defined as the “SSF+DLR group” (n=32).

Surgical Procedure

SSF group: Operations were performed in the supine position, under general anesthesia or spinal anesthesia. After the tourniquet was applied to the thigh area, a longitudinal 10-15 cm incision was made over the lateral malleolus. The dissection plane was between the peroneus tertius (anteriorly) and the peroneus longus and brevis (posteriorly). Then, the periosteum was cut and the ends of the fracture were identified. The fracture edges were cleaned and reduced. Depending on the type of fracture, either the lateral fibula anatomic locking plate or the posterior fibula anatomic locking plate and locked/unlocked cortical screws were applied. The ankle was taken to maximum dorsiflexion and 4 cortex screws of 52.5 (50.0-55.0) mm were placed from the posterior to the anterior after drilling the tibia and fibula (4 cortex drilling) through the dynamic hole on the plate in parallel to the joint line.

SSF+DLR group: The procedures applied in the SSF group were also performed for the SSF procedure in this group. Afterwards, an approximately 6-cm incision was made,

extending from the upper middle part of the talus to the distal side, oriented at a slight oblique angle from proximal-posterior to distal-anterior, and centered on the posterior aspect of the medial malleolus. The posterior tibial tendon sheath was incised longitudinally to allow better visualization of the deltoid ligament. Anteromedial mini capsulotomy was performed to evaluate the condition of the deltoid ligament and joint reduction. If the deltoid ligament was separated from the medial malleolus, 1 or 2 suture anchors were applied to the medial malleolus. If it was separated from the talus, 1 or 2 suture anchors were placed in the talus. After checking the strength of the anchors, the deltoid fibers were tied with suture anchor threads, and the posterior tibial tendon sheath was repaired. The number of suture anchors applied was 1 in 26 of the cases (81.3%) and 2 in 6 of the cases (18.8%). The suture anchor location was the medial malleolus in 24 cases (75.0%) and the talus (posterior) in 8 cases (25.0%).

In both groups, the cases were immobilized with a short leg cast for 6 weeks in the postoperative period. All cases started muscle strengthening exercises within 6 weeks postoperatively. Syndesmotic screws were removed under general anesthesia on the 6th-8th week postoperatively. The day after the procedure, patients were mobilized with partial weight-bearing.

Measurements

The parameters evaluated in this study were as follows:

• Patients' characteristics (gender, age, side, energy of trauma, fracture classification),

• Surgery features (time to operation, operation duration, plate type, syndesmotic screw size, union time, time to syndesmotic screw removal, count and placement of suture anchors, follow-up time).

• American Orthopedic Foot and Ankle Society (AOFAS) score,

• Short form (SF) - 36 score,

• Medial clear space (MCS),

• Radiographic score.

The AO Foundation/Orthopedic Trauma Association (AO/OTA) classification was used for fracture classification. All evaluations were performed by an experienced surgeon blinded to the procedure performed.

Functional Assessment (AOFAS)

AOFAS is a scale developed by the American Foot and Ankle Orthopedic Society to evaluate ankle functions. A maximum of 100 points describes good functional condition of the ankle, while a score of 0 describes poor clinical condition (16). The 1st year and 5th year AOFAS scores of the cases were recorded.

Quality of Life Assessment (SF-36 questionnaire)

The SF-36 was developed to evaluate quality of life. The last 4 weeks of life are taken into consideration in the evaluation of SF-36, and it consists of 36 items. Higher scores indicate better quality of life (17). The 1st year and 5th year SF-36 scores of the cases were recorded.

Radiographic Assessment

In the mortise view, the distance between the lateral border of the medial malleolus and the medial border of the talus was recorded as the MCS. If this interval is greater than 4 mm, it is considered to be abnormal and indicates lateral displacement of the talus (18). In addition to this finding, cases with tenderness and ecchymosis below the medial malleolus in clinical preoperative examination were considered to have deltoid ligament rupture. MCS values were recorded in the pre-operative period, postoperative period (before discharge), 1st year, and 5th year.

The radiographic osteoarthritis scoring system of Kraus et al. (19) was used in the evaluation of osteoarthritis. Higher scores on this scale indicate increased osteoarthritis. The 1st year and 5th year radiographic scores of the cases were recorded.

Statistical Analysis

All analyses were performed on SPSS v21 (SPSS Inc., Chicago, IL, USA). For the normality check, the Shapiro-Wilk test was used. Data are given as mean ± standard deviation or median (1st quartile-3rd quartile) for continuous variables according to the normality of distribution, and as frequency (percentage) for categorical variables. Normally distributed variables were analyzed with the independent samples t-test. Non-normally distributed variables were analyzed with the Mann-Whitney U test. Categorical variables were evaluated using the chi-square tests. Non-normally distributed variables were analyzed with the Wilcoxon Signed Ranks test for repeated measurements. Between-groups comparison of these variables were performed by analyzing differences between measurements with the Mann-Whitney U test or the Kruskall-Wallis test depending on the group count. Pairwise comparisons were performed with the Bonferroni correction method. Two-tailed p-values of less than 0.05 were considered statistically significant.

Results

Operation time was significantly longer in the SSF+DLR group compared to the SSF group (p<0.001). There was no statistically significant difference between the groups in terms of other characteristics (p>0.05, for each). The summary of patients' characteristics with regard to the surgery group is shown in Table 1.

While the MCS value was similar between the groups in the preoperative period (p=0.661), it was significantly lower in the SSF+DLR group in the postoperative, 1st year, and 5th year measurements (p<0.001, for each). Compared to preoperative MCS, postoperative MCS was significantly reduced in both groups (p<0.001, for each). Compared to the postoperative MCS value, 1st year MCS value increased significantly in the SSF group (p<0.001), whereas there was no significant change in the SSF+DLR group (p=0.599). Compared with the 1st year, neither group showed a significant change in terms of MCS value on the 5th year (p=1.000, for each).

The SF-36 score was higher in the SSF+DLR group at both the 1st year and 5th year comparisons (p<0.001, for each). In the SSF group, compared to the 1st year, the 5th year SF-36 value was significantly decreased (p<0.001), while there was no significant difference in the SSF+DLR group (p=0.805).

While the 1st year AOFAS score was similar between the groups (p=0.316), the 5th year AOFAS score was significantly higher in the SSF+DLR group (p<0.001). The 5th year AOFAS score decreased significantly (p<0.001) in the SSF group compared to the 1st year, while it increased significantly in the SSF+DLR group (p<0.001).

The radiographic score was significantly lower in the SSF+DLR group in both the 1st and 5th year comparisons

Table 1. Summary of patients' characteristics with regard to the surgery group

	Group			
	SSF (n=46)	**SSF+DLR (n=32)**	**Total (n=78)**	**p**
Age (year)	39.74±11.82	38.53±12.29	39.24±11.95	0.664
Gender				
Male	34 (73.90%)	22 (68.80%)	56 (71.80%)	0.618
Female	12 (26.10%)	10 (31.30%)	22 (28.20%)	
Side				
Right	24 (52.17%)	14 (43.75%)	38 (48.72%)	0.464
Left	22 (47.83%)	18 (56.25%)	40 (51.28%)	
Energy of trauma				
Low	34 (73.90%)	25 (78.10%)	59 (75.60%)	0.670
High	12 (26.10%)	7 (21.90%)	19 (24.40%)	
AO/OTA classification				
44B2.1	13 (28.26%)	11 (34.38%)	24 (30.77%)	0.927
44B3.1	8 (17.39%)	6 (18.75%)	14 (17.95%)	
44C1.1	17 (36.39%)	10 (31.25%)	27 (34.62%)	
44C2.1	8 (17.39%)	5 (15.63%)	13 (16.67%)	
Time to operation (days)	2.0 (2.0-3.0)	2.0 (1.0-3.0)	2.0 (2.0-3.0)	0.581
Operation time (minutes)	64.35±3.96	91.25±8.47	75.38±14.68	<0.001
Plate type				
Lateral	28 (60.87%)	21 (65.63%)	49 (62.82%)	0.669
Posterior	18 (39.13%)	11 (34.38%)	29 (37.18%)	
Syndesmotic screw size (mm)	52.5 (50.0-55.0)	50.0 (50.0-55.0)	50.0 (50.0-55.0)	0.792
Union time (weeks)	7.0 (7.0-8.0)	7.0 (7.0-8.0)	7.0 (7.0-8.0)	0.644
Time to remove the syndesmotic screw (weeks)	8.0 (7.0-8.0)	8.0 (7.0-8.0)	8.0 (7.0-8.0)	0.515
Follow-up time (weeks)	66.87±5.58	66.93±6.91	66.90±6.11	0.950

DLR: Deltoid ligament repair, SSF: Syndesmotic screw fixation, AO/OTA: The AO Foundation/Orthopedic Trauma Association, data are given as mean ± standard deviation or median (1st quartile-3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables

(p<0.001, for each). In both groups, the 5th year radiographic score was significantly increased compared to the 1st year (p<0.001, for each).

The summary of patients' measurements with regard to treatment groups is shown in Table 2.

Discussion

Although there have been many innovations in the approach to distal fibula fractures, the debate on ideal treatment method continues. In this study, in which the mid- and long-term results of DLR in addition to SSF in distal fibula fractures were evaluated, it was determined that the radiographic and functional results and quality of life were better in the SSF+DLR group compared to the SSF group. Of note, operation duration was longer in the SSF+DLR group.

Functional recovery after surgery is an important indicator of success and satisfaction. In our study, ankle functions were evaluated with the AOFAS score. Ankle functions worsened significantly in the SSF group at the 5th year compared to the 1st year but improved significantly in the DLR group during the same time interval. In addition, it was similar between the groups at the 1st year but was significantly better in the DLR group compared to the SSF group at the 5th year comparison. Consistent with our study, Gu et al. (5) reported that the AOFAS score was significantly better in DLR recipients among patients treated for ankle fractures. In some other studies, it has been shown that ankle functions improve after DLR in ankle fracture cases (6,7). In contrast, Li et al. (11) reported that postoperative functions were at a similar level between the groups treated with and without DLR application. In various studies supporting this study, it has been shown that ankle functions are not significantly different between the groups with and without DLR (8-10,12,13). However, in our study, it was shown that DLR had positive effects on ankle function, especially in the long term.

