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About the Journal

Bagcilar Medical Bulletin (Bağcılar Tıp Bülteni) (BMB) is periodical scientific publishing of Health Sciences University Turkey, İstanbul Bağcılar Training and Research Hospital. This editorially independent, unbiased, international journal periodically publishes peer-reviewed work in the all medical fields on an international scientific basis. Publication language is English for full text and Turkish and English for abstracts. The journal is published in English since December issue of 2016 as an e-journal.

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 branches will be accepted for evaluation in BMB.

The editorial policies are based on the "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (ICMJE Recommendations)" by the International Committee of Medical Journal Editors (2017, archived at http://www.icmje.org/) rules.

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

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Bağcılar Tıp Bülteni/Bagcilar Medical Bulletin, (BTB) Sağlık Bilimleri Üniversitesi, İstanbul Bağcılar Eğitim ve Araştırma Hastanesinin süreli bilimsel yayınıdır. Uluslararası, hakem değerlendirmeli, İngilizce ve açık erişim olarak yılda 4 sayı(Mart, Haziran, Eylül, Aralık) olarak yayınlanan bilimsel bir dergi olup, tıbbın tüm alanlarındaki bilgi birikiminin uluslararası bilimsel platformda yayılabilmesini amaçlamaktadır. Bu amaçla tıbbın her alanında yapılmış orijinal klinik ve deneysel çalışmalar ve ilginç olgu sunumları ile konusunda uzman yazarların yaptığı literatür derlemeleri yayın için değerlendirmeye alınır.

Bağcılar Tıp Bülteni/Bagcilar Medical Bulletin, yazıların İngilizce dilinde, yazıların özetlerinin Türkçe ve İngilizce dillerinde online olarak yayınlandığı bir dergidir.

Yayın politikaları "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (ICMJE Recommendations)" (2016, http://www.icmje.org/) temel alınarak hazırlanmıştır.

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T.C.Sağlık Bakanlığı Sağlık Bilimleri Üniversitesi, İstanbul Bağcılar Eğitim ve Araştırma Hastanesi adına Hastane Yöneticisi Ahmet Yaser Müslümanoğlu, Prof. M.D (Türkiye Cumhuriyeti Sağlık Bakanlığı Sağlık Bilimleri Üniversitesi, İstanbul Bağcılar Eğitim ve Araştırma Hastanesi, Üroloji Kliniği, İstanbul, Türkiye).

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Description

Bagcilar Medical Bulletin is a peer reviewed English journal aiming to publish original research, current review articles, case reports and letters related to all medical fields. The journal is currently published quarterly as online publication. The articles will become freely available to all readers in pdf format as soon as they have been accepted after peer review. Accepted articles will immediately appear as a part of the issue belonging to that publication period. The journal is currently published by Galenos Publishing House. The journal is using online manuscript submission, review and tracking systems.

Editorial Policies and Review Process

Publication Policy

Bagcilar Medical Bulletin considers for publication papers in the following categories:

- Original researches,
- Brief researches,
- Case reports,
- Reviews,
- Letters to the editor

The journal gives high priority to original studies in publication because of aiming to add the findings of searches in Turkey to international scientific knowledge, to share them within the international science milieu and to constitute the introduction of Turkish scientists. The review articles to be published in the journal are authorized by the editor to the relevant authors working on the subject.

General Principles

Papers that have not been published before or under evaluation by other publications are accepted for evaluation by the journal, if approved by each of the author. Publication board may amend manuscripts upon informed consent of authors. Editors and redactors are fully empowered to correct mistakes related to orthography, citation as given in National Library of Medicine MEDLINE/PubMed Resources.

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Bagcilar Medical Bulletin is committed to upholding the highest standards of publication ethics and observes the following principles of Publication Ethics and Malpractice Statement which is based on the recommendations and guidelines for journal editors developed by the Committee on Publication Ethics (COPE), Council of Science Editors (CSE), World Association of Medical Editors (WAME) and the International Committee of Medical Journal Editors (ICMJE).

All submissions must be original, unpublished (including as full text in conference proceedings), and not under the review of any other publication synchronously. Each manuscript is reviewed by one of the editors and at least two referees under double-blind peer review process. We reserve the right to use plagiarism detecting software to screen submitted papers at all times. We check for plagiary and fraudulent data; falsification (fabrication or manipulation of research data, tables, or images) and improper use of humans or animals in research. All manuscripts not in accordance with these standards will be removed from the publication. This also contains any possible malpractice discovered after the publication. In accordance with the code of conduct we will report any cases of suspected plagiarism or duplicate publishing.

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Biomedical Research-revised in 2006 http://www.wma.net/en/30publications/10policies/a18/

For this reason, regarding the subjects of clinical experiments, it should be indicated in the submitted manuscripts definitely that the above mentioned codes of conduct were applied. Besides approvals, from national or local ethical committees should be sent together with the papers as well. Manuscripts that report the results of experimental investigation with human subjects must include a statement that informed consent was obtained after the procedure(s) had been fully explained. In the case of children and those under wardship or with confirmed insanity, authors are asked to include information about whether the legal custodian's assent was obtained. And a letter of affirmation signed by all authors, confirming the collection of informed consents has to be sent to the journal.

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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).

Manuscript Organization And Format

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.

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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.

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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.

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.

Key Words

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.

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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.

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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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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

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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.

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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.

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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.

The manuscript should have an unstructured abstract representing an accurate summary of the article, key words, introduction, conclusion. Authors submitting review article should include a section describing the methods used for locating, selecting, extracting, and synthesizing data. These methods should also be summarized in the abstract.

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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.

Preparation of Manuscripts

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 /),

INSTRUCTIONS TO AUTHORS

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 /

References

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:

1. For articles in journals:

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(4):171-178.

2. For the supplement:

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

Sharan P, Sundar AS. Eating disorders in women. Indian J Psychiatry 2015:57(Suppl 2):286-295.

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:

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

INSTRUCTIONS TO AUTHORS

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:

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

5. For the citation from thesis:

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. 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

SUBMISSION TO JOURNAL

All new manuscripts must be submitted through the Bagcilar Medical Bulletin online manuscript submission and peer review system. Complete instructions are available at the website (). A cover letter should accompany with manuscripts, including the knowledge of:

•The findings of previous same studies should be informed and should be cited. The copies of previous same studies should be sent with manuscripts that might help to the editor in the decision process.

•The knowledge of "all authors have read and accepted the study in its form, all authors meet the criteria for being in authorship" should be stated.

•All helpful things for editorial ship should be stated: The comments of previous editor/reviewers and the response of authors should be added if the manuscript has been sent to another journal for consideration, previously. The editor requested this information to accelerate the publication process.

SUBMISSION CHECKLIST

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:

- Cover letter to the editor
  - The category of the manuscript
  - Acknowledgement of "the paper is not under consideration for publication in another journal"
  - Disclosure of any commercial or financial involvement
  - Reviewing the statistical design of the research article
  - Last control for fluent English
- Copyright Transfer Form
- Author Contribution Form
- ICJME Form for Disclosure of Potential Conflicts of Interest
- Permission of previous published material if used in the present manuscript
- Acknowledgement of the study "in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of in 2000.
- Statement that informed consent was obtained after the procedure(s) had been fully explained.
- 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".
- Title page
  - The title of the manuscript both in Turkish and in English
  - All authors and their affiliations
  - All authors' e-mail address, full postal address, GSM phone, business telephone and fax numbers
- Abstracts (400-500 words) Both in Turkish and in English
- Key words: 3 to 10 words (in Turkish and in English)
- Body text
- Acknowledgement
- Reference
- All tables (including title, description, footnotes)

YAZARLARA BİLGİ

Derginin Tanımı

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.

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 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.

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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 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

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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.

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 v.b. 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.

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

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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.

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

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belirtilmelidir. Gözden geçirme yazısı gönderen yazarlar veriyi bulma, seçme, ayırma ve sentezleme yöntemlerini belirtmelidir. Bu yöntemler aynı zamanda özde de yer almalıdır.

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 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.

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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.

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 sembollerde sadece standart kısaltmalar kullanılmalıdır, 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 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

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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).

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.

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MEDLINE'da yer almayan ve kısaltması olmayan dergi makalesi için: Sevinçer GM, Konuk N. Emotional eating. Journal of Mood Disorders 2013;3(4):171-178.

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2. Ek sayı için:

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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

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• 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

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• Kapak sayfası

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- Tüm yazarların yazışma adresi, iş telefonu, faks numarası, GSM, e-posta adresleri

• Özler (400-500 kelime) (Türkçe ve İngilizce)

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• Tam metin makale

• Teşekkür

• Kaynaklar

• Tablolar-Resimler, Şekiller

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ORIGINAL RESEARCH

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Clinical Significance of Cardiac Permanent Pacemaker Mode Option in Patients with Complete Atrioventricular Block

Atriyoventriküler Tam Bloklu Hastalarda Kalıcı Kalp Pili Mod Seçiminin Klinik Önemi

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Abstract

Objective: We assessed the impact of pacing mode on long-term clinical outcomes in cases with the complete atrioventricular block (CAB).

Method: We retrospectively analyzed 161 patients with CAB, who undergone a cardiac permanent pacemaker. Of the patients involved in the physiologic pacing (PP) group, 95 patients were with the VDD pacing mode and 14 patients were with the DDD pacing mode. In the ventricular pacing (VP) group, with the VVI pacing mode, there were 52 patients.

Results: The average age of the patients was 66±13 years and the average follow-up duration was 40.2±22.6 months. Atrial fibrillation (AF) was observed to be significantly more common in the VP group than in the PP group (p=0.007). However, the occurrence of stroke was similar between the two groups (p=0.753). Newly developed congestive heart failure (CHF) was seen more commonly in the VP group (p=0.015). When we evaluated the patients with and without CHF before pacemaker placement, the number of patients with CHF was reduced in the PP group (p=0.039) and insignificantly increased in the VP group (p=0.219).

Conclusion: We conclude that in patients with CAB, the use of PP, compared to VP, may decrease the rate of AF and CHF in the long-term.

Keywords: Artificial cardiac pacing, atrial fibrillation, atrioventricular block, heart failure, stroke

Öz

Amaç: Atriyoventriküler (AV) tam bloklu hastalarda kalıcı pacemaker mod seçiminin uzun dönem klinik sonuçları incelendi.

Yöntem: AV tam blok nedeni ile kalıcı pacemaker takılan toplam 161 hasta retrospektif olarak incelendi. Fizyolojik pacemaker (FP) grubu altında incelenen hastaların 95'inde VDD, 14'ünde DDD modu bulunmaktaydı. Ventriküler pacemaker (VP) grubu içinde incelenen 52 hastada VVI modu mevcuttu.

Bulgular: Ortalama yaş 66±13 yıl ve ortalama takip süresi 40,2±22,6 ay idi. Takip süresinde, VP grubunda, FP grubu ile karşılaştırıldığında daha fazla oranda atriyal fibrilasyon (AF) saptandı (p=0,007). İnme gelişimi açısından iki grup arasında bir fark bulunmadı (p=0,753). Pacemaker takılmadan önce konjestif kalp yetersizliği (KKY) bulunmayan hastalar incelendiğinde, takip süresi esnasında VP grubunda daha fazla oranda KKY gelişimi tespit edildi (p=0,015). Başlangıçta KKY bulunan ve bulunmayan hastalar birlikte incelendiğinde, takip süresi sonunda FP'li grupta KKY bulunan hastaların sayısı azalırken (p=0,039), VP'li grupta istatistiksel olarak anlamlı olmayan düzeyde bir artma saptandı (p=0,219).

Sonuç: AV tam bloklu hastalarda FP kullanımı, VP kullanımı ile karşılaştırıldığında, uzun dönemde AF ve KKY gelişimini azaltabilir.

Anahtar kelimeler: Atriyal fibrilasyon, atriyoventriküler blok, inme, kalp yetersizliği, yapay kalp pili

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Introduction

Physiologic pacing (PP) possibly provides a clinical benefit compared to ventricular pacing (VP) in the treatment of the complete atrioventricular block (CAB). Non-randomized studies suggest that PP is associated with a lesser incidence of stroke, atrial fibrillation (AF), heart failure than in the VP, and mortality decreases in patients with heart failure (1-8). Mortality rates were found similar between two groups in a recent retrospective study (9). The small randomized studies comparing PP to VP have demonstrated that mortality, the incidence of AF, and stroke are high in VP (10,11). For mortality and heart failure, the randomized studies with more patients established no significant differences between the PP and VP groups (12-14). For AF, only the Canadian Trial of Physiologic Pacing (CTOPP) found a risk reduction in the PP group (12), and for stroke, only the United Kingdom Pacing and Cardiovascular Events (UKPACE) trial found risk increase in the fixed-rate VP group (13).

Materials and Methods

All patients who received a cardiac permanent pacemaker (CPP) for CAB at our institution before June 2015 were reviewed. Patients with permanent AF, missing or inadequate records, follow-up period shorter than 6 months, and younger age group (<20 years) were excluded from the study.

The study group consisted of 161 patients (57% females), 68% with PP and 32% with VP. The mean age was 66±13 years and the mean follow-up period was 40.2±22.6 months. The follow-up visits occurred 1, 3, and 6 months after pacemaker implantation, and there were yearly visits thereafter. The patient's clinical condition, ambulatory ECG recordings, and 12-lead ECG records were analyzed. Stroke, AF, signs and symptoms of CHF before and after pacemaker implantation were evaluated. Hemorrhagic stroke and transient ischemic attack were not included in the stroke group. Patients with paroxysmal, persistent and permanent AF during the follow-up period were involved in the AF group.

Statistical Analysis

The results are specified as mean ± standard deviation. Statistical tests included chi-square analysis with the Yates' correction, Fisher's Exact test or McNemar test where pertinent, and Student's t-test. A p-value <0.05 was assessed as significant. All statistical studies were performed using SPSS for Windows, Version 9.0 (SPSS Inc., Chicago, IL, USA).

Results

No statistically significant difference was found compared to baseline characteristics between the treatment groups (Table 1).

As shown in Table 2, AF developed significantly more frequently in patients assigned to the VP group than in the PP group (34.6 vs 14.7%, p=0.007), and no significant difference existed among the patient groups concerning stroke (1.9% in VP vs 2.7% in PP group, p=0.753).

There were five patients with a history of CHF in the VP group and 13 patients in the PP group. We excluded these patients from analysis when we compared the newly developed CHF between the groups. This study demonstrates that the newly developed CHF in the group of VP is significantly more common than among those with PP (10.6% vs 1%, p=0.015, Table 3). Also, when we examined all patients with or without CHF before implantation of the pacemaker, CHF frequency was decreased significantly in

Table 1. Comparison of baseline characteristics and pharmacological agents according to pacing modes

			VP n=52	PP n=109	p
Age (year)			68±11	65±14	0.300
Follow-up (month)			44.4±24.4	38.2±21.5	0.100
Male (%)			46.1	42.2	0.762
History (%)					
	CAD		21.2	19.3	0.945
	Stroke		3.8	1.8	0.595
	PAF		3.8	4.6	1.000
	CHF		9.6	11.9	0.793
	Cardiac surgery				
		Valve	7.7	5.5	0.728
		CABG	5.8	6.4	1.000
Antiarrhythmic drugs (%)			26.9	37.6	0.246
Anticoagulant drugs (%)			13.5	11	0.849

CAD: Coronary artery disease, CHF: Congestive heart failure, PAF: Paroxysmal atrial fibrillation, PP: Physiologic pacing, VP: Ventricular pacing

Table 2. Event rates for atrial fibrillation and ischemic stroke

	VP (n=52)	PP (n=109)	p
Atrial fibrillation	18 (34.6%)	16 (14.7%)	0.007
Ischemic stroke	1 (1.9%)	3 (2.7%)	0.753

PP: Physiologic pacing, VP: Ventricular pacing

the PP group (p=0.039), and insignificantly increased in the VP group (p=0.219) during the study period (Table 4).

Discussion

This study aimed to assess if the pacing mode, whether PP or VP, contributed to the clinical benefit in the patients with CAB and implanted CPP. The retrospective studies showed mortality decrease in patients with heart failure, and improved clinical outcomes with respect to AF, stroke, and heart failure with PP. The small randomized studies have shown that the mortality, incidence of AF, and stroke were higher in the VP group. The randomized studies with more patients have failed to reveal a marked benefit for PP in terms of reduction of mortality and heart failure. AF risk was significantly lower in the PP group only in the CTOPP trial, and stroke risk was significantly higher in the fixed-rate VP group only in the UKPACE trial.

PP is believed to have an advantage over VP in that it mimics cardiac physiology more similarly by preserving atrioventricular synchrony and domination of sinus node (15-17), increases cardiac output which in turn may reduce heart failure, AF and stroke. PP improved left ventricular functions and hemodynamics, especially in patients with heart failure (18-23). VP may induce AF through changes in the atrial structure resulting from asynchronous ventricular contraction (19).

Our results showed a high incidence of AF in the VP group like that found in the CTOPP trial. Also, we found a high incidence of CHF in the VP group. This may be because of the loss of AV synchronization and decreased contribution of the atrium to ventricular filling. We found no significant difference concerning stroke between the two groups.

Table 3. Newly developed congestive heart failure

	VP (n=47)	PP (n=96)	p
New onset of CHF	5 (10.6%)	1 (1%)	0.015

CHF: Congestive heart failure, PP: Physiologic pacing, VP: Ventricular pacing

Table 4. The number of the patients with CHF before pacemaker implantation and at the end of follow-up period

	Before pacemaker implantation (CHF)	End of follow-up period (CHF)	p
VP (n=52)	5 (9.6%)	9 (17.3%)	0.219
PP (n=109)	13 (11.9%)	6 (5.5%)	0.039

CHF: Congestive heart failure, PP: Physiologic pacing, VP: Ventricular pacing

Study Limitations

The major limitations of our study are the small sampling size, retrospective design, although statistically insignificant, some baseline differences between the study groups.

Conclusion

We concluded that the PP compared to VP might reduce the incidence of AF and CHF. More randomized studies must be done for the selection of the best pacing mode in the patients with CAB.

Ethics

Ethics Committee Approval: The study protocol was approved by the local ethics committee of our institution (2020.09.1.05.122).

Informed Consent: Written informed consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: C.Ç., O.İ., Design: C.Ç., O.İ., Data Collection or Processing: C.Ç., O.İ., Analysis or Interpretation: O.İ., K.G., E.O., S.Ö., Literature Search: O.İ., K.G., E.O., S.Ö., Writing: O.İ., K.G., S.Ö.

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ORIGINAL RESEARCH

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Comparison of Transfix Screw Technique and Endobutton Technique in Terms of Tunnel Widening and Clinical Results in Anterior Cruciate Ligament Reconstruction

Ön Çapraz Bağ Rekonstrüksiyonunda Transfiks Vida Tekniği ile Endobutton Tekniğinin Tünel Genişlemesi ve Klinik Sonuçlar Yönünden Karşılaştırılması

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Abstract

Objective: The aim of the present study was to compare transfix screw technique and endobutton technique in terms of femoral and tibial tunnel enlargement and clinical outcomes in anterior cruciate ligament (ACL) surgery and to discuss non-anatomic transtibial system under current circumstances.

Method: This retrospective study was conducted on 50 patients who had ACL reconstruction in SCI Göztepe Training and Research Hospital between September, 1999 and March, 2003. Among the patients enrolled, 17 patients had endobutton and 33 had transfix screw technique for ACL reconstruction. The mean age of the patients who underwent ACL reconstruction through endobutton technique was 27.2 years whereas the mean age of those who had transfix screw method was 29.9 years. Femoral and tibial tunnel enlargement rates were reviewed for radiological comparison. Harner's quadrant location, Frontal femoral tunnel angles and Frontal tibial tunnel angles were similar in both groups, and they were found comparable radiologically. The differences between the early postoperative and late postoperative tunnel widths of both groups were compared. Clinical comparison was performed through the Hospital for Special Surgery Knee score (HSSKS).

Results: Tunnel widening was detected in a significant part of the cases who had both endobutton and transfix screw methods; and the cases with a tunnel dilatation difference at and over 2 mm were accepted as tunnel enlargement and evaluated in consideration of standard deviation.

Öz

Amaç: Bizim bu çalışmamızdaki amacımız ön çapraz bağ (ÖÇB) cerrahisinde transtibial sistemle yaptığımız transfiks vida tekniği ile endobutton tekniğini radyolojik ve klinik olarak karşılaştırmak ve bugünün koşullarında tartışmaktır.

Yöntem: Çalışma retrospektif olarak SSK Göztepe Eğitim ve Araştırma Hastanesi'nde Eylül 1999 ile Mart 2003 yılları arasında non-anatomik ÖÇB rekonstrüksiyonu yapılan 50 hasta ile yapıldı. Bunların 17'si endobutton, 33'ü ise transfiks vida tekniği ile ÖÇB rekonstrüksiyonu yapılan hastalardı. Endobutton tekniği ile ÖÇB ameliyatı yapılan hastaların ortalama yaşı 27,2 iken transfiks vida tekniği ile yapılan hastaların ise 29,9'du. Radyolojik karşılaştırmada femoral ve tibial tünel genişleme oranlarına bakıldı. Her iki teknikte Harner's kadranı dağılımı, Frontal tibial tünel açıları ve Frontal femoral tünel açıları benzer olup radyolojik olarak femoral ve tibial tünel genişleme oranları karşılaştırılabilir bulundu. Erken postoperatif ve geç postoperatif tünel genişlik oranları birbiriyle karşılaştırıldı. Klinik karşılaştırma ise Hospital for Special Surgery Knee score (HSSKS) ile yapıldı.

Bulgular: Hem endobutton hem de transfiks olgularının önemli bir kısmında tünel genişlemesi bulundu ve standart sapma dikkate alınarak 2 mm ve üzerinde tünel genişlik farkı olan olgular anlamlı tünel genişlemesi olarak kabul edilip değerlendirmeye alındı. Sonuç olarak endobutton CL'deki olguların %47'sinde, transfiks tekniğindeki olguların % 51,5'inde anlamlı tünel genişlemesi bulundu. Her iki teknik arsında tünel

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Abstract

Consequently, significant tunnel enlargement was detected in 47% of the cases in endobutton continuous loop (CL) reconstruction group and in 51.5% of the cases in transfix screw technique group. There was not any statistically significant difference in tunnel enlargement between two techniques (p>0.05). In the transfix technique, the HSKSS scores of the patients with femoral tunnel width difference over 2 mm were 90.2 whereas in cases without femoral tunnel width or minimal, this score was 91.1. In Endobutton technique, HSKSS scores of the patients with the femoral tunnel enlargement were 91, HSKSS scores of the cases without femoral tunnel enlargement were 91.25. There was no relation between femoral tunnel widening and HSKSS scores due to the value of p>0.005 in the Mann-Whitney U test. Postoperative rehabilitation period was similar in both groups; HSSKS scores of the cases who underwent transfix and endobutton techniques were compared (Table 9, 10). The p>0.05 meant that there was not any clinically significant difference between two groups.

Conclusion: Significant tunnel widening was found in both endobutton CL and transfix technique (using transtibial method) in ACL reconstruction with the hamstring tendon graft. However, there was no significant difference between the two techniques in terms of tunnel widening. It was observed that tunnel enlargement had no significant effect on clinical results in both groups. There was no significant difference between the two groups in terms of clinical results. Successful outcomes were obtained in ACL reconstructions through transtibial technique where extraarticular fixation was done. Recognition of both transtibial techniques for anatomic ACL reconstruction is essential for ACL revision procedures.

Keywords: Anterior cruciate ligament, endobutton technique, transfix technique, transtibial technique, tunnel widening

Öz

genişlemesi bakımından anlamlı istatiksel bir fark bulunmadı (p>0,05). Transfiks tekniğinde femoral tünel genişlik farkı 2 mm ve üzerinde olan hastaların HSKSS puanları 90,2 bulunurken femoral tünel genişlik farkı olmayan veya minimal olan olgularda bu puan 91,1 idi. Endobutton tekniğinde femoral tünelde genişleme olan hastaların HSKSS puanları 91, tünel genişlemesi olmayan olguların ise 91,25 idi. Bu durumun kliniğe yansımadığı Mann-Whitney U testinde p>0,005 değerinin bulunmasıyla anlaşıldı. Her iki grupta da ameliyat sonrası rehabilitasyon süresi benzer olup, transfiks ve endobutton teknikleriyle yapılan olguların HSSKS puanları karşılaştırıldı (Tablo 9, 10). P>0,005 olup her iki teknik arasında klinik olarak anlamlı bir fark saptanmadı.

Sonuç: Hamstring tendon grefti kullanılarak, transtibial yöntem ile yapılan hem endobutton CL, hemde transfiks tekniğinde anlamlı tünel genişlemesi bulundu. Fakat her iki teknik arasında tünel genişlemesi yönünden anlamlı bir fark yoktu. Her iki grupta da tünel genişlemesinin klinik sonuçlara yansımadığı tespit edildi. Her iki grupta da klinik sonuçlar bakımından anlamlı bir fark bulunmadı. Transtibial tekniğin kullanıldığı ve tespitin ekstraartiküler yöntemle yapıldığı ÖÇB rekonstrüksiyonunda geçmişte başarılı sonuçlar alınmıştır. Anatomik ÖÇB rekonstrüksiyonların yapıldığı günümüzde transtibial her iki tekniği bilmenin ÖÇB revizyonları için önemli olduğunu düşünüyoruz.

Anahtar kelimeler: Endobutton teknik, ön çapraz bağ, transfiks teknik, transtibial teknik, tunel genişlemesi

Introduction

Surgical procedures of anterior cruciate ligament (ACL) gathered speed by the replacement of extraarticular techniques with intraarticular techniques for ACL procedures in 1990s (1,2). ACL reconstruction was performed non-anatomically first; when importance of rotational stability in the knee was noticed after 2000s, anatomic ACL reconstruction procedures started and almost all procedures are performed through anatomic ACL reconstruction approach today. Although successful results are obtained by former transtibial technique, this method has been begun to be forgotten currently. We believe that this method should be recognized in detail and performed compulsorily due to increasing ACL revision surgery rates.

Many problems have been encountered in ACL reconstruction surgery from past to present. One of them is femoral and tibial tunnel enlargement. Many biological and mechanical factors have been blamed for tunnel widening. Antigenic immune response, non-specific inflammatory reaction, toxic substances created by materials, cell necrosis during the use of drill and synovial cytokines are biological factors that can cause bone tunnel enlargement. Unsuitable tunnel placements, stress loads and movement made by the graft in the tunnel, characteristics of fixation materials, excessive rehabilitation are the factors that are suggested to cause tunnel enlargement as mechanical reasons (3,4). Each of these factors that can reason for tunnel widening may impair bone tendon union. 10% failure and recurrent instability develop after ACL surgeries due to graft non-union.

The aim of the present study was to make a radiological and clinical comparison of transfix screw technique through transtibial system and endobutton technique in ACL surgery of which we used to perform by non-anatomic approach, and to discuss the results under current conditions.

Materials and Methods

This retrospective study was conducted on 50 patients who had ACL reconstruction in SCI Göztepe Training and Research Hospital between September, 1999 and

March, 2003. The study was conducted with the consent of all patients. Among the patients enrolled, 17 patients had endobutton and 33 had transfix screw technique for ACL reconstruction. The mean age of the patients who underwent ACL reconstruction through endobutton technique was 27.2 years whereas the mean age of those who had transfix screw method was 29.9 years. The duration between first trauma and ACL reconstruction was 24.3 months in transfix screw technique, and 30.9 months in endobutton technique. The distribution of meniscus rupture and chondral lesion was similar in two groups. Partial menisectomy was performed on all of the cases with meniscus rupture.

Bioabsorbable screws with a diameter of 1 mm larger than tibial tunnel diameter were used to fix the tibial tunnels in both groups. One staple was used additionally in transfix technique whereas 2 staples or washers were used in addition to bioabsorbable screw in endobutton technique. The mean follow-up periods were similar in both groups as 2.8 years for transfix screw method and 2.9 years for endobutton technique.

Radiological comparison of both groups was performed by anterior posterior (AP)/lateral X-rays and magnetic resonance imaging of the knee. Frontal femoral tunnel angle (Figure 1), frontal tibial tunnel angle (Figure 2), disintegration angle (Figure 3) and Harner's quadrants were reviewed by direct X-ray. The angles reviewed and Harner's quadrant location were similar in both groups, and they were found comparable radiologically. Femoral and tibial tunnel widening ratios were assessed for radiological comparison. Radiological measurement was

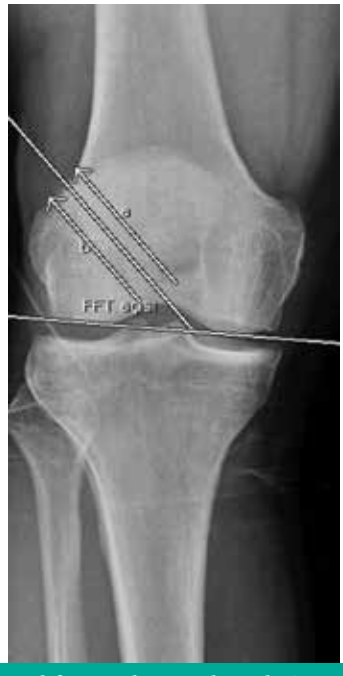

Figure 1. Frontal femoral tunnel angle in AP X-ray of the knee
FTT: Frontal tibial tunnel, AP: Anterior posterior

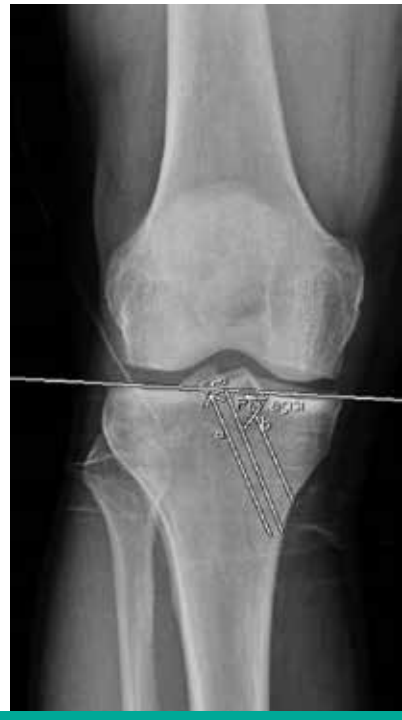

Figure 2. Frontal tibial tunnel angle in AP X-ray of the knee
FTT: Frontal tibial tunnel, AP: Anterior posterior

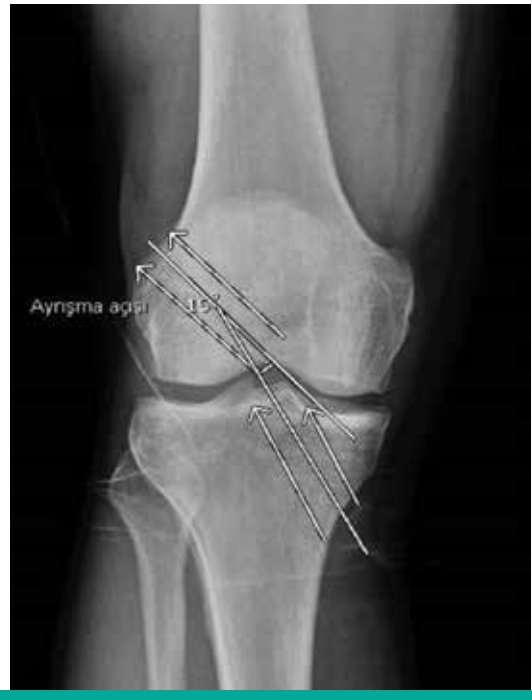

Figure 3. The disintegration angle between FFT and FTT
FTT: Frontal tibial tunnel, FFT: Frontal femoral tunnel

standardized by placing a square iron of 1 cm² into the film cassette.

Clinical comparison was performed through the Hospital for Special Surgery Knee score (HSSKS). HSSKS is a comprehensive measurement tool including subjective, objective and functional tests. Subjective complaints include pain, swelling, locking, release and frequent release. Objective issues include any previous surgical procedures (i.e. partial menisectomy), date of injury, surgery date, surgical procedure and examination of knee ligaments (Lachman, anterior drawer, posterior drawer tests and pivot shift etc). Functional assessment includes daily activities as well as working status, sports, running, jumping, standing and leaning onto the side. They are evaluated over 100 points. The ranging was assessed as follows; 96 to 100 points, quite good; 91 to 95 points, good; 86 to 90 points, moderate; 76 to 85 points, bad; and below 76, very bad. The highest score (approximately 40 to 50%) was obtained by functional activity and test response of the patient.

Statistical Analysis

Mean, standard deviation, median, minimum, maximum value frequency and percentage were used for descriptive statistics. The Mann-Whitney U test was used for the comparison of quantitative data. Paired sample t-test was used to detect standard deviation. SPSS 26.0 was used for statistical analyses.

Results

The difference between early postoperative and late postoperative tunnel width was evaluated by the Paired samples t-test. Accordingly, tunnel enlargement was detected in a significant part of endobutton and transfixes cases; the cases with tunnel enlargement difference at and over 2 mm were accepted as tunnel widening and evaluated in consideration of standard deviation. In this case, tunnel enlargement differences of 8 cases presented minimal increase or presented no change in Endobutton continuous loop (CL) whereas a significant enlargement of both femoral and tibial tunnel was seen in 7 cases and of femoral tunnel was seen only in 2 cases (Table 1). The largest width difference was found as 6 mm in the femoral tunnel, 4 mm in the tibial tunnel; the mean width difference of the tunnel was found as 3.8 mm and 2.6 mm in the femoral tunnel and tibial tunnel, respectively (average of the cases with significant tunnel widening). There was not any significant tunnel widening in 15 cases who had transfix technique; however, a significant enlargement was detected in both femoral and tibial tunnel in 14 cases, for femoral tunnel only in 3 cases and for tibial tunnel only in 1 case (Table 2). Accordingly, it was detected that femoral tunnel was dilated by 5 mm and tibial tunnel was dilated by 7 mm. The mean dilatation measure of femoral tunnel and tibial tunnel was 3.6 mm and 3.8 mm, respectively.

Consequently, significant tunnel enlargement was detected in 47% of the cases in endobutton CL reconstruction group, and in 51.5% of the cases in transfix screw technique group.

In Table 1, $p<0.001$ was detected in paired sample t-test with standard deviation of 20,598. A significant tunnel enlargement difference was detected with these findings. Same p-value was found for Table 2, below with standard deviation of 178,895.

In Tables 3 and 4 below, 63% of the cases with femoral tunnels on Harner's quadrant 3 through transfix technique presented a femoral tunnel width difference over 2 mm; however, such rate for the cases with the tunnels on Harner's quadrant 4 was 37%. It was investigated whether such tunnel width difference ratios were associated with

Table 1. Distribution of the cases with tunnel enlargement over 2 mm in endobutton technique

Endobutton CL			
Amount of femoral tunnel enlargement	**n=9**	**Amount of tibial tunnel enlargement**	**n=7**
2	1	2 mm	**3**
2.5 mm	-	2.5 mm	**2**
3 mm	1	3 mm	**1**
3.5 mm	4	4 mm	**1**
4	-	-	-
4.5 mm	1	-	-
5 mm	1	-	-
6 mm	1	-	-

CL: Continuous loop

Table 2. Distribution of the cases with tunnel enlargement over 2 mm in transfix screw technique

Transfix technique			
Amount of femoral tunnel enlargement	**n=17**	**Amount of tibial tunnel enlargement**	**n=15**
2	2	2	**2**
2.5 mm	1	3	**8**
3	6	3	**1**
4	3	5	**1**
4.5 mm	1	6	**2**
5	**4**	-	-

Harner's quadrant. The Mann-Whitney U test was applied for this. The p-value is >0.005 in this test and there was not any connection between Harner's quadrant and tunnel enlargement.

HSSKS scores of the patients with femoral tunnel width difference at and over 2 mm through transfix technique were found 90.2 whereas such score was 91.1 in the cases with none or minimal femoral tunnel width difference (Table 5, 6). The p>0.005 value detected by the Mann-Whitney U test meant that this was not reflected to the clinical presentation. There was not any significant difference in score comparison of the cases with femoral tunnel width difference at and over 2 mm (Table 7) and in the cases with none or minimal tunnel width (Table 8) (p>0.005).