One of the most important evaluation methods after fracture surgery is radiographic examination. In this respect, MCS values and radiographic scores of the cases were recorded in our study. In a study similar to ours, in which the results of groups treated for supination external rotation type IV ankle fracture with and without DLR were published, Choi et al. (20) reported that the MCS value decreased significantly in the postoperative period in both

Table 2. Summary of patients' measurements with regard to the treatment groups

	Group		
	SSF (n=46)	**SSF+DLR (n=32)**	**p[a]**
MCS (mm)			
Pre-operative	4.40 (3.80-4.60)[x]	4.40 (3.85-4.55)[x]	0.661
Post-operative	3.70 (3.50-3.90)[y]	2.90 (2.80-3.05)[y]	<0.001
1st year	4.15 (3.80-4.40)[z]	3.00 (2.90-3.15)[y]	<0.001
5th year	4.40 (3.90-4.40)[z]	3.00 (2.85-3.20)[y]	<0.001
p-value[b]	<0.001	<0.001	
SF-36			
1st year	74 (68-78)	78 (78-84)	<0.001
5th year	68 (66-74)	79 (78-84)	<0.001
p-value[b]	<0.001	0.805	
AOFAS			
1st year	76 (74-78)	77 (76-79)	0.316
5th year	66 (64-70)	80 (78-82)	<0.001
p-value[b]	<0.001	<0.001	
Radiographic score			
1st year	2 (1-2)	0 (0-1)	<0.001
5th year	9 (8-12)	2 (2-3)	<0.001
p-value[b]	<0.001	<0.001	

AOFAS: American Orthopedic Foot and Ankle Association, DLR: Deltoid ligament repair, MCS: Medial clear space, SF: Short form, SSF: Syndesmotic screw fixation

[a]: Comparison between groups, [b]: Comparison within groups, [x], [y], [z]: Different letters indicate significant differences between repeated measurements within groups.

Data are given as median (1st quartile-3rd quartile) for continuous variables

groups, but there was no significant difference between the groups. In a study comparing DLR and syndesmotic fixation results of lateral malleolar fractures, Rosa et al. (13) reported that MCS values were similar between the groups at the 24-month follow-up. Similarly, in another study, it was reported that there was no statistically significant difference between the groups in terms of MCS values (14). Unlike these studies, it was shown in two different studies that the postoperative MCS value decreased significantly when compared to the preoperative values in the groups with and without DLR, and also that the decrease in MCS in the DLR group was significantly higher than in the group without DLR (9,10). In our study, the follow-up period of the cases was longer. It was determined that the postoperative MCS value of both groups decreased significantly, but ultimately increased in the group without DLR. While the preoperative MCS was similar between the groups, it was significantly lower in the SSF+DLR group compared to the SSF group at all postoperative follow-up measurements. The permanence of stability in the SSF+DLR group may have been due to the fact that both medial and lateral support were present. In the SSF group, although lateral support is good, medial support is poor. Therefore, even if the postoperative recovery is satisfactory, the stability of the ankle may be reduced in the following time period due to insufficient medial support. Eventually, MCS value may increase, and the functional and radiographic outcomes may deteriorate.

In various studies examining different radiographic features, it has been shown that the radiographic results of cases with and without DLR are similar (10,15). There are also studies reporting that DLR improves radiographic results (7). To the best of our knowledge, this is the first study evaluating these effects of DLR with long-term follow-up. Accordingly, the osteoarthritis scores of the DLR cases were better at both the 1st and 5th year follow-ups. The reasons for better radiographic results in the SSF+DLR group may be the associated with the presence of relatively smoother joint line and better support of the ankle after DLR.

The contribution of surgery to the well-being of the cases will also increase the quality of life. This is one of the main goals of the surgery. In two different studies, the quality of life of patients with and without DLR was examined and it was reported that the postoperative quality of life was similar between those with and without DLR (8,13). In studies evaluating the quality of life of patients who underwent DLR alone, it was shown that the quality of life after DLR increased significantly (6,7). In our study, when compared to the SSF group, the quality of life of the SSF+DLR group at the 1st and 5th years was significantly better. In addition, it was determined that the quality of life at the 5th year had significantly decreased in the SSF group compared to the 1st year. Quality of life can be affected by many variables. If we interpret the difference in the quality of life found in our study within the scope of ankle surgery, it can be said that better radiographic and functional results after DLR may have been associated with the increased quality of life in patients.

The most important strength of our study is that it is the first study in which the mid- and long-term effects of DLR+SSF surgery were evaluated comprehensively -with respect to functional and radiographic results and quality of life- in patients with distal fibula fractures. In addition, to our knowledge, there are no previous studies that have examined the effects of additional DLR application on osteoarthritis findings in long-term follow-up. We believe the comprehensive analysis of patients and the long-term follow-up of patients are important highlights of our study.

Study Limitations

The facts that the study design is retrospective and it is a single-center study are important limitations. Muscle-strengthening exercises, nutritional status, body mass index, physical activity level, ankle protective behaviors, and complication development status were not examined. Different distribution of such variables among groups may have affected the results. The scores and some measurements of the cases were not evaluated in the preoperative and early postoperative periods, except for MCS. Therefore, it could not be interpreted whether the differences in scores (AOFAS, SF-36, and radiographic scores) that were present at the postoperative comparisons existed before the surgery, but considering the similarities between the groups, it is feasible to assume that the distribution of these scores before the operation was similar between the groups.

Conclusion

In this study, when compared to syndesmotic fixation in distal fibula fractures, it was found that performing DLR in addition to syndesmotic fixation (despite longer operation duration) is superior in terms of radiographic results, functional results, and quality of life in both the mid and long term. In addition, while results appeared to be worsening at long-term assessment in the SSF group, the positive results were persistent in the SSF+DLR group. Performing DLR in

appropriate cases in distal fibula fractures may contribute to better clinical outcomes in the mid-long term. These inferences can be supported by more comprehensive and prospective future studies.

Ethics

Ethics Committee Approval: All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The ethical approval was obtained from Maltepe University Faculty of Medicine Ethics Committee (no: 2021/900/41).

Informed Consent: Written informed consent was obtained from all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.Z.D., Ö.K.Ü., Design: M.Z.D., Ö.K.Ü., Data Collection or Processing: M.Z.D., Analysis or Interpretation: M.Z.D., Ö.K.Ü., Literature Search: M.Z.D., Ö.K.Ü., Writing: M.Z.D.

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ORIGINAL RESEARCH

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Evaluation of the Relationship Between the Severity of the Disease, the Neutrophil/Lymphocyte Ratio and CRP in Children with Bronchiolitis

Bronşiolit Tanısıyla İzlenen Çocuklarda Hastalığın Şiddeti ile Nötrofil/Lenfosit Oranı ve CRP Arasındaki İlişkinin Değerlendirilmesi

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Abstract

Objective: In this study, we aimed to evaluate the relationship among neutrophil-lymphocyte ratio (NLR), C-reactive protein (CRP) and disease severity in 0-2-year-old children diagnosed and hospitalized with bronchiolitis.

Method: This retrospective cross-sectional study includes 158 patients aged 0-2 years, who were hospitalized for bronchiolitis between 01.12.2018 and 04.01.2020 in University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital's Pediatrics Clinic. Patients' age, gender, laboratory results and disease severity scores were recorded. According to this, disease severity was categorized as mild, moderate and severe.

Results: No statistically significant difference was observed among the scores of disease severity, mean age of the groups and gender distribution (p=0.061, p=0.392). However, a statistically significant difference was found between the disease severity score and the neutrophil/lymphocyte (N/L) ratios (p=0.007). The N/L ratio of the "mild" group was seen as statistically significantly lower than that of the "moderate" and "severe" groups (p=0.003, p=0.006). No statistically significant correlation was detected among the disease severity score, mean age of the moderate and severe groups (r=0.081 p=0.311). A statistically significant difference was witnessed between the disease severity score and CRP values (p=0.014). The CRP values of the group with mild disease were realized to be significantly lower than that of the group with moderate severity (p=0.04).

Conclusion: An increase in the NLR along with CRP is associated with the clinical severity and is a beneficial parameter that can be used

Öz

Amaç: Çalışmamızda çocuk servisinde yatırılarak tedavi edilen bronşiolit tanısı alan 0-2 yaş arası çocuklarda nötrofil-lenfosit oranının (NLO) ve C-reaktif proteinin (CRP) hastalık şiddeti ile ilişkisinin değerlendirilmesi amaçlanmıştır.

Yöntem: Bu retrospektif kesitsel çalışmaya Sağlık Bilimleri Üniversitesi, İstanbul Bağcılar Eğitim ve Araştırma Hastanesi Çocuk Servisi'nde 01.12.2018-04.01.2020 tarihleri arasında bronşiolit nedeniyle yatırılarak takip edilen 0-2 yaş arası 158 hasta dahil edildi. Hastaların yaşı, cinsiyeti, laboratuvar sonuçları ve hastalık ciddiyet skorları kaydedildi. Bu skorlamaya göre hastalık ciddiyeti hafif, orta ve ağır olarak değerlendirildi.

Bulgular: Hastalık ciddiyet skoru ile grupların yaş ortalamaları arasında ve cinsiyet dağılımları arasında istatistiksel olarak anlamlı farklılık gözlenmemiştir (p=0,061, p=0,392). Hastalık ciddiyet skoru ile nötrofil/lenfosit (N/L) oranı değerleri arasında istatistiksel olarak anlamlı farklılık gözlenmiştir (p=0,007). Hafif grubun N/L oranı orta ve ağır gruplardan istatistiksel olarak anlamlı derecede düşük bulunmuş (p=0,003, p=0,006), orta ve ağır grupların hastalık ciddiyet skoru ile yaş değerleri arasında istatistiksel olarak anlamlı korelasyon gözlenmemiştir (r=0,081 p=0,311). Hastalık ciddiyet skoru ile CRP değerleri arasında istatistiksel olarak anlamlı farklılık gözlenmiştir (p=0,014). Hastalık ciddiyeti hafif grubun CRP değerleri ciddiyeti orta olan gruptan anlamlı derecede düşük bulunmuştur (p=0,04).

Sonuç: NLO'da artış CRP ile birlikte bronşiolit tanılı hastaların klinik ciddiyetiyle ilişkilidir ve çocuk servisinde yatan 0-2 yaş arası bronşiolit

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Abstract

for evaluating the prognosis of 0-2-year-old hospitalized patients with bronchiolitis.

Keywords: Bronchiolitis, CRP, disease severity, neutrophil lymphocyte ratio

Öz

tanılı hastaların prognozunu değerlendirmek için kullanılabilecek faydalı bir parametredir.

Anahtar kelimeler: Bronşiolit, CRP, hastalık ciddiyeti, nötrofil lenfosit oranı

Introduction

Acute bronchiolitis mostly affects infants and is characterized by acute respiratory distress. Edema is an inflammatory process characterized by obstruction of bronchioles with mucus and cellular debris. Respiratory syncytial virus (RSV), being the most common, rhinoviruses, influenza virus, parainfluenza viruses, coronaviruses, metapneumovirus and rarely other respiratory tract viruses can also be the cause.