Postoperative rehabilitation period was similar in both groups; HSSKS scores of the cases who underwent transfix and endobutton techniques were compared (Table 9, 10). The comparison was performed through the Mann-

Table 3. Distribution of femoral tunnel width difference over 2 mm according to Harner's quadrant in transfix screw technique

Transfix technique (n=17)			
Amount of femoral tunnel enlargement	**Harner quadrant 2**	**Harner quadrant 3**	**Harner quadrant 4**
2 mm	1	1	-
2.5 mm	-	-	**1**
3 mm	-	6	-
4 mm	-	1	**2**
4.5 mm	-	1	-
5 mm	-	**3**	**1**

Table 4. Distribution of the cases without significant tunnel widening according to Harner's quadrants in transfix screw technique

Transfix technique (n=16)	
Amount of femoral tunnel enlargement less than 2 mm or absent	
Harner quadrant 3	Harner quadrant 4
7	9

Table 5. HSSKS distribution scores of the cases with femoral tunnel enlargement at and over 2 mm in transfix screw technique

Transfix technique (n=17)				
	HSSKS			
Amount of femoral tunnel enlargement	**81-85 point**	**86-90 point**	**91-95 point**	**96-100 point**
2 mm	-	1	1	-
2.5 mm	-	-	1	-
3 mm	-	2	2	**1**
4 mm	-	-	2	**1**
4.5 mm	-	-	1	-
5 mm	**1**	**2**	**1**	-

HSSKS: Hospital for Special Surgery Knee score

Table 6. HSSKS distribution scores of the cases without femoral tunnel widening at and below 2 mm in transfix screw technique

Transfix technique			
Amount of femoral tunnel enlargement minimal or absent			
HSSKS			
80-85	**86-90**	**91-95**	**96-100**
2	5	6	3

HSSKS: Hospital for Special Surgery Knee score

Table 7. HSSKS distribution scores of the cases with femoral tunnel widening at and over 2 mm in endobutton technique

Endobutton CL (n=9)					
Amount of femoral tunnel enlargement	**HSSKS**				
	70-80 point	**81-85 point**	**86-90 point**	**91-95 point**	**96-100 point**
2 mm	-	-	-	-	**1**
3 mm	-	-	-	1	-
3.5 mm	-	-	2	2	-
4.5 mm	-	-	-	1	-
5 mm	-	-	1	-	-
6 mm	-	-	**1**	-	-

HSSKS: Hospital for Special Surgery Knee score, CL: Continuous loop

Table 8. HSSKS distribution scores of the cases without femoral tunnel widening at and below 2 mm in endobutton technique

Endobutton CL (n=8)				
Amount of femoral tunnel enlargement minimal or absent				
HSSKS				
70-80	**81-85**	**86-90**	**91-96**	**96-100**
1	1	1	3	2

HSSKS: Hospital for Special Surgery Knee score, CL: Continuous loop

Table 9. Distribution of HSSKS scores in the cases operated with transfix screw technique

Transfix technique				
HSSKS points				
70-80	**81-85**	**86-90**	**91-96**	**96-100**
1	3	10	14	5

HSSKS: Hospital for Special Surgery Knee score

Whitney U test. The p>0.05 meant that there was not any clinically significant difference between two groups.

Discussion

L'Insalata et al. (5) detected in their study conducted on ACL reconstructions through hamstring tendons that tunnel enlargement was more common than those performed by using patellar tendon graft. However, they did not explain that this was clinically meaningful. Similarly, Clatworthy et al. (6) detected in a study (in reconstructions on hamstring tendons) that the most enlargement of tunnel was in those using bioabsorbable screw, which was followed by metal interference screw, Bone Mulch screw and Endobutton CL. Clatworthy et al. (6) demonstrated in the aforesaid study that femoral tunnel enlargement could not be explained by ''bunge-cord'' effect in the cases in which Endobutton CL was used (6). The findings obtained in the present study were consistent with those obtained by Clatworthy et al. (6) detection of similar results in tunnel enlargement ratios of our cases both in Transfix and Endobutton CL techniques appears to prove that femoral tunnel enlargement by 65% of former tunnel diameter is due to tight rope effect. Because, tunnel enlargement occurs by 55% of former tunnel diameter in Transfix technique.

Moreover, the tibial tunnel was fixed by 1 staple and 1 bioabsorbable screw in majority of the cases with Transfix technique. However, double staples or washer were used in our Endobutton CL cases. This allowed us to compare tibial tunnel enlargement in both cases. The outcomes that we obtained were interesting because, some tibial tunnel enlargement quantity exceeded femoral tunnel width in Transfix screw technique. The mean tibial tunnel enlargement quantity was 2.6 mm in endobutton (calculated from those with significant tunnel enlargement), and 3.8 mm in Transfix screw technique. This was also consistent with the study conducted by Clatworthy et al. (6) However, tibial tunnel did not expand much although bioabsorbable screw was used in the cases without femoral tunnel enlargement.

Table 10. Distribution of HSSKS scores in the cases operated with Endobutton technique

Endobutton technique				
HSSKS points				
70-80	**81-85**	**86-90**	**91-96**	**96-100**
1	2	5	6	3

HSSKS: Hospital for Special Surgery Knee score

Does tunnel enlargement make any sense for the patients? If it does, what was the extent of enlargement to increase the instability? Ayala-Majias et al. (7) selected a retrospective cohort of 30 patients undergoing ACL recontruction with double semitendinosus plus double gracilis with longer than 10 -year follow-up to evaluate the relationship between tunnel position and widening and long term clinical results. They found that tibial tunnels widened more than femoral tunnels and tibial tunnel dilation was associated with long term degenerative changes but no with final knee instability (7). Nebelung et al. (8) evaluated 29 knees with a minimum follow-up 2 years after ACL reconstruction with endobutton tecnique. They have found no correlation between enlargement of the tunnel and the International Knee Documentation Comittee score or the residual joint instability (8). Çınar et al. (9) investigated the effects of anatomic and non-anatomic tunnel fixations on femoral tunnel widening and clinical results in ACL reconstruction with hamstring tendon graft. They found that there was marked and excessive tunnel enlargement in anatomic and non-anatomic tunnel fixations. They demonstrated that there was no relationship between tunnel widening and clinical results and ligament laxity (9). We could not find a relationship between tunnel enlargement and clinical outcomes in the both groups too; however, we detected that clinical status was moderate in the cases with tunnel widening by 50% and more of former tunnel diameter and HSSKS scores accumulated around 86 to 88. Majority of them were without instability; however, it was observed that they abstained from previous sports that they used to make before the surgery and they perform different sports. Furthermore, it should be stressed out that tunnel enlargement exceeding 50% of former enlargement diameter was 16% of our cases only.

Endobutton and Transfix screw are the materials providing extraarticular femoral fixation. The most superior characteristics include their resistance, strength against loading during femoral fixation with the strongest scraping forces (10-12). Another superior feature is not leading to posterior cortex wall fracture during fixation. Endobutton also has two other superior characteristics. One of them is serving as a material used for both hamstring tendons and patellar tendon bone graft, and the other is providing external rotation to the graft during tibial fixation of the graft. Despite such additional superior characteristics of Endobutton, usage was not common among surgeons in the past. Two settled views caused this. One view was that Endobutton causes tunnel

enlargement more than transfix due to tight rope effect; and it was shown that this was not correct. The second view was the desire to keep Endobutton as a priceless option for revision ligament surgery in the future. Femoral tunnel fixations were mostly used to be done inside the tunnel for that reason, and fixation failure was detected frequently (13). Furthermore, removal of femoral tunnel screws located intraarticularly is difficult and results with significant tunnel dilatation when removed (14). Anatomic ACL reconstruction is done nowadays and transtibial technique has almost been abandoned. Endobutton fixation material is commonly used to fixate femoral tunnel. Revision of ACL becomes difficult due to current femoral tunnel widening in the patients who had anatomic ACL reconstruction before with accurate femoral tunnel location. At this point, we believe that dominating transtibial technique is important. Because, the new femoral tunnel to be opened inside former tibial tunnel by keeping the frontal tibial angle at 60 degrees in average would be closer to anatomic location and longer than former tunnel. It is reported that if failure to thrive angle is over 75 degrees, it increases anterior laxity and causes loss of flexion (15). Furthermore, opening new femoral tunnel in transtibial technique allows an increase in disintegration probably due to the dilated tibial tunnel. This would enable to open the femoral tunnel more anatomically. Femoral tunnel grafting may not be needed. We observe better results of a patient whom we have performed ACL reconstruction 20 years ago and still follow up (Figure 4, 5). In the AP/lateral X-rays of the knee, femoral and tibial tunnels appear not to be enlarged. The knee examination revealed that Lachman 1 was positive, and the patient did not have any problem in the daily life. Furthermore, one of the noticeable points is the absence of osteoarthritis complaints.

Conclusion

Comparison of both techniques in the present study revealed no difference radiologically and for tunnel dilatation; and both fixation materials may be easily used if transtibial ACL revision would be done.

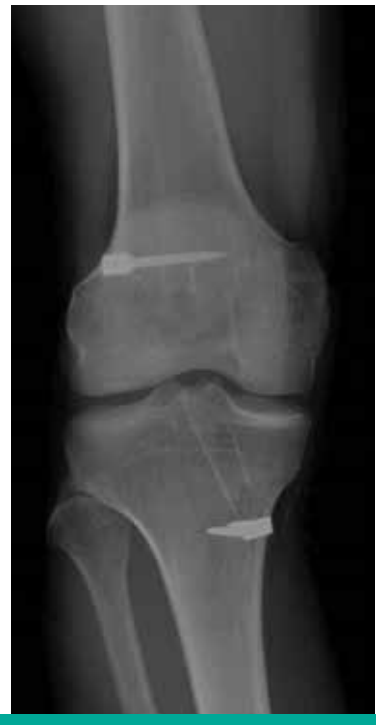

Figure 4. The AP knee X-ray of the patient who had non-anatomic ACL reconstruction through transtibial technique after 9 years; femoral tunnel was fixated by transfix screw. The patient has no complaint; he plays football etc

AP: Anterior posterior, ACL: Anterior cruciate ligament

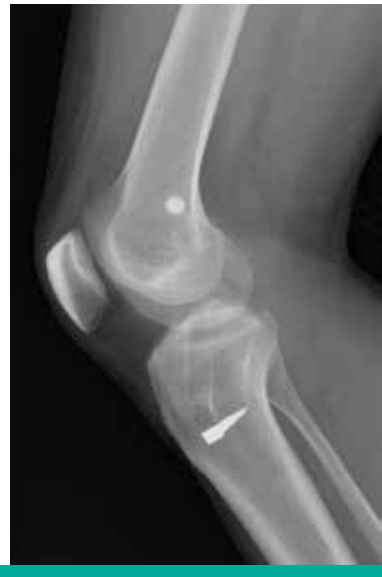

Figure 5. Lateral knee X-ray of the same patient, femoral tunnel appears to be opened at Harner's quadrant 4. no enlargement in femoral and tibial tunnels

Ethics

Ethics Committee Approval: Not applicable.

Informed Consent: The study was conducted with the consent of all patients.

Peer-review: Externally peer-reviewed.

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ORIGINAL RESEARCH

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Determination of Reference Range for B_{12} and Folate Levels According to Laboratory Data in an Adult Population

Yetişkin Bir Popülasyonda Laboratuvar Verilerine Göre B_{12} ve Folat Düzeylerinin Referans Aralığının Belirlenmesi

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Abstract

Objective: The aim of this study was to establish reference intervals (RIs) according to laboratory data in a population and to assess the vitamin B_{12} (B_{12}) and folate status related to RIs for all age and gender groups.

Method: The data were retrospectively provided from the laboratory information system of Balıkesir State Hospital. The selected patient population comprised 36.284 individuals (70.2% female, 29.8% male) between the age of 18 and 80 years. These participants were separated into six age-based subgroups (18-30, 31-40, 41-50, 51-60, 61-70 and 71-80 years). B_{12} and folate concentrations were measured by the ARCHITECT i2000sr (Abbott Diagnostics, Abbott Park, IL, USA) autoanalyzer. Extreme values were excluded by using IBM SPSS. The 95% RIs were obtained by the non-parametric method.

Results: The results of 20.850 patients for B_{12} and of 14.183 for folate were evaluated. The mean ages of patients for B_{12} and folate were 48.9±16.3 years and 49.7±16.6 years, respectively. Mean ± standard deviation concentrations of B_{12} and folate were 220±77 pmol/L and 13.9±6.5 nmol/L, respectively. 95% RIs were calculated as 97-397 pmol/L for vitamin B_{12} and 5.17-30.9 pmol/L for folate in the entire population. There are statistically significant differences between women and men for B_{12} and folate. In addition, there is a significant difference between age groups for folate but not for B_{12} concentrations.

Conclusion: In this study, differences between the reference ranges recommended by the manufacturer and the reference ranges of our own population were found. Our results indicate that determining the true reference range is vital.

Keywords: Folate, laboratory data, reference range, Turkey, vitamin B_{12}

Öz

Amaç: Bu çalışmanın amacı, bir popülasyondaki laboratuvar verilerine göre referans aralıklar (RIs) oluşturmak ve tüm yaş ve cinsiyet grupları için RIs ile ilişkili olarak vitamin B_{12} (B_{12}) ve folat durumunu değerlendirmektir.

Yöntem: Laboratuvar datası Balıkesir Devlet Hastanesi laboratuvar bilgi yönetim sisteminden retrospektif olarak elde edildi. On sekiz-80 yaş arası 36,284 hasta (kadın için %70,2, erkek için %29,8) seçildi. Data, altı alt yaş grubuna ayrıldı (18-30, 31-40, 41-50, 51-60, 61-70 ve 71-80 yaş). B_{12} ve folat konsantrasyonları ARCHITECT i2000sr (Abbott Diagnostics, Abbott Park, IL, ABD) otoanalizörü ile ölçüldü. Uç değerler IBM SPSS kullanılarak atıldı. RIs %95 dağılımda non-parametrik indirekt yöntem kullanılarak hesaplandı.

Bulgular: B_{12} için 20,850 ve folat için 14,183 hastanın sonuçları değerlendirildi. B_{12} ve folat hastalarının yaş ortalaması sırasıyla 48,9±16,3 ve 49,7±16,6 idi. B_{12} ve folatın ortalama ± standart sapma konsantrasyonları sırasıyla 220±77 pmol/L ve 13,9±6,5 nmol/L idi. Tüm popülasyon için %95 RIs, B_{12} vitamini için 97-397 pmol/L ve folik asit için 5,17-30,9 pmol/L olarak hesaplandı. B_{12} ve folat için kadın ve erkek arasında istatistiksel olarak anlamlı fark vardı. Folat için RIs yaş grupları arasında anlamlı bir fark vardı. Ancak B_{12} konsantrasyonları için önemli bir fark yoktu.

Sonuç: Bu çalışmada imalatçı tarafından önerilen RIs ile kendi popülasyonumuzun RIs'leri arasında fark bulunmuştur. Sonuçlarımız, her laboratuvarın kendi referans aralığını belirlemesinin önemli olduğunu göstermektedir.

Anahtar kelimeler: B_{12} vitamini, folat, laboratuvar verileri, referans aralığı, Türkiye

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Introduction

The deficiency of vitamin B_{12} is a severe nutritional problem all over the world, as subclinical deficiency can impact well-defined risk groups. However, vitamin B_{12} deficiency is foremost of prevalent vitamin deficiencies. There is no general agreement on cut-off level for vitamin B_{12} and its co-markers, including folate, methylmalonic acid, holotranscobalamin, and homocysteine (1).

A reference interval is defined as the interval that detects the reference values for medical laboratory tests, provided from the sample reference distribution of the values obtained from well-described healthy people with particular statistical methods (2). The both Clinical and Laboratory Standards Institute (CLSI) and Clinical and International Federation of Clinical Chemistry (IFCC) recommend that each professional laboratory should detect its own reference intervals (RIs) (2,3). Owing to laboratory and regional differences based on population, technical instruments, nutrition, and selection of the reference people, it is imperative for most of medical laboratories to detect their own RIs (1-4).

In estimating the RIs, there are direct and indirect methods to distinguish the reference groups that mostly represent the characteristic features of population. The direct method involves the selection of reference people from the major survey group according to pre-described standards. After this survey was completed, laboratory tests of the participants are measured (1). The indirect method, by contrast, involves the choice of test results in accordance with specific criteria from laboratory data in which the examination of the results is saved regardless of individuals' features (4).

RIs for these vitamins can vary significantly among populations. The aim of this study was to demonstrate RIs in a population and to assess the folate and vitamin B_{12} status related to RIs.

Materials and Methods

Study Group

The results were obtained retrospectively from the laboratory information system of Balıkesir State Hospital between the years of 2017 and 2019. The data used were approved by the hospital administration. This study was approved by the clinical research ethical committee of Medicine Faculty of Balıkesir University. The data of 36.284 patients (70.2% female, 29.8% male) between the ages of 18 and 80 years were selected after extreme values were excluded. The age groups of the patients were separated into six subgroups (18-30, 31-40, 41-50, 51-60, 61-70, and 71-80 years). The results of patients from intensive care units and inpatient clinics were excluded from the study. Any patients who had a vitamin deficiency, megaloblastic anemia, malignancy or chronic disease were also eliminated. In order to avoid duplicated results and prevent the interference of patients taking vitamin supplements, only the initial vitamin B_{12} and folate values of the subjects were included. Vitamin B_{12} and folic deficiencies were defined as low, <148 pmol/L for vitamin B_{12} and <6.8 nmol for folate (5).

Analytical Method

B_{12} and folate concentrations were measured by ARCHITECT i2000sr (Abbott Diagnostics, Abbott Park, IL, USA) autoanalyzer. For the internal quality control (IQC) of IQC material (three levels), the manufacturer was used. The analytical test performance which pertains to intra-assay coefficients of variability (CVs), inter-assay CVs, and total analytical error is shown in Table 1. The external quality assessment scheme (EQAS) results were evaluated in the EQAS immune-assay monthly program from BIO-RAD laboratories (BIO-RAD laboratories, Diagnostic group, California, USA) for the all periods included in the study. EQAS average CV and Z-score were 6.5% and 0.29 for vitamin B_{12} and were 8.5% and 0.29 for folate. Patient samples were collected into serum separator tubes for B_{12} and folate. The

Table 1. The analytical performances of B_{12} and folate

		Concentrations	Intraassay CVs (%)	Interassay CVs (%)	TAE
B_{12}, pmol/L	Level 1	191	5.3	7.3	11.85
	Level 2	378	4.8	6.0	
	Level 3	700	4.8	5.2	
Folate, nmol/L	Level 1	8.9	5.2	6.1	11.49
	Level 2	17.0	3.8	5.1	
	Level 3	34.1	3.1	3.4	

CV: Coefficients of variability, TAE: Total analytical error

samples were freshly analyzed on the same day. Samples with hemolysis, lipemia, or icterus were excluded.

Statistical Analysis

Extreme values were excluded by using IBM SPSS. The central 95% RIs were calculated using indirect non-parametric method. The results were expressed in the form of mean ± standard deviation (SD) and percentages (%). The normal distribution was tested by the Kolmogorov-Smirnov Z-test. According to the results from the Kolmogorov-Smirnov Z-test, the RIs of the groups were estimated by parametric or non-parametric methods in accordance with the IFCC recommendations. The distribution was detected to be non-parametric by the Kolmogorov-Smirnov Z-test. Upper and lower limit values of the RIs were calculated using the non-parametric method (percentile estimation method), and points corresponding to 95% of the distribution were sought (3). Confidence intervals of 90% of references' limit values were estimated according to guidelines (3).

The Mann-Whitney U test was used to compare gender groups, while a One-Way variance analysis was used to compare age subgroups. For multiple comparisons of groups that showed differences in variance analysis, the Tukey test was used for groups that had homogeneous variance, and the Tamhane test was used for groups that did not have homogeneous variance. P<0.05 was accepted as statistically significant.

Results

The results of 20.850 patients for B_{12} and 14.183 for folate were evaluated, after eliminating patients that had an exclusion criterion and extreme values. The mean ± (SD) and percentages according to gender for analyses conducted after the exclusion of extreme values are shown in Table 2.

The mean ages of patients for B_{12} and folate were 48.9±16.3 and 49.7±16.6 years, respectively. In total, the mean concentrations of B_{12} and folate were 222±77 pmol/L and 13.9±6.5 nmol/L, respectively. 95% RIs were calculated as 97-397 pmol/L for vitamin B_{12} and 5.17-30.9 pmol/L for folate for the entire population. There were statistically significant differences between women and men for B_{12} and folate. There was a significant difference among the age groups for folate, but no significant difference among the age groups for B_{12} concentrations. RIs of vitamin B_{12} and folate for age groups are shown in Tables 3 and 4.

Out of the entire study population, 17.8% had serum vitamin B_{12} concentrations <148 pmol/L and 8.5% had <6.8 nmol/L concentrations of the serum folate. The prevalence of vitamin B_{12} and folate deficiencies for gender and age groups are presented in Table 5.

Table 2. RIs for serum folic acid and vitamin B_{12} according to laboratory data in an adult population

		n (%)	Ages (Mean ± SD)	Mean ± SD	RIs Lower-upper (90%CI)	Manufacture's RIs
B_{12}, pmol/L	Female	14.736 (70.7)	47.8±16.1	222±77	107-397 (357-436)	138-654*
	Male	6.114 (29.3)	51.4±16.7	216±78	93-396	-
Folate, nmol/L	Female	10.254 (72.3)	48.7±16.1	14.4±6.7	5.2-33.2	7.0-43.4*
	Male	3.929 (27.7)	51.5±17.1	12.7±5.9	5.9-29.3	-

*: There is not a RIs according to gender. N: Number of patients, SD: Standard deviation, RIs: Reference intervals, CI: Confidence internal

Table 3. RIs for serum vitamin B_{12} according to age subgroups

Groups	n (%)	Ages (Mean ± SD)	B_{12}, pmol/L Mean ± SD	RIs	
				Lower (90% CI)	Upper (90% CI)
18-30	2.552/888	23.1±3.7	218±70	104 (97-114)	383 (345-421)
31-40	2.439/787	35.7±2.8	220±75	103 (93-113)	393 (354-432)
41-50	3.145/1.017	45.7±2.7	220±75	102 (92-112)	393 (354-432)
51-60	3.032/1.310	55.1±2.9	222±78	98 (88-108)	400 (360-440)
61-70	2.241/1.256	65.0±2.8	217±83	90 (81-99)	403 (363-443)
71-80	1.327/856	74.9±2.73	210±84	83 (75-91)	409 (368-450)
All	14.736/6.114	48.9±16.3	220±77	97 (87-107)	397 (357-436)

n: Number of female/male patients, SD: Standard deviation, CI: Confidence internal

Discussion

Presently, clinical laboratories use RIs frequently, a practice which is advised by the manufacturer. However, these RIs are not always representative of the members of the population in question (3). Thus, the IFCC and the CLSI recommend that each laboratory determines its own RIs. Each laboratory should examine the transferability of the expected values to its own patient population and determine its own reference interval (2,3). We identified the serum RIs for folate and vitamin B_{12} according to big laboratory data in an adult population. In this study, differences were found between the RIs recommended by the manufacturer and those determined by our own population. There was not a high prevalence for deficiency of folate and vitamin B_{12} in our population.

In this study, we determined RIs 97-397 pmol/L according to the total population for vitamin B_{12}. These values were lower than the upper and lower limits recommended by the manufacturer. In the conducted studies in our country, the RIs for vitamin B_{12}, the lower limit varies between 70 and 235 pmol/L, and the upper limit varies between 374 and 1.474 pmol/L (6-9). In the study of Bakan et al. (6), RIs were determined between 70 and 368 pmol/L in the Erzurum region, which has a lower socioeconomic status and is located in the east of our country. In the study of Oncel et al. (10), RIs were determined between 75 and 518 pmol/L in the Konya region, which has a lower socioeconomic status and is located in the middle of our country. In the study of Köseoğlu et al. (7), RIs were determined between 142 and 953 pmol/L in the Izmir region, which has a higher socioeconomic status and is located in the west of our country. Avcı and Aslan (11) determined RIs as 106-393 pmol/L for the entire population in a study with non-parametric methods using laboratory data similar to our study. The determined RIs in our study are similar to the values determined by Avcı and Aslan (11). In our study, for the RIs of vitamin B_{12}, there was a significant difference between genders.

The RIs determined according to the total population in this study were 5.2-30.9 nmol/L for folate. In the study conducted in Istanbul in our country, a direct method was used to determine RIs between 5.1 and 47 nmol/L (7). In a study conducted with a direct method in Izmir, the determined RIs were between 12.7 and 45.3 nmol/L (7). In a study conducted by Bakan et al. (6), the RIs determined with the direct parametric method were between 9 and 33 nmol/L for women and 9 and 28 nmol/L for men. In the study conducted with the direct method by Tanyalcin et al. (12), the determined RIs were between 8.9 and 41.1 nmol/L for women and 5.7 and 39.9 nmol/L for men. As evidenced by these two studies, RIs for folate were lower in men than in women. These results are similar to our results: both suggest that RIs differ according to gender (6,8,11).

Deficiency of vitamin B_{12} is a severe situation for health all over the world. It correlates with insufficient nutrition, which often results from socioeconomic conditions and increased vegetarian eating habits. Vitamin B_{12} and folate deficiencies have long been well-known to cause adverse effects on health, such as neuropathy and anemia (13). In this study, the most frequently used thresholds are 6.8 nmol/L and 148 pmol/L for folate and vitamin B_{12}, respectively (14). According to these thresholds, we determined a deficiency of 17.8% for vitamin B_{12}, and 8.5% for folate in our study's population. In our study, although the prevalence of vitamin B_{12} deficiency varied depending on age and gender, the highest rate for both genders was found in the 71-80 age group. The prevalence of folate deficiency was similar in both genders, with the highest rate in the 18-30 age group. When we evaluated the entire population, it was found that men had a higher prevalence

Table 4. RIs for serum folate according to age subgroups

Groups	F/M*	Ages (Mean ± SD)	Folate, nmol/L (Mean ± SD)	RIs	
				Lower (90%CI)	Upper (90%CI)
18-30	1.721/597	23.7±3.5	12.3±5.8	4.9 (4.4-5.4)	27.7 (24.9-30.5)
31-40	1.566/459	35.7±2.8	13.2±6.1	5.5 (4.7-5.7)	29.9 (26.9-32.9)
41-50	2.089/620	45.6±2.9	14.2±6.4	5.5 (5.0-6.1)	30.9 (27.8-34.0)
51-60	2.149/813	55.4±2.8	14.8±6.7	5.6 (5.0-6.2)	30.9 (27.8-34.0)
61-70	1.671/798	65.1±2.8	14.5±6.4	4.9 (4.4-5.4)	31.9 (28.7-35.1)
71-80	1.058/642	75.0±2.7	13.1±6.6	4.9 (4.4-5.4)	31.3 (28.2-34.4)
All	10.254/3.929	49.7±16.6	13.9±6.6	5.2 (4.6-5.7)	30.9 (27.8-33.9)

F/M (female/male): Number of female/male patients, there is a significant difference among the all age groups (p<0.001), N: Number of patients, SD: Standard deviation, CI: Confidence internal

of both vitamin B_{12} deficiency and folate deficiency compared to women.

Clinical biochemistry laboratories share a massive database. We selected the indirect method to determine the RIs of vitamin B_{12} and folate because of the volume of data for test results. The advantages of the indirect method include the fact that it is less expensive and less time-consuming than the direct method. In addition, it allows for the detailed evaluation of population subgroups and the division of these groups, if necessary. Furthermore, studies have recommended that the indirect method can be as accurate as the direct method when the truth indirect is applied (3,6,11). Namely, exclusion criteria, preanalytical variables, and the analytical performance of the laboratory are very important in the application of the indirect method. In our study, we excluded people with diseases that would affect the level of the vitamins we studied, including people with chronic diseases such as malignancy, chronic kidney failure, chronic heart failure, chronic blood diseases, thyroid diseases, diabetes mellitus and patients with vitamin deficiency. We also excluded hemolysis samples that could impact preanalytical test results. In our study, 35.9% of patient records were deleted when all exclusion criteria were applied. The participants were selected from a pool of patients who applied for general examinations and who had diseases which were not expected to affect vitamin B_{12} and folate metabolism. The patient density was mostly higher in polyclinics, such as internal medicine, physical therapy and rehabilitation, dermatology, ophthalmology, and orthopedics.

Our study has several limitations. The first limitation was that we could not evaluate hematological parameters according to the laboratory data we used to determine the reference range. Measuring B_{12} and folate concentrations is a key for detecting vitamin deficiencies. However, homocysteine, methylmalonic acid tests, and other hematological tests that investigate varying levels of deficiency in these vitamins facilitate the diagnosis of deficiency and the evaluation of the status of these vitamins. Therefore, it is necessary to evaluate the hematological parameters to demonstrate their effectiveness regarding clinical decisions related to RIs. The second limitation of our study is that diseases that affect the vitamin levels of our patients (according to the diagnoses found in the hospital information system) or other additional factors are excluded. However, it is difficult to detect preanalytical factors that may affect these test results. In this regard, the results can be confirmed by a direct reference range determination method of a healthy population. However, in this case, this is always taken into consideration. Laboratory data contain serious medical information. Thus, the indirect method is more advantageous, financially efficient, and easier to follow than the direct method, especially when considering the extraction of substantial laboratory data with determined exclusion criteria in the process of determining a population's specific reference range.

Conclusion

The use of true RIs is an essential responsibility for laboratorians. There are different geographical regions, different climates, different eating habits, and different socioeconomic conditions in our country. In this respect, it is also important to determine RIs according to region. In our study, we determined RIs of our region for vitamin B_{12} and folate using the indirect method and a vast quantity of laboratory data. Furthermore, our study is a key for the comparison of the RIs recommended by the manufacturing company, and also for the determination of vitamin B_{12} and folate concentrations in the population at hand.

Table 5. The prevalence of vitamin B_{12} and for folate deficiency in our study population

Groups	Vitamin B_{12}				Folate			
	F/M*	Female (%)	Male (%)	All (%)	F/M*	Female (%)	Male (%)	All (%)
18-30	406/404	15.9	16.2	16.0	188/111	10.9	18.6	7.5
31-40	457/1.067	18.7	13.0	17.3	121/52	7.7	11.3	9.2
41-50	494/178	15.7	17.5	16.1	123/64	5.9	10.3	6.3
51-60	473/232	15.6	17.7	16.2	94/76	4.4	9.3	6.0
61-70	491/226	21.9	18.0	20.5	92/85	5.5	10.7	7.9
71-80	293/230	22.1	26.9	24.0	93/102	8.8	15.9	11.5
All	2.614/1.112	17.7	18.2	17.8	711/490	6.9	12.5	8.5

*: Number of vitamin B_{12} and folate deficiency in female/male, F/M: Female/male

Ethics

Ethics Committee Approval: This study was approved by the Clinical Research Ethical Committee of Medicine Faculty of Balıkesir University (date: 21.09.2020, number: 2020/168).

Informed Consent: The results were obtained retrospectively from the laboratory information system of Balıkesir State Hospital between the years of 2017 and 2019. The data used were approved by the hospital administration.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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ORIGINAL RESEARCH

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The Step Wise Effect of Vessel Ligation Method on Intra and Postoperative Hypoparathyroidism in the Total Thyroidectomy

Total Tiroidektomide Vasküler Ligasyon Yönteminin İntraoperatif ve Postoperatif Hipoparatiroidizme Aşamalı Etkisi

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Abstract

Objective: The aim of this study was to determine the step-wise effects of vascular ligation method on the parathyroid function in intraoperative and early postoperative periods of total thyroidectomy.

Method: A total of 54 patients between the ages of 40 and 61 years, who underwent a total thyroidectomy for euthyroid multinodular goiter between June 2019 and December 2019, were included in this study. Thyroid lobes were separated step by step using the clamp-tie technique including an inferior approach, to preserve the parathyroid glands and recurrent laryngeal nerve. All patients underwent the same routine surgical and phlebotomy procedures. Serum parathyroid hormone (PTH) and Calcium (Ca) levels were measured 2 hours before the operation, during the operation while the inferior and superior poles of the right and left lobe were connected, and at the 12th postoperative hour, and all data were analyzed retrospectively.

Results: Of the 54 patients undergoing total thyroidectomy, 7 (12.9%) were male and 47 (87.04%) were female. The mean age was 45.65±8.23 years. In terms of PTH measured in the intraoperative period, a statistically significant decrease was found during the vessel ligation of the superior pole of superior lobe, and lobe excision ($p<0.05$). In the left lobe, an advanced decrease was detected after the vessel ligation of both poles and lobe excision ($p<0.001$). When the serum levels of Ca were measured in the intraoperative period, there was no significant change during the

Öz

Amaç: Vasküler ligasyon yönteminin, total tiroidektominin intraoperatif ve postoperatif erken dönemde paratiroid fonksiyonu üzerindeki aşamalı etkilerini belirlemek amaçlanmıştır.

Yöntem: Bu çalışmaya Haziran 2019 ile Aralık 2019 tarihleri arasında ötiroid multinodüler guatr nedeniyle total tiroidektomi uygulanan 40-61 yaşları arasında, toplam 54 hasta dahil edildi. Tiroid lobları, paratiroid bezleri ve rekürren laringeal sinir korunarak inferior yaklaşımlı klemp-bağlama tekniği kullanılarak adım adım ayrıldı. Tüm hastalara aynı cerrahi ve kan alma işlemi rutin olarak uygulandı. Serum paratiroid hormonu (PTH) ve Kalsiyum (Ca) düzeyleri operasyondan 2 saat önce, operasyon sırasında sağ ve sol lobun inferior ve superior polleri bağlandıkça ve postoperatif 12. saatte ölçüldü ve veriler retrospektif olarak incelendi.

Bulgular: Total tiroidektomi yapılan 54 hastanın 7'si (%12,9) erkek ve 47'si (%87,04) kadındı, yaş ortalaması 45,65±8,23 idi. İntraoperatif dönemde PTH açısından olgular değerlendirildiğinde sağ lob superior pol damar ligasyonu ve lob eksizyonunda istatiksel olarak anlamlı azalma saptandı ($p<0,05$). Sol lobda ise her iki pol damar ligasyonu ve eksizyonu sonrasında da ileri düzeyde azalma saptandı ($p<0,001$). Serum Ca açısından incelendiğinde intraoperatif dönemde sağ lob cerrahi işlemlerinde anlamlı değişiklik saptanmazken, sol lob damar bağlama ve lob eksizyon işlemleri sonrası Ca düzeylerinde anlamlı düşme saptandı ($p<0,05$). Postoperatif erken dönemde serum PTH ve Ca düzeylerinde

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Abstract

surgical procedures of the right lobe, whereas there was a significant decrease after the vessel ligation of the left lobe and the lobe excision procedures (p<0.05). There was a statistically significant decrease in serum PTH and Ca levels in the early post-operative period (p<0.05). A significant decrease in PTH levels of patients without hypocalcemia was observed after ligation of the superior pole of the right lobe, whereas in patients with hypocalcemia, this decline started after the removal of the right lobe (p<0.05). After the right lobe and left lobe excision and at the 12th postoperative hour, significant differences were detected in Ca levels between the groups with and without hypocalcemia. In addition, patients with hypocalcemia showed a significant decrease in Ca levels after left lobe excision and at the postoperative 12th hour (p<0.05 and p<0.001, respectively).

Conclusion: The step-wise effects of the vessel ligation method on intraoperative and postoperative PTH levels in total thyroidectomy may vary depending on the presence of hypocalcemia without making a significant difference in the risk of early postoperative complications.

Keywords: Calcium, hypocalcemia, parathyroid hormone, total thyroidectomy

Öz

istatiksel olarak anlamlı azalma saptandı (p<0,05). Sağ lobun superior polünün ligasyonu sonrası hipokalsemi olmayan hastaların PTH düzeylerinde anlamlı bir azalma gözlenirken, hipokalsemili hastalarda bu düşüş sağ lobun çıkarılmasından sonra başlamıştır (p<0,05). Sağ lob ve sol lob eksizyonu sonrası ve postoperatif 12. saatte, hipokalsemi olan ve olmayan gruplar arasında Ca düzeylerinde anlamlı farklar tespit edilmiştir. Ayrıca, hipokalsemili hastaların Ca düzeylerinde, sol lob eksizyonundan sonra ve postoperatif 12. saatte anlamlı düşüş görülmüştür (sırasıyla p<0,05 ve p<0,001).

Sonuç: Total tiroidektomide konvansiyonel damar ligasyon yönteminin intraoperatif ve postoperatif PTH düzeylerine aşamalı etkilerinin, erken dönem postoperatif komplikasyon riski insidansında anlamlı bir fark yaratmadan, hipokalsemi varlığına bağlı olarak değişebileceği gösterilmiştir.

Anahtar kelimeler: Hipokalsemi, kalsiyum, paratiroid hormon, total tiroidektomi

Introduction

Thyroidectomy is a widely performed operation in the practice of general surgery and has a complication rate lower than 5%. Nowadays, the most important complications of thyroidectomy performed mainly due to thyroid cancer and hyperparathyroidism are recurrent nerve injuries and transient or permanent hypoparathyroidism (1). In recent years, as the necessity of operation type includes the total thyroidectomies rather than subtotal types, the risk of these complications as well as the risks of incidental parathyroidectomy and related postoperative hypocalcemia increase in thyroidectomies (2). A statistically significant correlation was detected between incidental parathyroidectomy and hypocalcemia (3). Moreover, the bilateral thyroidectomy and central dissection also significantly increase the risk of developing postoperative hypocalcemia (4). Mastering the anatomy and knowing the anatomical variations are of primary importance, but parallel to the development in medical technologies, many hemostasis-producing techniques have also been developed (5-7). Although there are few studies in the literature about how these techniques including thermal devices result in any nerve injury and damage on the parathyroid glands (PGs), (7-9) the influence of vessel-ligation methods on intra and early postoperative PG function following a total thyroidectomy is not clear yet. In the present study, the step-wise effects of vascular ligation method on the parathyroid hormone (PTH) and Calcium (Ca) were investigated in the early and postoperative periods of total thyroidectomy by using an inferior approach and the results were discussed with the light of literature to elucidate the clinical outcomes of vessel ligation in thyroidectomy patients.

Materials and Methods

Patients

This study involved the data of 54 patients diagnosed with a euthyroid multinodular goiter operated by using an inferior approach, who were selected among 108 cases undergoing a total thyroidectomy in the Department of Surgery between June 2019 and December 2019. Prior to the study, the local ethics committee approval was obtained from the Clinical Research Ethics Committee of University of Health Sciences Turkey, Bağcılar Training and Research Hospital (decree number: 2020.01.1.05.005). All patients were informed about the study and informed consent was obtained from all patients regarding the use of their data in this scientific study.

The patients aged between 40 and 61 years, who were diagnosed as euthyroid multinodular goiter and experienced a post-operative temporary hypoparathyroidism, were included in the study. The patients undergoing a combined thyroidectomy and parathyroidectomy and patients with the indications of papillary thyroid cancer, follicular cancer, anaplastic cancer, medullar cancer, hypothyroidism, hyperthyroidism, retrosternal goiter and toxic goiter were excluded from the study. Demographic data, the duration of operation, the day of hospitalization, the volume of drainage, the number of reoperations, and mortality rates

were recorded.

Operative Techniques

Surgeries and postoperative care were standardized according to the literature (10,11). All thyroidectomies were performed by using an inferior approach under general anesthesia, which was a routine practice firstly applied by the same experienced surgeons in our clinic. The thyroid was approached via a low transverse collar incision. After the elevation of the platysma flap, superiorly and inferiorly, the strap muscles were divided in the midline and elevated sharply from the underlying thyroid gland. The dissection of the thyroid began with ligation division of the middle thyroid vein. Ligations were done with resorbable 2-0 and 3-0 vicryl sutures. Attention was directed toward the visualization of the inferior and superior PGs. The inferior thyroid artery (ITA) was ligated after the identification of the recurrent laryngeal nerve (RLN), first the inferior pole vessels were ligated, then superior pole vessels were ligated. During the dissection of the PGs and RLN, we preferred suturing the small vessels in this area. Each suture-ligation used for this area (around Berry's ligament) and the thyroid tissue by its capsule were elevated from the pretracheal fascia carefully (10). The dissection was carried across the midline and completed by mobilizing the isthmus and pyramidal lobe of the thyroid (10,11).

During the total thyroidectomy, the thyroid lobes of most patients were divided step by step by the inferior approach of clamp-tie technique, avoiding the PGs and RLNs. If there was any bleeding during the operation and the removal of tissue, the suture-ligation was used to provide hemostasis (10).

The duration of surgery was considered to be from the start of the skin incision until the wounds were covered with a dressing. Closure of the wound was performed using the conventional steps (11). Nerve monitoring system (Medtronic, NIM 3.0 version, USA) was used to monitor any nerve damage during the operation.

Serum PTH and Ca levels were preoperatively measured 2 hours before the operation, during the operation, and on the following 12 hours of the operation. Intraoperative levels of PTH and Ca were measured after the steps of the operation given below:

•Ligation of the inferior pole of the right lobe,

•Ligation of the superior pole of the right lobe,

•Excision of the right lobe,

•Ligation of the inferior pole of the left lobe,

•Ligation of the superior pole of the left lobe,

•Excision of the left lobe,

All data of the study were analyzed retrospectively.

Laboratory Methods

Intravenous blood samples of the patients were collected for eight times to measure the preoperative, intraoperative and postoperative serum PTH and albumin-adjusted Ca levels by standard methods using the Roche Diagnostics Modular Analytic system (Roche Diagnostics, Indianapolis, IN) in the biochemistry laboratory. PTH level was measured by an Elecsyse 170 immunoassay system, and the inter- and intra-assay CVs were 3.4% and 2%, respectively. The normal range for serum PTH level was accepted to be between 10 and 65 pg/mL. Hypocalcemia was defined as serum adjusted Ca <8.5 mg/dL, measured within 24 hours of total thyroidectomy (range: 8.5-12.5 mg/dL).

Postoperative Management and Follow-up

Postoperative complications including transient/permanent RLN palsy, transient/permanent hypocalcemia, bleeding and wound infection were recorded. Postoperative diagnosis of hypocalcemia was not only due the blood level of Ca, but also due to the clinical symptoms of hypocalcemia defined according to the literature (12). These symptoms include the neural hyperexcitability, confusion, disorientation, and hallucinations. On respiratory examination, inspiratory or expiratory wheeze, laryngeal stridor, dysphagia, and bronchospasm may be observed. On cardiac examination, bradycardia, tachycardia, S3, and signs of heart failure may be present. Chvostek signs and Trousseau signs may be indicative for hypocalcemia (12).

Oral Ca + calcitriol was not routinely given to all patients unless the level of adjusted Ca was under 8.5 mg/dL, the level of PTH was lower than 10 pg/mL and the patients showed any postoperative clinical symptoms of hypocalcemia defined above. The patients with normal levels of PTH but with the level of adjusted Ca under 8.5 mg/dL with postoperative clinical symptoms of hypocalcemia were prescribed only two ampules of intravenous Ca (Ca Picken 10% ampule containing 225 mg Ca Gluconate Monohydrate) twice within the first 24 hours. If the symptoms were not relieved, the injection of Ca was resumed. If needed, oral Ca (Calcimax-D3® containing 2.500 mg Ca carbonate and 880 IU vitamin D3, Basel Ilac, İstanbul, Turkey) and/or oral calcitriol (Rocaltrol® containing 0.25 µg calcitriol, Deva Ilac, İstanbul, Turkey) were prescribed twice daily

until the first clinic visit. Patients requiring Ca ± calcitriol supplements after their first postoperative visit were followed-up, and their Ca and PTH levels and clinical symptoms for hypocalcemia were checked until they could maintain normocalcemia and normoparathyroidism without supplements (13).

Statistical Analysis

All statistical analyses were performed by the GraphPad Instat Statistics Software. The normality test was performed by the Kolmogorov-Smirnow test. Two parametric data were compared by the Paired t-test, and two non-parametric data were compared by the Mann-Whitney U test. Three or more parametric data were compared by the ANOVA and Tukey-Kramer Multiple Comparisons test. Three or more non-parametric data were compared by the Kruskal-Wallis test (non-parametric ANOVA) and Dunn's Multiple Comparisons test. The significance levels were determined as $p<0.05$, $p<0.01$, and $p<0.001$.

Results

Of 54 patients who had undergone total thyroidectomy, 7 (12.9%) were male and 47 (87.04%) were female patients with an overall mean age of 45.65±8.23 years (range: 40-61 years). There was no vocal cord paralysis (unilateral/bilateral) following the surgery in any of the patients. The mean duration of operation was 110.2±8.9 min and that of hospitalization was 2.4±0.3 days. The mean drainage volume was 50.2±9.3. None of the patents needed any reoperation and no mortality due to the operation occurred. The most frequent postoperative complication was hypocalcemia that was transient in five patients (9.3%), and there was no permanent hypocalcemia in any of the patients. Although the preoperative mean level of Ca of all patients appeared to be under normal range, not all patients showed the clinical symptoms of hypocalcemia; therefore, treatment for hypocalcemia was only applied to the patients with transient hypocalcemia. RLN palsy, bleeding or wound infection were not observed following the operation (Table 1).

Comparing preoperative, intraoperative and postoperative hormone levels of the patients (Table 2), a significant decrease in PTH levels started following the ligation of the superior pole of the right lobe ($p<0.05$) and this decrease continued until postoperative 12th hour with an increasing level of significance depending on time and step of the operation. The lowest level of PTH was observed at the postoperative 12th hour in comparison to the preoperative levels ($p<0.001$). On the other hand, Ca levels began to decrease following the ligation of the inferior pole of the left lobe ($p<0.05$) and this decrease also continued in time, and the lowest level of Ca was observed at the postoperative 12th hour ($p<0.001$).

Patients were divided into subgroups according to the presence of hypocalcemia. No statistically significant intergroup difference was found among preoperative, intraoperative and postoperative PTH levels depending on the presence of hypocalcemia (Table 3). However, a considerable decrease in PTH levels of the patients without hypocalcemia was

Table 1. Postoperative parameters of the patients

Parameter	Value	Total (n=54)
Operation duration (min)	Mean ± SD	110.2±8.9
Hospitalization (day)	Mean ± SD	2.4±0.3
Drainage volume (mL)	Mean ± SD	50.2±9.3
Reoperation	n (%)	0
Mortality	n (%)	0
Postoperative complications	n (%)	-
Transient RLN palsy	-	0
Permanent RLN palsy	-	0
Transient hypocalcemia	-	5 (9.3)
Bleeding	-	0
Wound infection	-	0

RLN: Recurrent laryngeal nerve, SD: Standard deviation

Table 2. Preoperative and postoperative hormone levels of the patients (n=54)

	Parathyroid hormone (pg/mL) Mean ± SEM	Calcium (mg/dL) Mean ± SEM
Preoperative levels	60.27±6.54	7.32±0.16
Intraoperative levels		
Ligation of the inferior pole of the right lobe	53.31±5.76	7.25±0.18
Ligation of the superior pole of the right lobe	50.18±5.32*	7.19±0.16
Excision of the right lobe	47.55±3.98*	7.15±0.18
Ligation of the inferior pole of the left lobe	37.78±3.07**	7.05±0.18*
Ligation of the superior pole of the left lobe	35.20±3.36***	6.94±0.18*
Excision of the left lobe	29.97±3.15***	6.70±0.17***
Postoperative 12th hour	19.99±2.11***	6.56±0.20***
p	0.0001	0.0001

*: $p<0.05$, **: $p<0.01$, ***: $p<0.001$ vs preoperative levels, SEM: Sport and exercise medicine

observed following the ligation of the superior pole of the right lobe (p<0.01), while this decrease in the patients with hypocalcemia began after the removal of the right lobe (p<0.05). Reductions in PTH levels of both groups continued after the 12th hour of the operation (Table 3).

Comparing the preoperative, intraoperative and postoperative Ca levels according to the presence of hypocalcemia (Table 4), a statistically significant difference was detected between two groups following the excision of the right lobe and the excision of the left lobe (p<0.05). There was also a statistically notable difference among Ca levels of two groups at the postoperative 12th hour of the operation (p<0.001), and additionally at that time, the lowest level of Ca was observed among the patients without hypocalcemia. Moreover, the patients with hypocalcemia had a significant decrease in Ca levels after the excision of the left lobe and at the postoperative 12th hour of the operation (p<0.05 and 0.001, respectively).

Discussion

The most important complications of thyroid surgery with a great effect on the patient's quality of life are recurrent nerve injury and transient or permanent hypoparathyroidism (5,6). A temporary hypoparathyroidism is common (24.1%) but the permanent hypoparathyroidism is rare (1.2%) following a total thyroidectomy (14). The most common cause of acquired hypoparathyroidism is the removal or devascularization of the PG due to a traumatic surgery (5). Thus, in the present study, the step-wise effects of vascular ligation method on the PG function were investigated in the early and postoperative periods of total thyroidectomy performed by using and inferior approach, and the findings showed a significant decrease in PTH levels following the ligation of the superior pole of the right lobe, which continued until the postoperative 12th hour ever-increasingly, depending on the time and step of the operation; however, the levels of PTH were in normal range.

There are many studies investigating the effects of the selected surgical technique and vascular ligation methods

Table 3. Preoperative and postoperative parathyroid hormone levels (pg/mL) of the patients compared to the presence of hypocalcemia

	No hypocalcemia (n=49)	Hypocalcemia (n=5)	p
Preoperative levels	61.16±6.91	51.80±7.03	0.605
Intraoperative levels			
Ligation of the inferior pole of the right lobe	53.49±6.31	51.60±2.71	0.486
Ligation of the superior pole of the right lobe	50.77±5.72	44.52±4.48	0.802
Excision of the right lobe	47.89±4.22	44.26±4.23	0.808
Ligation of the inferior pole of the left lobe	37.73±3.29**	38.30±2.75	0.757
Ligation of the superior pole of the left lobe	35.68±3.52**	30.68±3.99*	0.487
Excision of the left lobe	29.92±3.44***	30.41±1.97*	0.487
Postoperative 12th hour	20.12±2.21***	18.74±2.50*	0.808

*: p<0.05, **: p<0.01, ***: p<0.001 vs preoperative levels

Table 4. Preoperative and postoperative calcium levels (mg/dL) of the patients compared to the presence of hypocalcemia

	No hypocalcemia (n=49)	Hypocalcemia (n=5)	p
Preoperative levels	7.33±0.18	7.20±0.08	0.505
Intraoperative levels			
Ligation of the inferior pole of the right lobe	7.30±0.20	6.80±0.34	0.243
Ligation of the superior pole of the right lobe	7.24±0.17	6.64±0.39	0.318
Excision of the right lobe	7.22±0.19	6.48±0.23	0.029+
Ligation of the inferior pole of the left lobe	7.11±0.19	6.44±0.64	0.368
Ligation of the superior pole of the left lobe	7.00±0.19	6.42±0.41	0.247
Excision of the left lobe	6.78±0.19	5.90±0.32*	0.047+
Postoperative 12th hour	6.67±0.22*	5.48±0.12***	<0.0001+++

*: p<0.05, ***: p<0.001 vs preoperative levels, +: p<0.05, +++: p<0.001 vs no hypocalcemia

on the PG in thyroidectomies, but there is no consensus on their superiority to each other (7,8,11). Since we used only an inferior approach of clamp-tie technique for thyroidectomy and aimed to determine the changes in PTH and Ca levels, an iatrogenic damage on the PGs of patients can be excluded from our study. Although there are many studies predicting whether hypoparathyroidism will be temporary or permanent in which consensus on this issue cannot be reached (15,16), we ignored these controversial ideas by selecting the patients without any hypoparathyroidism. We conducted this study on determining the indicative levels of PG function and hypocalcemia by excluding the thermal effect of devices completely and by entering to the thyroid gland by an inferior approach of clamp-tie and then performing all the hemostasis by vessel ligation. In this approach, the RLN is found in the soft areolar tissue in the tracheoesophageal groove proximal to the ITA crossing point. One advantage of this technique is that the RLN is found proximally prior to extra-laryngeal branching and away from thyroid bed scarring that might have been caused by prior surgery (10).

In the present study, the preoperative mean levels of Ca in all patients appeared to be lower than normal ranges. This is probably due to our patients experiencing a malnutrition or an insufficient sun exposure during a year, who live in a population with relatively low socioeconomical levels compared to the other regions of Turkey.

Studies have reported that there is no significant difference in safety and in terms of the risk of complications between a total thyroidectomy and subtotal thyroidectomy (17). Since the secondary interventions after a subtotal thyroidectomy may cause more damage to the parathyroid gland due to adhesions, we suggest performing the largest possible surgery, i.e. total thyroidectomy, in the first surgery. For this reason, we applied total thyroidectomy to all our patients. Some studies gave a high incidence of postoperative hypocalcemia by total thyroidectomy as 30% reported by de Araujo Filho et al. (18). However, this is still statistically different from the preoperative levels, as in our study in which Ca levels began to decrease following the ligation of the inferior pole of the left lobe and this decrease also continued by time and each step of the thyroidectomy, and the lowest level of Ca was observed at the postoperative 12th hour. The enhanced decrease in Ca and PTH levels after the ligation of the left lobe was an expected outcome due to the removal of the right lobe, already performed before the removal of the left lobe.

Moreover, the most frequent postoperative complication was transient hypocalcemia observed in 9.3% of the patients, suggesting a lower risk of complication of hypocalcemia. Therefore, we may recommend a total thyroidectomy by using an inferior approach to all patients who are going to undergo a thyroidectomy.

Most researchers have claimed that the postoperative hypofunction of PGs occurs due to an ischemia, as a secondary to the ligation of the ITA. This is a logical inference, since it is well-known that the blood supply to the PGs glands comes mainly from this artery (18). Therefore, some studies evaluated the moderate influence of different surgical techniques in postoperative hypocalcemia and found the association of the distal ligation of ITA branches during a total thyroidectomy with lower mean postoperative Ca and PTH levels (19,20). Although no conclusive results in favor of proximal or distal ligation have been reported, the distal ligation of ITA is a simple surgical maneuver, allowing to isolate carefully inferior parathyroid gland preserving the inferior laryngeal nerve. Therefore, we have always ligated the distal part of ITA, whereas a proximal ligation was also preferred in some cases, with a lower incidence. In these specific situations, the ligation of ITA along the main trunk is needed to achieve a better bleeding control, without any additional complication during surgery. This is promoted by the outcome of our study of the absence of any bleeding, besides the absence of RLN palsy and a wound infection, supporting a routine ligation of the distal part of ITA during a total thyroidectomy.

Conclusion

This study has shown that the step-wise effects of vessel ligation method on intra and early postoperative parathyroid functions following total thyroidectomy may vary based on the presence of hypocalcemia, without a significant difference in the incidence of risk of postoperative complications. The vessel ligation in thyroidectomy should be performed by a delicate manipulation of the thyroid glands by an experienced surgeon, and in the closest proximity of thyroid gland to preserve the PGs and their functions. If the parathyroid is removed or avulsed accidentally during the thyroidectomy, perioperative auto-implantation to the forearm or sternocleidomastoid muscle is suggested. In future studies, comparing the techniques of thyroidectomies is recommended, including an intraoperative identification of PGs or preoperative Ca supplementation to the patients with hypocalcemia.

Ethics

Ethics Committee Approval: Prior to the study, the local ethics committee approval was obtained from the Clinical Research Ethics Committee of University of Health Sciences Turkey, Bağcılar Training and Research Hospital (decree number: 2020.01.1.05.005).

Informed Consent: All patients were informed about the study and informed consent was obtained from all patients regarding the use of their data in this scientific study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: G.E., Y.E., Design: G.E., M.K., Y.E., Data Collection or Processing: G.E., H.Y., N.A.H., S.M., R.K., Y.A., M.T., T.S., Analysis or Interpretation: G.E., H.Y., N.A.H., S.M., R.K., Y.A., M.T., T.S., Literature Search: G.E., H.Y., N.A.H., S.M., Writing: G.E., M.K., H.Y., N.A.H., S.M., R.K., Y.A., M.T., T.S., Y.E.

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ORIGINAL RESEARCH

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Comparative Evaluation of the First-grade and Senior Medical School Students' Knowledge and Attitudes Toward Thoracic Surgery

İlk ve Son Sınıf Tıp Fakültesi Öğrencilerinin Göğüs Cerrahisi Hakkındaki Bilgi ve Tutumlarının Karşılaştırmalı Değerlendirilmesi

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Abstract

Objective: Comparison of the knowledge and attitudes of first and last year medical students about thoracic surgery.

Method: The answers of the five questionnaires which were directed to the first and last year medicine faculty students were evaluated comparatively. The first 4 questions were about the knowledge of thoracic surgery and the last question was about the wishes of thoracic surgery expertise in the future.

Results: There were 71 of first year and 68 of last year medicine students in this survey research. There were no correct answers to all of the first 4 questions. It was found that 15.49% of the first grade and 85.29% of the 6th grade correctly knew the organs in the chest cavity. The first grade students could not give the correct answer to the question which was about the diseases of thoracic surgery, whereas only six participants in the sixth grade gave the correct answer. The students in both grades responded that the stage of the disease was important in the treatment of lung cancer. For the question evaluating the treatment methods of thoracic surgery, both student groups did not answer correctly. And both of student groups had inaccurate information on the treatment of rib fracture. While 29.57% of the first grade students considered to be a thoracic surgeon, none of the sixth grade students were willing to be a thoracic surgeon.

Conclusion: The knowledge of thoracic surgery is increasing at higher grades but it is still insufficient. The fact that the thoracic surgery is considered risky compared to other departments and the medical specialty exam scores which are effective in the decision on the specialization have a negative effect on medical students to choose thoracic surgery as a future career.

Keywords: Medical education, medical faculty, medical specialty, medical students, thoracic surgery

Öz

Amaç: İlk ve son sınıf tıp fakültesi öğrencilerinin göğüs cerrahisi hakkındaki bilgi ve tutumlarının karşılaştırılmasıdır.

Yöntem: İlk ve son sınıf tıp fakültesi öğrencilerine yöneltilen 5 anket. İlk 4 soru göğüs cerrahisi bilgisini sorgularken son soru gelecekte göğüs cerrahisi isteklerini irdeledi.

Bulgular: Ankete 1. sınıftan 71 ve 6. sınıftan 68 kişi katıldı. İlk 4 sorunun tümüne doğru cevap veren bulunmadı. Göğüs boşluğunda bulunan organları 1. sınıfların %15,49'u, 6. sınıfların ise %85,29'unun doğru olarak bildiği saptandı. İki grupta da en sık timüs ve yemek borusunun yerleşimi ile ilgili hatalar yapıldı. Göğüs cerrahisi alanına giren hastalıkların değerlendirildiği soru da birinci sınıflar doğru yanıt veremezken, 6. sınıflardan sadece 6 kişi doğru yanıt verdi. Göğüs cerrahisi branşının tedavi yöntemlerinin değerlendirildiği soruyu iki grup da doğru olarak yanıtlayamazken iki grup öğrencileri büyük oranda kot fraktürü tedavisine yönelik yanlış bilgilere sahipti. Birinci sınıfların %29,57'si (n=21) göğüs cerrahisi alanında tıpta uzmanlık eğitimi düşünürken 6. sınıflardan göğüs cerrahisi uzmanı olmak isteyen saptanmadı.

Sonuç: Göğüs cerrahisi branşının bilinirliği tıp fakültesi öğrencilerinin sınıfı ilerledikçe artmakta fakat yine de yetersiz kalmaktadır. Göğüs cerrahisinin diğer bölümlere göre riskli kabul edilmesi ve uzmanlık seçiminde etkili olan tıbbi uzmanlık sınavı, tıp öğrencilerinin gelecekteki bir kariyer olarak göğüs cerrahisi seçimini olumsuz etkilemektedir.

Anahtar kelimeler: Göğüs cerrahisi, tıbbi uzmanlık, tıp eğitimi, tıp fakültesi, tıp öğrencisi

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Introduction

Since the introduction of technological advances to thoracic surgery (mechanical ventilation, double-lumen tube insertion, etc), this field of medicine has remained less recognized in the society and among healthcare workers due to the complex physiological and mechanical properties of the thoracic anatomy, name similarities, and its establishment as an independent specialty department recently. The access of most patients to thoracic surgeons occurs after they were referred by other physicians and medical staff. Therefore, the knowledge and awareness of thoracic surgery across physicians and healthcare professionals from other specialties of medicine are critical.

This survey study aimed to compare the awareness level of thoracic surgery among the first- and the senior-grade medical school students, who are the future physicians. By this study, we aimed to contribute to the awareness levels of medical students about thoracic surgery so that they could refer the right patient to a relevant clinic and we aimed to reveal the underlying reasons for medical students' disfavor of specializing in thoracic surgery, which became one of the least preferred fields of surgery for specialization, still displaying an ever-decreasing trend.

Materials and Methods

The study included volunteering first-grade and senior students attending the medical school of Balıkesir University in the 2019-2020 academic year. We developed a form comprising the informed consent and the questionnaire questions. We distributed the study form to eligible students to obtain their answers for the 5 questions in the questionnaire (Suppl 1). No demographic information other than age and sex and no information with the potential to reveal the identity of the participants were requested.

For comparisons, the participants were divided into two groups as the first-grade and senior students, which were named group 1 and group 2, respectively.

Our study was approved by the Local Ethics Committee (decision no: 2019/155). This study was conducted in compliance with the principles of the Declaration of Helsinki (version: B.10.4.ISM.4.06.68.48/184).

Statistical Analysis

Simple statistical analyses were performed using Microsoft Excel 2007. Further analyses were performed with SPSS (Statistical Package for the Social Sciences Version 24.0, SPSS Inc. Sciences Version 22.0, SPSS Inc. Chicago, IL, USA). The categorical values were given as frequency (n) and percentage (%) for descriptive analysis and the continuous data were expressed in mean ± standard deviation (SD).

Results

A total of 139 students, comprising 71 (51.1%) in group 1 and 68 (48.9%) in group 2, participated in the survey. The mean age was 21.14±2.8 years (mean ± SD) (minimum-maximum =17-27 years) and 61 (43.9%) participants were male and 78 (56.1%) were female.

The first question asking the names of the organs in the thorax was answered correctly by 15.49% (n=11) and 85.29% (n=58) of the group 1 and group 2 participants, respectively (Table 1).

The second question asked the diseases included in the specialty area of thoracic surgery. Group 1 failed to answer this question correctly and only 8.82% (n=6) of the group 2 participants gave the precisely correct answers (Table 2).

The third question that asked the participants to mark the correct options was answered correctly by one person from group 1 (1.4%) and 4 people from group 2 (5.88%). The respondents most commonly answered that the stage of the disease was critical in the treatment of lung cancer (group 1 =73.23%, group 2 =82.35%). While 48 (67.6%) participants in group 1 answered that medical treatment of asthma and chronic obstructive pulmonary disease (COPD) was provided by thoracic surgeons, there were no participants in group 2 who gave this answer. While 18 participants (25.35%) in group 1 correctly answered that the surgical procedures for lung cancer would accelerate disease progression, no participants from group 2 marked this option. Twenty-three (32.39%) participants from group 1 and 28 (41.17%) from group 2 answered that thoracic

Table 1. Responses to the first question about the organs in the chest cavity

Question 1	Group 1 n (%)	Group 2 n (%)
Heart	70 (98.59)	68 (100)
Spleen	63 (88.73)	68 (100)
Lung	71 (100)	68 (100)
Esophagus	39 (54.92)	66 (97.05)
Kidney	69 (97.18)	68 (100)
Thymus	33 (46.47)	60 (88.23)
Stomach	68 (95.77)	68 (100)
Liver	59 (83.09)	68 (100)
Breast	66 (92.95)	68 (100)

surgeons were authorized to perform sympathectomy for the treatment of regional hyperhidrosis. There were 39 (54.92%) participants in group 1 and 6 (9.67%) in group 2, who answered that the identification of lumps in the breast would require to be examined by a thoracic surgeon.

No participants in neither group gave the correct answers to all of the options of the fourth question that inquired the awareness of the types of operations performed by thoracic surgeons. Sixty-two (87.32%) participants in group 1 and 30 (44.11%) in group 2 failed to give the correct answer that the use of compression vests for the entire trunk had no place in the treatment of rib fractures. The fifth question inquired whether the participants would aim to specialize in thoracic surgery. Twenty-one (29.57%) participants in group 1 answered yes to this question, while there were no participants who would like to specialize in thoracic surgery in group 2. Two people in each of the two groups left this question without comments. When the group 1 participants, who answered yes to this question, were asked the rationale for their preference, the most common option was "i am fond of surgery'', marked by 18 (85.71%) students. There were 48 (67.60%) participants in group 1 and 66 (97.05%) participants in group 2 stating that they would not prefer thoracic surgery for specialization. The reason for not preferring thoracic surgery was the preference for a "less risky specialty" (n=20) in group 1, while the participants in group 2 (n=28) reported an "inclination to internal medicine specialty areas". The second most common reason for disfavoring thoracic surgery was the option "i will decide based on my medical specialty exam (MSE/TUS) score" in both groups (group 1, n=14, group 2, n=22).

Table 2. Responses of both groups through the question about the specialty area of thoracic surgery

Question 2	Group 1 (n=71)	Group 2 (n=68)
Pneumothorax	46	64
Lung cancer	67	54
Breast cancer	37	0
COPD	58	10
Pneumonia	62	60
Pulmonary hydatid cyst	14	26
Local hyperhidrosis	14	26
Thoracic traumas	44	60
Smoking cessation procedure	28	8
Cystic disease of breast	32	2
Esophagus cancer	32	40
Chest wall deformities	55	56
Diaphragm pathologies	37	50
Asthma	45	4
Thymus tumors	29	50

COPD: Chronic obstructive pulmonary disease

Discussion

Until the 1990s, when the thoracic surgery was defined as an independent functional medical specialty department in Turkey, thoracic surgery interventions were performed by surgeons from different disciplines, resulting in inappropriate awareness of this field of medicine (1). In this study, we conducted a survey across the first-grade and senior medical school students, aiming to compare the awareness about thoracic surgery between the groups and address the underlying reasons why or why not medical school students consider a specialization in thoracic surgery.

The first question inquired the organs in the thoracic cavity. The number of correct answers was low among first-grade medical students, classified as group 1. This finding clearly indicates that human anatomy should be better taught in high school. The same question was answered correctly by 85.29% of the senior students, classified as group 2. It was found out that 11.76% (n=8) and 2.94% (n=2) of the senior students did not know the location of the thymus and the esophagus, respectively, despite the education they received in the medical school. We can interpret this finding either by suggesting that the senior student participants did not pay enough attention to the survey questions or by critical inadequacies in medical education.

The second question inquired which subject matters were included in the field of the thoracic surgery specialty. The first-grade students failed to answer this question correctly and 8.82% (n=6) of the senior students answered this question precisely. The low rates of correct answers received from the first-grade students to this question can be explained by the Yıldırım et al.'s (1) study, which reported that the term ''thoracic surgery'' was misunderstood as chest diseases or understood as referring to breast surgery by hospital staff other than physicians and ordinary individuals in the community. The low rates of correct answers received from the senior students suggest the likelihood of potential critical issues in the clinical practice to be experienced soon by these future physicians when they will need to perform in multidisciplinary teams or see patients in need of thoracic surgery interventions.

Supplement 1. Translation of the questionnaire

1. Which of the following belongs in the rib cage?

- Spleen
- Lung
- Esophagus
- Kidney
- Thymus
- Stomach
- Liver
- Breast

2. Which of the following diseases are in the field of thoracic surgery?

- Pneumothorax
- Lung cancer
- Breast cancer
- Chronic obstructive pulmonary disease
- Pneumonia
- Pulmonary hydatid cyst
- Hyperhidrosis
- Chest traumas
- Smoking cessation
- Cystic diseases of breast
- Esophagus cancer
- Chest wall deformities
- Diaphragm pathologies
- Asthma
- Thymus tumors

3. Which of the following is correct?

- Diagnosis and treatment of asthma and chronic obstructive pulmonary disease should be managed by thoracic surgeons.
- Even in the early stage, any surgical procedure through to lung cancer will accelerate the progression of the disease.
- Thoracic sympathectomy surgery applied in palmar hyperhidrosis can be performed by thoracic surgeons.
- Surgery is the most appropriate treatment method of pulmonary hydatid cysts in adults.
- Primary spontaneous pneumothorax is more common in smokers, young, tall men. Pneumothorax follow-up and treatment is in the field of thoracic surgery.
- Self-examination of breasts is very important in early diagnosis. If a mass is suspected, it is necessary to consult a thoracic surgeon immediately.
- The stage of the disease is very important in the treatment of lung cancer. Depending on the stage of the disease, surgery and/or other oncological treatment methods can be chosen.

4. Which of the thoracic surgery operations described below are incorrect?

- Videothoracoscopy is the general name of thoracic surgeries performed with the help of a camera.
- Lobectomy is the surgical anatomic removal of one lobe of the lung.
- Mediastinoscopy is a bronchoscopy procedure performed to take samples from the mediastinal lymph nodes.
- Tube thoracostomy is the process of draining the air, blood or fluid that should not be in the pleural space.
- Thoracic sympathectomy is the surgical removal of the sympathetic nerves that provide sweating in especially regional hyperhidrosis of the hands and axilla.
- All chest corset is the method that provides thoracic stabilization in the treatment of rib fractures.

Supplement 1. Continued

5. Would you like to specialize in medicine in the field of thoracic surgery in the future?

a. If yes, why?

- I am fond of surgery.
- Low scores required to be accepted for thoracic surgery residency.
- I lost one of my relatives from lung cancer.
- Thoracic surgery would provide more satisfaction compared to other surgical branches
- There are more academic carrier opportunities in thoracic surgery.

b. If not, why?

- I have affinity of the participant for specialty areas of internal medicine.
- I would decide based on the medical specialty examination scores.
- I prefer a specialty that earns more.
- It is not popular enough.
- I would prefer a less risky field of specialty than thoracic surgery.

The majority of the participants from both groups answered the third question correctly, which inquired the thoracic surgery curriculum in general, covering the diseases mentioned in the second question. Most of the participants in either group correctly answered that the disease stage was important in the treatment of lung cancer (group 1 =73.23%, group 2 =82.35%). The participants in group 1 repeated the same misconception in the previous question that the medical treatment for asthma and COPD were provided by thoracic surgeons (67.6%, n=48). This misconception was resolved in group 2 (n=0), owing to further medical school education received by these students. The low rate of awareness of sympathectomy for regional hyperhidrosis in either group has been a warning sign to us, highlighting the need that this subject matter should be better emphasized in the thoracic surgery curriculum for the school of medicine students.

Because of the high number of students in medical schools, thoracic surgery education is mostly provided theoretically, resulting in inadequacies in practical training. No survey participants provided the correct answers to the fourth question that inquired the definitions of operation types in the area of thoracic surgery, supporting the observation about the practical training inadequacies. In both groups, the least known term was "videothoracoscopy" (group 1 =12.67%) (group 2 =23.52%), which can be associated with the recent introduction of this new method. A similar finding was reported by another study, in which specialist physicians in our country were surveyed about the types of thoracic surgery interventions. That study found that 27.2% of specialist physicians did not know the definition of videothoracoscopy precisely (2).

While 21 (29.57%) participants in group 1 answered yes to the fifth question, which asked whether the participant would like to specialize in thoracic surgery, no participants in group 2 would like to specialize in this field of medicine. A survey study on 352 students from 32 medical schools across the United Kingdom reported that, of all survey participants, 10.8% wished to specialize in thoracic surgery; however, this rate was found as low as 4.7% among the 5th-grade medical school students (3). A similar figure was found by a study from the United States, reporting a rate of 6% (4).

In our research, the option ''i am fond of surgery'' was the most commonly selected rationale by the participants. The second most common rationale for the participant's preference was the low scores required to be accepted for thoracic surgery residency (n=6). This rationale was followed by the third most common rationale that thoracic surgery would provide more satisfaction compared to other surgical branches (n=5).

Regarding the rationale for disfavoring, the first-grade students most commonly selected the option that they would prefer a less risky field of specialty than thoracic surgery (n=20). This rationale was followed by the one that the participant would decide based on the MSE/TUS scores (n=14). The third most common rationale was the affinity of the participant for specialty areas of internal medicine (n=12). In group 2, "a close interest in specialty areas of internal medicine (n=28)" was preferred most commonly. This rationale was followed by the option that the participant would like to decide based on the MSE/TUS scores (n=22). The third most commonly selected option was ''the preference for a less risky area of specialty other

than thoracic surgery'' (n=16). These results reveal that the performance anxiety about MSE (TUS), the recent increase in the number of malpractice file suits, and heavy penalties to physicians have affected the plans of medical students about specialization.