The most common cause of lower respiratory tract disease in infancy is acute bronchiolitis (1). Although it can be encountered in all seasons, it is mostly seen in winter, especially between October and May. It generally affects infants. It is the most common cause of hospitalization in this age group (2,3). Airway inflammation, epithelial cells, macrophages, cytotoxic T-cells and eosinophils play a role in the pathogenesis of bronchiolitis (1). Moreover, it has been shown that neutrophil assembly is predominant in acute bronchiolitis (4). It has been reported that chemokines associated with high levels of neutrophils are increased in nasal and tracheal fluid samples taken from infants with RSV bronchiolitis (5). It has been shown previously that inflammation associated with IL-8 is correlated with the severity of the disease in patients with bronchiolitis (6). The diagnosis of bronchiolitis is mainly based on clinical findings, but acute phase reactants are also important in evaluating the clinical course of the disease. The most commonly used acute phase reactants in the clinic are blood leukocyte count (WBC), erythrocyte sedimentation rate (ESR), serum C-reactive protein (CRP) and serum procalcitonin (5,6). Neutrophil/lymphocyte ratio (NLR), which is lately being used frequently, is a parameter used to evaluate inflammation and the clinical course of diseases.

In our study, it was planned to evaluate the relationship between NLR (which is an easily accessible and inexpensive parameter) and bronchiolitis severity score.

Materials and Methods

In this study, 158 patients in the 0-2 age group, who were hospitalized and treated with the diagnosis of bronchiolitis in University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital Pediatric Clinic between 1 December 2018 and 4 January 2020, were evaluated. Ethical approval for the study was obtained from University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital Ethics Committee (decree no: 2020.01.1.02.002, date 10.01.2020). Written informed consent was obtained in accordance with the Declaration of Helsinki.

Patients with severe immune deficiency, chronic neurological or cardiac disease and the children whose families did not approve to participate in the study were excluded from the study.

The diagnosis of bronchiolitis was made based on clinical findings. The patients had increased respiratory rate, chest retractions and wheezing. Prolonged expirium and sibilant rhonchi were detected. It was learned that the patients had upper respiratory tract infection symptoms such as runny nose, cough and mild fever 1-2 days before applying to the clinic. Radiologically, excess aeration in both lungs (parallelization of the ribs, flattening of the diaphragm, reduction in the mediastinum and heart area), peribronchial infiltrates and atelectasis were observed.

Grading of the disease: A scoring system taking into account the respiratory rate per minute, wheezing, retractions and general condition of the patient was used to evaluate the severity of the disease (7). According to this scoring system, patients were divided into three groups as mild, moderate and severe (Table 1).

Table 1. Acute bronchiolitis classification

	Mild	Moderate	Severe
Apnea	Absent	Absent	+
Respiratory rate/min	<50	50-70	>70
Heart rate/min	<140	140-160	>160
Retractions	Mild	Moderate	Severe
SaO_2	>93%	86-92%	<85%
Cyanosis	Absent	Absent	+
Necessary FiO_2 for SaO_2>93%		0.21-0.4	>0.4

For complete blood count, 1-2 mL of blood was taken into an EDTA tube and studied in a Beckman Coulter (LH750) machine, and the NLR of the patients was calculated.

Statistical Analysis

In this study, statistical analyses were performed with the NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) package program. In the evaluation of the data, the distribution of variables was examined with the Shapiro-Wilk normality test as well as descriptive statistical methods (mean, standard deviation, median, interquartile range), One-Way analysis of variance in intergroup comparisons of normally distributed variables, independent t-test in comparison of paired groups, Kruskal-Wallis test in intergroup comparisons of non-normally distributed variables, Dunn's multiple comparison test in subgroup comparisons, chi-square test in comparisons of qualitative data, Pearson correlation test in comparison of variables with each other. The results were evaluated at the significance level of $p<0.05$.

Mean, standard deviation, median, lower limit and upper limit summary criteria were given for continuous variables such as laboratory values. According to the distribution of these variables in the comparison of the groups; the t-test or One-Way analysis of variance was used in independent groups in normal distribution, the Mann-Whitney U test or Kruskal-Wallis test was used if not normally distributed. Number and percentage summary criteria were given for categorical variables such as gender and age. Chi-square test statistics were used to compare these in groups.

Results

Of the 158 patients included in the study, 96 (60%) were male and no statistically significant difference was found between gender and disease severity (p=0.392) (Table 2). According to the disease severity scoring, 42 cases were mild with a mean age of 4.86±4.41 months, 9 cases were moderate with a mean age of 7.36±6.31 months, and 19 cases were severe with a mean age of 6±5.31 months. No statistically significant difference was observed between the disease severity score and the mean age (p=0.061) (Table 2).

The mean N/L ratio of the group with mild severity score was 0.69±0.52, the median value was 0.54 (0.31-0.88), the mean N/L ratio of the group with moderate severity score was 1.66±1.99, the median value was 0.84 (0.44-2.34), and the mean N/L ratio of the group with severe severity score was 1.6±1.51, and the median value was 1.10 (0.49-1.94). Statistically significant difference was observed between the groups (p=0.007) (Table 3).

The mean CRP of the group with low disease severity score was found to be statistically significantly lower than that of the group with moderate disease severity (p=0.014), and no statistically significant difference was observed between the other groups (p>0.05) (Table 3). The relationship between CRP and disease severity score is given in Graph 1.

The mean N/L ratio of the group with mild disease severity score was found to be statistically significantly lower than that of the groups with moderate and severe severity score (p=0.003, p=0.006), and no statistically significant difference was observed between the groups with moderate and severe disease severity scores (p=0.003, p=0.006 =0.533) (Table 4) (Graph 2).

Table 2. Relationship between patient's age and gender and disease severity score

		Disease severity score						p
		Mild n=42		Moderate n=9		Severe n=19		
Age (months)		4.86±4.41		7.36±6.31		6±5.31		0.061
Gender	**Male**	23	54.76%	63	64.95%	10	52.63%	0.392
	Female	19	45.24%	34	35.05%	9	47.37%	

Table 3. Relationship between CRP and N/L ratio and disease severity score

		Disease severity score			
		Mild n=42	Moderate n=9	Severe n=19	
CRP	**Mean ± SD**	12.49±30.4	23.5±46.38	16.87±36.19	**0.014**
	Median (IQR)	4.35 (1.22-12.65)	11.04 (3.07-22.85)	4.33 (1.84-18.18)	
N/L ratio	**Mean ± SD**	0.69±0.52	1.66±1.99	1.6±1.51	**0.007**
	Median (IQR)	0.54 (0.31-0.88)	0.84 (0.44-2.34)	1.10 (0.49-1.94)	

CRP: C-reactive protein, SD: Standard deviation, N/L: Neutrophil/lymphocyte, IQR: Interquartile range

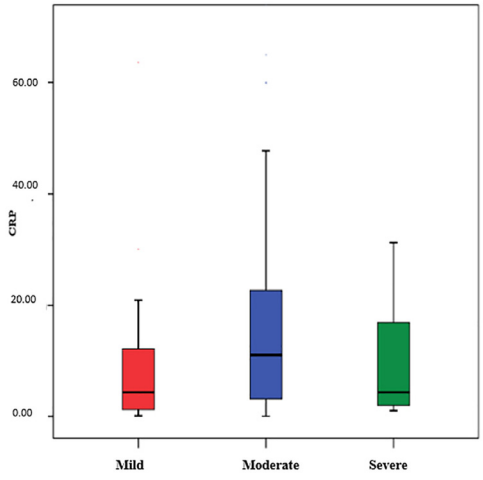
The mean CRP of the group with low disease severity score was found to be statistically significantly lower than that of the group with moderate disease severity (p=0.04), no statistically significant difference was observed between the other groups (p>0.05) (Table 4) (Graph 3).

While no statistically significant correlation was found between the disease severity score and age (r=0.081, p=0.311), a statistically significant positive correlation was observed between the disease severity score and the mean N/L ratio (r=0.206 p=0.009) (Table 5).

Discussion

The diagnosis of bronchiolitis is based on symptoms and physical examination findings, supported by complete blood count, serological tests and chest X-rays (8). Acute bronchiolitis is a limited inflammation of the tracheobronchial tree with edema and increased secretion in the mucosa of the large airways, and the use of antibiotics is usually unnecessary in treatment (9,10). The clinical course may be more severe in cases with immunodeficiency, chronic lung disease, congenital heart disease or a history of premature birth. Laboratory tests (CRP values/CRP, mean platelet volume) were found to have no effect on predicting clinical severity (11,12).

As a parameter, NLR is an inexpensive and easy to measure for determining the severity of diseases. NLR has been used in many studies and has recently been a frequently studied value in oncology and cardiovascular system patients (13-15). A decrease in the number of lymphocytes, an increase in the number of neutrophils and a relative increase in NLR have been shown in previous studies in case of systemic inflammatory response (16-18).