Conclusion

The results of this research demonstrated inadequacies in both secondary and higher education. These results suggest the likelihood of errors in the future when referring and consulting patients who presented to clinics other than thoracic surgery. Furthermore, we are of the opinion that the medical student's prioritization of MSE (TUS) scores and the attempts to avoid potential risks of thoracic surgery will unfavorably affect physicians and future medical practices further.

Ethics

Ethics Committee Approval: Our study was approved by the Local Ethics Committee (decision no: 2019/155). This study was conducted in compliance with the principles of the Declaration of Helsinki (version: B.10.4.ISM.4.06.68.48/184).

Informed Consent: Consent of partipiciant has been taken.

Peer-review: Externally peer-reviewed.

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ORIGINAL RESEARCH

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C-reactive Protein to Albumin Ratio as a Prognostic Predictor in Larynx Cancer

Larinks Kanserinde Prognostik Bir Belirteç Olarak C-reaktif Protein Albümin Oranı

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Abstract

Objective: During the past decade, several inflammation-based prognostic systems have been reported in the field of clinical oncology. Recently, C-reactive protein and albumin ratio (CAR) have showed their impact on a large variety of tumor types. The aim of this study is to evaluate the impact CAR on prognosis and 5-year survival (5yS) in patients operated for larynx cancer.

Method: One hundred eighteen patients operated in our center between 2010 and 2015 were eligible for retrospective analysis. We evaluated the impact of the CAR and neutrophil to lymphocyte ratio (NLR) on the 5yS. Univariate and multivariate Cox regression analyses were performed to determine the associations of CAR.

Results: The optimal cut-off level of CAR was at 0.993. A low and high CAR was assigned to 40.7% and 59.3% of patients, respectively. The 5yS rates of patients with a high CAR were worse than those in the low group (79.2% vs 73.2% p<0.05). Disease stage (p<0.001) and high level of NLR were also significant predictors of 5yS. CAR at diagnosis was associated with an unfavorable progress. Patients with stage III-IV disease had a significantly higher pretreatment CAR than patients with stage I-II disease [respectively 1.83±0.52 standard deviation (SD) and 0.58±0.38 (SD), p<0.01]. ROC analysis of overall survival of larynx squamous cell carcinoma revealed that CAR had a greater area under curve value (0.786) compared to NLR (0.695) (p<0.01).

Conclusion: CAR is an independent prognostic marker in larynx cancer after being adjusted by other accompanying factors and the CAR could be a readily available biomarker in clinical setting.

Keywords: Albumin, C-reactive protein, larynx cancer, prognosis

Öz

Amaç: Geçtiğimiz on yıl boyunca, klinik onkoloji alanında enflamasyon temelli birkaç prognostik sistem bildirilmiştir. Son zamanlarda, C-reaktif protein ve albümin oranı (CAO), çok çeşitli tümör tipleri üzerinde prognostik belirteç olarak kendini göstermiştir. Bu çalışmanın amacı, larinks kanseri nedeniyle opere edilen hastalarda CAO'nun prognoz ve 5 yıllık sağkalım üzerine etkisini değerlendirmektir.

Yöntem: 2010-2015 yılları arasında merkezimizde ameliyat edilen 118 hasta retrospektif analiz için uygun bulunmuştur. CAO ve nötrofil lenfosit oranın (NLO) 5 yıllık sağkalım üzerindeki etkisi değerlendirildi. CAO ile sağkalım ve prognoz arasındaki ilişkileri belirlemek için tek değişkenli ve çok değişkenli Cox regresyon analizi yapıldı.

Bulgular: CAO'nun optimal cut-off seviyesi 0,993 olarak hesaplandı. Hastaların sırasıyla %40,7 ve %59,3'ünde düşük ve yüksek CAO saptandı. Yüksek CAO'lu hastaların 5 yıllık sağkalım oranları düşük gruptakilere göre daha kötü idi (%79,2'ye karşı %73,2, p<0,05). Hastalık evresi (p<0,001) ve yüksek NLO değeri de 5 yıllık sağkalım için anlamlı faktörler olarak izlendi. Tanıda CAO kötü prognoz ile ilişkili idi. Evre III-IV hastalığı olan hastalar, evre I-II hastalığı olanlara göre anlamlı olarak daha yüksek bir ameliyat öncesi CAO'ya [sırasıyla 1,83±0,52 standart sapma (SS) ve 0,58±0,38 (SS), p<0,01] sahipti. Gırtlak skuamöz hücreli karsinomun genel sağkalımının ROC analizi, CAO'nun NLO'ya (0,695) kıyasla daha yüksek (eğri altındaki alan) eğri altındaki alan değerine (0,786) sahip olduğunu ortaya koydu (p<0,01).

Sonuç: CAO, eşlik eden diğer faktörlerden bağımsız olarak, larinks kanserinde bir prognostik faktördür ve CAO klinik ortamda kullanıma hazır bir biyobelirteç olabilir.

Anahtar kelimeler: Albümin, C-reaktif protein, larinks kanseri, prognoz

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Introduction

Larynx cancer is the second most frequent cancer of the upper aerodigestive tract following oral cavity (1). Most of the pathologic diagnoses are squamous cell carcinoma, approximately for 85% to 95% of the laryngeal malignant neoplasms (2). In 2019, 12,410 new larynx cancer cases were diagnosed and 3.760 died from this disease. Laryngeal cancer occurs more frequently in men than in women (5.2 cases per 100,000 vs 1.1 per 100,000, respectively) (3). Approximately 43% of patients present with advanced (stage III or IV) disease at diagnosis. Unlike other regions, laryngeal cancer is one of a few oncologic diseases in which the 5-year survival rate has decreased over the past 20 years, from 66% to 60%, although the overall incidence is decreasing (4).

During the past decade, several inflammation-based prognostic systems have been reported in the field of clinical oncology (5). Neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), platelet (PLT) and mean platelet volume (MPV) are the most popular ones. Among them, it is well-known that the serum levels of C-reactive protein (CRP) and albumin ratio (CAR) are the most valuable ones (6). CRP is a positive acute-phase protein used for diagnosis in individuals with infection or inflammation and for the evaluation of the effectiveness of the treatment (7). Albumin is a negative acute-phase reactant. Even though albumin decreases mainly in acute inflammation, it is known to be decreased in chronic process of inflammation and it also reflects the nutrition status (8).

Head and neck cancers (HNC) often cause symptoms associated with dysphagia, suggesting that nutrition levels of these patients are generally affected. There are a few studies which have reported the association between the modified Glascow Prognostic score (mGPS) and the prognosis of HNC (9,10). CRP and albumin may separately or together have a prognostic value, either in the short term or in the long term of inflammation. CRP CAR has been reported as an alternative and basic version of GPS as a useful inflammatory index for assessing the status of cachexia (8).

In this retrospective cohort study, we investigated whether the CAR would be as useful as the NLR for predicting the prognosis and the postoperative survival of larynx cancer

Materials and Methods

A retrospective review was performed using the clinical records of the patients who had undergone elective surgery for Larynx Squamous Cell Carcinoma (LSCC). All the procedures had been performed by the same surgical team at the University of Health Sciences Turkey, Bağcılar Training and Research Hospital, between January 2010 and December 2015. The study protocol and the written informed consent were approved by the Committee of Ethics in Human Research of the University of Health Sciences Turkey, Bağcılar Training and Research Hospital with the approval number 2019.12.2.01.091

Inclusion and Exclusion Criteria

The inclusion criteria of this study were as follows: 1) being histologically diagnosed as LSCC and operated by our department, 2) having pre-treatment blood sampling for complete blood count (CBC), CRP and albumin measurement, and 3) regular follow-up.

Patients who had any inflammatory, systemic or autoimmune disease and/or malnutritional condition, secondary malignancy and any trauma and medication history that might affect the level of blood parameters were excluded from the study.

Surgery Type

All cancer patients were assessed with a comprehensive head and neck examination, including flexible direct laryngoscopy and imaging (computerized tomography scans and chest X-rays). Tumors were classified according the TNM classification of the American Joint Committee on Cancer (AJCC) (8^{th} edition, 2017). The patients underwent two types of surgeries according to the stage of the tumor as well as the laryngeal exposure as primary treatment. Endoscopic resection was performed using en-bloc or piecemeal techniques for early stage tumors. Open surgery included partial (laryngofissure cordectomy, supraglottic or supracricoid horizontal laryngectomy) and total laryngectomy, and the minimum follow-up duration of the patients included in the study was 24 months.

Clinical Data Extraction

We reviewed baseline characteristics of participants, including age, gender, disease stage, smoking status, tumor histology, factors related to the primary treatment (the start and the end of the treatment, treatment regimen, type of surgery, treatment of neck, radiotherapy doses, duration of treatment, interruptions, radiologic (magnetic resonance, positron emission tomography scan) follow-up and 5 years of outcomes and survival rates, the incidence of recurrence and second primary malignancy by using a standard data extraction system. Tumors were classified according to the

TNM classification of the AJCC (8th edition, 2017). Blood samples were tested prior to the initial treatment. We noted the blood parameters including CBC, CRP and albumin. Then, we calculated CAR and NLR values of the study groups and the control group. Then, we investigated the most sensitive and specific indicator parameter associated with larynx cancer

Statistical Analysis

The chi-square or Fisher's Exact test was used to compare the categorical variables, which was presented as the numbers and percentages of patients. Univariate analyses were conducted using the log-rank test analysis. Multivariate analysis of these variables in survival was performed using the Cox proportional hazards model. For advanced comparisons of CAR, white blood cells, hemoglobin (Hgb), PLR, and MPV, we used the Mann-Whitney U test, as Post-hoc test. To detect the most significantly associated parameter with the activity of RAS, the receive operating characteristic (ROC) curve analysis was carried out to assess the cut-off of CAR. The optimal cut-off values were identified as the values that maximize the Youden index (sensitivity + specificity - 1). Survival curves were estimated with the Kaplan-Meier method. The associations of CAR with survival were evaluated in univariable and multivariable cox regression models. For statistical analysis of all data, we used SPSS software for Windows (SPSS Inc., Chicago, IL, USA). All tests were two-sided and a p-value <0.05 was considered statistically significant.

Results

One hundred thirty one patients were operated in our tertiary clinic between 2010 and 2015. During the follow-up period, 7 of these patients died from disease independent reasons and 6 patients died in follow-up. Thus, 118 patients were included in the study. The median follow-up period was 51.2 months (range: 8-60 months). One hundred twelve of the 118 (94.9%) patients were men, and 6 (5.1%) were women. The demographic characteristics of the patients are described in Table 1. The median age was 65 years (range: 45-78 years). Most of them were older than 65 years (n=84, 71.2%). The majority of the patients had a disease stage of IV (40.7%) and stage III (28.8%). 22% of the patients were stage I and 8.1% of the patients were stage II. The distribution of the primary tumor was as follows: glottic (n=98), supraglottic (n=15), and subglottic (n=5).

Table 1. Clinicopathological characteristics of patients stratified by CAR and NLR (CAR C-reactive protein to albumin ratio, NLR neutrophil to lymphocyte ratio)

	n=118	%	CAR Mean ± SD	NLR Mean ± SD	Hb Mean ± SD	p CAR	p NLR
Gender						0.659	0.762
Male	112	94.9	1.81±0.98	3.01±0.89	13.83±0.69	-	-
Female	6	5.1	1.84±0.42	3.04±0.96	14.41±0.51	-	-
Age						0.637	0.654
<65 years	84	71.2	1.81±0.44	2.99±0.95	13.92±0.73	-	-
>65 years	34	28.8	1.94±0.05	3.07±0.76	13.70±0.58	-	-
Localization						0.092	0.08
Glottic	98	83.1	1.85±0.21	3.04±0.94	13.86±0.72	-	-
Supraglottic	15	12.7	1.80±0.11	2.82±0.55	13.78±0.44	-	-
Subglottic	5	4.2	1.54±0.18	2.98±0.83	14.01±0.83	-	-
Stage						<0.01	0.567
I	10	8.5	0.36±0.46	2.89±0.78	13.96±0.59	-	-
II	26	22	0.63±0.45	3.14±0.93	14.02±0.66	-	-
III	34	28.8	1.65±0.59	2.88±0.67	13.72±0.55	-	-
IV	48	40.7	2.01±0.56	3.05±1.03	13.85±0.81	-	-
Lymph node metastasis						0.045	0.07
Yes	47	39.9	1.85±0.44	3.02±0.16	13.92±0.73	-	-
No	71	60.1	1.77±0.05	2.99±0.91	13.70±0.58	-	-
Total	118	100	1.82+0.86	3.01±0.89	13.86±0.69	-	-

SD: Standard deviation, CAR: C-reactive protein to albumin ratio, NLR: Neutrophil to lymphocyte ratio, Hb: Hemoglobin

Local recurrences occurred in 20 patients (16.9%) and locoregional recurrences developed in 47 (39.9%) patients. Twenty eight (23.7%) patients died due to disease in the five years. The 5-year overall survival (OS) rate for the entire cohort was 76.3%. Using the roc chart, we found that the range of cut-off value for CAR was 0.993 as the optimal cut-off level for assessing 5-year survival (Figure 1). Patients were divided into two groups based on the cut-off value of CAR ≥0.993 (n=70, 59.3%) and CAR <0.993(n=48, 40.7%). Using the same technique, we found that the range of cut-off value for NLR was 3.05 as the optimal cut-off level for assessing 5-year survival (Figure 2). Patients were divided into two groups based on the cut-off value of NLR ≥3.05 (n=38, 32.2%) and NLR <3.05 (n=80, 67.8%).

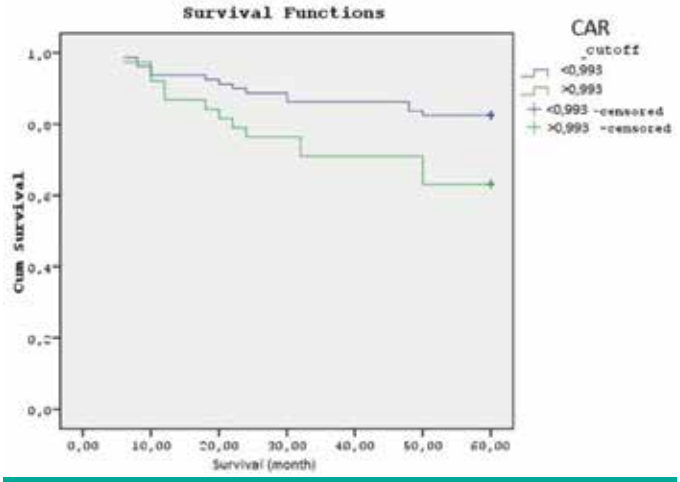

Figure 1. Kaplan-Meier curves for overall survival according to CAR at diagnosis. OS stratified by CAR at diagnosis (CAR <0.99 vs CAR ≥0.99)

CAR: C-reaction protein to albumin ratio, OS: Overall survival

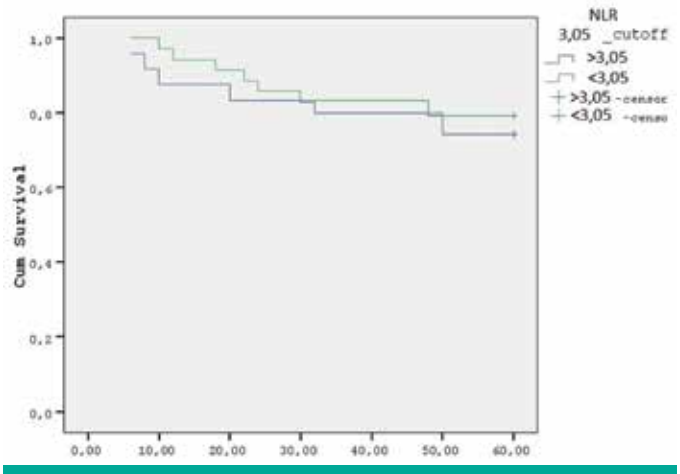

Figure 2. Kaplan-Meier curves for overall survival according to NLR at diagnosis. OS stratified by CAR at diagnosis (NLR <3.05 vs NLR ≥3.05)

NLR: Neutrophil to lymphocyte ratio, OS: Overall survival, CAR: C-reaction protein to albumin ratio

In contrast to the patients with high CAR, patients with low CAR had longer 5-year survival (74.3% vs 79.2%, p<0.05) (Figure 1). Similarly, longer 5-year survival was also significantly observed in patients with low NLR compared to high NLR (73.2% vs 79.5%, p<0.05). Figure 3 represents the graph of the ROC analysis of the parameters including CAR and NLR. ROC analysis of OS of LSCC revealed that CAR had a greater area under curve (AUC) value (0.786) compared to NLR (0.695) (p<0.001).

According to stage, patients with stage III-IV disease had a significantly higher pretreatment CAR (1.83±0.52) than patients with stage I-II disease (0.58±0.38, p<0.01) (Table 1). Similarly, in terms of lymphatic metastasis, positive patients had a significantly higher pretreatment CAR (1.85±0.44) than patients with negative lymphatic metastatic disease (1.77±0.05, p=0.045) (Table 1). However, there was no significant association between CAR-NLR and gender (p=0.077), age (p=0.087) and localization of tumor. Moreover, CAR was identified as a significant prognostic factor for the OS when adjusted by clinicopathological factors, other inflammation based factors and other tumor markers (adjusted hazard ratio 2.13, 95% confidence interval 1.38-3.4, p=0.002).

Discussion

There are numerous factors that contribute to the prognosis of laryngeal cancers such as location of tumor, age, gender,

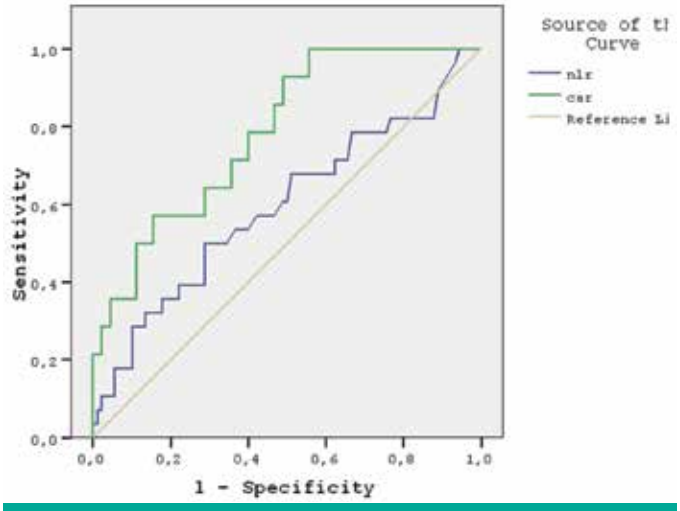

Figure 3. The graph of the ROC analysis of the parameters including CAR and NLR

NLR: Neutrophil to lymphocyte ratio, CAR: C-reaction protein to albumin ratio, ROC: Receive operating characteristic

alcohol, cigarette usage, histology, histological grade, anterior commissure involvement, performance status, Hgb level and duration of primary treatment (11). LSCC patients are at the highest risk for recurrence in the first three years following the treatment. After this, the chance of recurrence is low, and any lesion represents a new primary cancer (12).

In the literature, the link between cancer and inflammation has been evaluated previously (13). Several potential mechanisms have been suggested for the relationship between inflammatory response and cancer (14). Tumor growth or invasion could activate tissue inflammation and then tumor overgrowth induces hypoxic necrosis and local tissue damage, this is also thought to activate an inflammatory response. And the other hypothesis is that cancer cells and associated leukocytes could trigger the production of the inflammatory cytokines and chemokines which facilitate cancer growth, invasion and angiogenesis, such as tumor necrosis factor, vascular endothelial growth factor interleukin (IL)-1, -6, and -8. As a result, disruption of the host immune response and resistance to cytotoxic drugs might occur (15). The CRP concentration has been found to be useful in evaluating both the severity of inflammation and treatment method in cases of respiratory tract inflammation and myocardial infarction (16,17). Determination of CRP is a cheap, consistent and reproducible test and is available in almost every hospital.

There is an increasing interest in the use of blood parameters as prognostic factors in cancers. Neutrophil, lymphocyte, CRP and PLT counts, either as individual values or in relation to each other, could be associated with the cancer prognosis (17-20). NLR and the CAR were reported to have a significantly prognostic value as the markers of inflammation (5,18,19). NLR, a novel potential marker for identifying inflammation in various diseases, is a valuable marker, easily accessible and cheap parameter unlike the expensive inflammatory markers such as IL-6, IL-1b. Ozyalvacli et al. (20) have reported that high NLR is a significant diagnostic factor of distinction of breast cancer. NLR is also found to be an important prognostic marker for stage II or III gastric cancer associated with poor prognosis (21).

CRP is an acute-phase reactant synthesized by hepatocytes, which is regulated by proinflammatory cytokines, particularly IL-6 (22). In patients with cancer, there is evidence of the stereotyped acute-phase protein reply of increased CRP and decreased albumin, and this relationship is similar to different tumor types (23).

Several studies have investigated the association between inflammatory mediators and HNC. Nakayama et al. (9) reported for the first time the clinical value of the mGPS in patients with HNC. In a different study, the relationship between inflammatory indices, including the CRP and albumin levels, and the disease prognosis showed salivary duct carcinoma (24). Kinoshita et al. (15) have demonstrated that the CAR is an independent prognostic marker in patients with hepatocellular carcinoma. Similar to this finding, after the analysis of 1.572 patients who were treated for nasopharynx carcinoma (NPC), Zhang et al. (25) reported that CAR might be an useful prognostic indicator in patients with NPC, independent of disease stage. According to the literature, it can be said that the CAR would be applicable as a new inflammation-based prognostic system that could add a new aspect to prognostication and classification potential.

We found that patients with an elevated CAR were more likely to be LSCC with high stage tumor. Moreover, the multivariate analysis demonstrated that patients who had advanced stage disease and CAR higher than 0.99 had more possibility of locoregional recurrence and poor survival rates than patients with low CAR levels. This may also lead to poor prognosis in patients with high CAR. When compared to NLR, higher NLR might also be an indicator of poor prognosis in patients with LSCC, but CAR had a greater AUC in the ROC analysis. According to these results, CAR appears to be more valuable than NLR for predicting the outcome of the surgery and prognosis in survival in larynx malignancy.

Study Limitations

The primary limitation of the study was its retrospective design since it included only a limited number of parameters obtained from the medical data of the patients. Nevertheless, this study may provide an inspiration for further prospective investigations of many other blood test parameters associated with inflammation in patients with larynx cancer.

Conclusion

In this study, we retrospectively analyzed the utility of CAR in 118 eligible patients with LSCC in our cancer center. To our knowledge, this is the first study to analyze the correlation between CAR and prognosis in patients with LSCC. The results of this study demonstrated that high CAR was independently associated with poor prognosis in patients with LSCC as well as advanced stage and high NLR at the time of diagnosis.

Ethics

Ethics Committee Approval: All procedures performed in studies were in accordance with the ethical standards of Committee in University of Health Sciences Turkey, Bağcılar Training and Research Hospital with number and date 2019.12.2.01.091/27.12.2019.

Informed Consent: A consent form from each patient was taken.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.B.C., S.K., Design: Ş.Ö., B.C.G., Data Collection or Processing: B.C.G., H.D.T., Analysis or Interpretation: A.B.C., S.K., Literature Search: M.F.O., Ş.Ö., Writing: A.B.C., B.C.G.

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

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ORIGINAL RESEARCH

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Palliation in Malignant Esophageal Stricture and Fistulas with Self-expandable Metallic Stents

Malign Özofagus Darlık ve Fistüllerinin Self-ekspandibl Metalik Stentlerle Palyasyonu

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Abstract

Objective: We aimed to present the effectiveness of self-expandable metallic stents (SEMS) in dysphagia score and fistula closure, which are used in palliation for dysphagia and tracheoesophageal fistula seen in primary and secondary advanced esophagus tumors.

Method: We reviewed the files and records of 34 patients who underwent stent implantation due to esophageal stricture and/or fistula in our clinic between 1997 and 2002. The patients were assessed regarding age, gender, the reason for stent insertion (stricture or fistula), localization of stricture or fistula, pre-procedural and post-procedural dysphagia scores (DS), stent specifications, tumor histopathology, complications and need for re-stenting.

Results: In our clinic, 36 SEMS were inserted to 34 patients during this period. The median age was 64 years (range: 44-82 years). There were 24 men and 10 women. Of the patients considered as inoperable, 15 (44%) had primary esophagus carcinoma while 19 (46%) had secondary esophagus carcinoma including 9 gastric carcinomas, 8 lung cancers, 1 larynx cancer and 1 acute myeloid leukemia. The anatomic localizations included cervical esophagus in one patient (3%), thoracic esophagus in 16 patients (47%), and distal esophagus in 17 patients (50%). There was stricture in 25 patients (73.5%), stricture plus fistula in 6 patients (17.6%), and fistula alone in 3 patients (8.8%). Thirty-six self-expandable stents were implanted in 34 patients for stricture and fistula palliation, including 30 (29 covered, 1 non-covered) Ultraflex stent, 3 Wallstent esophageal stents, and 3 Flamingo stent, a modified Wallstent for gastroesophageal junction tumors. The dysphagia score was 4 (unable to swallow anything) in 5, 3 (difficulty to swallow liquids) in 20, and 2 (difficulty to swallow solid foods) in 6 of 31 patients with a stricture. The mean dysphagia score was found as 2.96 before the procedure whereas 0.19 after the procedure. There was minimal difficulty to swallow solid foods (DS:1) in 6 patients and no dysphagia (DS:0) in 25 patients after the procedure. The fistula tract was closed by SEMS in all 9 cases (3 with fistula and 6

Öz

Amaç: Özofagusun primer veya sekonder ileri düzey tümörlerinde ortaya çıkan disfaji ve trakeoözofageal fistül palyasyonunda kullanılan self-ekspandibl metalik stentlerin (SEMS), disfaji skoru ve fistül kapatılması üzerine etkinliğini sunmayı amaçladık.

Yöntem: Kliniğimizde 1997-2002 yılları arasında özofagus darlık ve/veya fistülü nedeni ile stent uygulaması yapılan 34 hasta işlem kayıtları ve hasta dosyaları üzerinden incelendi. Hastalar yaş, cinsiyet, stent uygulanma sebebi (darlık ve fistül varlığı), darlık veya fistül lokalizasyonu, işlem öncesi ve sonrası disfaji skorları (DS), kullanılan stent özellikleri, tümörlerin histopatolojisi, gelişmiş olan komplikasyonlar, restent ihtiyacı olup olmamasına göre değerlendirildi.

Bulgular: Kliniğimizde 34 hastaya 36 self ekspandibl metalik stent uygulandı. Hastaların yaş aralığı 44-82 ve ortalama yaş 64 olarak bulundu. Hastaların 24'ü erkek, 10'u kadındı. İnoperabl olarak kabul edilen hastaların 15'i (%44) primer özofagus karsinomu, 19'u (%56) sekonder özofagus karsinomu idi. Bu sekonder özofagus karsinomları 9 mide, 8 akciğer, 1 larenks kanseri, 1 akut myeloid lösemi olarak dağılım göstermekteydi. Tümörlerin anatomik yerleşimi; 1 (%3) servikal, 16 (%47) torakal ve 17 (%50) distal özofagus şeklindeydi. Hastaların 25'inde (%73,5) darlık, 6'sında (%17,6) darlık ve fistül, 3'ünde (%8,8) sadece fistül mevcuttu. Darlık ve fistül palyasyonu için 34 hastaya uygulanan 36 self ekspandibl stentin 30'u ultraflex (1 kapsız, 29 kaplı), 3'ü wallstent, 3'ü wallstentin gastroözofageal bileşke tümörleri için modifiye edilmiş formu olan Flamingo stent idi (Boston-Scientific). DS; darlık tespit edilen 31 hastanın 5'inde afaji (DS:4), 20'sinde ise sıvı gıdaları yutmada güçlük (DS:3) ve 6 hastada katı gıda yutmada güçlük (DS:2) mevcuttu. Yutma güçlüğü olan bu 31 hastanın DS işlem öncesi 2,96 olarak bulunmuşken, işlem sonrası 6 hastada katı gıdaları yutmada minimal güçlük (DS:1), kalan 25 hastada ise disfaji semptomu tamamen ortadan kalkmış olup (DS:0) ve ortalama DS:0,19 olarak bulundu. Fistül traktının palyasyonu amaçlanan 9 (3 fistül, 6 fistül + darlık) hastanın tamamının fistül traktı self ekspandibl metalik

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Abstract

with fistula plus stricture) in which fistula tract palliation was intended. No major complication was detected in 36 stent interventions performed in 34 patients while minor complication rate was 17.6% including stent migration in 2 patients, complete obstruction at the distal tip due to food plug in 2 and granulation tissue in one patient, and less than 50% expansion of the stent in one patient. Re-stenting was performed in 2 patients with minor complications. The re-stenting rate was 5.8% in our study.

Conclusion: SEMS are among first-line modalities in the palliation of malignancy-related esophagus stricture and fistula. Palliation of esophagus stricture and fistulas due to primary or secondary esophagus malignancies using SEMS is a safe, effective, and readily tolerable method. The accurate positioning of a stent in a safe manner can be achieved using fluoroscopy during procedure. Endoscopy before and after procedure improves the success and effectiveness of the procedure.

Keywords: Dysphagia, esophagus, self-expandable metallic stent, tracheoesophageal fistula

Öz

stentlerle kapatıldı. Otuz dört hastaya uygulanan 36 stent aplikasyonu sonucunda hastalarda majör komplikasyon saptanmadı, minör komplikasyon oranı ise %17,6 olarak bulundu. Minör komplikasyon olarak 2 hastada migrasyon, 2 hastada gıda tıkacına, 1 hastada granülasyon dokusuna bağlı distal uçta tam obstrüksiyon, 1 hastada da stentin %50'nin altında açılması görüldü. Minör komplikasyon görülen hastalardan ikisine restenting uygulandı. Tekrar stentleme oranımız %5,8'di.

Sonuç: SEMS maligniteye bağlı özofagus darlık ve fistüllerinin palyasyonunda ilk sıradaki seçeneklerden biridir. Özofagusun primer veya sekonder kanserlerine bağlı gelişen özofagus darlık ve fistüllerin SEMS ile palyasyonu güvenli, etkili, hasta açısından kolaylıkla tolere edilebilen bir yöntemdir. Bu stentlerin doğru lokalizasyona güvenli bir şekilde yerleştirilmesi, uygulama sırasında radyolojik olarak floroskopi kullanılması ile sağlanabilir. İşlem öncesi ve sonrasında yapılan endoskopi de işlemin başarısını ve etkinliğini artırmaktadır.

Anahtar kelimeler: Disfaji, özofagus, self-ekspandibl metalik stent, trakeoözofageal fistül

Introduction

The most common presenting complaint is dysphagia in primary or secondary advanced, esophageal tumors. Esophageal lumen should be narrowed more than 50-75% for the onset of dysphagia (1).

Although primary esophageal cancer is the most common cause of malignant esophageal stricture, tumors associated with direct invasion of the esophagus such as gastric cancer or metastatic tumors (secondary esophageal cancers) can lead stenosis, causing symptoms through external compression to esophagus (1,2).

Another relevant clinical entity caused by malignant esophageal cancers and metastatic tumors is the fistula tract between the esophagus and trachea or bronchi. In these patients, severe cough occurs with food intake; subsequently, aspiration pneumonia develops. It has been found that untreated patients die within one month. The fistula incidence is 14.75% in tracheal cancers, 6% in esophageal cancers, and 0.16% in lung cancers (3).

Since symptoms occur in the late period, curative treatment cannot be possible in the majority of patients with esophageal cancer. Despite many advances in surgery, radiotherapy, and chemotherapy, 5-year survival is less than 10% (4). Thus, palliative treatment is the only option in patients with advanced cancers. Malnutrition caused by dysphagia, the most common complaint, is an important factor affecting mortality and morbidity in the patients (5).

The goal of palliative treatment is to eliminate problems such as dysphagia and tracheoesophageal fistula (TEF) and to improve the quality of life in patient. For optimal palliation, the treatment modality should be safe, effective, tolerable, inexpensive, and readily available. Although balloon dilatation, laser therapy, and plastic prosthesis have been used for palliation, self-expandable metallic stents (SEMS) are widely used today (6-8). Most recently, iodine-125 coated stents are implanted in an attempt to intraluminal brachytherapy (9).

In the present study, we share outcomes about 36 self-expandable metallic stent implantations performed under C-arm fluoroscopy in 34 patients with malignant esophageal stricture and/or fistula tract in the shed of literature.

Materials and Methods

Our study was conducted retrospectively by examining patient files. We reviewed files and records of 34 patients who underwent stent implantation due to esophageal stricture and/or fistula in our clinic between 1997 and 2002. The patients were assessed regarding age, gender, the reason for stent insertion (stricture or fistula), localization of stricture or fistula, pre-procedural and post-procedural dysphagia scores (DS), stent specifications, tumor histopathology, complications, and need for re-stenting.

Pre-procedural Preparation

In all patients referred to our clinic from oncology or surgery departments, who were diagnosed as primary or secondary inoperable esophageal cancer-causing dysphagia and/or fistula with an indication of stent palliation, the esophagus was assessed before stent implantation by

radiological evaluation using non-ionic contrast material to demonstrate stenotic segment and fistula tract.

On erect radiographs, localization and length of malignant stricture, as well as the length of the stent to be used, were determined. Also, it was decided whether dilatation was required before stent implantation by measuring lumen size. The DS was recorded before the procedure according to the World Health Organization dysphagia classification (Table 1). In patients without a fistula tract, endoscopy was performed in addition to radiological evaluation. The patients were stratified according to the presence of stricture alone, stricture plus fistula, or fistula alone. It was aimed to relieve stricture in patients with stricture alone while it was aimed to close the fistula tract in remaining patients.

On passage radiographs, localization, output, and associated airway segment were identified. On radiographs at the right lateral decubitus position, the targeted stent localization was evaluated regarding its relationship with vertebrae and other adjacent structures. Before the procedure, stent localization was determined according to its relationship with vertebrae by opaque markers on skin. The calculations were made on radiographs to implant appropriate stent at an appropriate position. The patients were stratified according to the presence of stricture alone, stricture plus fistula, or fistula alone. It was aimed to relieve stricture in patients with stricture alone while it was aimed to close the fistula tract in remaining patients.

In all patients presenting with dysphagia, endoscopic evaluations were made and biopsy was performed for histopathological diagnosis at the endoscopy unit of the surgery department. During endoscopy, the localization of mass lesion was determined and polypoid lesions that might hamper stent expansion were resected. No endoscopy was performed due to the high risk for complications in patients with the fistula tract on radiological evaluation.

Stent Implantation

Stent implantation was performed under fluoroscopy by a C-arm digital radiography device at the right lateral decubitus position with a head elevation of 30°. The procedure was performed under anesthesia with oxygen supplementation via nasal cannula and the patient was monitored throughout the procedure.

Table 1. World Health Organization dysphagia classification

Stage	Dysphagia
Stage 0	No dysphagia, able to consume normal diet
Stage 1	Moderate passage, occasional difficulty in solid foods
Stage 2	Mild passage, able to swallow semi-solid foods but not solid foods
Stage 3	Poor passage, only able to swallow liquid foods
Stage 4	No passage, unable to swallow including liquids

The stricture was passed using Jaqwire with hydrophilic tip or Zebra guidewire (Boston-Scientific) via the transoral route. After the confirmation of passage beyond the stenotic segment, a guidewire was replaced by a 6 F regular catheter. The distal tip of stricture was determined by contrast material infusion via a catheter in cases with advanced stricture where the distal tip could not be visualized. At this point, the catheter was replaced by Amplatz super-stiff guidewire (0.038 inches, Boston Scientific) and stent transporter was advanced over a guidewire. The stent was positioned at pre-determined localization by the assistance of reference imaging with opaque markers and gradually opened. Attention was drawn to locate the distal tip of the stent just below mass lesion while proximal tip was at 1.5-2.0 cm above the mass lesion. The stent grid was released using a string attached. A few minutes after complete stent removal, 10 F transporter with 21 olives at the distal tip was removed.

Follow-up after Stent Implantation

A control radiograph was taken at the first hour after implantation; and stent localization was compared with a template on reference image to decide whether stent was positioned at appropriate localization.

After stent implantation, the patients were hospitalized for over 24 hours and immobilization was ensured. Anti-reflux treatment was initiated, and analgesics were prescribed to prevent pain during stent opening. Only liquids were allowed during the first 24 hours. The patient was then mobilized in the absence of complications such as stent migration or failure to open on control radiograph at the 24^{th} hour. The dysphagia score was assessed after the procedure and the patient was discharged with a diet containing semi-solid foods and anti-reflux treatment. In the presence of stent migration, the stent was retracted to proximal at endoscopy unit while balloon dilation was performed when complete stent opening was failed due to compression.

On day 7 after discharge, passage radiographs were obtained. Patients were questioned about dysphagia and information was provided regarding potential complications of a stent. It was recommended to visit our clinic in the development of any complaint which might be associated with a stent.

This study was conducted according to the Declaration of Helsinki and approval was obtained from local Ethics Committee. Informed consent was obtained from all patients.

Statistical Analysis

The assessment of DS was performed using SPSS for Windows version 15.0. DS before and after stenting were compared by using the Wilcoxon Signed-Rank test. A p-value of <0.01 was considered to be statistically significant.

Results

In our clinic, 36 SEMS were inserted to 34 patients during this period. The median age was 64 years (range: 44-82 years). There were 24 men and 10 women. Of the patients considered as inoperable based on endoscopy and radiology findings, 15 (44%) had primary esophagus carcinoma while 19 (46%) had secondary esophagus carcinoma including 9 gastric carcinomas, 8 lung cancers, 1 larynx cancer and 1 acute myeloid leukemia (Table 2).

The anatomic localizations included cervical esophagus in one patient (3%), thoracic esophagus in 16 patients (47%), and distal esophagus in 17 patients (50%). There was stricture in 25 patients (73.5%), stricture plus fistula in 6 patients (17.6%), and fistula alone in 3 patients (8.8%). Thirty-six SEMS was inserted in 34 patients for stricture and fistula palliation, including 30 (29 covered, 1 non-covered) Ultraflex stent, 3 Wallstent esophageal stents, and 3 Flamingo stents, a modified Wallstent for gastroesophageal junction tumors (Figure 1).

When pre-procedural DS were compared to those obtained after the procedure, it was seen that DS was 4 (unable to swallow anything) in 5, 3 (difficulty to swallow liquids) in 20, and 2 (difficulty to swallow solid foods) in 6 of 31 patients with stricture and the mean DS was 2.96 before the procedure, while there was minimal difficulty to swallow solid foods (DS:1) in 6 patients and no dysphagia (DS:0) in 25 patients after the procedure and the mean dysphagia score was 0.19 after the procedure (Table 2). The dysphagia score was calculated as 2.9±0.6 before the procedure and 0.2±0.4 after the procedure, indicating a significant difference (p<0.0001, dependent sample t-test).

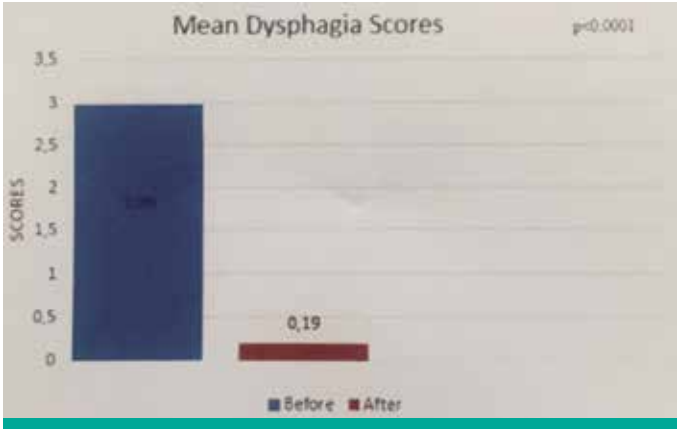

Figure 1. Mean dysphagia scores before and after SEMS procedure

SEMS: Self-expandable metallic stents

The fistula tract was closed by SEMS in all 9 cases (3 with fistula and 6 with fistula plus stricture) in which fistula tract palliation was intended. In these patients, a stent was placed asymmetrically as distal one-third being below the orifice and proximal two-third being above the orifice.

Table 2. Gender, stent indication, stricture/fistula localization, dysphagia scores, stent type, histopathological diagnosis and complications in the patients

	Count
Gender	
Male	24
Female	10
Stent indication	
Stricture	25
Stricture + Fistula	6
Fistula	3
Stricture/fistula localization	
Proximal (Cervical)	1
Mid (Thoracis)	16
Distal	17
Dysphagia score before procedure	**2.96 (mean)**
Grade 4	5
Grade 3	20
Grade 2	6
Dysphagia score after procedure	**0.19 (mean)**
Grade 1	6
Grade 0	25
Stent type	
Ultraflex	30
Wallstent	3
Flamingo	3
Histopathological diagnosis	
Primary esophagus carcinoma	15
Gastric cancer	9
Lung cancer	8
Larynx cancer	1
AML	1
Major complication	0
Minor complication	6

AML: Acute myeloid leukemia

By asymmetrical placement, it was prevented from the proximal passage of materials between external stent surface and esophagus mucosa by increasing the closure area of the coated stent at the segment above the stent. Also, a longer stent segment was left above orifice against the likelihood of stent migration.

Complications

The complications causing severe stent-related morbidity and mortality were classified as major complications while those not affecting morbidity or mortality were minor complications.

Major complications: These included stent-related esophageal perforation, TEF formation, massive bleeding due to the fistula tract between the esophagus and aorta, and gastrointestinal system obstruction caused by stent migration.

Minor complications: These included stent migrations not causing GIS obstruction, stent opening less than 50%, distal granulation tissue secondary to reflux, tumor ingrowth, and food plug.

No major complication was detected in 36 stent interventions performed in 34 patients while minor complications were observed in 6 patients. Complete stent migration was detected in a patient with distal esophageal adenocarcinoma on day 3 after implantation. As the stent-maintained lumen patency allowing intake of semi-solid foods, no re-stenting was considered initially. However, re-stenting was performed on month 6 when progression was observed in dysphagia symptoms. The second stent was migrated 3 cm towards distal and stabilized at that position.

In another patient who underwent stent implantation due to fistula palliation, the stent was migrated 3 cm towards distal within the first 24 hours; thus, the stent was pulled to proximal and the fistula tract was closed completely. On month 2, stricture secondary to granulation tissue at a non-covered segment of the stent was developed. The granulation tissue was resected via endoscopy, achieving lumen patency.

In a patient with distal esophageal cancer, long segment and obstructive stricture were developed secondary to granulation tissue at the distal end on week 3 after stent implantation. Thus, another stent was implanted into the stent already in place.

The stent opening was 50% at the proximal tip in a patient presenting with dysphagia secondary to esophagus cancer and stricture at the thoracic segment. In the endoscopy, it was seen that there was infundibulum of a diverticulum adjacent to the proximal tip of the stent, which could not be detected on radiological studies because of stricture at the same level. It was concluded that a stent could not be opened completely due to scar tissue and fibrosis at the infundibulum of a diverticulum. Stent proximal was dilated via endoscopy using balloon dilatation.

Stent obstruction secondary to food plug was developed in 2 patients on week 3. The plug was removed via endoscopic and sufficient passage was re-established.

In conclusion, it was observed all stents (100%) were at appropriate localization within the first hour in 36 stent implantations in 34 patients. No major complication was observed during stent implantation. The minor complication rate was 17.6% (6/34). Re-stenting was performed in 2 patients due to minor complications with a re-stenting rate of 5.8% in our study.

Discussion

The palliation in malignancy-related stricture and fistula in the esophagus has a significant influence on the morbidity and mortality of patients. The goal of palliative treatment is to eliminate symptoms and to improve the quality of life in these patients. For optimal palliation, the treatment modality should be safe, effective, tolerable, inexpensive, and readily available.

In the literature, there are many different treatment modalities in the palliation of dysphagia, including balloon dilatation, plastic prosthesis, and SEMS which is more widely used.

The balloon dilatation to ensure the lumen continuum has limited use due to short-term effects and the need for repeated interventions (6). Again, laser therapy is not used in long, tortuous, narrow segments, and lesions causing extrinsic compression (8).

Radiotherapy ensures dysphagia palliation in 60-80% of patients; however, it takes 2 months to exert its effects. In 25% of patients receiving radiotherapy, dysphagia persists due to fibrotic, cicatricial contraction (10,11).

The SEMSs were first introduced by Frimberger and have been modified depending on requirements since the early 1990s. The SEMSs are palliative treatment modalities that fulfill the majority of the above-mentioned needs (12-14). These stents can be implanted via endoscopy, radiological-assistance, or both.

When outcomes are compared between endoscopic or radiology-assisted stent implantation, the correct positioning rate is high in both techniques (95% in the endoscopic technique vs. 100% in fluoroscopic technique). In the literature, perforation has been reported in the endoscopic technique when passing highly narrowed segments. The endoscopist cannot identify the degree of luminal stenosis due to blood, mucus, and tumor tissue within a lumen. The esophagus is perforated while passing stenosis and it is generally not recognized by the endoscopist. If an uncovered stent is implanted due to stenosis, the perforated area will be enlarged due to radial forces applied by a stent. Also, if there is fistula formation with a thin orifice, these orifices could not be recognized and can be perforated in this region. Although the stent will be implanted via the endoscopic technique, radiological imaging studies should have to be performed before intervention (15-17).

In the fluoroscopy technique, the correct stent positioning rate is 100%. During the procedure, whether a stent is opened at the correct position can be monitored by fluoroscopy using radiopaque markers on the stent and localization of stricture on reference imaging (17). In the endoscopic technique, only one end of stricture can be visualized; thus, the stent can be opened at a higher or lower position. In fluoroscopic technique, fistula localization can be determined and stent can be implanted at appropriate localization. The recent appearance of the fistula is assessed using non-ionic, water-soluble contrast material just before stent implantation; thus, the stent can be placed at appropriate localization. It is challenging to identify small fistulas via endoscopy. Thus, it is more accurate to employ fluoroscopic control in the palliative treatment of fistulas using stent (18).

In our clinic, all SEMSs implanted via fluoroscopic techniques were placed at correct localization (100%). The mean dysphagia score was 2.96 before stent implantation while it was 0.19 after the procedure. The marked reduction in dysphagia score demonstrated the effectiveness of SEMSs in the palliation of dysphagia.

The SEMS was introduced in clinical practice in the early 1990s and has been modified according to the needs in practice over time. Today, it becomes the most widely used palliative treatment modality in esophageal stricture and fistula due to primary or secondary esophageal cancers.

The stent size can vary according to the length of the lesion. There are silicone-coated forms to prevent stent penetration into the tumor or non-coated forms solely used in the palliation of strictures (19). These stents can be inserted into appropriate localization either via an endoscopic or fluoroscopic manner (20,21).

In our study, no stent-related major complication was observed; however, the minor complication rate was found as 17.6% stent migration in 2 patients, complete obstruction at the distal tip due to food plug in 2 and granulation tissue in one patient, and less than 50% expansion of the stent in one patient. Re-stenting was performed in 2 patients with minor complications. The re-stenting rate was 5.8% in our study, which was below those reported in the literature (7.4-41%) (21,22).

In the literature, the stent-related major complications have been reported as 4-12% while minor complications as 16-64% (13-16). The lower minor complication rate in our study may be due to the fact that self-rated subjective assessments such as retrosternal pain and foreign body sensation, which are considered minor complication criteria in the literature, were not included in our assessment as minor complications. We think that the elimination of structures which may affect stent opening during preparation before stent implantation and using endoscopic data during fluoroscopic stent implantation improved stent success and reduced complication rate in our study.

In a study on 119 cases by Song et al. (14), esophageal stents were implanted via fluoroscopic technique and it was seen that all stents were at the correct position. Of the cases, recurrent stricture was observed due to migration in 10 patients whereas due to bleeding in 3 and due to stent penetration into the tumor in 7 patients. Two patients with bleeding died.

In another study on 44 cases by Ludwig et al. (23), esophageal stents were implanted via fluoroscopic technique and it was seen that there was recurrent stricture due to tumor in 10 patients, stent migration in 2 patients and stent-related TEF development in one patient. Re-stenting was performed in 13 patients (32%) (23). Knyrim et al. (13) implanted self-expandable stents in 21 patients and TEF was developed in 2 patients while tumor-related stricture in 3 patients. Re-stenting was performed in 3 patients (14%). In the study using endoscopy and fluoroscopy together, MacManus et al. (24) failed to implant stent at the correct position in 11 of 186 stent implantations and reported perforation during procedure and stent migration in 2 patients. Life-threatening bleeding was observed in 3 patients (24).

In a case series including 62 patients, Vakil et al. (25) implanted esophageal stents via endoscopic technique under fluoroscopy. The stent opening was <50% in 2 patients while stent could not be positioned at desired localization in 2 patients and bleeding was developed in 8 patients (mild bleeding in 4 and severe bleeding in 4 patients). At long-term follow-up, stent migration was observed in 4 patients. Re-stenting was needed in 5 patients due to several complications (25).

When compared to literature, we achieved a higher success rate in inappropriate stent localization, dysphagia relief, and fistula treatment while stent-related complication rate in our study.

In-stent implantation, the implantation of an appropriate stent ineligible patient under appropriate conditions improves success rate with lower complication rates. The eligible patients are decided by the collaboration of clinicians and radiologists. In our study, the number of patients is limited since stent implantation is not performed in lesions 2 cm proximal to the cricopharyngeal muscle and large mass lesions localized between the trachea and esophagus but it also reduces complication rate.

Study Limitations

This study has some limitations including limited assessment criteria in patients who underwent stent implantation, limited sample size, and lacking long-term.

Conclusion

SEMS are among first-line modalities in the palliation of malignancy-related esophagus stricture and fistula. These stents can be implanted via either fluoroscopic or endoscopic techniques.

Fluoroscopic or fluoroscopy-assisted endoscopic SEMS implantation is safer with a higher rate of accurate stent positioning compared to SEMS implantation via endoscopy alone.

In conclusion, palliation of esophagus strictures and fistulas due to primary or secondary esophagus malignancies using SEMS is a safe, effective, and readily tolerable method. The accurate positioning of a stent in a safe manner can be achieved using fluoroscopy during the procedure. Endoscopy before and after the procedure improves the success and effectiveness of the procedure.

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Ethics

Ethics Committee Approval: This study was approved by the İstanbul Yeni Yüzyıl University, Ethics Committee for Science, Social and non-interventional Health Science Research (decision number: 2020/08-494). This study was approved by the Local Ethics Committee.

Informed Consent: Informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

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A Retrospective Study of Patients with Acute Pancreatitis in an Internal Medicine Clinic

Akut Pankreatitli Hastaların Geriye Dönük İncelenmesi

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Abstract

Objective: Acute pancreatitis (AP) is the rapid inflammation of the pancreas which may be life threatening, even though the disease course may range from mild to severe. We sought to investigate the characteristics of cases followed with a diagnosis of AP at our clinic.

Method: Patients diagnosed and followed with AP from 2015 to 2017 at the Istanbul Kanuni Sultan Süleyman Training and Research Hospital were analyzed retrospectively. Demographic features, etiological factors, duration of hospitalization, antibiotic usage and complications were investigated.

Results: Of the 160 patients with AP, 65 (40.6%) were male and 95 (59.4%) were female. The mean age of the patients was 56.2±19.1 years. At hospital admission, fever and abdominal pain were observed in 5% of the patients, abdominal pain and itching were present in 1.3%, while abdominal pain and jaundice were reported in 3.8%. Etiology of AP was defined as gallstones in 42.5%, alcohol in 4.4%, hyperlipidemia in 0.6%, posttraumatic causes (including endoscopic retrograde cholangiopancreatography) in 5.6%, drugs in 3.8%, malignancy in 1.3%, and autoimmunity in %3.8, and the remaining 38% were evaluated as idiopathic pancreatitis. Three patients with cardiac complications were either admitted to the intensive care unit (2 patients) or died (1 patient).

Conclusion: Gallstone-related AP was determined to be the most common cause of AP in this study, and idiopathic causes were shown in the second rank. Endoscopic retrograde cholangiopancreatography should be planned if there is clinical deterioration and cholangitis. Serious complications (such as cardiac) may develop in patients defined to have mild disease. Thus, clinicians must be aware of this possibility and should be on high alert for possible cardiac complications which may lead to mortality or intensive care admission.

Keywords: Acute pancreatitis, etiology, retrospective analysis

Öz

Amaç: Olguların seyri hafif ve ağır arasında değişkenlik gösterse de, akut pankreatit (AP) hayatı tehdit etme ihtimali olan akut bir pankreas iltihabıdır. Bu çalışmada kliniğimizde AP tanısı ile takip edilmiş olguların irdelenmesi amaçlandı.

Yöntem: İstanbul Kanuni Sultan Süleyman Eğitim ve Araştırma Hastanesi'nde 2015-2017 yılları arasında takip edilmiş olan AP olguları geriye dönük incelemeye alındı. Hastaların demografik özellikleri, etiyolojik faktörler, yatış süresi, antibiyotik kullanımı ve komplikasyonları araştırıldı.

Bulgular: Akut pankreatitli 160 hastanın 65'i erkek (%40,6), 95'i kadındı (%59,4). Yaş ortalaması 56,2±19,1 yıl idi. Olguların %42,5'inde safra taşı, %4,4'ünde alkol, %0,6'sında hiperlipidemi, %5,6'sında post travmatik (endoskopik retrograd kolanjiopankreatografi dahil), %3,8'inde ilaç, %1,3'ünde malignite, %3,8'inde otoimmün ve geri kalan %38'inde idiyopatik AP geliştiği tespit edildi. Hastaneye başvuru sırasında olguların %5'inde ateş ve karın ağrısı, %1,3'ünde karın ağrısı ve kaşıntı, %3,8'inde karın ağrısı ve sarılık görüldü.

Sonuç: AP etiyolojisinde en sık safra taşı tespit edilmiş olup, idiyopatik nedenler ikinci sırada gelmektedir. Klinik kötüleşme ve kolanjit varsa endoskopik retrograd kolanjiyopankreatografi planlanmalıdır. Hafif seyirli olarak tanımlanan hastalarda da ciddi komplikasyonlar gelişebilir (örneğin; kardiyak). Klinisyenler, ölüm veya yoğun bakım ihtiyacına neden olabilecek kardiyak komplikasyonların gelişme ihtimaline karşı tetikte olmalıdırlar.

Anahtar kelimeler: Akut pankreatit, etiyoloji, retrospektif inceleme

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Introduction

Acute pancreatitis (AP) is an inflammatory condition of the pancreas that has a broad clinical spectrum ranging from local injury to systemic inflammatory response syndrome and organ failure. It is a common gastrointestinal condition throughout the world, which challenges the healthcare system due to associated morbidity and treatment costs. The incidence is reported to be 5 to 30 per 100,000 population, and the average mortality rate is 5% but varies depending on the severity of cases (1).

The most common causes of AP include gallstones and alcohol, which are identified in up to 80% of cases. The rest of the cases are associated with less common causes such as drug reactions, pancreatic solid and cystic malignancies, and hypertriglyceridemia. Definitions of key terms were based on the 2012 Atlanta Classification of AP; Diagnosis of AP (two of the following) (2).

- Abdominal pain (acute onset of a persistent, severe, epigastric pain often radiating to the back)

- Serum lipase activity (or amylase) at least 3 times greater than the upper limit of normal

- Characteristic findings of AP on computed tomography (CT) or magnetic resonance imaging. Contrast-enhanced abdominal CT scan findings of acute interstitial edematous pancreatitis include focal or diffuse enlargement of the pancreas with heterogeneous enhancement with intravenous contrast. When contrast-enhanced CT is performed on three or more days after abdominal pain, necrosis, complications, and severity can be predicted (Table 1) (2).

The Ranson criteria is a scoring system that has been used frequently to evaluate AP severity. The most important disadvantage of the Ranson criteria is that it does not provide accurate information within the first 24 hours. Systemic inflammatory response criteria and bedside acute pancreatitis severity index (BISAP) criteria have been recommended for the first 24-48 hours in recent years (3). Although conservative treatments are very effective in mild cases, in severe AP, intensive care follow-up, broad-spectrum antibiotic therapy, enteral feeding, endoscopic retrograde cholangiopancreatography (ERCP) and sphincterotomy may be required (4).

We have retrospectively analyzed the etiology of the patients followed-up with AP at our clinic in order to evaluate the frequency of various signs and symptoms at hospital admission, antibiotic use, complications, and prognosis.

Materials and Methods

The medical records of 160 patients hospitalized in the internal medicine clinic of our hospital between the years of 2015 and 2017 were analyzed retrospectively. Patients who were diagnosed with AP during the study period were included in the study. Their demographic characteristics, laboratory results and imaging findings were assessed and recorded.

The 2012 revision of the Atlanta Classification of AP was used for the diagnosis of AP (2). Briefly, the presence of 2 of the following 3 criteria was accepted as definite AP: (i) severe epigastric pain radiating to the back, (ii) an increase of at least 3-fold the upper reference value of amylase or lipase (in our hospital laboratory amylase <100, lipase <60) (iii) findings conclusive for AP on CT or magnetic resonance imaging. Ultrasonography (USG) evaluation was performed after emergency room admission in patients that required differential evaluation during diagnosis. Patients who were diagnosed without imaging findings and later developed non-mild AP also underwent imaging with CT.

At admission (0 hours) and at the 48th hour, the severity of disease was classified according to the Ranson criteria and mild pancreatitis was defined in patients scoring <3 points, while severe pancreatitis was defined in patients with ≥3 points. Also, the expected mortality rate was calculated via the BISAP criteria as <1% for 0 points and 25% for 5 points. Then, the relationship between disease severity and etiological factors, age, gender, duration of hospitalization, antibiotic use, C-reactive protein (CRP) levels, and prognosis was examined.

Statistical Analysis

The Statistical Package for Social Sciences (SPSS) version 22.0 (SPSS Inc., Chicago, IL, USA) statistics software was used for all statistical analyses. The CRP values and duration of hospitalization were presented as mean ± standard deviation. For categorical values, count (n) and percentage (%) were used. The comparison of CRP values from admission to 48-hour results were performed with the related-samples Wilcoxon test. The results were interpreted according to the significance level of $p \leq 0.05$.

Results

A total of 160 patients were included in the study, 95 (59.4%) were female and 65 (40.6%) were male. The mean age of the patients was 56.2±19.1 years. At hospital admission, fever and abdominal pain were observed in 5% of cases,

abdominal pain and itching were present in 1.3%, while abdominal pain and jaundice were reported by 3.8% of the patients.

In the current study group, gallstone-induced AP was observed in 68 (42.5%) patients, idiopathic pancreatitis in 60 (37.5%) patients, and alcohol-induced pancreatitis in 7 (4.4%) patients. All patients with alcohol-induced AP were male. With regard to other causes, we found that drug-induced AP was observed in 6 (3.8%) patients, autoimmune AP in 6 (3.8%) patients, traumatic AP in 9 (5.6%) patients, hyperlipidemia-related AP in 1 (0.6%) male patient, and

Table 1. Radiological definition of acute pancreatitis

1. Interstitial edematous pancreatitis
Acute inflammation of pancreatic parenchyma and peripancreatic tissues, but no necrosis. Criteria for contrast-enhanced computed tomography:
▪ Pancreatic parenchyma increases with intravenous contrast agent
▪ No signs of peripancreatic necrosis
2. Necrotizing pancreatitis
Inflammation associated with pancreatic parenchymal necrosis and/or peripancreatic necrosis
Contrast-enhanced computed tomography criteria:
▪ Absence of pancreatic parenchyma involvement with intravenous contrast agent and/or
▪ Presence of signs of peripancreatic necrosis
3. Acute peripancreatic fluid collection
Pancreatitis with interstitial edema and peripancreatic fluid without peripancreatic necrosis. Applies to peripancreatic fluid areas seen within the first four weeks without a pseudocyst.
Contrast-enhanced computed tomography criteria:
▪ Occurs in the case of interstitial edematous pancreatitis
▪ Homogeneous collection with liquid density
▪ Limited to normal peripancreatic facial planes
▪ No identifiable wall surrounding the collection
▪ Adjacent to the pancreas (no intrapancreatic extension)
4. Pancreatic pseudocyst
Maturation usually requires 4 weeks after the onset of acute pancreatitis; occurs after pancreatitis with interstitial edema.
This entity usually occurs more than four weeks after the onset of interstitial edematous pancreatitis to mature.
Contrast-enhanced computed tomography criteria:
▪ Well circumscribed, usually round or oval
▪ Homogeneous fluid density
▪ No non-liquid component
▪ Well-defined wall (ie, completely encapsulated)
▪ Maturation usually requires >4 weeks after the onset of acute pancreatitis; occurs after interstitial edematous pancreatitis
5. Acute necrotic collection
A collection containing variable amounts of both fluid and necrosis associated with necrotizing pancreatitis; the necrosis can involve the pancreatic parenchyma and/or the peripancreatic tissues
Contrast-enhanced computed tomography criteria:
▪ Occurs only in the setting of acute necrotizing pancreatitis
▪ Heterogeneous and non-liquid density of varying degrees in different locations (some appear homogeneous early in their course)
▪ No definable wall encapsulating the collection
▪ Location-intrapancreatic and/or extrapancreatic
6. Walled-off necrosis (WON)
A mature, encapsulated collection of pancreatic and/or peripancreatic necrosis that has developed a well- defined inflammatory wall. WON usually occurs >4 weeks after the onset of necrotizing pancreatitis.
Contrast-enhanced computed tomography criteria:
▪ Occurs only in the setting of acute necrotizing pancreatitis
▪ Heterogeneous and non-liquid density of varying degrees in different locations (some appear homogeneous early in their course)
▪ No definable wall encapsulating the collection
▪ Location-intrapancreatic and/or extrapancreatic

malignancy related AP in 3 (1.9%) patients (all male) (Table 2).

The patient with hyperlipidemia-related AP had a history of multiple attacks of pancreatitis. In 2 patients, AP had developed after ERCP intervention. Two of the patients with gallstone-induced pancreatitis were pregnant and had no complications. Drug-induced AP was seen in 6 (3.8%) patients. The drugs thought to be responsible for AP development were sitagliptin, exanatide, carbamazepine, azathiopurine, and also HRT treatment.

In 86 cases (58.5%), normal findings were seen in abdominal USG. In 49 cases (33.3%), sludge or stones were detected in the biliary tract. It was noted that only 9 (6.1%) patients' USG reports showed inflammatory findings in the pancreas (supporting AP diagnosis). The CT imaging results were conclusive for edematous pancreatitis in 106 (66%) patients, while necrotizing pancreatitis was detected in 10 (6.3%) patients. Local complications were detected in 14 patients (8.8%). An ampulla tumor was detected in 1 patient. In total, 29 patients who had good clinical condition and demonstrated a regression of inflammatory markers did not undergo CT scan.

With regard to the Ranson criteria, 106 patients were expected to have good prognosis (<3 points) with mild edematous pancreatitis, and 54 patients were expected to have poor prognosis (≥3 points) with severe AP. When scores obtained from the BISAP criteria were assessed, we found that a patient with 5 points had died. In addition, among the 3 patients with 3 points, 2 were admitted to the intensive care unit and one was followed-up in the general surgery clinic with necrotizing pancreatitis.

The mean duration of hospitalization in our study was 6.31±4.68 days. The antibiotics preferred during hospitalization were: ceftriaxone in 54.6%, ceftriaxone and metronidazole in 16.6%, and imipenem in 11.1%.

Table 2. Etiological factors of acute pancreatitis

Etiology	n	%
Gallstones	68	42.5
Idiopathic	60	37.5
Trauma	9	5.6
Alcohol	7	4.4
Drugs	6	3.8
Autoimmunity	6	3.8
Malignancy	2	1.3
Ampulla tumor	1	0.6
Hyperlipidemia	1	0.6

With regard to the local and systemic complications of AP, we identified thrombocytopenia in 1 patient (0.6%), respiratory system complications in 9 patients (5.6%), hyponatremia in 1 patient (0.6%), hypokalemia in 1 patient (0.6%), and gastrointestinal bleeding in 1 patient (0.6%). Furthermore, in 2 patients (1.2%), pancreatitis caused diabetic ketoacidosis, while acute coronary syndrome occurred in 4 patients (2.5%) and cardiac problems developed in 4 patients (2.5%). A temporary increase in creatinine levels was detected in 2 patients (1.2%) with chronic renal failure. Finally, ileus occurred in 1 patient (0.6%) (Table 3).

The mean CRP levels at the time of hospitalization (39.5±63.6) and at the 48t^{h} hour (106.1±108.2) were compared, demonstrating a statistically significant increase ($p<0.05$).

Discussion

The current study reports the frequency and distribution of the characteristics of patients diagnosed with AP at our center. A slight female predisposition was determined, the great majority of patients had gallstone-related or idiopathic AP, and alcohol-related AP was considerably rare compared to that in publications from other countries. The latter is a common finding in Turkish studies and is associated with lower alcohol consumption. The results for clinical findings, antibiotic use, prognosis and complications did not yield any noteworthy findings and were similar to previous studies.

In a study by Yalçın et al. (5) from Turkey, 67.5% of the patients were female, 32.5% were male and the mean age was 55.17±19.75 (minimum: 18, maximum: 93) years. Apart from the slightly lower frequency of females in our study, the results were similar. With regard to etiology, Yalçın et al. (5) reported the three most common causes of AP as biliary pathologies (70.1%), hyperlipidemia (5.7%) and alcohol (4.8%), while 16.1% of cases were classified as idiopathic (5). Alcohol-induced pancreatitis is common in western countries, whereas gallstone-related AP is almost

Table 3. Systemic complications in acute pancreatitis

Complication	n	%
Respiratory system	9	5.6%
Renal complications	6	3.75%
Gastrointestinal complications	2	1.2%
Diabetic ketoacidosis	2	1.2%
Cardiac problems	4	2.5%
Hematologic complications	1	0.6%

always ranked in first place in our country (6). Gallstone pancreatitis is more common in women than in men and alcohol-induced pancreatitis is more common in men. In our country, alcohol-induced AP cases comprise around 10-15% of all pancreatitis cases (7). In the study by Gülen et al. (8), biliary causes represented 68.1% of the etiological distribution, alcohol was found in 14%, other causes were 6.1% and idiopathic causes were 11.8%. In the study by Demiral et al. (9), the most common cause was gallstones (80.9%), followed by hyperlipidemia (4.5%). These results are mostly similar to our findings and indicate the importance of gallstone-related and idiopathic AP development in our country. In a study in the United Kingdom, it was reported that approximately half of cases with AP originated from gallstones and a quarter from alcohol (10). In our study, we detected gallstone-related AP in 42.5% of cases and idiopathic pancreatitis in 38%. The frequencies of other less-common etiologies were as follows: posttraumatic (5.6%), drug-induced (3.8%), alcohol-induced (4.4%), autoimmune (3.8%), malignancy-related (1.3%) and hyperlipidemia-related (0.6%).

In the USA, it has been reported that 1-2% of AP cases are related to malignancies (11). Similarly, in our study, malignancy was detected in only 2 (1.3%) cases. One of these patients had the Gray-Turner sign. Although this symptom is not specific, it is a symptom of retroperitoneal bleeding in pancreatic necrosis and has been reported to be detected in 1-3% of cases (12).

The sensitivity of USG in AP is estimated to be 75-85% (13). In our study, USG was normal in 86 cases (58.5%) and gallstones or sludge in the biliary tract was detected in 49 cases (33.3%). Even though 135 of the 160 patients had undergone USG after admission, we found that only a fraction (6.1%) of the patients' diagnoses had been supported by USG findings. This is very low compared to the literature and may be due to the insufficiency of examination with USG in the emergency conditions and minimal changes in the pancreas in the acute period.

CT is considered as the most important diagnostic tool to assess diagnosis, prognosis and complications in AP. Imaging with CT can demonstrate 90-95% of pathologies that develop in AP. It must be noted that since pancreatic necrosis findings are evident after 48-72 hours, early CT may not be reliable. In our study, CT findings were normal in 42 patients (26.3%) during the initial admission to the hospital. Complications were observed in CT in only 3 cases (1.9%).

AP is a disease that has a mild course (self-limiting and returning to normal) in 70-80% of patients, while it is severe and progressive with high mortality in 20-30% (14). Necrotizing pancreatitis develops in 5-10% of all pancreatitis cases, which was similar to our finding of 6.3%. Nine patients (5.6%) experienced pleural effusion and 6 patients (3.8%) experienced renal complications. Other studies have reported that acute kidney injury occurs in 3-15% of cases (15). It is obvious that the most mortal complications are cardiac complications, which were rather rare (2.6%) in our study group. Although edematous pancreatitis was identified in these patients, 1 patient who died and 2 patients who were admitted to the intensive care unit had experienced serious cardiac problems. Another complication seen in AP is diabetic ketoacidosis, a condition that is within the differential diagnoses of AP and can also be observed as a complication.

The mean Ranson criteria score of the patients was 2±1.3. Accordingly, 106 cases had expectation of good prognosis and 54 cases had expectation of poor prognosis. Alcohol-induced AP cases had been found to have a good prognosis expectation according to Ranson score. Alcohol-related etiology was seen as a major risk factor in the prognosis of pancreatitis in a study by Frey and colleagues (16). However, in meta-analysis conducted by De Bernardinis et al. (17), the Ranson score was suggested to be a weak marker in predicting the prognosis of pancreatitis. Although the number of patients in this study was limited, our findings also support the notion that the Ranson criteria may not be a good scoring system to determine prognosis in patients with AP. We believe clinicians must be aware of the possibility of rare but serious complications even in patients with mild disease, as demonstrated by our results.

According to a large epidemiological study conducted between 1988 and 2003 in the USA, the mean duration of hospitalization in patients with AP was 6.9 days (18). This is similar to our findings that showed a mean duration of hospitalization as 6.31±4.68 days. In the same study from the USA, the mortality of disease was shown to have had a decreasing trend, from 12% to 2% (18). In the present study group, mortal disease had occurred in 1.6% of patients, indicating a continuation of this trend. The advances in medicine and patient care, in addition to the increased chance for intensive care admission (for patients with poor general condition), may be among the reasons for this low mortality rate.

Conclusion

Gallstone-related AP was determined to be the most common cause of AP in this study, and our results showed a higher frequency in females. Although alcohol consumption-related AP frequency was lower compared to the literature, our results were in support of the majority of previous studies from Turkey. Although mortality rates have decreased throughout the past 2-3 decades, it is evident from our results that serious complications may develop in patients defined to have mild disease by various scoring criteria. Thus, clinicians must be aware of this possibility and should be on high alert for possible cardiac complications which may lead to mortality or intensive care admission.

Ethics

Ethics Committee Approval: The present study was conducted after being approved by the Local Ethics Committee of Bakırköy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey (reference no: 2017T234, date: 14/08/2017).

Informed Consent: This is a retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: B.B.İ., K.İ., Ö.T., A.K., Design: B.B.İ., K.İ., Ö.T., A.K., Data Collection or Processing: B.B.İ., K.İ., Ö.T., A.K., Analysis or Interpretation: B.B.İ., K.İ., Ö.T., A.K., Writing: B.B.İ., K.İ., Ö.T., A.K.

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An Experience of Telemedicine During COVID-19 Pandemic: Follow-up of Patients with Obesity Via Phone Interviews

COVID-19 Pandemisi Sırasında Bir Teletıp Deneyimi: Obezitesi Olan Hastaların Telefon Görüşmeleriyle Takibi

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Abstract

Objective: Telemedicine means to provide healthcare services to remote patients using modern information technology like audio/video communications, computer and telemetry. During global Coronavirus diseases-2019 (COVID-19) pandemic, home isolation was advised for general population, especially for individuals who were at higher risk for infection, like people living with obesity. Here, it was aimed to evaluate the data obtained with a telemedicine method performed for obesity center patients' follow-ups during COVID-19 pandemic lockdown period and highlight the need for alternative follow-up methods for chronic diseases like obesity during crisis times.

Method: All registered obesity center patients were included in the study. Phone calls were made by the directing doctor and patients were asked about their diet compliance, exercise level, the way they felt, present weight, any problems about their accompanying diseases or obtaining their medications. Recommendations were made (healthy nutrition, hydration, home exercises, coping with distress, the necessity of home isolation, precautions needed to be taken when they have to go out). The answers were categorized and number of patients for each category were determined.