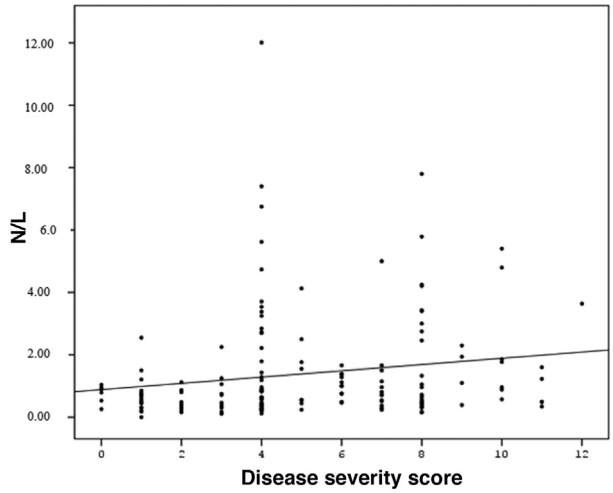
Graph 1. Relationship between CRP and disease severity score

CRP: C-reactive protein

Table 4. Comparison of CRP and N/L ratios of the groups

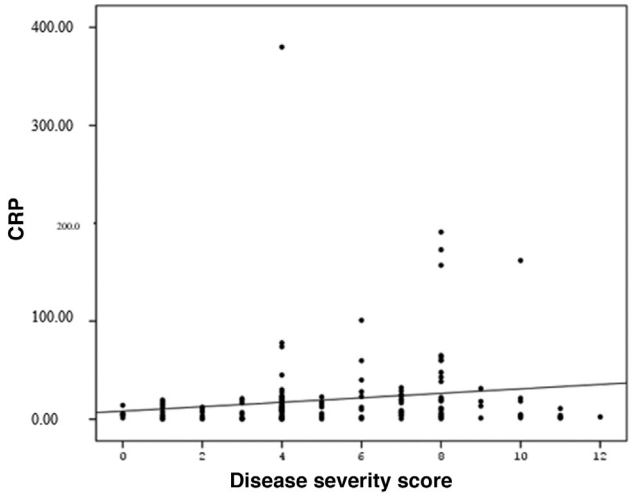
	CRP p	N/L p
Mild/moderate	**0.04**	**0.003**
Mild/severe	0.342	**0.006**
Moderate/severe	0.240	0.533

CRP: C-reactive protein, N/L: Neutrophil/lymphocyte



Graph 2. Relationship between N/L ratios and disease severity score

N/L: Neutrophil/lymphocyte



Graph 3. Relationship between CRP and disease severity score

CRP: C-reactive protein

It is important to accurately determine the treatment plan of pediatric bronchiolitis patients. Auxiliary parameters are needed in the decision-making process. For this purpose, various scoring systems have been developed. Some blood tests are also used as a parameter of these scoring systems to help in diagnosis and treatment (19). Huang et al. (20) reported that NLR was associated with disease severity in patients with community-acquired pneumonia. Zahorec (21) reported that lymphocyte percentage decreased in sepsis and systemic inflammatory response in their study. This is explained by the increase in neutrophil ratio and decrease in lymphocyte ratio in inflammatory response states. Hwang et al. (22) reported that NLR could be used as an inexpensive and easy prognostic marker in septic and critically ill patients. In our study, it was observed that as the severity of bronchiolitis increased, neutrophils increased, and lymphocytes decreased, which was reflected as an increase in NLR. At the same time, in our study, it was observed that the CRP value increased in proportion to the severity of the disease, and the increase in both CRP and NLR in proportion to the severity of the disease is an indicator of the increase in these parameters with inflammation, which is compatible with the previous literature.

In a study by de Jager et al. (23), it was found that there was a correlation between high NLR and increased mortality in chronic diseases. In another study by de Jager et al. (24), high NLR was found to be more valuable than leukocyte and neutrophil values in predicting bacteremia in the emergency department. In a study by Yoon et al. (25) on tuberculosis and bacterial pneumonia patients, NLR was found to be significantly higher in bacterial pneumonia patients.

In our study, the increase in NLRs in accordance with the severity of the disease in pediatric patients with bronchiolitis supports previous studies. As the severity of the infection increases, the neutrophil ratio increases and the lymphocyte ratio decreases. Bronchiolitis can have a serious course especially in young children and may result in pediatric intensive care unit admittance. Therefore, we think that NLR, which is an inexpensive and easy parameter, can be meaningful and important in terms of showing the course of the disease.

Table 5. Relationship between age (months), CRP and N/L ratio and disease severity score

		Disease severity score
Age (months)	**r**	0.081
	p	0.311
CRP	**r**	**0.159**
	p	**0.046**
N/L	**r**	**0.206**
	p	**0.009**

CRP: C-reactive protein, N/L: Neutrophil/lymphocyte

In a study by Çelik Güzel et al. (26) it was found that while NLR increased as the severity of the disease increased in children with acute bronchiolitis similar to our study, CRP did not increase in line with the severity of the disease. In our study, CRP also increased in line with the severity of the disease.

Bircan et al. (27) reported that the severity of pneumonia was related to the level of CRP, and that there was a statistically significant difference between CRP, WBC and ESR values in inpatients and outpatients. In another study conducted in our country, the severity of pneumonia was found to be associated with high CRP and WBC levels, while there was no difference in ESR and fibrinogen. In addition, a statistically significant relationship was found between mortality and high CRP (28).

Study Limitations

The limitations of our study are that it was a retrospective study and NLR was not compared with a healthy control group of same age and gender. The positive side of our study is that disease severity scoring was used to evaluate the patients.

Conclusion

NLR is a systemic inflammatory response marker that has been used increasingly in recent years. The fact that it is cheap, easily accessible and useful as clinically demonstrated in previous studies increase its value.

Increased neutrophil lymphocyte ratio and CRP are associated with the clinical severity of bronchiolitis, and can be used to determine the severity of the disease in pediatric patients aged 0-2 years with a diagnosis of bronchiolitis.

Ethics

Ethics Committee Approval: Ethical approval for the study was obtained from University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital Ethics Committee (decree no: 2020.01.1.02.002, date 10.01.2020).

Informed Consent: Written informed consent was obtained in accordance with the Declaration of Helsinki.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: Ö.G., M.E., Design: Ö.G., M.E., Data Collection or Processing: Ö.G., A.Ö., Ö.B., Analysis or Interpretation: Ö.G., M.E., Ö.B.G., Drafting Manuscript: M.E., Ö.B.G., Ö.B., Critical Revision of Manuscript: Ö.B.G., A.Ö., Final Approval and Accountability: M.E., Ö.B.G., A.Ö., Technical or Material Support: Ö.B., M.E., Supervision: M.E., Ö.B.G.

Conflict of Interest: No conflict of interest was declared by the authors.

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ORIGINAL RESEARCH

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Investigation of the Effect of Protamine-heparin Dose Ratio Adjustment on Intraoperative Graft Patency and Postoperative Bleeding

Protamin-heparin Doz Oranının Değiştirilmesinin İntraoperatif Greft Açıklığı ve Postoperatif Kanama Üzerine Etkisinin İncelenmesi

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Abstract

Objective: The use of systemic anticoagulation and protamine is an indispensable issue for cardiopulmonary bypass. We aimed to investigate the effect of protamine administration in different doses on intraoperative graft opening and postoperative bleeding amounts.

Method: Eighty patients scheduled for isolated coronary artery bypass surgery were divided into two equal groups. One group was administered at a ratio of 1:1 (group 1) and the other group (group 2) at doses of 1:0.75 (heparin: protamine). The demographic characteristics of the groups, operative data, and postoperative follow-up parameters were compared. Transit time flow measurement (TTFM) measurements were performed on the grafts used. The amounts of bleeding and transfusion were compared.

Results: Demographic characteristics and operative data of both groups were similar. Pulsatility index value was found to be high in TTFM measurements in the saphenous vein used in one patient in group 1 (thrombus in the saphenous vein). In group 2, a high flow was found in the left internal mammary artery in one patient (vasospasm). Although the erythrocyte suspension transfusion amount was partially higher in group 2, it was not statistically significant (p=0.909). The amount of fresh frozen plasma used in group 2 was significantly higher (p=0.001). Also, there was no significant difference in terms of drainage amounts (p=0.968).

Conclusion: An unnecessary excess of protamine dose does not have a positive effect on bleeding and transfusion amounts. On the contrary, it may facilitate intraoperative graft occlusion. Studies with larger patient numbers are needed for stronger interpretations.

Keywords: Bleeding, coronary bypass, graft patency, protamine

Öz

Amaç: Kardiyopulmoner baypas için sistemik antikoagülasyon vazgeçilmez bir konudur. Bu amaçla kullanılan heparin kadar bu etkiyi ortadan kaldıran protamin de çok önemlidir. Ancak az yapılması kadar fazla yapılması da birtakım yan etkilere neden olabilmektedir. Çalışmamızda farklı dozlarda yapılan protamin uygulamasının intraoperatif greft açıklığı ve postoperatif kanama miktarları üzerine etkisinin araştırılması amaçlanmıştır.

Yöntem: İzole koroner arter baypass cerrahisi yapılması planlanan 80 hasta iki eşit gruba ayrıldı. Bir gruba 1:1 oranında (grup 1) diğer gruba (grup 2) ise 1:0,75 (heparin: protamin) dozlarında uygulama yapıldı. Grupların demografik özellikleri, operatif verileri (baypas süresi, klemp süresi, sıcaklık, aktif pıhtılaşma zamanı değerleri vb.), postoperatif takip parametreleri karşılaştırıldı. Hastalara kullanılan greftlerde transit time flow measurement (TTFM) ölçümleri yapıldı. Kanama miktarları ve transfüzyon miktarları kaydedildi ve karşılaştırıldı.

Bulgular: Gruplar arasında demografik özellikler açısından farklılık görülmedi. Operatif veriler (kardiyopulmoner bypass süresi, klemp süresi, sıcaklık vb.) açısından her iki grubun verileri benzer nitelikteydi. Grup 1'de bir hastada kullanılan safen vendeki TTFM ölçümlerinde pulsatilite indeksi değeri yüksek bulundu (safen vende trombüs). Diğer grupta da bir hastada sol internal meme arterinde akım yüksek bulundu (vazospazm). Eritrosit süspansiyonu transfüzyon miktarları grup 2'de kısmen fazla olmasına rağmen istatistiksel olarak anlamlı değildi (p=0,909). Grup 2'de kullanılan taze donmuş plazma miktarı anlamlı olarak fazla idi (p=0,001). Yine aynı şekilde drenaj miktarları açısından anlamlı bir farklılık yoktu (p=0,968).

Sonuç: Heparin ve protamin kalp cerrahisi için vazgeçilmez iki ilaçtır. Ancak protamin dozunun gereksiz miktarda fazla yapılmasının kanama ve transfüzyon miktarları için olumlu bir katkısı olmamakla beraber aksine intraoperatif greft tıkanıklıkları için kolaylaştırıcı etki yapabilmektedir. Bu konuda daha güçlü yorumlar için daha geniş hasta sayıları ile çalışmalara ihtiyaç duyulmaktadır.

Anahtar kelimeler: Greft açıklığı, kanama, koroner baypas, protamin

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Introduction

Heparin and protamine are indispensable drugs for open heart surgery. Heparin-protamine balance gains importance in all surgical interventions using a cardiopulmonary bypass (CPB) device. Thanks to the presence of an effective antidote such as protamine sulfate, heparin can be used safely at high doses in cardiac surgery (1). Protamine is widely used to eliminate the effect of heparin after weaning from CPB (2). Like many drugs used, both overdose and low dose administrations may have some unwanted consequences. Although it is actually applied to eliminate the effect of heparin, it can have an anticoagulant effect when applied in large amounts (3,4). There are studies showing that protamine causes dysfunction in platelet functions and thus may cause coagulation disorders (5,6). Since it is a drug with serious side effects, dose adjustment is very important. These side effects are particularly important after a major surgical intervention, such as cardiac surgery, where the risk of bleeding is high and difficulties in hemodynamic stabilization may be experienced. In many centers where cardiac surgery is performed, heparin dose is calculated according to body weight. This may cause high-dose heparin administration, especially in the overweight patient group, and consequently, high-dose protamine after surgery (7). Low activated clotting time (ACT) values that will occur with the effect of high doses of protamine will predispose to thrombus formation and thromboembolic events at different levels, especially in newly anastomosed grafts. In addition, unwanted consequences may occur in patients who already have bleeding potential, as the heparin-protamine balance cannot be fully adjusted.