Results: The number of patients that were called was 101, 86 for those who answered and 15 for those who did not respond. When their last registered weight in kg was compared with the present weight declared by the patient, 40.7% had weight gain (n=35), 50% had weight loss (n=43) and 9.3% (n=8) patients had same weight. When they were asked about their food consumption, 27.9% (n=24) of patients were following the recommended diet, 29% (n=29) were not following any recommendations about their diet and 33% (n=33) were partially

Öz

Amaç: Teletıp odyo/video iletişimi, bilgisayar ve telemetri gibi modern bilişim teknolojisini kullanarak uzaktaki hastalara sağlık hizmeti verilmesidir. Global Koronavirüs hastalığı-2019 (COVID-19) pandemisi süresince, genel popülasyona; özellikle obezitesi olan bireyler gibi yüksek enfeksiyon riski olan kişilere ev izolasyonu önerilmiştir. Burda, COVID-19 pandemisi izolasyon döneminde obezite merkezi hastalarının takibi için kullanılan teletıp yöntemi verilerinin değerlendirilmesi ve kriz zamanlarında obezite gibi kronik hastalıklar için alternatif takip metodlarının gerekliliğine dikkat çekilmesi amaçlanmıştır.

Yöntem: Obezite merkezinde kayıtlı tüm hastalar çalışmaya dahil edildi. Merkez yönetici hekimi tarafından telefon aramaları yapıldı ve hastalara diyet uyumları, egzersiz düzeyleri, nasıl hissettikleri, mevcut kiloları, eşlik eden hastalıkları ya da ilaçlarını temin etmede zorluk yaşayıp yaşamadıkları soruldu. Tavsiyelerde bulunuldu (sağlıklı beslenme, sıvı alımı, ev egzersizleri, stresle baş etme, ev izolasyonu zorunluluğu, dışarda olmak zorunluysa alınması gereken önlemler). Yanıtlar sınıflandırıldı ve her kategori için hasta sayısı belirlendi.

Bulgular: Toplam 101 hasta arandı, 86 hasta yanıt verdi ve 15 hasta yanıt vermedi. Son kayıtlı kilolarıyla karşılaştırıldığında %40,7 (n=35) hasta kilo almıştı, %50 (n=43) hasta kilo vermişti ve %9,3 (n=8) hasta kilosunu korumuştu. Hastaların % 27,9'u (n=24) tavsiye edilen diyete uyuyordu, %29'u (n=29) diyet konusunda hiçbir tavsiyeye uymuyordu ve %33'ü (n=33) diyet önerilerine kısmen uyuyordu. En sık yapılan yanlış tüm gün ve gece boyunca atıştırmaktı. Hastaların %30,2'si (n=26) düzenli olarak ev egzersizi yapıyordu, %50 (n=43) hiç egzersiz yapmıyordu ve %19,8 (n=17) kısmen ev egzersizleri yapıyordu. En sık yapılan egzersiz evde-yürüme programlarıydı. Kendilerini nasıl hissettikleri sorulduğunda %53,5 (n=46)

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Abstract

following their dietary recommendations. The most common mistake was snacking throughout the day and at nighttime. When they were asked about their physical activity level, 30.2 % (n=26) of patients were doing home exercises regularly, 50% (n=43) were not exercising at all and 19.8 % (n=17) were partially doing home exercises. The most common home exercise was home-walking programmes. When they were asked how they felt, 53.5% (n=46) of patients declared to be generally good, 24.4% (n=21) were generally bad and 22.1 (n=19) were partially good. The most common complaint was sleep disturbances and anxiety.

Conclusion: Telemedicine is an easy, safe and effective follow-up method for chronic diseases like obesity at extraordinary times like the pandemic period we are going through. Its application can be broader after medical and legal regulations become clear to let both the patients and the healthcare professionals who use this method be safe in all aspects.

Keywords: COVID-19 pandemic, obesity, telemedicine

Öz

hasta genel olarak iyi, %24,4 (n=21) hasta genel olarak kötü, %22,1 (n=19) hasta kısmen iyi olduklarını belirtti. En sık şikayet uyku bozuklukları ve anksiyeteydi.

Sonuç: Teletıp, içinde bulunduğumuz pandemi periyodu gibi olağanüstü zamanlarda, obezite gibi kronik hastalıklar için kolay, güvenli ve etkin bir takip metodudur. Bu yöntemin uygulama alanı, kullanan hastalar ve sağlık profesyonelleri için her anlamda güvenli olmasını sağlayacak medikal ve legal düzenlemeler yapıldıktan sonra genişleyebilecektir.

Anahtar kelimeler: COVID-19 pandemisi, obezite, teletıp

Introduction

Telemedicine means to provide healthcare services to remote patients using modern information technology like audio/video communications, computer and telemetry. It is a convenient method as it can provide health-care services across geographic, time, social and cultural barriers. World Health Organization makes a distinction between telemedicine and telehealth, emphasizing that telehealth is performed generally for preventive medicine purposes and telemedicine is performed for treatment purposes (1).

Starting late 2019 and early 2020, 2019 novel Coronavirus diseases-2019 (COVID-19) caused a global pandemic and has affected our country since March 2020, too. Turkish Ministry of Health declared the general precautions needed to be taken for the pandemic by healthcare facilities immediately. Our obesity center therapeutic education programme and obesity outpatient clinic were temporarily discontinued according to these precautions (2,3).

Home isolation was advised for general population, especially for individuals who had high infection risk, like the elderly, immunosuppressed ones, or those with chronic illnesses. Obesity was among those chronic illnesses and people living with obesity were advised to stay at home strictly (2,3).

Home isolation had some consequences like overeating, inactivity, increased stress levels, sleep disturbances which could easily lead to weight gain. Several studies from different countries highlighted this problem even for people with normal weight and the risk was bigger for individuals living with obesity. Thus, we decided to use telemedicine methods to follow up our patients (4-6).

Here, it was aimed to evaluate the data obtained with a telemedicine method performed for obesity center patients' follow-ups during COVID-19 pandemic and highlight the need for alternative follow-up methods for chronic diseases like obesity during crisis times.

Material and Methods

All registered obesity center patients were included in the study (98 female, 3 male, totally 101 patients). First, phone messages were sent informing the patients that they were going to be called by their doctor for follow-up. Then, the phone calls were made by the directing doctor. Patients were asked about their diet compliance, exercise level, how they felt, present weight, any problems about their accompanying diseases or obtaining their medications. Their questions were answered. Recommendations that needed to be followed at home during pandemic period for obesity and also for protection from COVID-19 were made (healthy nutrition, hydration, home exercises, coping with distress, the necessity of home isolation, precautions needed to be taken when being outside was a must). The answers were categorized and numbers of patients for each category were determined.

Study was conducted according to the Helsinki 2000 declaration. Verbal consent was obtained from all patients after all procedures had been fully explained. Ethical approval was obtained from University of Health Sciences

Turkey, İstanbul Training and Research Hospital Ethical Committee (2444/12.06.2020).

Statistical Analysis

Statistical analysis was performed using SPSS 22.0 for Windows program. Descriptive analysis (number, percentage, mean ± standard deviation) was used for statistical analysis.

Results

The number of patients that were called was 101, 86 patients answered and 15 patients did not respond (3 calls were made within a 3 day-period and when there was still no answer at all times, the patient was accepted non-responding). General characteristics of the patients are summarized in Table 1.

When their last registered weight in kg was compared with the present weight declared by the patient, 40.7 % had weight gain (n=35), 50% had weight loss (n=43) and 9.3% (n=8) patients had same weight (Table 2).

Table 1. General characteristics of the patients

Gender	Female	Male
Number of patients (no)	83	3
Age (years) (mean ± SD)	50.92±9.4	59.5±5.1
BMI (kg/m²)	35.05±5.2	33.6±0.37
WC (cm)	115.7±10.01	133±9.84
DM rate (number/%)	32/38.5	2/66.6
HT rate (number/%)	39/49.9	2/66.6
CRD rate (number/%)	4/4.8	0
CAD rate (number/%)	4/4.8	1/33.3
HL rate (number/%)	36/43.37	1/33.3
Hypothyroidism (number/%)	16/19.3	0
Malignancy (number/%)	3/3.6	0

SD: Standard deviation, BMI: Body mass index, DM: Diabetes mellitus, HT: Hypertension, CRD: Chronic renal disease, CAD: Coronary artery disease, HL: Hyperlipidemia

When they were asked about their food consumption, 27.9% (n=24) of patients were following the recommended diet, 29% (n=29) were not following any recommendations about their diet and 33% (n=33) were partially following their dietary recommendations. The most common mistake was snacking during the day and at night (Table 2).

When they were asked about their physical activity level, 30.2% (n=26) of patients were doing home exercises regularly, 50% (n=43) were not exercising at all and 19.8% (n=17) were partially doing home exercises. The most common home exercise was home-walking programmes (Table 2).

When they were asked about how they felt, 53.5% (n=46) of patients declared to be generally good, 24.4% (n=21) were generally bad and 22.1 (n=19) were partially good. The most common complaints were sleep disturbances and anxiety (Table 2).

All patients declared that they were glad to be called for follow-up and it motivated them. And, it was striking that one patient asked whether she was going to be called again, declaring if so, she was going to pay more attention to her lifestyle recommendations.

Discussion

COVID-19 pandemic affected great diversity of people from all around the world. Preliminary reports from China led us about general precautions that should be taken to prevent the spread of the disease, diagnosis and treatment methods and highlighted the populations who were at higher risk (7).

Along with several other diseases/conditions, patients with obesity were declared to be at high risk for COVID-19 infection. Diminished immune system and increased inflammatory state were blamed for the susceptibility to

Table 2. Classification of patients' lifestyle changes during pandemic period

Weight status	Weight gain	Weight loss	Same weight
No/% of patients	35/40.7	43/50	8/9.3
Weight change [mean ± SD (kg)]	2.85±2.59	2.41±1.76	0
Diet status	Following recommended diet	Not following recommended diet	Partially following recommended diet
No/% of patients	24/27.9	29/33.7	33/38.4
Exercise status	Doing recommended home exercises	Not exercising at all	Partially doing recommended home exercises
No/% of patients	26/30.2	43/50	17/19.8
Their mood	Generally good	Generally bad	Partially good
No/% of patients	46/53.5	21/24.4	19/22.1

SD: Standard deviation

COVID-19 in obesity and also, for the consequences of the disease (8).

Obesity (48.3%) was one of the most common underlying diseases in COVID-19 infection along with hypertension (49.7%), chronic lung disease (34.6%), diabetes mellitus (28.3%) and cardiovascular disease (27.8%) according to centers for diseases control and prevention report. People with obesity had more serious illness, needed more hospital admission and ventilation support. Also, it was pointed out that healthcare could be tricky for people with severe obesity as adequate equipment was not available in every hospital for these individuals (9).

Thus, home isolation was advised to all individuals living with obesity. Living indoors protected people from coronavirus, but at the cost of weight gain as well as increased anxiety, depression, social isolation, decreased sunlight exposure and possible behavioral addiction disorders (10). Snacking, binge eating, eating more meals than ever, having more junk food than ever, decreased physical activity levels and increased sitting time were reported (11).

In our study, 60% of the patients did not gain weight although one third of the patients did not follow their diet and half of the patients did not exercise at all. It was striking that some patients with obesity actually did lose weight. This was attributed to different reasons: The media declared obesity as one of the reasons of morbidity and mortality in COVID-19 and this might have triggered people with obesity to try harder to lose weight, stay healthy and be able to avoid increased mortality risk related to obesity. Also, some people might have had uncontrolled diabetes or even sarcopenia during pandemic period. Similar results were obtained in a study in Italy, too. In this study by Di Renzo et al. (5), although nearly half of the patients declared they had gained weight, some did quit smoking, some tried to have organic products in their diet and adhered to Mediterranean diet and some increased physical activity, especially resistance training to stay healthy.

Risk of COVID-19 infection, self-quarantine and economical burdens of the situation led to mental distress to nearly everyone who was affected by the pandemic. Depression, perceived discrimination, post-traumatic stress disorder, even suicidal ideation were reported. Mental health of even health-workers was of a concern. It was accepted normal to have anxiety to some extent, but still social isolation was hazardous to people who were already prone to depression (12-14).

In our study, although one fourth of the patients had serious anxiety, majority of the patients could find a way to cope with the psychological consequences of the pandemic. This could be attributed to close family relations and active support among family members in our society as a part of our traditional life.

Home-based exercise, dance, active video-games, any chance to increase physical activity were recommended to cope with anxiety, to improve body composition, postural balance and also cognitive functions in older ages (15). Exercise helped maintaining both physical and mental well-being (16). Making right information sources available, providing effective communication and general and medical needed supplies, making self-isolation a people's choice for health maintenance, and reducing the boredom could help people to get over the distress related to pandemic (17). A study suggested that a telephone support line provided by psychiatric nurses could help to provide a social network (18).

Telemedicine is recommended for mildly ill patients and patients with ongoing chronic diseases. This would both provide the supportive care needed and minimize the exposure to other ill patients (19).

While using telemedicine for patients, standard local regulations must be followed. The audio/video visit should be planned. The time spent, method of telehealth and all visit notes should be documented. Usual visit questions should be asked and answers should be noted. Patients' chief complaint, review of systems, history of complaints, history of patient should be obtained. And in the end, it must be decided whether the patient himself/herself should be seen in person. Otherwise, recommendations must be given and next appointment should be arranged if necessary (19).

In our study, patients were informed via telephone messages informing them they were gonna be called by their doctor in obesity center for follow-up. As there are no specific regulations about tele-medicine, only hospital approval was taken in advance. When the doctor made the call, after getting verbal consent from the patients, they were asked about their present condition regarding obesity and coping with pandemic. All answers, time of calls and recommendations made were recorded. As all patients were seen and examined by the same doctor before and their detailed files were available, the phone-call visit was convenient. However, the doctors should be careful while using telemedicine for a patient they have

never seen before as medical and legal issues may occur. Although in a study in 2019, the authors found no reported cases of medical malpractice in direct-to-consumer telemedicine, malpractice risk is still present (20). Thus, ethical, legal and financial aspects should be analyzed in detail and be decided whether it is worth practicing telemedicine (21,22). But at extraordinary times like COVID-19 pandemic, it is a convenient tool that can be used without hesitation for patients with chronic diseases like obesity (23).

Conclusion

Telemedicine is an easy, safe and effective follow-up method for chronic diseases like obesity at extraordinary times like the pandemic period we are going through. Its application can be broader after medical and legal regulations become clear to make both the patients and the healthcare professionals who use this method to be safe in all aspects.

Ethics

Ethics Committee Approval: Ethical approval was obtained from University of Health Sciences Turkey, İstanbul Training and Research Hospital Ethical Committee (2444/12.06.2020).

Informed Consent: Verbal consent was obtained from all patients after all procedures had been fully explained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: F.A., Design: F.A., Data Collection or Processing: F.A., H.U.A., M.E.P., Analysis or Interpretation: F.A., H.U.A., M.E.P., Literature Search: F.A., H.U.A., M.E.P., Writing: F.A.

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ORIGINAL RESEARCH

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Pulmonary Function Test and Thoracic Computed Tomography in the Evaluation of Dyspnea in Patients with Goiter

Guatrlı Olgularda Dispnenin Değerlendirilmesinde Solunum Fonksiyon Testi ve Toraks Bilgisayarlı Tomografi

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Abstract

Objective: The uses of flow volume loop (FVL) section of pulmonary function test (PFT) and thorax computed tomography (TCT) are examined in the evaluation of dyspnea, which is one of the leading symptoms of compression due to goiter.

Method: Thirty-six patients who were admitted to the Chest Diseases and Tuberculosis Clinic of University of Health Sciences Turkey, Bağcılar Training and Research Hospital between August 2019 and January 2020 with the complaint of dyspnea and who were diagnosed with goiter were enrolled in this prospective study. To determine the compression of the goiter on the trachea, PFT and TCT were performed in all cases. The patients were evaluated in terms of age, gender, smoking history, complaints, respiratory system physical examination findings, FVL, type of goiter, presence of TCT findings of external compression and deviation of trachea due to goiter. The degree of external compression on trachea according to the TCT were grouped as follows grade 0: No compression on the trachea, grade 1: Compression narrowing the tracheal lumen diameter less than 50%, grade 2: Compression narrowing the tracheal lumen diameter more than 50%. FVL in PFT was grouped as normal and upper airway obstruction (UAO).

Results: Twenty-six of the 36 cases were female (72.22%). The median age was 54.50 (range, 32-80) years. When the location of the goiter was evaluated, it was found that 25 (69.44%) of the cases had retrosternal goiter (RSG) and 11 (30.56%) had cervical goiter (CG). In terms of FVL, 28 (77.78%) were compatible with UAO and 8 (22.22%) with normal condition. Tracheal deviation was detected in 18 (50%) cases. External compression of trachea was detected in 28 (77.78%) cases, grade 1 in 14 (38.89%) cases and Grade 2 in 14 (38.89%) cases. FVL was found to be

Öz

Amaç: Guatra bağlı basının önde gelen semptomlarından biri olan dispnenin değerlendirilmesinde solunum fonksiyon testindeki (SFT) akım volüm halkası (AVH) ve toraks bilgisayarlı tomografinin (TBT) kullanımının değerlendirilmesi amaçlandı.

Yöntem: Ağustos 2019-Ocak 2020 tarihleri arasında Sağlık Bilimleri Üniversitesi Bağcılar Eğitim ve Araştırma Hastanesi Göğüs Hastalıkları ve Tüberküloz Kliniği'ne nefes darlığı şikayeti ile başvuran guatr tanılı 36 hasta bu prospektif çalışmaya alındı. Guatrın trakeaya basısını değerlendirmek için olguların tümüne SFT ve TBT yapıldı. Olgular yaş, cinsiyet, sigara öyküsü, şikayet, solunum sistemi muayene bulguları, AVH, guatr çeşidi, TBT'deki guatra bağlı trakea basısı ve deviasyonu açısından değerlendirildi. TBT'deki trakea basısı grade 0: Trakeaya bası yapmamış, grade 1: Trakea çapını %50'den daha az daraltan bası, grade 2: Trakea çapını %50'den daha fazla daraltan bası bulgusu şeklinde gruplandırıldı. SFT'deki AVH normal ve üst hava yolu obstrüksiyonu (ÜHYO) ile uyumlu olarak gruplandırıldı.

Bulgular: Çalışmadaki 36 olgunun 26'sı kadındı (%72,22). Yaş ortalaması 54,50 (32-80 aralığında) yıldı. Guatr yerleşim yeri olarak 25'i (%69,44) retrosternal guatr (RSG), 11'i (%30,56) servikal guatrdı (SG). Akım volüm halkasına (AVH) göre 28 (%77,78) olgu ÜHYO ile uyumlu, 8 (%22,22) olgu normal AVH ile uyumlu idi. Trakeal deviasyon 18 (%50) olguda saptandı. Trakeal dış bası 28 (%77,78) olguda saptanmıştı ve bunların 14'ü (%38,89) grade 1, 14'ü (%38,89) grade 2 şeklindeydi. AVH grade 0, 1, 2 grubunda sırasıyla %25, %85,71, %100 oranlarında ÜHYO ile uyumlu saptandı (p=0,0001). Grade 0 grubunda normal AVH görülmesi grade 1 ve grade 2'ye göre istatistiksel olarak anlamlı oranda yüksek saptandı (p=0,001). Guatr yerleşim yerine göre bakıldığında RSG

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Abstract

compatible with UAO in grade 0, 1, and 2 with the percentages of 25%, 85.71%, and 100%, respectively (p=0.0001). Normal FVL appearance in Grade 0 group was statistically significant when compared to grade 1 and grade 2 (p=0.001). According to goiter type, the compatibility of FVL with UAO was higher in the RSG group with a statistical significance (p=0.002).

Conclusion: Although TCT is useful in evaluating the boundaries of the disease and surgical anatomy in patients with goiter, preoperatively, the FVL of the PFT should be considered as a priority over TCT to support the clinical correlation of dyspnea due to goiter.

Keywords: Dyspnea, flow volume loop, goiter, thoracic computed tomography

Öz

grubunda ÜHYO ile uyumlu AVH saptanması istatistiksel olarak anlamlı derecede yüksekdi (p=0,002).

Sonuç: Guatrlı hastalarda her ne kadar TBT, hastalığın sınırlarını ve cerrahi anatomiyi değerlendirmede yararlı olsa da, guatra bağlı nefes darlığının klinik korelasyonunu desteklemek amaçlı preoperatif olarak SFT'nin AVH, TBT'den daha öncelikli olarak değerlendirilmelidir.

Anahtar kelimeler: Akım volüm halkası, dispne, guatr, toraks bilgisayarlı tomografi

Introduction

Goiter is defined as the growth of the thyroid gland in diffuse and nodular manner. The incidence of this disease, which is more common in women, is around 4-5% (1). It can be seen as cervical goiter (CG) or retrosternal goiter (RSG) according to the location. In RSG, more than 50% of the thyroid gland is under the sternal notch, in the mediastinum (2). Cough, dyspnea, stridor, choking sensation, and difficulty in swallowing, which are considered as goiter-related external compression symptoms, are also considered as surgical indications as well as the radiological findings of external compression in thoracic computerized tomography (TCT) (3).

TCT and pulmonary function tests (PFT) are used to evaluate external compression symptoms. Especially the flow volume loop (FVL) section in PFT helps the clinicians to evaluate the external compression of trachea. The y-axis shows the flow, and the X-axis shows the volume in FVL (4). In a correctly performed test, the two curves complement each other and appear convex (Figure 1, 2). In cases with upper airway obstruction (UAO) such as goiter, flattening is seen in the convex part of the loop (Figure 3, 4). If the external compression on the trachea causes restriction in airflow during inspiration or expiration, it is defined as variable airway obstruction. In fixed airway obstruction, airway diameter does not change throughout inspiration or expiration and the airflow is equally affected during the respiratory cycle (5).

The size of the thyroid gland, its characteristics, location, external compression on trachea, or its deviation can be examined with TCT; therefore, it plays an important role in preoperative evaluation.

In this study, we evaluated the use of PFT and TCT in cases with dyspnea related to the goiter. We compared the FVL in PFT and radiological findings in TCT.

Materials and Methods

The study was planned after the approval of the Ethics Committee of University of Health Sciences Turkey, Bağcılar Training and Research Hospital (ref number of: 2019.08.1.02.059/02.08.2019).

A total of 36 goiter cases, who were admitted to the Chest Diseases and Tuberculosis Clinic at University of Health Sciences Turkey, Bağcılar Training and Research Hospital between August 2019 and January 2020 with dyspnea, were enrolled in the study. Informed consents were taken from patients.

Patients with asthma, chronic obstructive pulmonary disease (COPD), acute bronchitis, acute upper respiratory tract infection, lung cancer and anemia, which can cause similar dyspnea symptoms and affect FVL, and those who failed in performing FVL were excluded from the study. All patients underwent PFT with a Mır-Mınıspır model handheld digital spirometry device. At least 3 respiratory maneuvers were performed by the PFT technician and the best FVL was recorded. PFTs were carried out according to the acceptability and repeatability criteria of ATS/ERS guidelines (6).

TCT was performed with Philips-Brilliance CT 64-Ds tomography device to evaluate the radiological findings of external compression and deviation of trachea due to goiter.

The cases were evaluated in terms of age, gender, smoking history, complaints, respiratory examination results, FVL, goiter type, radiological findings of external compression and deviation of trachea due to goiter. The external

compression on trachea was grouped as grade 0, 1, 2. Grade 0: No external compression on the trachea, grade 1: External compression narrowing the trachea diameter by less than 50%, grade 2: External compression narrowing the trachea diameter by more than 50%.

Statistical Analysis

In this study, the NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) package program was used for statistical analyses. In the evaluation of the data, the descriptive statistical methods (mean, standard deviation) were used as well as the Shapiro-Wilk normality test to test the distribution of the variables. The independent t-test was used in comparing the binary groups of variables with normal distribution and the chi-square test was used in the comparison of qualitative variables. The results were evaluated at the significance level of $p<0.05$.

Results

Twenty-six of 36 patients were female (72.22%). The median age was 54.50 (range, 32-80) years. When considered in terms of the goiter location type, it was found that 25 (69.44%) were RSG and 11 (30.56%) were CG. 12 (33.33%) had a smoking history. All of them (100%) had dyspnea, 6 (16.67%) patients had dysphagia and 5 (13.89%) had cough in addition to dyspnea. The physical examination of respiratory system was normal in 29 (80.56%) patients and 5 (13.89%) of them had stridor. In 2 (5.56%) of them, rhonchus was heard. All patients with stridor were in the grade 2 group in terms of external compression on the trachea.

When PFTs were evaluated, 28 (77.78%) of the cases were found to be compatible with UAO in terms of FVL and 8 (22.22%) with normal condition. A total of 15 (41.67%)

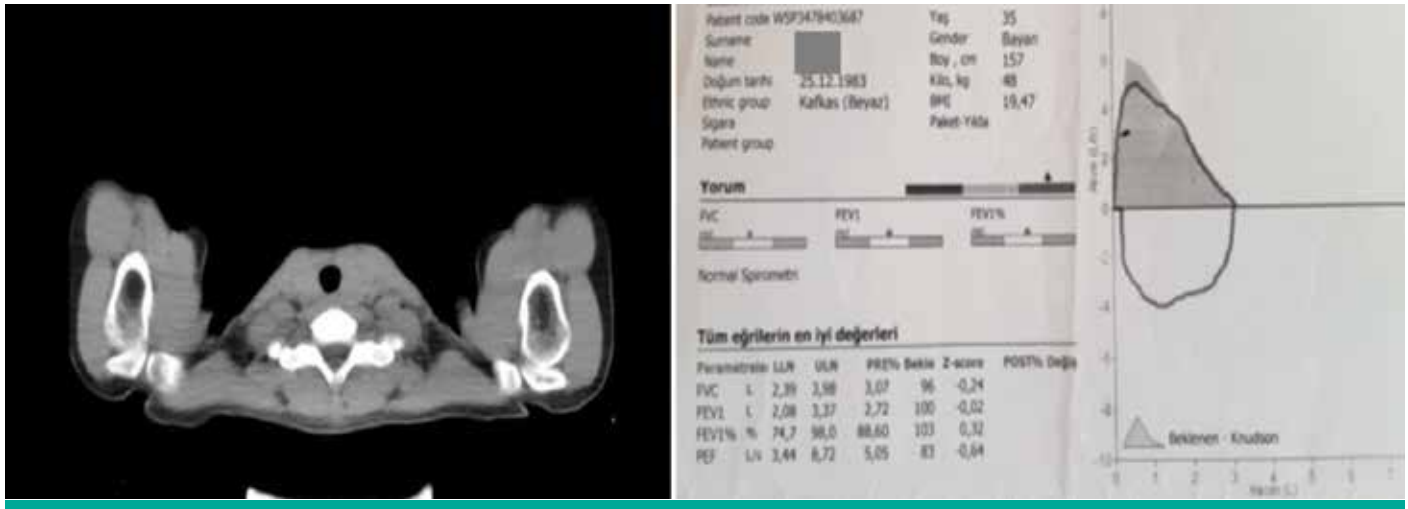

Figure 1, 2. Thoracic computerized tomography without an external compression on the trachea and normal flow volume loop of a 35-year-old female

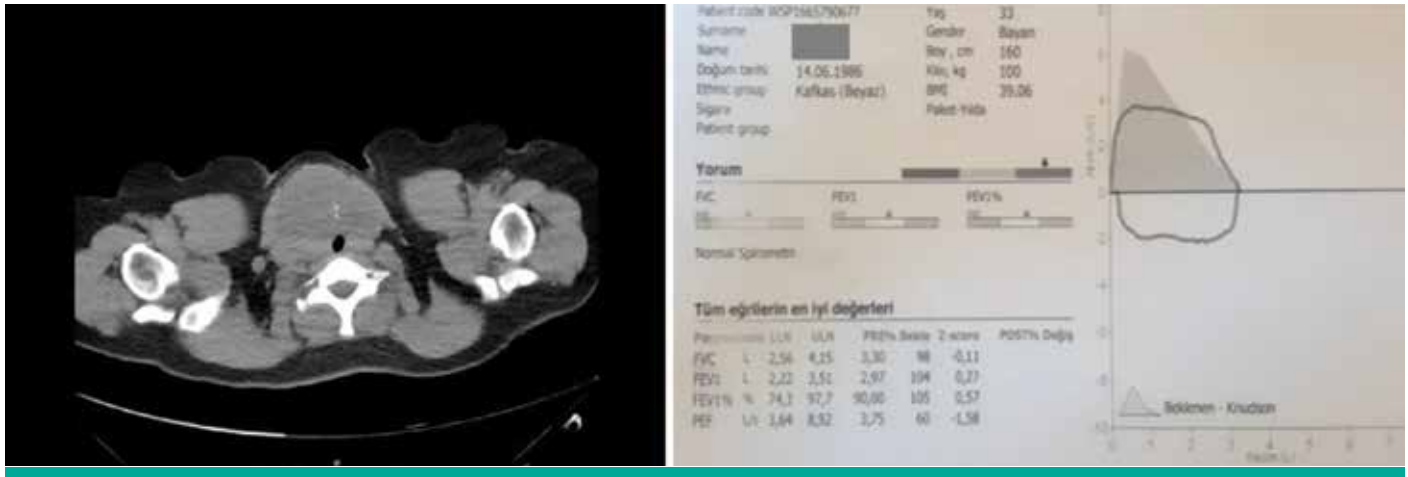

Figure 3, 4. Thoracic computerized tomography with an external compression on the trachea and flow volume loop compatible with upper airway obstruction of a 32-year-old female

patients with UAO had fixed airway obstruction and 13 (36.11%) had variable airway obstruction. Goiter-related tracheal deviation was detected in 18 (50%) patients; 12 (66.67) had deviation to the right and 6 (33.33%) to the left. External compression on the trachea was detected in 28 (77.78%) patients, 14 (38.89%) in the grade 1 group and 14 (38.89%) in the grade 2 group. Radiological findings on TCT of RSG and CG groups are shown in Table 1.

Thirty of 36 patients were diagnosed histopathologically by performing goiter surgery or needle aspiration biopsy. A total of 24 (80%) patients had benign and 6 (20%) had malignant cytology, and finally 19 patients underwent surgery (52.78%).

The relationship between FVL and external compression on the trachea (grade) is shown in Table 2. In grades 0, 1, and 2, FVL was found to be compatible with UAO at the rates of 25%, 85.71%, and 100%, respectively (p=0.0001). When evaluated according to the goiter type, the UAO in the RSG group was higher than in the CG group with a statistical significance (p=0.002).

The percentage of narrowing in the tracheal lumen was 88% in the RSG group and 54.5% in the CG group, which was statistically significant (p=0.026). The external compression percentage in grade 2 level was 48% in RSG, which was higher than CG (18.2%), but that was not statistically significant (p=0.06). Normal FVL in the grade 0 group was statistically significant when compared to grade 1 and grade 2 (p=0.001).

Table 1. Radiological findings of external compression on the trachea on thoracic computerized tomography in retrosternal goiter and cervical goiter

	RSG*		CG†		
	n	%	n	%	p
Tracheal deviation	15	60	3	27.3	0.070
External compression on trachea	22	88	6	54.6	0.026
Grade 0	3	12	5	45.5	-
Grade 1	10	40	4	36.4	-
Grade 2	12	48	2	18.2	0.060

*RSG: Retrosternal goiter, †CG: Cervical goiter

Table 2. The relationship between flow volume loop and grade of external compression on the trachea

	Grade 0		Grade 1		Grade 2		
FVL*	n	%	n	%	n	%	p
Normal	6	75	2	14.29	0	0	-
Compatible with UAO†	2	25	12	85.71	14	100	0.0001

*FVL: Flow volume loop, †UAO: Upper airway obstruction

Discussion

TCT and less commonly PFT are generally used to evaluate dyspnea, which is one of the external compression symptoms related to goiter. However, TCT is a more expensive and invasive method when compared to PFT. The FVL in PFT is an easy and practical test that can be used to evaluate UAO due to external compression on the trachea caused by goiter. However, its disadvantages are that its diagnostic sensitivity is low in mild obstructions and the typical image of UAO is masked when coexisting diseases such as COPD and asthma are present (7,8).

Albareda et al. (9) conducted a study and reported that 54% of RSG patients had symptoms due to external compression of goiter and 26% had FVL compatible with UAO. In terms of FVL, 24% of the cases had variable airway obstruction and 2% had fixed airway obstruction (9). In our study, all of the patients (100%) had external compression symptoms; therefore, we found UAO at a higher rate of 92% (52% of which was fixed, and 40% were variable airway obstructions in the RSG group). Regarding the higher number of cases with external compression of the trachea at grade 2 level, our UAO rates, especially fixed airway obstruction rates, may be higher.

In their study, Stevens et al. (10) examined the effect of FVL in deciding surgery in goiter patients. They found FVL to be normal in 33 of the 38 cases and abnormal in 5. Two of the patients with abnormal FVL were compatible with external compression, and 3 were compatible with obstructive/restrictive lung diseases. Seven of the 33 patients, who had normal FVL, underwent surgery (local compression, abnormal cytology, and grave's disease). They claimed that FVL had no effect on deciding on surgery. In this study, only 4 patients had dyspnea and 14 patients had combined symptoms (10). In our study, patients with co-existing obstructive/restrictive lung diseases were not included in the study because FVL could have been affected in this respect. All of the patients were symptomatic and had the complaint of dyspnea. Twenty eight (77.78%) had abnormal but 8 (22.22%) had normal FVL. FVL was compatible with UAO in these 28 cases. A total of 19 (52.78%) patients underwent surgery. Six patients underwent surgery due to malignancy and other patients due to local compression on the trachea caused by goiter. In our study, we found that FVL had an effect on deciding surgery, especially in those who had local compression.

In Stevens et al.'s (10) study, 2 cases had external compression, 2 had tracheal deviation in TCT and FVL was

normal in the cases with external compression. It may be due to the fact that the degree of the external compression was mild; no information was given in the study about it. In our study, since all of them were symptomatic, external compression was detected in 28 (77.78%) and tracheal deviation in 18 (50%) patients. FVL was compatible with UAO in 26 of those who had external compression, which was statistically significant. Such a difference between the two studies may be related to the greater number of patients with external compression.

Menon et al. (11) examined the prevalence of UAO and the correlation among clinical findings in goiter patients. They found radiological findings of external compression of the trachea in TCT in 9.3% and FVL was compatible with UAO in PFT in 14.3% of patients, and no correlation was found between TCT findings and FVL. However, it should be addressed that 26.8% of the study population had RSG, and only 32% were symptomatic (11). In our study, 69.44% of the patients had RSG and all were symptomatic; therefore, the UAO rate was 77.78% and external compression rate was 77.78%, which showed a higher rate and a correlation.

Thusoo et al. (12) detected radiological findings of tracheal deviation and/or external compression on chest X-rays in 32% of goiter patients. In their study, 40% of the population were symptomatic. They also detected FVL compatible with UAO in 60%, the most common was variable airway obstruction. In contrast to our study, smokers were excluded in this study and only chest X-rays were used instead of TCT. It was found that 77.78% of our patients were compatible with UAO in FVL; 41.67% had fixed and 36.11% had variable airway obstruction (12). Since our rate of patients with RSG was higher, FVL compatible with UAO was also higher and the fixed airway obstruction was the most common obstruction type.

In previous studies, it was detected that 69-73% of patients with RSG and CG had tracheal deviation as the common radiological finding. External compression was relatively more common in patients with RSG [35 (73%)] compared to the cases with SG [9 (58%)]. Tracheal deviation was also radiologically detected in 50% and external compression in 77.78% of patients and the rates were similar to those reported in previous studies (13).

Patients with goiter should be referred to chest physicians in the presence of dyspnea, especially if they have RSG. After ruling out the other causes of dyspnea that are not related to external compression due to goiter, patients should be evaluated with PFT with priority, and then with TCT to see if there is an external compression or not. Depending on the degree of the external compression, surgery should be decided with a multi-disciplinary approach including the general surgeons. According to the interpretation of our study, a patient who has goiter and dyspnea should undergo PFT at first and then if FVL is normal, it should be considered as grade 0 or grade 1. In this situation, there should be no need for further evaluations such as TCT. If FVL is compatible with UAO in grade 1 or grade 2, then it is necessary to evaluate the patients with TCT. The presence of fixed airway obstruction especially with grade 2 level means that there is a surgical indication.

Study Limitations

A limitation of our study is that it involves a small number of patients so there is a need for further studies with larger study populations to support this issue.

Conclusion

Although TCT is preoperatively useful in evaluating the boundaries of the disease and surgical anatomy in patients with goiter, the FVL of the PFT should be considered as a priority over TBT to support the clinical correlation of dyspnea due to goiter.