There are many factors that can cause bleeding in cardiac surgery. Most important of these factors are preoparative drugs, changes in the inflammatory system, the negative effect of the heart-lung machine on the coagulation system, hypothermia, and a decrease in hematocrit levels (8,9). It is very important to reduce the factors that may cause non-surgical leakage bleeding as much as possible.

Another important issue in coronary artery bypass surgery is that the grafts made have good flow. Especially in the early period, technical problems, vascular structures and blockages may occur with thrombotic mechanisms. It is also important to be able to detect graft thrombosis that may occur with overdose of protamine. One of the intraoperative methods that can be used for this purpose is transit time flow measurement (TTFM).

The aim of this study is to investigate the changes in the protamine dose and the amounts of bleeding and transfusion and also to examine the effect of dose adjustment on intraoperative graft patency. This study is the first to examine the effect of protamine dose adjustment on intraoperative graft patency.

Materials and Methods

Method of Study, Patient Selection

A work permit was obtained from the ethics committee of the institution, to which our clinic is affiliated (Atatürk University Clinical Research Ethics Committee. decision no: 18, decision date: 01.10.2020). After getting ethics committee approval, patients who were prospectively planned for isolated coronary artery bypass grafting surgery in our clinic between January 2021 and July 2021 were informed and their consent was obtained. LITA graft was used in both groups. Saphenous vein was used for other grafts (mean 2.9±0.74 grafts were used in group 1 and 2.77±0.69 grafts were used in group 2). Only the perfusionist knew which group the patients would be in, and they were divided into two groups, respectively.

When choosing patients in both groups, the inclusion criteria were determined as that isolated coronary artery bypass grafting operation would be performed under CPB and patients would be at the age of 18-75 years.

On the other hand, using anticoagulants and antiaggregants 48 hours before the operation, receiving dialysis treatment, and needing mechanical support after the operation were determined as the exclusion criteria.

The patients in the first group were administered protamine at a ratio of 1:1 according to the total amount of heparin administered during the CPB period, as in routine practice. Three quarters of the routine protamine dose was administered to the patients in the second group and ACT control was performed. TTFM evaluation was performed on all grafts in all patients after protamine. Demographic data, Euroscore II values, intraoperative and postoperative blood transfusion amounts, pre- and postoperative laboratory values, ACT values (preop, post-protamine, 1st hour in intensive care), TTFM values (after protamine) and follow-up parameters were compared.

ACT Measurement Method

Measurements were made with the Actalyke^{R} MINI (Activated Clotting Time Test System-Helena Laboratories, Beamont, Texas USA, 77704) device in the operating room.

This device uses the 2-point clot detection feature and starts ACT measurement immediately after the ACT Tube is inserted. Celite is used inside the tube (Actalyke® C-ACT).

TTFM Measurement Method

The technique was developed to evaluate graft quality and to measure the blood flow through the graft with its special probe. The device our clinic used is the MediStim VQ1101, MediStim ASA (Oslo, Norway). With this technique, the diastolic filling, mean flow, and pulsatility index (PI) can be measured. The first measurements were made when the anastomoses of the grafts were finished and the heart started to work again (the mean arterial pressure was 50-60 mmHg). Later, second measurements were made after protamine was administered when CPB was terminated. Based on the data from similar studies and recommendations from the manufacturer, we accepted the PI value as the main criterion for flow quality. Intergroup comparisons were made according to the post-protamine data.

Heparin-protamine Applications

ACT was checked before heparin was administered to patients in both groups, as in routine practice. Heparin was administered according to body weight (400 IU/kg). When ACT fell below 480, an additional dose of heparin was administered with the decision of the perfusionist. At the end of the surgical procedure, after weaning from CPB, all of the protamine dose (1:1, ie 1.0 mg/100 IU) calculated for complete neutralization was applied to the first group. In the second group, three-quarters of the full neutralization dose was administered. In the second group, three-quarters of the full neutralization dose was administered based on previous studies (8-10).

As the study endpoints, the primary endpoint was ACT values (200 and above), and the secondary endpoint was the amount of drainage, transfusion amount and bleeding revision.

Statistical Analysis

NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used for statistical analysis. While evaluating the study data, in addition to descriptive statistical methods (Average, standard deviation, median, frequency, ratio, minimum, maximum), the distribution of the data was evaluated using the Shapiro-Wilk test. The Mann-Whitney U test was used to compare two groups that did not show normal distribution of quantitative data. The Student's t-test was used to compare the quantitative data between two groups showing normal distribution. The significance was evaluated at the level of $p<0.05$.

Results

Eighty patients, including 40 patients in each group, were included in the study. Two patients were excluded from the study because they were discharged with the help of an intraaortic balloon pump after the operation. There was no difference between the groups in terms of age, gender, body mass index, Euroscore II values, and comorbid factors (Table 1). None of the patients used anticoagulants other than low molecular weight heparin in the preoperative period (last 48 hours). There was no significant difference in the preoperative and postoperative laboratory data of the patients (Table 2). All patients were cooled to 32 degrees (rectal) body temperature during operations and were operated by the same surgical team. There was no difference in intraoperative data (such as CPB duration, cross-clamping time, minimum body temperature, blood gas monitoring) between the groups (Table 3).

Table 1. Demographic data

	Group 1 (n=40)	Group 2 (n=40)	p
Age (years)	64.95±7.7	62.43±9.68	0.200[a]
Gender (M/F)	29 (72.5%)/11 (27.5%)	32 (80%)/8 (20%)	0.599
COPD (n/%)	7 (17.5%)	7 (17.5%)	0.999
Hypertension (n/%)	19 (47.5%)	22 (55%)	0.655
Hyperlipidemia (n/%)	12 (30%)	14 (35%)	0.811
Diabetes mellitus (n/%)	14 (35%)	12 (30%)	0.811
PVD (n/%)	2 (5%)	1 (2.5%)	0.556
BMI (kg/m^2)	30.2±2.84	29.5±2.73	0.264[a]
BSA (m^2)	1.98±0.16	1.95±0.13	0.256[a]
Euroscore II	1.08±0.54	1.19±0.42	0.314[a]

COPD: Chronic obstructive pulmonary disease, BMI: Body mass index, PVD: Peripheral vascular disease, BSA: Body surface area, [a]: Student's t-test

The results of the ACT values that form the basis of the study are given in Table 4. There was no difference in terms of preop ACT values (p=0.114). There was no difference in terms of ACT values measured while CPB was continuing (p=0.412). However, ACT values measured after protamine were high in group 2, which was statistically significant (p=0.001). While the amount of protamine administered in group 1 was 32225±4500 IU on average, it was 26145±3250 IU in group 2. Although there was no statistically significant difference in the TTFM values measured after protamine in the patients, in the higher dose protamine group, a fresh thrombus was detected in the control performed because the saphenous vein graft (circumflex artery) was not flowing well, and the patency was restored with embolectomy. In the other group, low flow was measured in the left internal mammarian artery (LIMA) anastomosis of one patient.

Table 2. Preoperative and postoperative laboratory data

		Group 1 (n=40)	Group 2 (n=40)	p
WBC (K/mm^3)	Preop	7.96±1.87	7.94±1.94	0.977[a]
	Postop 1 day	12.35±2.42	12.07±2.48	0.614[a]
Hgb (g/dL)	Preop	14.02±1.63	13.69±1.27	0.249[b]
	CPB entry	7.34±0.57	7.48±0.62	0.321[a]
	CPB 20 minute	7.27±0.58	7.55±0.64	***0.046[a]**
	CPB output	7.44±0.57	7.61±0.54	0.188[a]
	Postop 1 day	8.77±0.72	8.59±0.54	0.294[b]
Hematocrit (%)	Preop	41.88±5.02	40.37±4.46	0.158[a]
	CPB entry	22.53±1.74	23.03±1.72	0.200[a]
	CPB 20 minutes	21.41±2.61	23.12±1.65	0.346
	CPB output	28.15±2.22	22.84±1.36	0.329[a]
	Postop 1 day	26.87±1.9	26.31±1.67	0.160[a]
Platelet (K/mm^3)	Preop	234±67.53	233.85±67.32	0.992[a]
	Postop 1 day	190.33±32.18	185.95±39.46	0.588[a]
Calcium (mg/dL)	Preop	9.24±0.8	9.43±0.68	0.247[a]
	CPB entry	1.26±0.1	1.28±0.09	0.282[a]
	CPB 20 minutes	1.29±0.09	1.38±0.11	0.321
	CPB output	1.28±0.1	1.3±0.08	0.285[a]
INR	Preop	1.04±0.1	1.07±0.1	0.189[a]
	Postop 1 day	1.11±0.09	1.1±0.08	0.605[a]
aPTT (sec)	Preop	31.3±3.82	34.08±5	****0.007[a]**
	Postop 1 day	29.78±3.86	32.3±5.61	***0.038[b]**

[a]Student's t-test, [b]Mann-Whitney U test, *p<0.05, **p<0.01, WBC: White blood cell, Hgb: Hemoglobin, INR: International normalized ratio, aPTT: Activated partial thromboplastin tim

Table 3. Operative/postoperative data and total drainage amounts

	Group 1 (n=40)	Group 2 (n=40)	p
CPB time (min)	90.93±10.94	89.85±15.28	0.718[a]
X-clamp time (min)	50.13±8.82	52.33±9.77	0.294[a]
Body temperature (°C)	31.87±0.85	31.29±4.63	0.310[b]
Total drainage (mL)	822.63±162.24	820.75±241.06	0.968[a]
Bleeding revision (n/%)	1/2.5%	2/5%	0.624
Extubation time (hour)	7.27±1.5	6.86±1.15	0.180[a]
Red cell suspension transfusion (unit)	2.83±1.06	2.8±0.88	0.909[a]
Fresh frozen plasma (unit)	3.88±0.82	2.58±0.93	****0.001[a]**
Intraoperative FFP (unit)	1.89±0.61	1.93±0.58	0.341[a]

Student's t-test[a], Mann-Whitney U test [b], *p<0.05, **p<0.01, CPB: Cardiopulmonary bypass

Table 4. ACT values of both groups

	Group 1 (n=40)	Group 2 (n=40)	p
ACT preop	132.18±10.27	135.75±9.74	0.114[a]
CPB entry	714.55±157.38	684.58±167.75	0.412[a]
CPB 20 minute	699.1±111.85	706.15±120.39	0.787[a]
CPB output	651.98±66.46	684.15±125.78	0.157[a]
After protamine	136.05±8.66	146.4±8.24	**0.001[a]

[a] Student's t-test, **p<0.01, ACT: Activated clotting time, CPB: Cardio pulmonary bypass

However, this situation was considered due to spasm in LIMA and the problem was solved with local application of papaverine.