Ethics

Ethics Committee Approval: The study was planned after the approval of the Ethics Committee of University of Health Sciences Turkey, Bağcılar Training and Research Hospital (reference number of: 2019.08.1.02.059/02.08.2019).

Informed Consent: Informed consents were taken from patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: E.Y., Design: E.Y., Data Collection or Processing: G.Ö., Analysis or Interpretation: G.Ö., Writing: E.Y., G.Ö.

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

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ORIGINAL RESEARCH

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Evaluation of Etiologic Factors and Electrophysiologic Findings in Patients with Peroneal Neuropathy

Peroneal Nöropatisi Olan Hastalarda Etiyolojik Faktörlerin ve Elektrofizyolojik Bulguların Değerlendirilmesi

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Abstract

Objective: Peroneal neuropathy is the most common entrapment mononeuropathy in the lower extremity. The common site of injury is around the fibular head where the nerve becomes superficial. Compressive pathologies are the most frequently seen etiologies. The treatment plan is designed according to the etiology. Electrophysiologic investigations are accepted as the gold standard for the diagnosis of peroneal neuropathy. In this study, we aimed to evaluate the etiologic factors and electrodiagnostic findings in peroneal neuropathy.

Method: We retrospectively analyzed the etiological and electrodiagnostic test findings of patients with clinical features compatible with peroneal neuropathy, who presented to the Electromyography Laboratory of İstanbul Medipol University Hospital between January 2016 and December 2019. Patients with polyneuropathy or a disease that may cause polyneuropathy such as diabetes mellitus, those with lumbosacral radiculopathy or plexopathy, and those with neurodegenerative diseases were excluded.

Results: A total of 30 patients with clinical features compatible with peroneal neuropathy (19 males, 11 females, median age 30 years; range 21 to 66) were enrolled in the study. Four (13.3%) patients had a comorbid disease. The median duration (minimum-maximum) of the symptoms was 20.5 (2-140) weeks. The affected side of the peroneal nerve was 43.3% right, 43.3% left, and 13.3% bilateral. The common cause of peroneal nerve injuries was due to compression (40%). Potential causes of compression in five out of 12 cases were iatrogenic. Weight loss was found in 10% of patients and one patient (3.3%) had a history of a recurrent ganglion cyst. Approximately 23% of lesions were due to traction injury and 23%

Öz

Amaç: Peroneal nöropati, alt ekstremitede en sık görülen tuzak mononöropatidir. Yaygın yaralanma bölgesi, sinirin yüzeysel olduğu fibula başındadır. En sık görülen etiyolojiler kompresif patolojilerdir. Tedavi planı etiyolojiye göre tasarlanır. Elektrofizyolojik incelemeler peroneal nöropati tanısında altın standart olarak kabul edilmektedir. Bu çalışmada peroneal nöropatide etiyolojik faktörleri ve elektrodiagnostik bulguları değerlendirmeyi amaçladık.

Yöntem: İstanbul Medipol Üniversite Hastanesi Elektromiyografi Laboratuvarı'na Ocak 2016-Aralık 2019 tarihleri arasında başvuran peroneal nöropati ile uyumlu klinik özellikleri olan hastaların etiyolojik ve elektrodiagnostik test bulgularını retrospektif olarak inceledik. Polinöropatili veya diabetes mellitus gibi polinöropatiye neden olabilecek bir hastalığı olan hastalar, lumbosakral radikülopati veya pleksopatisi olanlar ve nörodejeneratif hastalığı olanlar çalışma dışı bırakıldı.

Bulgular: Çalışmaya peroneal nöropati ile uyumlu klinik özelliklere sahip 30 hasta (19 erkek, 11 kadın, medyan yaş 30 yıl, 21-66 aralıkta) alındı. Dört (%13,3) hastada ek hastalık vardı. Medyan (minimum-maksimum) semptom süresi 20,5 (2-140) haftaydı. Peroneal sinirin etkilenen tarafı %43,3 sağ, %43,3 sol ve %13,3 bilateral idi. Peroneal sinir yaralanmalarının en sık nedeni kompresyona bağlıydı (%40). On iki olgudan beşinin olası kompresyon nedenleri iyatrojenikti. Hastaların %10'unda kilo kaybı saptandı ve bir hastada (%3,3) tekrarlayan ganglion kisti öyküsü vardı. Lezyonların yaklaşık %23'ü traksiyon yaralanmasına bağlıydı ve olguların %23'ü idiyopatikti. Elektrofizyolojik incelemelere göre, 16 olgu ağırlıklı olarak aksonal yaralanma olmaksızın demiyelinizan idi. Kalan 14 olguda (%46,6) aksonal yaralanma saptandı ve aksonal yaralanmalı olguların

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Abstract

of cases were idiopathic. According to electrophysiologic investigations, 16 cases were predominantly demyelinating without axonal injury. The axonal injury was detected in the remaining 14 cases (%46.6) and half of the cases with axonal injury were accompanied by demyelinating injury. Six cases had mild, 3 cases had severe, and 5 cases had a total axonal injury.

Conclusion: Compression is the most commonly seen etiological factor in peroneal neuropathy. Electrophysiologic investigations play a significant role in the differential diagnosis, prognosis, management plan, and follow-up of recovery. Further detailed studies are needed to clarify the relationship between electrophysiologic findings and prognosis to form an algorithm for the treatment and follow-up.

Keywords: Electrodiagnosis, entrapment neuropathy, peroneal nerve

Öz

yarısına demiyelinizan yaralanma eşlik etti. Altı olguda hafif, 3 olguda ağır ve 5 olguda total aksonal yaralanma vardı.

Sonuç: Kompresyon, peroneal nöropatide en sık görülen etiyolojik faktördür. Elektrofizyolojik araştırmalar ayırıcı tanıda, prognoz, tedavi planı ve iyileşmenin takibinde anahtar rol oynar. Tedavi ve takip için bir algoritma oluşturmak için elektrofizyolojik bulgular ile prognoz arasındaki ilişkiyi netleştiren daha detaylı çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Elektrodiagnoz, peroneal sinir, tuzak nöropati

Introduction

The peroneal nerve is derived from the L4, L5, and S1 nerve roots, which travel through the lumbosacral plexus and eventually join the sciatic nerve. Within the sciatic nerve, the fibers are destined to become the peroneal nerve run separately from the fibers forming the tibial nerve. Before separation from the sciatic nerve at proximal to popliteal fossa, peroneal nerve fibers innervate the short head of biceps femoris and distally form the common peroneal nerve, also known as common fibular nerve. The common peroneal nerve supplies the sensation of the upper lateral leg. It passes around the fibular head where it becomes superficial and bifurcates into the superficial and deep peroneal nerves. This naming is according to the relationship between branches and bone. The superficial and deep peroneal nerves innervate the dorsiflexors of the ankle, toes, and the evertors of the ankle, respectively (1,2).

Peroneal neuropathy is the most common entrapment neuropathy in the lower limb. It accounts for 15% of all peripheral entrapment neuropathies and takes third place after median and ulnar neuropathies. The common site of injury is around the fibular head, where the nerve is superficial and eligible for compression and trauma. However, more distal lesions at the level of the calf, ankle, and foot affecting the deep and superficial peroneal nerve as well as proximal lesions occur less frequently. Patients often present with foot drop and sensory disturbance over the dorsum of the foot and lateral calf (1,2).

Many etiological factors may contribute to peroneal neuropathy such as external compression (casts, immobilization), direct trauma (fracture), traction injuries (forcible ankle inversion), mass lesions (ganglion, tumor), entrapment (fibular tunnel), vascular conditions, diabetes mellitus, weight loss, leprosy and idiopathy. However, the most encountered mechanism is compression and it can develop by prolonged squatting, habitual leg crossing, immobilization, or even ankle-foot orthoses (1-4).

For the diagnosis of neuropathy, a detailed history of symptoms, distribution, duration and course of the neuropathy should be obtained. The presentation of sciatic neuropathy, lumbosacral plexopathy, or L5 radiculopathy may be similar to peroneal neuropathy. In addition to a good clinical examination and laboratory investigations, electrodiagnostic tests (EDT) play a key role in the differential diagnosis. EDT identifies the site of the lesion, reveals the underlying pathology, establishes the prognosis by determining the severity of the injury, and helps to monitor recovery (1,3). In this study, we aimed to evaluate the etiologic factors and electrodiagnostic findings in peroneal neuropathy.

Materials and Methods

Subjects

A total of 5.570 electrodiagnostic studies were screened retrospectively. The number of cases diagnosed with the entrapment neuropathy was 1.252. A total of 30 patients with clinical features compatible with peroneal neuropathy (19 males, 11 females, median age 30 years, range 21 to 66), who presented to the electromyography (EMG) Laboratory of İstanbul Medipol University Hospital between January 2016 and December 2019, were retrospectively analyzed.

Patients meeting the following criteria were included in the study: (1) weakness present in at least one of the muscles innervated by the peroneal nerve (ankle dorsiflexion, toe extension, foot eversion) with or without sensory loss

involving anterolateral leg and dorsum of foot, (2) needle EMG findings consistent with peroneal neuropathy. The exclusion criteria were as follows: (1) polyneuropathy or a disease that might cause polyneuropathy such as diabetes mellitus, (2) neurological examination findings like weakness of muscles not innervated by the peroneal nerve (hip abduction, knee flexion, foot inversion, and dorsiflexion), positive straight leg raise test, fasciculation, hyperreflexia, spasticity, (3) EDT findings suggestive of the sciatic mononeuropathy, lumbosacral radiculopathy or plexopathy, motor neuron disease (4) a history of lumbosacral radiculopathy or plexopathy, and (5) neurodegenerative diseases.

Imaging modalities including magnetic resonance imaging and conventional radiograph were conducted in cases with suspected lumbar pathologies or anatomical anomalies.

Demographic data such as age, gender, comorbid diseases (coronary artery disease, malignity, etc) and clinical characteristics including the side of the peroneal nerve injury, duration of symptoms, and etiology of injury were noted. The study protocol was approved by the İstanbul Medipol University Ethics Committee (10840098-772.02-E.34268).

Electrodiagnostic Tests

All patients had a detailed neurologic examination. Standard motor and sensory nerve conduction studies and needle EMG were performed by the same author (F.A.) using a Dantec, Keypoint G3 EMG & Evoked Potential Response Unit Equipment. Needle EMG was performed for the leveling of the injury. The peroneal motor nerve conduction study was carried out recording the extensor digitorum brevis muscle, stimulating the ankle, below the fibular head, and lateral popliteal fossa. Also, recording the tibialis anterior muscle (stimulating below the fibular head and lateral popliteal fossa) was performed when there was no conduction block at the fibular neck. The superficial peroneal sensory nerve conduction study was performed recording the lateral ankle and stimulating the lateral calf at the level of 10-12 cm proximal to the ankle. Motor unit action potentials (MUAPs) and the presence of active denervation were analyzed using concentric needle electrodes. When recruitable MUAPs on needle examination in the affected muscles were absent, complete nerve injury was considered. When preserved voluntary control of MUAPs in the affected muscle was detected, incomplete nerve injury was considered.

Statistical Analyses

Data were analyzed using the IBM SPSS for Windows version 23.0 software (IBM Corp. Armonk, NY, USA). The Shapiro-Wilk test was used to evaluate the normality of data. Descriptive analyses were presented as median, minimum, and maximum for continuous variables. Categorical data were summarized as counts and percentages.

Results

Our clinical rate for peroneal entrapment was 7.5 cases per year and the percentage of peroneal entrapment among entrapment neuropathies was 2.3%. Thirty patients with peroneal nerve injury were included in the study. 63.3% of the patients were male and the median (minimum-maximum) age of the patients was 30 (21-66) years. Four (13.3%) patients had a comorbid disease. The median (minimum-maximum) symptom duration was 20.5 (2-140) weeks. The side of the peroneal nerve injury was 43.3% right, 43.3% left, and 13.3% bilateral. The demographic and clinical characteristics of the patients were summarized in Table 1.

Etiological factors of peroneal nerve injury were summarized in Figure 1. The common causes of peroneal nerve injuries were due to compression (40%). Underlying predisposing factors were lying on with pressure on the fibular head (4 cases, 13.3%), pressure wrapping around the knee including (2 cases, 6.7%), prolonged squatting or excessive exercise (5 cases, 16.7%), and habitual leg crossing (1 case, 3.3%). Five out of 12 cases with compressive etiologies were iatrogenic. Casting (2 cases),

Table 1. Demographic and clinical characteristics of patients with peroneal nerve injury

	n	%	Median (min-max)
Age (year)	-	-	30 (21-66)
Gender	-	-	
Male	19	63.3	
Female	11	36.7	
Symptom duration (week)	-	-	20.5 (2-140)
Comorbidities			
Coronary artery disease	1	3.3	-
Malignancy (lymphoma, lung cancer, esophagus cancer)	3	9.9	-
Side of the peroneal nerve injury			
Left	13	43.3	-
Right	13	43.3	-
Bilateral	4	13.3	-

n: Number of individuals, min: Minimum, max: Maximum

prolonged bed rest in the intensive care unit (2 cases), and protracted positioning during surgery (1 case) were the iatrogenic reasons that we obtained. Weight loss after bariatric surgery was found in 10% of patients (3 cases) and one patient (3.3%) had a history of a recurrent ganglion cyst. Approximately 23% of lesions (7 cases) were due to the traction of the nerve. 23% of patients (7 cases) did not have any etiological factor and remained idiopathic.

Results of nerve conduction studies and EMG are shown in Table 2. According to EDT, 16 cases were predominantly demyelinating without axonal injury. The axonal injury was detected in the remaining 14 cases (%46.6) and half of the cases with axonal injury were accompanied by demyelinating injury. Six cases were mild, 3 cases were severe, and 5 cases were total axonal injury. Prolonged bed rest in the intensive care unit, sustained compression, and casting were found in the history of patients with severe axonal injury. It was found that surgical treatment was applied to 5 cases with total axonal injury, 1 case with a ganglion cyst, and 1 case without axonal injury. The rest 23 cases were managed by watchful waiting and conservative treatment composed of lifestyle modifications, pain management, exercise, and splints if necessary. Unfortunately, outcomes of treatments were unavailable because of the recall bias and the lack of objective assessment.

Table 2. Results of nerve conduction studies and electromyography

Measured parameters		n	%
CMAP	Absent	7	23.3
	Reduced	23	7.7
SNAP	Absent	5	16.7
	Reduced	11	36.7
	Normal	14	46.7
Denervation potentials	Absent	18	60
	Present	12	40
MUAPs	Absent	5	16.7
	Neurogenic	9	30

n: Number of nerves, CMAP: Compound muscle action potential, SNAP: Sensory nerve action potential, MUAPs: Motor unit action potentials

Discussion

Entrapment neuropathies of the lower limb may arise from compression, trauma, or iatrogenic injury. Factors like the site of the injury, the severity of the lesion, etiology are important for the prognosis and deciding the treatment plan (1). With this regard, we aimed to identify the etiological factors causing peroneal neuropathy and electrophysiological findings in our study. There is no publication identifying the frequency of peroneal neuropathy, but the most common entrapment neuropathy of the lower extremity is peroneal neuropathy at the level of the fibular head because of its superficial course around the fibula and susceptibility to stretch injury than tibial nerve (1,3-5). Especially, ankle sprains with inversion and flexion cause traction injury with the mechanism of tearing of the vasa nervorum (6). The percentage of peroneal neuropathy due to traction was found 23.3% in our study. Traumatic injuries like fibular fractures and knee dislocation are also risk factors for peroneal neuropathy (7-9). Noble et al. (10) found the rate of peroneal neuropathy as 1-2% in patients with tibia or fibula fractures.

The most common and probable cause of peroneal neuropathy is external compression at the fibular head which may originate from habitual leg crossing, prolonged squatting, inappropriate positioning in bedridden patients, occupational factors, casting, and braces (5). The percentage of compressive etiologies in our study was 40% and this is compatible with the literature.

Weight loss is another risk factor for peroneal neuropathy. Some case reports implicate the relationship between

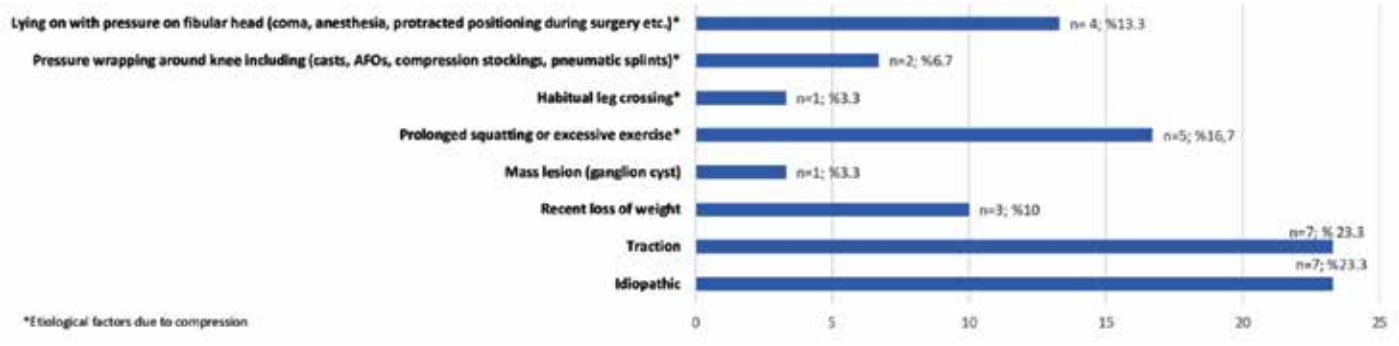

Figure 1. Etiological factors of peroneal nerve injury
n: Number of cases

weight loss and peroneal neuropathy (11-13). In one case series, the frequency of weight loss was reported as 20% in peroneal neuropathy (14). In our study, the frequency of weight loss was 10% and all patients who lost weight from 5 to 14 kg had a history of bariatric surgery. Only one patient had bilateral entrapment of the peroneal nerve.

Internal compression also presents with the same symptoms and is caused by mass lesions like neuroma, Baker cyst, tumors, and ganglion cysts (5). In one study, the percentage of mass lesions in peroneal neuropathy is found as 13%, and the mostly detected mass lesion is intraneural ganglion cyst (15). Additionally, the common peroneal nerve is the most common site of an intraneural ganglion cyst in the peripheral nervous system (16). Ganglion cysts are space-occupying lesions and cause internal compression resulting in progressive peroneal neuropathy (17,18). We had one case of a ganglion cyst (3.3%).

Possible mechanisms for iatrogenic peripheral nerve injuries are direct nerve injury, mechanical factors (compression, stretch, ischemia), the toxicity of injected drugs, and double crush syndrome (19). Antoniadis et al. (20) reported that common peroneal nerve affected 13% among 340 iatrogenic nerve injuries treated surgically. According to our results, the iatrogenic peroneal nerve injury ratio was 16.6% and compression was the main mechanism detected. Systemic diseases like diabetes mellitus and inflammatory diseases are other etiological factors for peroneal neuropathy (1).

Peroneal neuropathy is classified as idiopathic when none of these predisposing factors are present. Aprile et al. (21) reported the rate of idiopathic peroneal neuropathy as 16% among 69 cases. According to our results, 23.3% of our cases were idiopathic.

Electrophysiologic investigations are accepted as the gold standard for the diagnosis of peroneal neuropathy (1,2). It is also important for the differential diagnosis. Symptoms of peroneal neuropathy may be drop foot or sensation deficits. And presentations of L5 radiculopathy, sciatic mononeuropathy, lumbosacral plexopathy, and polyneuropathy may be similar. Other diseases that should be considered in the differential diagnosis are cerebral and spinal cord lesions, motor neuron disease, and anterior compartment syndrome of the leg (2,22). Electrophysiologic investigations help to distinguish these various diseases by localizing the lesion precisely and determinate the severity of the condition. Thus, electrodiagnostic studies are “sine qua non” for peroneal neuropathy (1). Karakis et al. (23) showed that predominantly axonal pathologies were seen in the peroneal neuropathy in childhood and adolescence (72%) but this should be attributed to the percentage of traumatic etiology (56%) in their study. According to our results, pathophysiology was predominantly demyelinating in 53.4%, axonal in 23.3%, and mixed in 23.3%. The total axonal injury was seen at 16.6%. Two out of 5 cases with total axonal injury were associated with compression, but the duration of symptoms was longer than 6 months for both. The remaining three cases were iatrogenic due to prolonged bed rest in the intensive care unit and casting. It should be concluded from here that the duration of symptoms and the mechanism of injury are important risk factors for the development of total axonal injury.

Neuropathies of the lower limb cause morbidity and disrupt functionality. Peroneal neuropathy has a favorable prognosis generally. Poor prognostic predictors are the findings of denervation in EMG, age, and severe weakness at onset (24,25). Needle EMG helps prognostication by indicating the presence of denervation. In our study, denervation potentials in the needle EMG were found to be 40%.

Derr et al. (26) showed that peroneal neuropathy with non-traumatic compression origin had a good prognosis. In the case of external compression, the recommended treatment methods are watchful waiting, lifestyle modifications including the relief of the pressure, doing exercise, and usage of ankle-foot orthoses to prevent possible deformity. If there is peroneal neuropathy induced by internal compression, then surgical treatment should be chosen. Patients with progressive symptoms or who do not improve with conservative treatment should be referred for surgical treatment (24,27).

There are some limitations of this study that should be mentioned. The study was conducted retrospectively in a single center with a small population. EDT were done at varying times after the peroneal nerve injury and patients have not been followed up for their recovery process.

Conclusion

Peroneal neuropathy is the most common entrapment mononeuropathy of the lower extremity, and the nerve is affected especially around the fibular head. Compressive pathologies are the most frequently seen etiologies. Electrophysiologic investigations play a key role in the differential diagnosis, prognostication, management plan, and follow-up of recovery. Further detailed

studies are needed to clarify the relationship between electrophysiologic findings and prognosis to form an algorithm for the treatment and follow-up.

Ethics

Ethics Committee Approval: The study was approved by Ethics Committee of İstanbul Medipol University with decision no: 10840098-772.02-E.34268.

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: S.T., F.A., N.H., Design: S.T., A.R., F.A., Data Collection or Processing: S.T., N.H., F.A., Analysis or Interpretation: A.R., N.H., Literature Search: A.R., F.A., Writing: S.T., N.H.

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ORIGINAL RESEARCH

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Clinical and Demographic Characteristics of the Culture Results of Patients Applying to the Emergency Department

Acil Servise Başvuran Hastaların Kültür Sonuçlarının Klinik ve Demografik Özellikleri

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Abstract

Objective: Culture examination is a frequently used diagnostic method in emergency departments. This study was performed to investigate the frequency of culture examinations that were sent from the emergency department and also the rate of positive results and the most frequently isolated pathogens.

Method: This is a retrospective cohort study. We retrospectively investigated the cultural results of the patients who were admitted to the emergency department between 1st Jan 2016 and 31st March 2017. The demographic datum, medical diagnosis, the culture type, and the results were recorded from the hospital records.

Results: Totally 70,934 culture tests were sent from 45,100 patients between study dates. 1.1% of the cultures were sent from the emergency department. There was colonization at 16.8% of the cultures; this ratio was 33.6% in the cultures that were sent from the emergency department. The cultures were more frequently positive in emergency medicine when we compared them to those in the whole hospital. The positivity rate was higher in wound and abscess cultures but very low in gaita cultures.

Conclusion: The further detailed studies about the cultures sent from the emergency department on the basis of a specific disease and antibiotic resistance will be instructive about prophylactic antibiotic use in the emergency department.

Keywords: Bacteremia, culture analysis, emergency department, microbiology

Öz

Amaç: Kültür muayenesi, acil servislerde sıklıkla kullanılan bir tanı yöntemidir. Bu çalışma, acil servisten gönderilen kültür incelemelerinin sıklığını, ayrıca olumlu sonuçların oranını ve en sık izole edilen patojenleri araştırmak amacıyla yapıldı.

Yöntem: Bu çalışma retrospektif bir kohort çalışmasıdır. 1 Ocak 2016-31 Mart 2017 tarihleri arasında acil servise başvuran hastaların kültür sonuçlarını geriye dönük olarak incelendi. Hastane kayıtlarından demografik veriler, tıbbi tanı, kültür tipi ve sonuçlar kayıt altına alındı.

Bulgular: Çalışma tarihleri arasında 45.100 hastadan toplam 70.934 kültür testi gönderildi. Kültürlerin %1,1'i acil servisten gönderildi. Kültürlerin %16,8'inde kolonizasyon vardı. Acil servisten gönderilen kültürlerde bu oran %33,6 idi. Acil tıpta kültürler, tüm hastaneyle karşılaştırdığımızda daha sık pozitifti. Pozitiflik oranı yara ve apse kültürlerinde daha yüksek, gaita kültürlerinde ise çok düşüktü.

Sonuç: Acil servisten belirli bir hastalık ve antibiyotik direnci temelinde gönderilen kültürlerle ilgili daha detaylı çalışmalar, acil serviste profilaktik antibiyotik kullanımı konusunda yol gösterici olacaktır.

Anahtar kelimeler: Acil servis, bakteriyemi, kültür analizi, mikrobiyoloji

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Introduction

Infectious diseases are among the frequent applications to the emergency register. There are many admissions to emergency departments from infections such as pneumonia, urinary system infection, soft tissue infection, meningitis, sepsis, and neutropenic fever. In these patients, it is important to take a culture in the emergency department to support the diagnosis and guide the appropriate antibiotic treatment. It is especially important to start antibacterial therapy urgently in some conditions, such as sepsis, meningitis, and neutropenic fever. It is essential to take samples such as blood, cerebrospinal fluid (CSF), and urine in emergency services, to deliver them to the laboratory in a short time, to reproduce in their cultures, and to initiate effective antimicrobial treatments according to the result.

Blood cultures are a frequently used diagnostic method in emergency departments, but the necessity of this is discussed in the literature (1). Although guidelines do not provide much information about when to take a blood culture sample,Infectious Disease Society of America (IDSA) offers suggestions on this subject (2). However, as the most appropriate time, the period when the concentration of microorganisms is highest in the blood is the 30-60 minute period before fever. However, since it is not always possible to predict this period in many patients, blood culture should be taken as soon as possible after the fever begins to rise. Blood cultures should be taken before antibiotic therapy is initiated.

In this study, we aimed to evaluate the positivity rates and the number of culture tests requested from the emergency department and to identify the most frequently isolated pathogens.

Materials and Methods

Study Design and Population

This study was planned retrospectively. It was started after the approval of the Ethics Planning Board numbered 2017/582 at the 49th Board Meeting held on 13.06.2017 from the Ethics Committee of the Turkish Republic Ministry of Health, University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital. Results from patients who applied to the Emergency Medicine Clinic between January 1, 2016, and March 31, 2017 were analyzed retrospectively. The demographic data of the patients, the diagnosis made in the emergency department, the place where the culture samples were taken, and the culture results were obtained from the medical records of the patients in the electronic information system of our hospital.

Statistical Analysis

The data obtained in the study were analyzed with SPSS 20.0 for the Windows package program. Of the continuous variables, those with normal distribution were expressed as mean ± standard deviation, and those without normal distribution were expressed as median (minimum-maximum). Normal distribution was evaluated by histogram and the Kolmogorov-Smirnov test. Categorical variables were expressed as numbers (percent). The significance of the difference between the averages of the two groups was evaluated using the Mann-Whitney U test and the Student t-test in normal distributions. The significance of the difference between the groups in categorical variables was evaluated with the chi-square test. $P<0.05$ level was considered statistically significant.

Results

During the study period, 70,934 samples were sent from 45,100 patients. Seven hundred seventy four (1.1%) of the examinations were requested by the emergency department. Reproduction was detected in 16.8% (n=11,907) of all cultural studies. In cultures sent from the emergency department, reproduction was detected in 260 samples (33.6%), 2.2% of all cultures detected reproduction were sent from the emergency department. When cultures requested from all hospitals and emergency services were compared, positivity was found more frequently in emergencies (p=0.001).

During the study, growth was detected in a total of 260 culture samples from 236 patients. From the blood, CSF, and urine samples of the patients, reproduction was observed in only one variety from 214, 2 separate from 20, and 3 separate culture samples from 2 of them. 64.2% (n=167) of patients with reproduction were women. The average age was 46.56±21.48 years; The median age was 46 years (0-89 years). The mean age of women (43.0±21.3 years) was lower than that of men (52.9±20.5 years) ($p<0.001$).

Wound culture and urine culture were the most common examples of cultures sent from the emergency department (Table 1). The positive rates of culture samples sent from the emergency department both in the emergency department and in all hospital samples are shown in Table 1. The positivity rate is seen mostly in catheter cultures in the emergency room and wound cultures throughout the

hospital. The least positive rates were seen in feces cultures in both the emergency room and all hospital-wide samples.

Table 2 shows the distribution of pathogens detected in reproduction in culture. The most frequently detected pathogen was *E. coli* (n=67, 25.8%) followed by *S. aureus* (n=52, 20.0%).

Table 3 lists the most frequently isolated pathogens from all cultures. The most common pathogen in culture samples taken after abscess drainage was *S. aureus* (n=13, 41.9%), followed by *S. pyogenes* (n=4, 12.9%). Reproduction was observed in three of the sputum culture samples, and *P. aeruginosa*, *P. fluorescens*, and *S. schleiferi* reproduction were detected. Only two of the stool culture samples had reproduction and Salmonella reproduction was detected in both. The most frequent pathogen in urine culture samples was *E. coli* (n=46, 59.0%), followed by *K. pneumoniae* (n=13, 16.7%). The most common pathogen in culture samples taken from the catheter tip was *S. aureus* (n=4, 66.7%). In blood culture samples, the most common pathogen in the aerobic culture was *S. aureus* (n=7, 31.8%) and the most frequent pathogen in the anaerobic culture was *S. aureus* (n=4, 33.3%). This was followed by *E. coli* (n=3, 25.0%) in aerobic culture and *S. hominis* (n=6, 27.3%) in anaerobic culture. The most common pathogen in culture samples taken from sterile body fluids was *S. aureus* (n=5, 16.0%), followed by *E. coli* and *S. agalactiae* (n=4, 16.0%). The most common pathogen in the culture samples taken from the wound was *S. aureus* (n=17, 21.0%), followed by *S. epidermidis* (n=13, 16.0%).

Table 1. Reproduction rates of culture types sent by the emergency department in all hospitals and emergency rooms

	All patients		Emergency department	
	n	Positive rate (%)	n	Positive rate (%)
Abscess (aerob) culture	374	57.5%	33	63.6%
Abscess (aerob) culture	405	29.4%	2	50.0%
Fecal culture (aerob)	1.048	4.2%	19	10.5%
Urine culture (aerob)	55,034	15.0%	386	19.2%
Blood culture (aerob)	2.514	22.9%	46	37.0%
Blood culture (anaerobe)	1.601	20.5%	28	32.1%
Catheter tip culture	331	42.9%	5	100.0%
Sterile body fluid (aerob)	493	25.2%	66	27.3%
Wound culture (aerob)	2.493	64.3%	121	65.3%

Discussion

The time it takes to get the results of the culture causes empirical treatment to be applied in some cases. This increases the importance of the regional antibiotic profile and resistance rates. In our study, 2.2% of the culture examinations evaluated in the microbiology laboratory were requested by the emergency department. In the study of Ece Terek and Tunçel Başoğlu (3), which included 348 isolates (37.1%) produced from 937 urine samples sent to a university hospital microbiology laboratory, this rate

Table 2. Pathogen distribution detected in cultures

	n	%		n	%
Acinetobacter baumannii	2	0.8	Salmonella species	2	0.8
Acinetobacter baumannii & calcoaceticus complex	1	0.4	***Staphylococcus aureus***	***52***	***20.0***
			Staphylococcus epidermidis	***20***	***7.7***
Candida albicans	4	1.5	Staphylococcus gallinarum	1	0.4
Enterobacter aerogenes	3	1.2	Staphylococcus haemolyticus	5	1.9
Enterobacter cloacae	5	1.9	Staphylococcus hominis	10	3.8
Enterococcus faecalis	11	4.2	Staphylococcus lugdunensis	3	1.2
Enterococcus faecium	4	1.5	Staphylococcus saprophyticus	1	0.4
Escherichia coli	***67***	***25.8***	Staphylococcus schleiferi	2	0.8
Klebsiellaoxytoca	2	0.8	Staphylococcus xylosus	1	0.4
Klebsiella pneumoniae	***21***	***8.1***	Streptococcus agalactiae	5	1.9
Morganellamorganii	1	0.4	Streptococcus anginosus	2	0.8
Paracoccusyeeii	1	0.4	Streptococcus constellatus	1	0.4
Proteus mirabilis	7	2.7	Streptococcus dysgalactiae	4	1.5
Pseudomonas aeruginosa	9	3.5	Streptococcus mitis	1	0.4
Pseudomonas fluorescens	1	0.4	Streptococcus pyogenes	9	3.5
Pseudomonas species	1	0.4	Streptococcus species	1	0.4

was reported as 5.9%. In our study, growth was detected in 16.8% of all culture tests sent by all departments of the hospital. In the cultures sent by the emergency service, 33.6% growth was detected. Similar to our study, in a study by Yücel et al. (4), in which the results of all cultures sent to patients who applied to a university hospital emergency service were examined, it was reported that reproduction was detected in 17% of the cultures sent by the emergency service. In our study, it was seen that the cultures sent by the emergency department were higher in the positive rate. It was thought that the probable reason for this might have been because patients who were considered to have infections in our emergency department generally gave cultures in the outpatient clinic conditions but only if there was high suspicion and if prophylactic antibiotic treatment would be initiated in a short time.

Table 3. The most frequently isolated pathogens in cultures

	n	%
Abscess (aerop) culture		
Staphylococcus aureus	**13**	**41.9**
Streptococcus pyogenes	**4**	**12.9**
Escherichia coli	3	9.7
Sputum culture (aerob)		
Pseudomonas aeruginosa	1	33.3
Pseudomonas fluorescens	1	33.3
Staphylococcus schleiferi	1	33.3
Fecal culture (aerob)		
Salmonella species	2	100
Urine culture (aerob)		
Escherichia coli	**46**	**59**
Klebsiella pneumoniae	**13**	**16.7**
Enterococcus faecalis	4	5.1
Catheter tip culture		
Staphylococcus aureus	**4**	**66.7**
Enterococcus faecalis	1	16.7
Escherichia coli	1	16.7
Blood culture (aerob)		
Staphylococcus aureus	**7**	**31.8**
Staphylococcus hominis	**6**	**27.3**
Staphylococcus epidermidis	3	13.6
Blood culture (anaerobe)		
Staphylococcus aureus	**4**	**33.3**
Escherichia coli	**3**	**25**
Staphylococcus epidermidis	2	16.7
Sterile body fluid (aerob)		
Staphylococcus aureus	**5**	**20**
Streptococcus agalactiae	**4**	**16**
Escherichia coli	**4**	**16**
Wound culture (aerob)		
Staphylococcus aureus	**17**	**21**
Staphylococcus epidermidis	**13**	**16**
Escherichia coli	10	12.3

In the study, 64.2% of the patients in whom cultures were sent by the emergency department were women; the average age was 46.56±21.48 years; the median age was 46 years (range 0-89). Yücel et al. (4) reported that their average age was 52±21 years (in the range of 17-100) and the numbers of women and men were equal in their studies. In the study conducted by Yürümez et al. (5), similar to our study, they reported that the mean age was 45.6±19.5 years, and 54.4% of the patients were male. In the study conducted in Germany, in which 18,785 culture samples were included, 78% of the patients were female and the average age of all patients was 62±24 years (6). The average age in Germany is almost the highest among those in the European Union countries, so the average age was considered to be higher in hospital applications and accordingly in the samples taken. (7). Likewise, regional differences within the country can change the average age of the patient population.

In our study, in the general distribution of the pathogen detected in culture growth, the most common pathogen was *E. coli* (25.8%) followed by *S. aureus* (20.0%). In the study of Yücel et al. (4), similar to our study, they found the most frequent growth of *E. coli* with 47.2% when all samples were taken into consideration. In the study conducted by Çetin et al. (8) in a university hospital in one year, which involved intensive care patients, a reproduction rate of 28.8% was detected in 1859 culture samples taken from intensive care patients, and the most frequent pathogens were reported as coagulase-negative streptococci. In the study of Ertürk et al. (9) conducted similarly in a hospital in a university, reproduction rate of 33% was detected in the samples sent from patients in the intensive care unit. Of the microorganisms that grew, 152 (51%) were Gram-negative, 102 (34%) were Gram-positive bacteria and 43 (14%) were yeast (9). All hospitals have infection control committees under the control of the Ministry of Health and carry out studies to prevent bacterial colonization, especially in intensive care units. However, certain pathogens can be seen in certain services (10,11). Accordingly, microorganisms and culture positivity rates were thought to change.