There was no difference between the two groups in terms of the amounts of intraoperative and postoperative blood transfusions (erythrocyte suspension, fresh frozen plasma and platelet suspension). Postoperative total drainage amounts were also similar between the groups. One patient from group 1 was revised due to bleeding (bleeding focus was in the saphenous vein branch) at the 5th hour postoperatively. The bleeding was excluded from the study because it was due to surgery.

Discussion

Protamine is an indispensable drug to eliminate the effect of systemic anticoagulation with heparin in cardiac surgery performed with CPB. When protamine is used in an appropriate amount, besides neutralizing the effect of heparin, administration of high doses can increase the amount of bleeding by making an anticoagulation effect with the opposite effect (2). Therefore, the amount of application is very important. In the light of available information, it is recommended that the dose of heparin/protamine be 1/1. However, discussions on this issue are still going on. In this study, we examined the effect of different doses of protamine on postoperative blood transfusion and drainage amounts, as well as intraoperative graft patency.

It has been shown in various studies that if the protamine dose is more than necessary for the neutralization of heparin, it increases the coagulation disorder state rather than improvement in hemostasis (8,9). For the occurrence of this situation, there are studies suggesting that it reduces thrombin formation and inhibits factor V activation (10). In the study conducted by Meesters et al. (8), a significant difference was shown in terms of thrombin levels between the patient groups who received two different doses. It was observed that the amount of blood transfusion due to low thrombin levels increased in the group with excess protamine (8). In our study, no difference was found between the groups in terms of blood transfusion amounts. We did not make a measurement in terms of thrombin levels, but we think that not high protamine dose may be effective in this regard.

Protamine structurally has a peptide structure consisting of 32 amino acids. With its cationic structure, it neutralizes the anionic heparin at a ratio of 1:1 (6). The metabolism and mechanism of action of protamine in the body change with the presence of heparin. While it has a shorter duration of action in the presence of heparin, a longer half-life occurs in the absence of heparin (11). In addition, while the heparin-protamine complex is metabolized from the liver, only protamine is eliminated by the kidneys (12). All this literature information shows that protamine applied above the heparin dose may have different effects than the desired effect. The main hematological side effects are its ability to cause thrombocytopenia (13) and decrease in platelet aggregation via thrombin (14). It has been shown in various studies that these possible side effects are in applications with a protamine/heparin ratio above 1. The absence of an application above this rate in our study suggests that our patients can be protected from these side effects. Even if the thrombotic situation in the saphenous vein graft was not sufficient to make a definite interpretation in a patient in whom the protamine dose was applied exactly, it suggests that the anticoagulant effect may also be at 1:1 doses because some of the heparin made before the pump may lose its effectiveness with the effect of the elapsed time. It is known that there are many factors that are effective in the occurrence of intraoperative or early postoperative graft occlusion in saphenous vein grafts. It should be kept in mind that excessive doses of protamine used to reduce surgical bleeding may contribute to this event.

Besides hematological side effects of protamine, immunological and inflammatory side effects have also been described. These mechanisms include hypotension, bradycardia, pulmonary vasoconstriction, and allergic reactions (15,16). Protamine administration is performed

during the period when CPB is terminated in cardiac surgery. Therefore, most of these side effects can be overlooked since they are associated with the surgery performed. Since the main focus of our study was not side effects, an analysis could not be made in this direction. However, the fact that these side effects have also been shown is important in terms of showing us the drawbacks of overdose of protamine. Particularly, hypotension (17) and pulmonary hypertension (18) side effects are very important as they may lead to unnecessary medical interventions after cardiac surgery (19). In fact, a study by Ocal et al. (20) showed that severe right ventricular failure and pulmonary hypertension developed with the effect of protamine.

The ability of protamine used after cardiac surgery to neutralize heparin is traditionally followed by ACT values. Returning to ACT values before the administration of heparin is considered as the main goal. In our study, where different protamine doses were applied, if ACT values were 20% higher than the first measurement in the measurements made after heparin, although additional doses of protamine were planned, this application was not required in any patient. Although it was higher on average in the low-dose protamine group compared to the other group, this height was not more than 20% in any patient. This situation made us think that adequate neutralization can be achieved even with lower protamine doses because the heparin left from the heparin used in CPB and needing to be neutralized is actually lower than the first dose of heparin.

Postoperative bleeding in cardiac surgery is a very disturbing situation. Surgeons who are afraid of this situation prefer high protamine dose to low. However, the data in the literature show that unnecessary protamine dose has an increasing effect rather than reducing postoperative bleeding. In our study, the fact that there was no difference in the amount of bleeding between the groups with different protamine doses seems to be consistent with this information.

Study Limitations

-Although there are studies showing that ACT alone is not sufficient for protamine dose adjustment, protamine dose adjustment was made by following the ACT value within the routine practice in our clinic.

-Since we do not use a system that determines the effect of heparin remaining from heparin used in CPB, the protamine dose was calculated according to the amount of heparin administered in total. Although this is the traditional approach, there are important studies claiming that this is not enough.

-While TTFM measurements measuring graft patency were performed, other causes that would disrupt the flow were excluded from the scope of the study. This situation made it difficult to interpret the effect of protamine on this issue (because other factors that could affect TTFM measurements were not analyzed in the study). Only problems caused by acute thrombus were included in the evaluation.

Conclusion

Two of the most important points in heart surgery are good graft patency and few bleeding complications. The effect of heparin for anticoagulation in CPB is neutralized by protamine. An excess of protamine dose sufficient to eliminate the effect of heparin does not have a positive additional effect on the amount of postoperative bleeding. In addition, although no analysis has been performed for other parameters that may affect TTFM measurements, we think that low-dose protamine will contribute positively to early intraoperative graft patency. Large randomized studies are needed on this subject.

Ethics

Ethics Committee Approval: A work permit was obtained from the ethics committee of the institution, to which our clinic is affiliated (Atatürk University Clinical Research Ethics Committee. decision no: 18, decision date: 01.10.2020).

Informed Consent: Consent certificate was taken from all patients for the study.

Peer-review: Externally peer-reviewed.

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CASE REPORT

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A Case Diagnosed Late with Suspicion: A Foreign Body Aspiration

Geciken ve Şüphe ile Çözülen Bir Tanı: Yabancı Cisim Aspirasyonu

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Abstract

Foreign body aspiration is the cause of a frequently seen respiratory problem in the pediatric population. It may be life threatening if diagnosed late. The clinical symptoms as well as physical examination findings are similar to those of upper and lower respiratory tract infections; therefore, it is easily missed.

A 15-month-old male patient came to emergency room with respiratory problems that started acutely. Physical examination showed symptoms that were consistent with upper respiratory tract obstruction; therefore, the patient was started on inhaler treatments. The chest X-ray and the primary examination with a laryngoscope showed no specific results. The patient was then admitted to pediatric intensive care unit in order to continue his treatment. The patient showed improvement in time; however, his condition declined as the dosage of the inhaler treatment was decreased. Second examination with a laryngoscope was performed and a foreign body in the larynx was found. The foreign body was removed in the operating room and the complaints of the patient were completely gone. Foreign body aspiration is a clinically important situation for the pediatric population due to the fact that it is seen very commonly and causes acute respiratory problems. The clinical findings are similar to those of upper and lower respiratory tract obstructions or infections and it can be diagnosed easily with a careful physical examination.

Keywords: Delayed diagnosis, foreign body aspiration, laryngoscopy, pediatrics

Öz

Yabancı cisim aspirasyonu, çocukluk çağında sık görülen bir solunum sıkıntısı nedenidir. Geç tanı konulduğunda hayatı tehdit eden durumlara yol açabilir. Klinik şikayetleri ve fizik muayene bulguları üst ve alt hava yolu enfeksiyonlarına benzer klinik tablolar oluşturduğundan tanıda kolaylıkla gözden kaçabilir.

On beş aylık erkek hasta çocuk acil servisimize ani başlayan solunum sıkıntısı ile başvurdu. Fizik muayene bulguları üst solunum yolu tıkanıklığı düşündüren hastaya ilk başta nebül tedavisi uygulandı. Çekilen toraks bilgisayarlı tomografisinde ve yapılan ilk laringoskopik muayenede özellik saptanmayan hasta takip ve tedavisinin devamı için çocuk yoğun bakım ünitemize yatırıldı. İlk başta tedaviye iyi yanıt veren fakat tedavinin azaltılmasıyla birlikte şikayetleri tekrar artan hastaya ikinci laringoskopik muayene yapıldı ve larinkste yabancı cisme rastlandı. Ameliyathane koşullarında çıkarılan cisim sonrası hastanın şikayetleri tamamen geriledi.

Yabancı cisim aspirasyonları çocukluk çağında sık görülmesi, ani solunum sıkıntısına yol açması, klinik bulguları ile üst ve alt solunum yolu tıkanıklığı ya da enfeksiyonu yapan nedenleri taklit etmesi ve dikkatli muayene ile kolaylıkla tanısının konulması nedeniyle çocukluk çağının önem arz eden durumudur.

Anahtar kelimeler: Gecikmiş tanı, laringoskopi, pediyatri, yabancı cisim aspirasyonu

Introduction

Foreign body aspiration to the tracheal-bronchial system is a commonly seen problem with important morbidity and mortality rates (1,2). It is seen mostly in male patients under three years old and causes 7% of deaths in this age group (3). Clinical findings differ depending on the location of the foreign body as well as whether the blockage is complete or partial (4). In some cases, because it can be confused with other reasons for respiratory problems, it

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may be diagnosed late. In our case study, we present a case of a male patient who came to the emergency room (ER) with acute respiratory problems, who was then followed at the pediatric intensive care unit (PICU) with physical findings of upper respiratory tract obstruction and treated accordingly. A further examination was performed with laryngoscope once the patient was non-responsive to medical treatment.

Case Report

A 15-month-old male patient came to the ER with respiratory problems, wheezing and coughing for the past three days. The patient's symptoms developed very acutely and he applied to several other centers. The provided treatments did not help the patient's symptoms; therefore, he came to our ER. Preliminary physical examination showed that overall status of the patient was average, and he was conscious. Respiratory system examination showed stridor and suprasternal retractions. Other system examinations had no particular findings. First blood gases showed pH: 7.41, pCO_3: 32 mmHg, HCO_3: 2.7, lactate: 0.9 and base excess: 3.6. There was no specific finding in the chest X-ray (Figure 1). The patient was started on ampicillin sulbactam and cephotaxime as antibiotics, salbutamol, budesonide and adrenalin as inhaler treatment and methylprednisolone and magnesium sulphate as bronchodilator treatment. Computed chest tomography was performed since the respiratory problems had an acute beginning, and an increase in peribronchial intensity and atelectasis in the right lung was seen. No foreign object was seen in the laryngoscopic examination performed by the ear nose throat doctor. The symptoms of the patient continued despite the treatment and interventions in the ER and the patient was then transferred to PICU.

Physical examination of the patient in the PICU showed the overall status of the patient to be average, conscious with Glasgow Coma scale of 15 (eyes: 4, verbal: 5, motor: 6). Respiratory system examination showed stridor with suprasternal retractions. 32 breaths per minute, heart rate of 100 beats/minute and blood pressure of 120/75 (90) mmHg were also noted. Examination of other systems showed no findings. Blood gases showed pH: 7.36, pCO_2: 39 mmHg, HCO_3: 21.2, lactate: 1.4, base excess: 2.3. Complete blood count showed leukocyte number as 15,280 (normal: 4.000-12,000), biochemical parameters showed C-reactive protein as 7.9 mg/L (normal: 0-5) and procalcitonin level resulted as 1.23 ng/mL (normal 0.02-0.5). The patient was started on ampicillin sulbactam 150 mg/kg/day in 3 equal doses, dexamethasone 0.15 mg/kg/dose in 4 doses, 3% hypertonic saline inhaler 3 cc/dose in 4 doses, ipratropium bromide inhaler 250 mcg/dose in 4 doses, salbutamol 0.15 mg/kg/dose in 8 doses and 1/1.000 inhaler epinephrine 3 mL/dose in 4 doses. The patient's condition improved with the treatment; however, once the dosing of the medication was decreased, the patient's symptoms increased. On the sixth day of the patient's follow-up, his condition got worsened and the patient was consulted to a ear, nose and throat specialist once more. The second laryngoscopic examination showed suspicion of a foreign body, unable to be identified to the edema in the lateral side of the vocal cord, and the patient was taken to the operating room. Direct laryngoscopic examination under anesthesia showed a foreign body located in the left pyriform sinus. The foreign body was removed using forceps (Figure 2). It was pumpkin seed shell (Figure 3). Following the operation, the patient's symptoms decreased immediately and was followed at the PICU one more day. Then, he was transferred to pediatric ward.

Discussion

Foreign body aspiration is commonly seen in children under 3 years old but can be seen in all age groups and is a pediatric emergency (5). Children under 3 years old are in constant movement in order to discover their surroundings and because their fine motor skills start developing, they bring everything they find into their mouths. However, since their dental development is not complete, they mostly

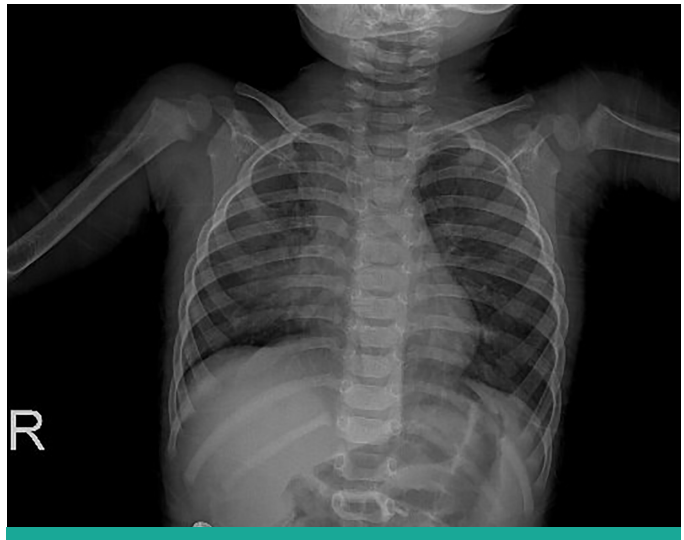

Figure 1. Chest X-ray in the ER
ER: Emergency room

fail at chewing (6). This increases the risk of aspiration of crustacean food.

Patient history is very important in the foreign body aspiration cases. The presence of someone who has witnessed the aspiration moment and the information that they provide help the diagnosis. However, in 1/3rd of the cases, no such witness is seen or the information provided is not trustworthy (7,8). In this case, there are specific physical examination symptoms that the physician must be alert about. Most commonly seen examination findings are the decrease of respiratory sounds on one side, wheezing, stridor and respiratory difficulty. On the other hand, physical examination can be completely normal as well (4). In our case, the patient had a history of eating nuts few days prior to coming to the hospital and the symptoms starting acutely were the reasons why foreign body aspiration was considered and even though the first laryngoscopic examination showed no results, the second examination helped the diagnosis.

Figure 2. Foreign body seen in the rigid laryngoscopy

Figure 3. Pumpkin seed shell taken out using rigid laryngoscopy

Imaging can be used in all cases suspected of foreign body aspiration. The most common imaging technique is chest X-ray. However, in 1/3rd of the cases, the X-ray can be normal, and normal imaging does not exclude foreign body aspiration (4). Computer tomography can be used in order to evaluate the infectious situations following the obstruction. In cases where the foreign body is not radiopaque, the diagnosis is very difficult. If the foreign body is stuck in the trachea, because it can cause edema, it may be difficult to see it in a laryngoscopy. In our case, the foreign body was not visible in the chest X-ray and the computer tomography because it was not radiopaque. First laryngoscopic examination showed no foreign body because of the location of the object as well as the edema it caused. In such cases, it is important to repeat the imaging techniques (9). In our case, because the symptoms did not improve with medical treatment and clinical suspicion continued, laryngoscopy was repeated and the patient was diagnosed with foreign body aspiration.

Most common treatment in foreign body aspiration is the removal of the object using rigid laryngoscope (10). In all cases suspected of foreign body aspiration, laryngoscopy should be performed (11).

Foreign body aspiration should be considered in children who have respiratory problems which start acutely, does not decrease despite the appropriate treatment and are repeating. Patient history, physical examination and radiologic findings should be considered together in order to reach the diagnosis. Identifying a foreign body aspiration early on and doing the treatment accordingly can save a child's life and increase their life quality.

Ethic

Informed Consent: For the study, written and verbal consent was obtained from the family.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: V.T., Ü.K.B., S.M. B.C.G., Design: V.T., Ü.K.B., S.M. B.C.G., Data Collection or Processing: V.T., Ü.K.B.,

S.M., Analysis or Interpretation: V.T., Ü.K.B., S.M., Drafting Manuscript: V.T., Ü.K.B., S.M., B.C.G., Critical Revision of Manuscript: Ü.K.B., Final Approval and Accountability: V.T., S.M., B.C.G., Ü.K.B.

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CASE REPORT

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COVID-19 (SARS-CoV-2) Infection in Neonates: A Single-center Case Series

Yenidoğanlarda COVID-19 (SARS-CoV-2) Enfeksiyonu: Tek Merkezli Bir Olgu Serisi

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Abstract

More than five million people worldwide have been infected with Coronavirus disease-2019 (COVID-19), and it has been reported that children are less infected than adults and newborns are less infected than children. The symptoms of COVID-19 are mild in children compared to adults and can often be asymptomatic. However, after 1 year of the epidemic, serious cases began to be reported in children, especially with mutant strains. Pediatricians need to know the diagnosis and course of these infections in newborns in terms of case management. There is still a lack of definitive information on the infection and transmission of COVID-19 in newborns. In this case series, four cases of community-acquired neonatal COVID-19 infection followed in our clinic are presented.

Keywords: COVID-19, neonate, SARS-CoV-2

Öz

Tüm dünyada beş milyondan fazla insan Koronavirüs hastalığı-2019 (COVID-19) ile enfekte oldu ve çocukların erişkinlere kıyasla daha az enfekte olduğu ve yenidoğanların çocuklardan daha az enfekte olduğu bildirilmiştir. COVID-19'un semptomları çocuklarda erişkinlere kıyasla daha hafiftir ve sıklıkla asemptomatik olabilirler. Ancak salgının 1. yılından sonra özellikle mutant suşlarla birlikte çocuklarda da ciddi olgular bildirilmeye başlanmıştır. Çocuk doktorlarının, yenidoğanlarda bu enfeksiyonların tanısını ve seyrini bilmeleri olgu yönetimi açısından önemlidir. Yenidoğanlarda COVID-19 enfeksiyonu ve bulaşı konusunda hala kesin bilgi eksikliği vardır. Bu olgu serisinde kliniğimizde izlenen toplumdan edinilmiş dört neonatal COVID-19 enfeksiyonu olgusunu sunulmuştur.

Anahtar kelimeler: COVID-19, SARS-CoV-2, yenidoğan

Introduction

In December 2019, Coronavirus disease-2019 (COVID-19) [severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2)] was first identified in Wuhan, China. The infection spread rapidly all over the world. The World Health Organization has declared a global pandemic (1). The symptoms of COVID-19 in children are similar to those in adults, but in children, the symptoms are variable. COVID-19 affects children, boys, and girls equally, with a reported average age of 7.6 years. Fever or chills and cough are the most frequently reported symptoms in children. Clinical findings overlap with many other clinical syndromes such as pneumonia, bronchiolitis, and gastroenteritis (2-5).

In newborns, the clinic is often similar to the pediatric age group. Acute respiratory failure can be seen in advanced neonatal cases. In the neonatal period, cases are frequently taken on an in-family basis. Although cases that can be transmitted vertically in the intrauterine period have been reported, a vertical transmission has not been clarified yet. However, very few neonates were found positive for pandemic COVID-19 infection and the clinical features of infected newborns were different (6,7).

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We aimed to present a series of COVID-19 cases diagnosed as polymerase chain reaction (PCR) positive in tertiary neonatal intensive care because it is rarely seen in the neonatal period. From all presented cases, parental consents were obtained.

Case Reports

Case 1

A 25-day-old male newborn was admitted to the hospital with the complaints of fever and cough that had been ongoing for two days. He had been born with cesarean section, weighed 3.900 g in 39 3/7 weeks of gestation. Upon physical examination, the actual weight was 4.900 g, the axillary temperature was 38 °C, and respiratory rate was 70 breaths per minute. Rhonchus was heard in his breathing sounds. Chest X-ray revealed right paracardiac and left basal irregular opacities. Lymphopenia, thrombocytopenia, or elevated liver enzymes were not detected. C-reactive protein (CRP) (0.8 mg/L) and procalcitonin (0.1 ng/mL) were normal. Her mother had runny nose and cough symptoms. She had no history of travel but she had contacted with a health worker partner. The real-time reverse transcription-polymerase chain reaction (RT-PCR) test for the detection of COVID-19 in nasopharyngeal swabs was positive in both the mother and newborn. In the mother's partner, the test was negative. Ampicillin-gentamicin and Oseltamivir were started. We did not start hydroxychloroquine treatment since mechanical respiratory support treatment was not required. Antibiotic treatment was completed in 7 days. A pulmonary CT scan was not performed due to lack of respiratory distress, increased tachypnea, and decreased fever. The control RT-PCR test was positive following the treatment. RT-PCR tests were found to be positive on the 14th and 16th days of admission. The RT-PCR test results were negative on the 21st and 22nd days of admission. The neonate was closely monitored for 3 weeks and he was discharged from the hospital asymptomatically on the 22nd day of the hospitalization.

Case 2

A five-day-old female newborn was admitted to the hospital with the complaints of reduced feeding and jaundice. She had been born with cesarean section, weighed 1.850 g in 34 3/7 weeks of gestation. Upon physical examination, the patient was icteric, weighed 1.800 g, the axillary temperature was 36.5 °C, there was thrush in the mouth, and a diaper rash was observed. The mother's breast was normal. Respiratory sounds and chest X-ray were normal. The total bilirubin level was 20 mg/dL, platelet and lymphocyte count, CRP (0.4 mg/L), and procalcitonin (0.1 ng/mL) were normal. Ampicillin-gentamicin and phototherapy were started. On the 5th day of hospitalization, it was learned that he had contact with the COVID-19 positive grandmother. RT-PCR test in nasopharyngeal swab was positive in both the mother and newborn. Antibiotic treatment was completed in 7 days. On the second week of life, she exhibited a decrease in sucking and mild tachypnea with mild intercostal retractions. A capillary sample blood gas analysis and a chest radiograph were normal. The serum level of CRP was normal (0.5 mg/L). After 48 h, the symptoms resolved. In the second week, again the RT-PCR tests were positive. There was redness in one eyelid on her 21st postnatal day, lasting for three days. Tobramycin was started for susceptible conjunctivitis. In the third week of hospitalization, two RT-PCR tests of the newborn at 24-hour intervals were found to be negative. She was discharged asymptomatically on the 23rd day of her hospitalization.

Case 3

An 11-day-old female newborn was admitted to the hospital with the complaints of fever-reduced feeding. She had been born with the weight of 2.800 g in 39 6/7 weeks of gestation. Upon physical examination, the actual weight was 2.870 g, the axillary temperature was 39 °C, and respiratory rate was 56 breaths per minute. Feeding was reduced and the front fontanel was taut. Respiratory sounds and chest X-ray were normal. Lymphopenia, thrombocytopenia, or elevated liver enzymes were not detected. CRP was normal. Her mother had no symptoms and she had no history of travel and she had not contracted with a health worker partner, but a member of the family was diagnosed with COVID-19. RT-PCR test for the detection of COVID-19 in nasopharyngeal swab was positive in the first test, negative during hospitalization but the test taken 24 hours later was positive. Lomber punction was planned and protein level 520 mg/dL and glucose 20 mg/dL were found in the cerebrospinal fluid while blood glucose was 127 mg/dL and cerebrospinal fluid was seen purulent. Ampicillin and cefotaxime were started in meningitis doses. Antibiotic treatment was completed in 14 days A pulmonary CT scan was not performed due to lack of respiratory distress, increased tachypnea, and decreased fever. Streptococcus agalactia was reproduced in blood culture and there was not any reproducement in cerebrospinal fluid. The RT-PCR test results were negative on the first and 15th day of admission. The neonate was closely monitored for 17 days and she was discharged from the hospital as asymptomatic

after finishing the treatment of meningitis on the 28th day of the hospitalization.

Case 4

A 13-day-old female newborn was admitted to the hospital with the complaints of reduced feeding. Her acceptance weight was 3.340 g and had been born at 39+2 weeks of gestation. Upon physical examination, she was tachypneic and had retractions. Breathing sounds were normal. Lymphopenia, thrombocytopenia, or elevated liver enzymes were not detected. CRP was 0.21 mg/L. She had no history of travel but she had no contact with a health worker. RT-PCR test for the detection of COVID-19 in nasopharyngeal swab was positive in both the mother and newborn We did not start hydroxychloroquine treatment since mechanical respiratory support treatment was not required. Ampicillin and cefotaxime were started. Antibiotic treatment was completed in 7 days. A pulmonary CT scan was not performed due to lack of respiratory distress, increased tachypnea, and decreased fever. The control RT-PCR test was negative following the treatment. RT-PCR tests were found to be negative on the 11th day of admission. The neonate was closely monitored for 12 days and she was discharged from the hospital as asymptomatic on the 12th day of the hospitalization.

Discussion

More than 95% of newborns of SARS-CoV-2-positive mothers are well at birth. Symptoms seen in newborns are largely associated with early delivery and adverse uterine environments caused by critical maternal COVID-19. Mild infection symptoms that do not require respiratory support have been identified in some newborns of infected mothers, but most of these cases have been associated with community-acquired transmission (8,9). In our cases, it was determined that they acquired this virus later than the COVID-19 positive cases in their families.

Symptoms and signs of COVID-19 in neonates remain blurry. In a systematic review of infants <3 months with SARS-CoV-2 infection, 4% were asymptomatic, 92% were hospitalized, 20% were admitted to the intensive care unit, and 3% required mechanical ventilation. Symptoms included fever (73%), cough (38%), rhinitis (36%), respiratory distress (26%), malnutrition (24%), vomiting (14%), and diarrhea (14%) (10).

In thirty-seven symptomatic neonatal patients from all over Turkey in a national study, most common findings were fever, cough, and hypoxemia with the rates of 49%, 41%, and 27%, respectively. While oxygen administration (41%) and non-invasive ventilation (16%), mechanical ventilation requirement (3%) was found. CRP elevation and high prothrombin times of the cases were found to be correlated with case severity (11).

There were diagnosed fever, cough, tachypnea, nutritional problems, hyperbilirubinemia, unexpected early-onset moniliasis, and diaper dermatitis in our cases.

Laboratory findings are variable in children diagnosed with COVID-19. In a systematic review of laboratory-confirmed COVID-19 cases in children, in most children, complete blood count was normal; low leukocyte count was found in 17% and neutropenia or lymphocytopenia in 13%. High CRP (>0.5 mg/dL) or procalcitonin (>0.5 ng/mL) was identified in approximately one third of the cases. Serum aminotransferases, creatine kinase, and lactate dehydrogenase elevations have been reported as another common laboratory abnormality (3,12,13). Lymphopenia, thrombocytopenia, or elevated liver enzymes were not detected and CRP and procalcitonin levels were normal in our cases.

COVID-19 infection is still an infection with unknowns. Although cases often show mild symptoms in the neonatal period, it should be kept in mind that follow-up is necessary and that newborns are different from the pediatric age group.

Ethic

Informed Consent: From all presented cases, parental consents were obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: E.C., Ç.C.G., Design: E.C., Ş.H., Data acquisition and process: E.C., Ç.C.G., Ş.H., Data analysis and interpretation: E.C., Ş.H., Literature review: E.C., Ç.C.G., Ş.H., Manuscript writing: E.C., Ş.H., Manuscript review and revisation: E.C., Ş.H.

Conflict of Interest: No conflict of interest was declared by the authors.

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LETTER TO THE EDITOR

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The Amount of Propofol Used Should be Specified in Milligrams Instead of Milliliters

Kullanılan Propofol Miktarı Mililitre Yerine Miligram Olarak Belirtilmelidir

Rümeysa Karaçuha Sürücü

Samsun Training and Research Hospital, Clinic of Anesthesiology and Reanimation, Samsun, Turkey

Dear Editor in Chief,

Esophagogastroduodenoscopy (EGD) is a common diagnostic procedure which requires sedation for most patients (1,2). Propofol is an agent often used alone or in combination in endoscopic procedures such as EGD and/or colonoscopy. The median effective dose (ED50) of propofol for loss of consciousness is 1 to 1.5 mg/kg after a bolus. The duration of hypnosis is dose dependent and 5 to 10 minutes after 2-2.5 mg/kg (3).

I read the article entitled "The correlation of pain catastrophizing scale and sedation in patients undergoing gastroscopy'' belonging to Duman Aydın et al. in Bagcilar Medical Bulletin 2021;6(1):1-6. In the section of ''material and methods'' in this study, it was stated that intravenous propofol was administered to patients during EGD at a dose of 1 mg/kg, and doses of 0.3-0.5 mg/kg were added to patients with pain or movement during the procedure. In the results section, the amount of propofol used for sedation was 80.3±16.2 mL, both in the text and in the table. Detailed information about propofol dilution is not provided in the article. 1% propofol contains 10 mg/mL of active substance. When used in a pure state, the amount of 80.3±16.2 mL indicates that 803±162 mg is used, which will correspond to a very high amount for short-term (average of 5.53±2.15 minutes in the study) operations. In my opinion, it would be more appropriate to specify the amount of propofol used in sedation in mg instead of mL in the article.

Keywords: Esophagogastroduodenoscopy, propofol, sedation

Anahtar kelimeler: Özefagogastroduodenoskopi, propofol, sedasyon

Ethics

Peer-review: Internally peer-reviewed.

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ERRATUM

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DOI: 10.4274/BMB.galenos.2020.e001 ‘‘When we analyzed analgesic needs, we showed that patients having normal PCS scores needed significantly lower doses of analgesic premedication than patients having higher PCS scores (median rank scores 21.61 mL vs 40.97 mL, p<0.001) (Table 3). Similarly, patients having low DyNRS values (<4) needed significantly lower doses of analgesic premedication than patients having higher DyNRS values (≥4) (median rank values 30.99 mL vs. 36.60 mL, p=0.044) (Table 3).” expression in the Results, has been corrected as: “When we analyzed analgesic needs, we showed that patients having normal PCS scores needed significantly lower doses of analgesic premedication than patients having higher PCS scores (median rank scores 21.61 mg vs 40.97 mg, p<0.001) (Table 3). Similarly, patients having low DyNRS values (<4) needed significantly lower doses of analgesic premedication than patients having higher DyNRS values (≥4) (median rank values 30.99 mg vs. 36.60 mg, p=0.044) (Table 3).’’

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