In the study, the positivity rate of sputum culture was 29.4% throughout the hospital and 50.0% in the samples sent by the emergency department. In the retrospective study of Yücel et al. (4), in which 1.485 patient samples from the

microbiology laboratory of a university for a period of 15 months were included, reproductive rate of sputum cultures sent by the emergency department was reported as 43% (4). In our study, reproduction was observed in three of the sputum culture samples, and *P. aeruginosa*, *P. fluorescens* and *S. schleiferi* reproduction were detected in these. In the study of Yücel et al. (4) reproduction was reported in three of the sputum cultures, with methicillin-resistant coagulase-negative staphylococcus, *P. aeruginosa*, and *S. aureus* (4). In the study conducted by Çetin et al. (8), a reproduction rate of 30% was detected in sputum culture samples taken from intensive care patients and the most common breeding pathogens were reported as *Enterobacteriaceae*. In the studies of Talay et al. (12), it was aimed to determine the resistance profile of antibiotics against the factors reproduced in the non-specific culture results of the patients hospitalized with the lower respiratory tract infection and to investigate the empirical treatment approaches in these cases, and 41 patients with reproduction from 84 cases were evaluated. Reproducing microorganisms were reported as *S. pneumonia* (39%), *K. pneumonia* (31.7%), and *P. aeruginosa* (19.5%), respectively. In our study, sputum culture was desired very little. Comparison studies have been seen at higher rates compared to our study since there are cultures sent from chest disease outpatient clinics. In our study, it is not possible to comment on the most common pathogen since the number of cases is very few. Also, the most frequently detected pathogens in studies have been reported as *S. pneumonia*, *K. pneumonia*, and *P. aeruginosa*.

In the study, the positivity rate of stool culture was 4.2% throughout the hospital and 10.5% in the samples sent by the emergency department. Only two of the stool culture samples had reproduction and Salmonella reproduction was detected in both. In the study of Yücel et al. (4), reproduction rate of stool cultures sent by the emergency department was reported as 0% in the study. Güney and Başustaoğlu (13). reported that an enteric pathogen was found in 6.6% of the total 379 stool cultures and the most common of these were campylobacter (56%) and salmonella (44%). The fecal culture was found to be very positive both in our study and in previous studies. When we evaluated our study and other studies together, it was thought that it would be appropriate to evaluate whether the cultures determined to be so positive were necessary.

Studies have shown that the factors that cause urinary tract infections are Gram-negative rods and enterococci, often caused by fecal flora (14). In the study of Ece Dağlar et al. (15), urine samples sent to Tavşanlı and Uşak State Hospital Microbiology Laboratories were retrospectively analyzed, standard microbiological methods were used for the isolation of bacteria from clinical samples, and antimicrobial sensitivity was investigated by disk diffusion method. They detected reproduction in 8.3% of these urine samples; 84.9% of the reproducing bacteria were Gram-negative and 15.1% were Gram-positive bacteria. The most frequently isolated Gram-negative bacteria were 45.1% *E. coli* and the most common Gram-positive bacteria were reported as 10.9% *Enterococcus* sp (15). In the study conducted by Çetin et al. (8), a reproduction rate of 30.2% was detected in urine culture samples sent from intensive care patients and the most frequent pathogens were *E. coli* and *Candida* spp. reported to follow. In our study, the urinary culture positivity rate was 15.0% throughout the hospital and 19.2% in the samples sent by the emergency department. Yücel et al. (4) reported reproduction rate as 18% in the administration cultures sent by the emergency department in the study. The most common pathogen in urine culture samples was *E. coli* (59.0%), followed by *K. pneumonia* (16.7%). In the study of Ece Terek and Tunçel Başoğlu (3), the most frequent strains detected in urine cultures were 52% *E. coli*, followed by *E. faecalis* with 15.5% (3). Urine culture is a frequent examination both in emergency departments and other units. In general, *E. coli* is more frequently isolated. In our study, results consistent with the literature were obtained.

In the study, the catheter tip culture positivity rate was 42.9% throughout the hospital and 100% in samples sent by the emergency department. In the study of Yücel et al. (4), reproduction rate of catheter tip cultures sent by the emergency department was reported as 50%. In the culture samples taken from the catheter tip, the most common pathogen was *S. aureus* (66.7%). In the study of Ergin et al. (16) in which intravascular catheter cultures were evaluated in patients in intensive care units, it was reported that the catheter culture was 35% positive and the most common pathogens were coagulase-negative staphylococci (14%) and methicillin-resistant *S. aureus* (2%). Again, in the study of Çetin et al. (8), a reproduction rate of 31% was determined in urine culture samples sent from intensive care patients and the most common reproductive pathogens were coagulase-negative streptococci and it was reported that *S. aureus* followed it. It was reported in the study of Sünbül et al. (17) that were reproduced in the catheter culture at the rate of 61% in pediatric intensive care patients, and

the most common pathogens were coagulase-negative staphylococcus and methicillin-resistant *S. aureus*. In our study, *S. aureus* was detected most frequently in samples sent from the catheter tip, regardless of coagulase and methicillin resistance.

Blood cultures are a common diagnostic method in emergency departments, but the need for this is discussed in the literature (1). Although guidelines do not provide much information about when to take a blood culture sample, IDSA offers suggestions on this subject (2). In our study, the aerobic blood culture positivity rate was 22.9% throughout the hospital and 37.0% in the samples sent by the emergency department, the positivity rate in anaerobic cultures was 20.5% throughout the hospital and 32.1% in the samples sent by the emergency department. Yücel et al. (4) reported the reproduction rate of blood cultures sent by the emergency department as 15% in their study. The most common pathogen in the blood culture samples was *S. aureus* (31.8%) and the most common pathogen in anaerobic culture was *S. aureus* (33.3%). This was followed by *E. coli* (25.0%) in aerobic culture and *S. hominis* (27.3%) in anaerobic culture. In the study of Yücel et al. (4), the most frequently detected pathogen was reported as coagulase-negative streptococci. In the study of Yürümez et al. (5), the most frequently detected pathogen in anaerobic blood culture was reported as E.coli, similar to our study. In the study carried out by Oğuz et al. (18) in pediatric emergency patients, 5.8% of the samples showed that there was a reproduction, 91.7% of this reproduction was gram-positive and 8.3% was Gram-negative bacteria. In the study of Karakoç et al. (19), it was reported that the rate of significant growth in blood cultures was 18.3%. In the study conducted by Çetin et al. (8), a reproduction rate of 30% was detected in blood culture samples sent from intensive care patients and the most frequent pathogens were reported as coagulase-negative streptococci and less frequently *A. baumannii*. Similar studies have been conducted on the usefulness of blood culture in many different patient populations. A 2006 study suggests that the rate of beneficial cultures is 2.8% and that blood culture should be taken only in the case of urinary tract infection, community-acquired pneumonia, and cellulitis in people who are immunocompromised (20). In another study conducted in 2007, it was stated that 6% of all culture samples had reproduction and only 0.18% of all patients changed the treatment process (20). In our study, there was no study on how much blood cultures directed treatment, and it is not possible to evaluate this in the emergency room as the culture results are concluded at the earliest 2 days later. Detailed studies on the value of the samples taken in the emergency departments and how much they direct the treatment will give more accurate results in this regard.

In the study, the rate of sterile body fluid culture positivity was 25.2% throughout the hospital and 27.3% in samples sent by the emergency department. The most common pathogens in culture samples were detected in the samples of *S. aureus*, *E. coli*, and *S. agalactiae* (16.0%). In the study of Yücel et al. (4), the growth rate in sterile body fluid cultures sent from the emergency department was reported to be 16%. In the study, the most common pathogen grown in culture samples taken from sterile body fluids was *S. aureus* (16.0%), followed by *E. coli* and *S. agalactiae* (16.0%). In the study conducted by Çetin et al. (8), a growth rate of 33.3% was found in sterile body fluid samples taken from patients in the intensive care unit, and the reproducing pathogens were reported as *S. aureus*, *Enterobacteriaceae* and *A. baumannii*.

In some studies, the most frequently isolated pathogen in soft tissue infections is known as *S. aureus* (21,22). In our study, the rate of wound culture positivity was 64.3% throughout the hospital and 27.3% in samples sent by the emergency service. Yücel et al. (4) reported the growth rate in wound cultures sent from the emergency department as 61% in their study. In the culture samples taken from the wound, the most common pathogen was *S. aureus* (21.0%), followed by *S. epidermidis* (16.0%). Yücel et al. (4) reported the most common pathogen in wound cultures sent by the emergency service as *E.coli* and *S. aereus*. In our study, the rate of abscess culture positivity was 57.5% throughout the hospital and 63.6% in samples sent from the emergency service. Yücel et al. (4) reported that the growth rate in abscess cultures sent by the emergency service was 50%. In our study, in the culture samples taken after abscess drainage, the most common pathogen was *S. aureus* (41.9%), followed by *S. pyogenes* (12.9%). Yücel et al. (4) reported *E. coli* as the most frequently detected bacterium in abscess cultures. In the study conducted by Çetin et al. (8), the most frequently grown pathogens in wound culture samples sent from patients in the intensive care unit were reported as coagulase-negative streptococci.

Study Limitation

The most important limitation in this study is that the study was performed in a single-center and retrospective manner; therefore, the symptoms and examination information of the patients could not be obtained. The data cover only adult emergency data, child emergency data are not included. In the study, antibiogram results of reproductive samples

were not evaluated. Therefore, it is not possible to make any comments regarding the prophylactic antibiotic use recommendations. It is not known in which environment and how the cultures were taken and whether they were brought to the laboratory environment in appropriate conditions and time, and how long the cultivation was done after coming to the laboratory, and these could not be standardized since retrospective studies were performed. The patients' co-morbid diseases, immune suppression status, and other infective diseases, if any, have not been known, so the possible effects of co-morbid diseases on the culture growth of patients have not been evaluated.

Conclusion

Culture tests are frequently used in hospitals and emergency rooms. The pathogens isolated from the cultures differ according to the region, culture type, and disease type. Knowing the most frequently detected pathogens both in hospitals and in clinics is effective in prophylactic antibiotic use decisions and information is given to healthcare workers about the possible measures that may be required during the spread of possible hospital-borne or community-borne infections. The culture positivity rate was higher in the samples sent from the emergency rooms than in those in the general hospital. While culture positivity rate is high in wound and abscess cultures, it is very low in stool cultures. Detailed studies, including disease-based and antibiotic resistance of cultures sent from the emergency departments, will guide the initiation of prophylactic treatment. New studies on this subject are needed.

Ethics

Ethics Committee Approval: This study was planned retrospectively. It was started after the approval of the Ethics Planning Board numbered 2017/582 at the 49th Board Meeting held on 13.06.2017 from the Ethics Committee of the Turkish Republic Ministry of Health, University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital.

Informed Consent: Patient consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: Ş.Ö.H., İ.Ö., Design: Ş.Ö.H., M.A.K., Data Collection or Processing: M.A.K., İ.Ö., Analysis or Interpretation: Ş.Ö.H., M.A.K., Literature Search: Ş.Ö.H., Writing: Ş.Ö.H.

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

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CASE REPORT

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Posterior Reversible Encephalopathy Syndrome in Two Patients with Severe Preeclampsia

Şiddetli Preeklampsi Geçiren İki Hastada Posterior Reversible Ensefalopati Sendromu

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Abstract

Posterior reversible encephalopathy syndrome (PRES) is an entity that occurs due to vasogenic brain edema in predominantly posterior sections of the brain and is characterized by headache, altered mental status, vision loss or seizures. In this report, we present two women who developed PRES secondary to severe hypertension in pregnancy. Our goal is to outline the clinical features of the disease, diagnostic methods, management, and maternal outcomes. The etiology of PRES may vary in a wide range including hypertension, kidney failure, preeclampsia/eclampsia, collagen vascular diseases, and sepsis. Prompt recognition and treatment of the syndrome after severe preeclampsia or eclampsia have major importance in order to prevent permanent damage to the brain.

Keywords: Eclampsia, hypertension, preeclampsia, posterior reversible encephalopathy syndrome

Öz

Posterior reversibl ensefalopati sendromu (PRES), başağrısı, mental instabilite, görme kaybı, nöbetler ile karakterize, ağırlıklı olarak beynin başta oksipital lob olmak üzere posterior kısımlarını tutan vazojenik ödem durumudur. Etiyoloji hipertansiyon, böbrek yetmezliği, kollajen vasküler hastalıklar, sepsis, preeklampsi/eklampsi gibi durumları içeren geniş bir yelpazede olabilir. Beyinde kalıcı hasarı önlemek icin erken teşhis ve hızlı yönetim esastır. Bu olgu bildiriminde, sezaryenden 2 gün sonra şiddetli preeklampsi ve ardından HELLP sendromuna ilerleyen bir postpartum hasta ile eklampsi geçiren bir başka postpartum hastamızda gelişen PRES sendromunu ele almaktayız. Amacımız, PRES'nin klinik özelliklerini, diagnostik metodları, yönetimi ve maternal sonuçlarını ortaya koymaktır.

Anahtar kelimeler: Hipertansiyon, preeklampsi, eklampsi, posterior reversibl ensefalopati sendromu

Introduction

Posterior reversible encephalopathy syndrome (PRES) was first described by Hinchey et al. (1). PRES has become a more recognized medical term due to alerting neurologic symptoms. There are readily available imaging techniques that enable clinicians to make the diagnosis. It is characterized by headaches, seizures, nausea or vomiting, vision problems due to posterior cerebral white matter edema but the syndrome is not always reversible, and it is often not confined to either the white matter or the posterior regions of the brain (2,3). The incidence of PRES is not known. The etiology of those disturbances may vary in a wide range including hypertension, kidney failure, preeclampsia/eclampsia, collagen vascular diseases, sepsis, consumption of immunosuppressive agents, etc. It is more common in women even when patients with eclampsia are excluded (1-3). As definition, preeclampsia is a systemic vascular disorder characterized by new-onset hypertension and proteinuria after 20 weeks of gestation and eclampsia is defined as a seizure occurring in association with preeclampsia (4).

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Prompt recognition and treatment of the syndrome are important in the prevention of the permanent damage that can occur in this otherwise typically reversible condition. The management of PRES is mostly based on the investigation and resolution of the underlying cause. If the underlying cause is diagnosed and treated effectively, clinical symptoms may subside in a week (1,2).

There are a few theories to explain the pathophysiology of PRES. The most popular theory is that the autoregulation of the blood perfusion in brain vessels is disrupted due to uncontrolled hypertension (2). Sudden elevations in blood pressure cause the extravasation of proteins to the intercellular area and this results in vasogenic edema. However, this theory does not explain the cerebral hypoperfusion which can sometimes be seen in PRES and why PRES may occur in normotensive patients as well. In this perspective, the association of PRES with systemic inflammatory conditions such as autoimmune diseases, sepsis or preeclampsia has revealed a theory which claims that PRES might be associated with endothelial dysfunction (5). Compatible with both theories, the pathogenesis of preeclampsia or eclampsia makes a predisposition to developing PRES syndrome. Therefore, it is a potentially devastating disease for which obstetricians should be prepared in preeclamptic pregnant women.

In these case presentations, we aimed to present two preeclamptic women who recovered without any sequela in intensive care unit (ICU) after developing PRES. Both of patients provided informed consents regarding their medical information to be used in this study. With this article, we would like to show the importance of early diagnosis and optimal management of the entity.

Case Reports

Case 1

A 32-year-old primigravida woman was admitted at 35 weeks of gestation due to hypertension of 170/100 mmHg. Her hemoglobin level, hematocrit, white blood cell count and platelet level were 9.6 g/dL, 32%, 9.25x10^3/µL and 155 10^3/µL, respectively. Her liver function enzymes, namely aspartate aminotransferase (AST), alanine aminotransferase (ALT), were 47 and 35 U/L. She had +1 proteinuria in urine analysis and her fundoscopic examination was in normal limits without having any sign of intracranial hypertension. Her high blood pressure was taken under control with 250 mg of alpha methyl dopa per 6 hours. The intrauterine growth retardation was detected in fetus according to ultrasonographic measurements which were consistently indicating 31 weeks of gestation. Betamethasone injections were applied in order to support the pulmonary function. During her prenatal care, late decelerations resistant to resuscitations occurred and she underwent an urgent cesarean section due to the diagnosis of fetal distress. She did not have any complications in postoperative 48 hours. At day 3, her blood pressure raised to 180/110 mmHg and subsequent generalized seizure with urinary incontinence occurred. Parenteral magnesium sulfate and glyceryl trinitrate infusion were promptly started. Urgent neurology, internal medicine, and anesthesia consultations were done. 4 mg steroid injection for twice per day, metabolic panel, fibrinogen, and peripheral blood smear were ordered. Liver enzymes came up to be elevated 10 times (AST: 562 U/L, ALT: 199 U/L), fibrinogen level was found to be slightly low (198 mg/dL) and platelet counts suddenly decreased to 44.000 10^3/µL. In the peripheral blood smear, the hematologist found too many acanthocytes to count and the actual platelet number was 34.000 10^3/µL. HELLP syndrome was diagnosed and the patient was transferred to ICU. One volume of plasmapheresis was planned. Meanwhile, she became sluggish and her consciousness gradually deteriorated. She was not opening eye neither to verbal command nor to pain. Her Glasgow Coma score was 6 (one for no eye-opening, one for no verbal response and 4 for withdrawal from pain). Urgent cranial magnetic resonance imaging (MRI) and MRI venography were carried out. Diffuse high signal intensity on T2-weighted (Figure 1) and fluid-attenuated inversion recovery (Figure 2) images were interpreted to be edematous lesions located in the cerebellum and through the temporoparietal junction to the cortex of the brain. The lesions were found to be compatible

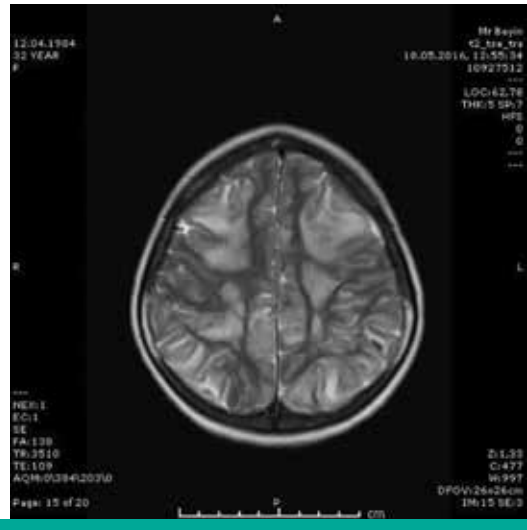

Figure 1. Hypointense lesions on T2- weighted sections

with PRES. 200 cc Mannitol IV push was administered to decrease extracellular fluid retention in the brain. Close observation was undertaken with an intermittent metabolic panel and coagulation markers. After the completion of plasmapheresis, prednol 1 mg/day per kilogram was ordered. Her liver enzymes and coagulation markers were gradually normalized. With the anti-edematous and supportive treatment, patient clinically improved in 3 days and she was out of ICU on the postoperative day 8. After spending 3 days in inpatient service for full recovery, she was discharged to home.

Case 2

A 28-year-old nulliparous woman was admitted for the diagnosis of preeclampsia and in-utero growth restriction at the gestational age of 28 weeks and 1 day pregnancy.

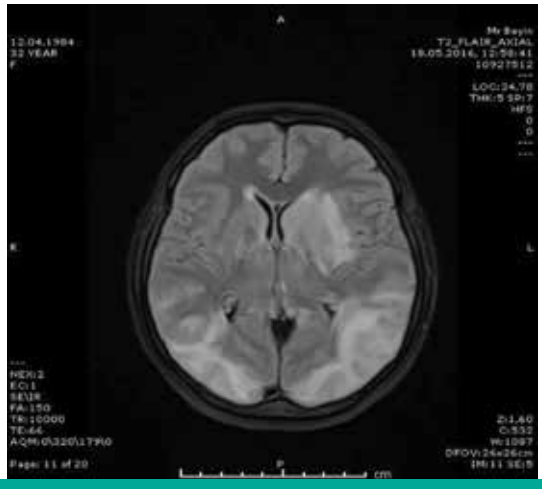

Figure 2. Hypointense lesions on FLAIR sections
FLAIR: Fluid-attenuated inversion recovery

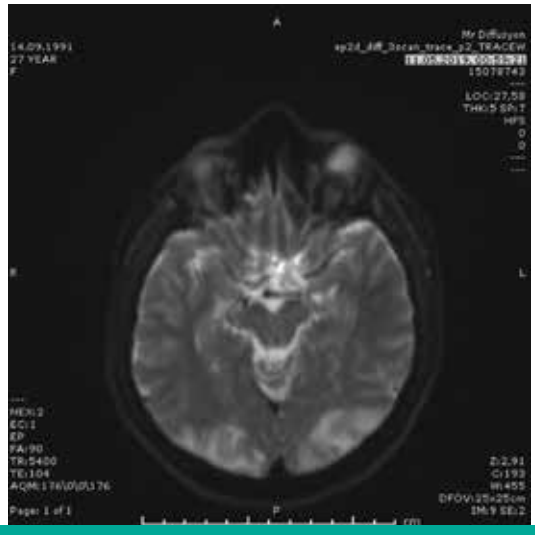

Figure 3. Hyperintense lesions on diffusion-weighted MRI
MRI: Magnetic resonance imaging

Her initial blood pressure was 150/110 mmHg and there was +3 protein in urine analysis. Abdominal circumference of fetus was in the 3rd percentile and there were notches in the bilateral uterine arteries. Her initial liver function enzymes were in the normal limits (ALT: 21, AST: 20 U/L), platelet count was 175,000 10^3/μL and proteinuria in 24-hour urine was 9.149 mg. Two consequent doses of 12 mg betamethasone injections were applied for pulmonary maturation. As severe preeclampsia was diagnosed, antihypertensive treatment and 2 gr/h of magnesium sulfate infusion were started. She was taken to the close observation of perinatalogist. At the 4th day of hospitalization, the doppler examination of umbilical arteries were normal but there was minimal ascites in the maternal abdomen. By day 5, she developed prodromal findings such as generalized headache and scotomas in the visual field and the blood pressure elevated once again to 170/90 mmHg, she underwent urgent C-section. There were no complications during or the first 24 hours of surgery. After that, her blood pressure peaked and she developed diplopia. Once the blood pressure was stabilized after the increase in the dose of antihypertensive treatment, the diplopia was regressed. However, on the postoperative day 2, she developed a generalized tonic-clonic seizure, her blood pressure reached to 200/110 mmHg, pulse was 98 and oxygen saturation was 91%. Airway was applied immediately, oxygen flow was started at the rate of 10 Lt/min. She was protected from the sharp edges at the surrounding and bilateral IV routes were inserted. Loading dose of magnesium sulfate and 5 mg of hydralazine sulfate were pushed. The blood pressure regressed to 180/90 mmHg and the seizure came to the end. She had stabilized as the anticonvulsant therapy was started. Shortly after, she was consulted to neurology because of persistent hypertension, lethargy, generalized headaches and diplopia. Computerized tomography (CT) scan was performed and her fundoscopic examination results were found to be in normal limits with no signs of papilledema or findings of hypertensive retinopathy. Since her cranial CT showed a hypodense lesion at the site of posterior cerebral artery (PCA), diffusion MRI was ordered immediately in order to investigate PRES syndrome related to eclampsia or other differential diagnoses. MRI showed hyperintensity (Figure 3) in the perfusion area of PCA, which was found to be compatible with PRES syndrome. Mannitol 100 mg 4x1 and dexamethasone 2x8 mg infusions were started per neurology consultation. Because of persistent hypertension, lethargy and diplopia for more than 6 hours, she was transferred to ICU for the monitorization of mental status and vitals. The persistent hyperintensive lesions in

the left occipital and bilateral frontal lobes in the second cranial MRI confirmed the vasogenic edema due to PRES. The antihypertensive treatment, levatiracetam 3x500 mg, furosemide 2x40 mg and sedative agents were administered in ICU. As she was extubated and neurologic examination was normal, she was transferred back to inpatient service on the postoperative day 8.

Discussion

In our cases, PRES syndrome most possibly occurred secondary to late postpartum eclampsia (LPE). In LPE, the seizures are seen 2 days to 4 weeks after the delivery. LPE can be challenging to diagnose since those pregnant women may not have obvious findings of preeclampsia such as high blood pressure or proteinuria but both of those patients had an obvious preeclampsia presentation.

Preeclampsia is attributed to generalized endothelial dysfunction of the vessels due to the cytotoxic trophoblastic factors that originated from the placenta. It is still unknown if this damage in the endothelial lining is the cause or the result of hypertension. In both situations, the blood-brain barrier disruption causes fluid and protein transudation to the intercellular area, and this may lead to brain edema. Also, the cerebral autoregulation of blood perfusion cannot be sustained after repetitive abrupt hypertensive changes in brain blood vessels and this situation further increases the interstitial fluid and exacerbates vasogenic edema (6,7). This mechanism also explains the possible pathogenesis of seizures seen in our patients.

As the name indicates, the lesions of PRES are generally located in the posterior territory of the brain. This is thought to be secondary to decreased sympathetic innervations around the basilar artery and its branches. The classic response of arterioles to hypertension is vasoconstriction in order to limit hyperperfusion and possible extravasation of plasma. This response is regulated by sympathetic nerves and the posterior regions that have relatively scarce sympathetic innervations become more prone to develop vasogenic edema (8).

Although the relationship between PRES and preeclampsia/eclampsia has not been clearly explained, we believe that the trophoblastic cytokines cause generalized endothelial dysfunction and play a major role in the development of PRES similar to our cases with preeclampsia and eclampsia (5).

The management of PRES should be based on the underlying pathology. In our cases, the definitive treatment of preeclampsia, which is the delivery of the baby, was already carried out. Prompt blood pressure control and regulation of electrolyte disturbances are the mainstays of treatment. To decrease the cerebral edema and prevent convulsions, we administered anti-edematous medications such as mannitol and steroids (methylprednisolone/dexamethasone). Anti-convulsive agents are also suggested for symptomatic treatment.

Conclusion

PRES should always be considered as one of the differential diagnosis in preeclamptic or eclamptic women who present with altered mental status, convulsions or headaches. Prompt diagnosis and treatment of underlying cause will likely expedite the resolution of cerebral edema and full recovery is expected in days to weeks.

Ethics

Informed Consent: All forms of consent are available to share the patient's photos and data after surgery.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.D., K.D., Design: M.D., K.D., Data Collection or Processing: S.B., Analysis or Interpretation: Y.T., Writing: S.B.

Conflict of Interest: The authors declare that there is no conflict of interest with regard to this manuscript.

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CASE REPORT

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A Rare Cause of Renal Vein and Inferior Vena Cava Thrombosis: A Case of Embryonal Testicular Carcinoma

Renal Ven ve Inferior Vena Kava Trombozunun Nadir Bir Nedeni: Embriyonel Testis Karsinomu Olgusu

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Abstract

Thrombosis is rarely the manifestating symptom of testicular cancers. Patients are usually admitted with painless testicular mass or less frequently pain or hydrocele. Here, we present a young male with germ cell tumor of testis, referred with renal vein and inferior vena cava thrombosis.

Keywords: Germ cell tumor, inferior vena cava, renal vein, thrombosis

Öz

Tromboz, testiküler kanserlerin nadiren ilk bulgusudur. Hastalar genellikle ağrısız testis kitlesi ya da nadiren ağrı veya hidrosel ile başvurur. Renal ven ve inferior vena kavada tromboz ile başvuran testis germ hücreli tümörü olan genç bir hastayı sunmaktayız.

Anahtar kelimeler: Germ hücreli tümör, inferior vena kava, renal ven, tromboz

Introduction

The incidence of testicular germ-cell tumors is 3-10/100,000, which makes it the most frequent cancer among young males (1). It accounts %1 of all cancers but also the 95% of all testicular cancers (2). The most common presenting symptom is painless swelling of one testicle; however less frequently, patients may be admitted with pain, hydrocele or an incidentally found lesion in the retroperitoneum (3). Lack of symptoms in the early stages causes delays in the diagnosis of testicular cancer (TC) in young patients compared to patients older than 50 years (4). We report a case who presented with incidentally found inferior cava vein thrombosis.

Case Report

A 32-year-old young male had fatigue and night sweating for more than 3 months, accompanied by 4 kilogram weight loss in 3-4 weeks. Abdomen and thorax tomographic examination revealed out multiple lymphadenomegalies, and consequently renal doppler ultrasonography indicated thrombosis in the right renal vein and vena cava inferior which reached out inferior hepatic vein and totally occluded

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both veins (Figure 1). He was referred to our hospital after being initiated anticoagulant therapy in another hospital. Laboratory examination showed high sedimentation rate (55 mm/h), proteinuria (spot urine prot/cre: 1.4 gr) and lactate dehydrogenase: 979 U/L. Patients were hospitalized in internal medicine service and low molecular weight heparin therapy (Clexane® 0.8) was continued. Additional blood analysis indicated elevated levels of alpha feto-protein (775 ng/m) and beta human chronic gonadotropin (11,011 IU/mL). On physical examination, no significant finding except painless irregular scrotal mass in 5x10 mm size and containing calcifications was observed. He consulted to urology department and underwent surgery.

After uneventful postoperative period, histopathologic examination indicated pure embryonal carcinoma (Figure 2, 3). The patient was referred to medical oncology, and chemotherapy was initiated. Control Doppler ultrasonographic examination pointed out the recovery of occlusion on the vena cava inferior and renal vein.

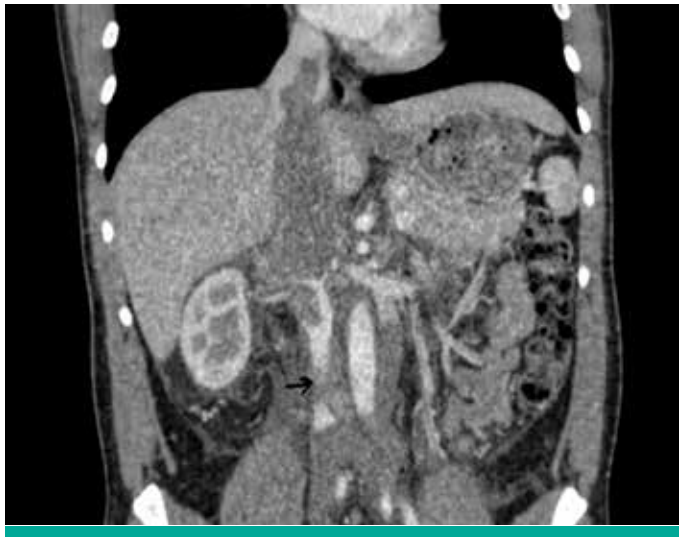

Figure 1. Tomographic examination indicating thrombosis in vena cava inferior

Discussion

Because approximately 70% of TC are localized in the testicle at the time of diagnosis, thrombosis as a presenting sign of testicular lesion is extremely rare and usually seen in seminamatous cancers related to direct tumor invasion or neoplastic thrombosis (5). Urological cancers constitute approximately %5 of malignancy related thrombosis (6). Germ cell tumors (GCT) has higher tendency to hematogenous spread but inferior vena cava (IVC) invasion of GCT is seen less than %3 in an autopsy series (7). Masui et al. (8) defined risk factors of IVC thrombosis as; right sided testicular tumors with large abdominal mass greater than 5 cm, hepatic metastasis or receiving high dose corticosteroids. The diagnosis of IVC thrombosis is usually done by high index of suspicion in TC patients with retroperitoneal mass >5 cm (9).

The management of GCT associated IVC thrombosis may require multidisciplinary approach. Chemotherapy alone is rarely effective in the resolution of IVC thrombosis in GCT's, and antithrombotic therapy or even thrombectomy is usually required. A case report presented a patient with TC who experienced pulmonary thromboembolism during anticoagulant therapy (10). To minimize the risk of pulmonary thromboembolism, some authors perform IVC filter insertion prior to orchiectomy and chemotherapy (8). Our patient showed a rapid response to anticoagulant therapy, and IVC thrombosis recovered in 4-week period.

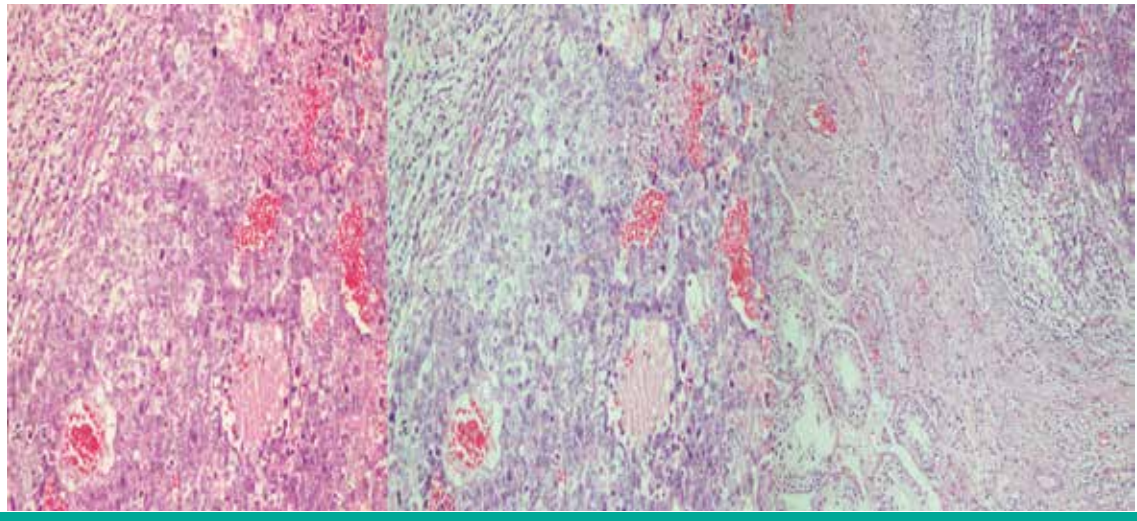

Figure 2. Tumoral tissue consisting of atypical pleomorphic cells showing mitotic activity (HE x 200)

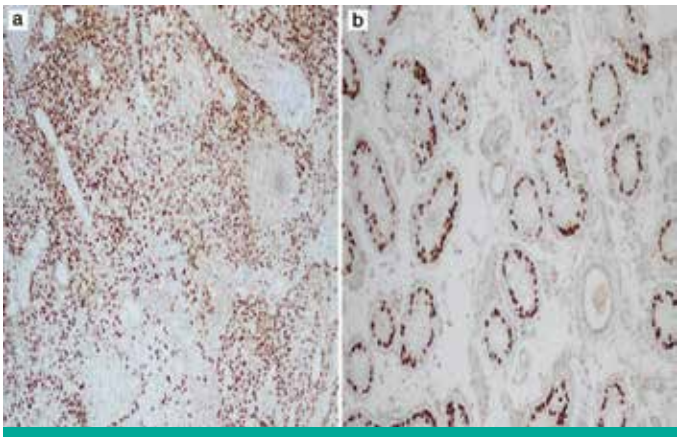

Figure 3. a) OCT 3/4 expression on the tumor cells (OCT 3/4x100), b) OCT 3/4 expression on seminiferous tubules (OCT 3/4x100)

OCT: Optical coherence tomography

According to the Hidden study, venous thromboembolism (VTE) is the most frequent preventable cause of death in hospitalized patients (6). Thromboprophylaxis for cancer patients and antithrombotic therapies when a thrombus is detected play vital role to decrease the risk of pulmonary thromboembolism and sudden death.

TCs should be considered in young males presenting with VTE without an evident risk factor for thrombosis. Physical examination of young individuals that are referred with thrombosis plays crucial role, because before starting numerous radiologic interventions and hematologic tests, single scrotal examination may help to establish the diagnosis. Initiation of immediate therapy and collaboration of the departments of internal medicine, urology and cardiovascular surgery are essential in the management of TC patients VTE.

Ethics

Informed Consent: Written consent was received from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.A., A.E.A., Ü.K., Design: S.A., A.E.A., Ü.K., Data Collection or Processing: S.A., M.Y., İ.Ş., İ.U., A.Z., Ş.Ö., Analysis or Interpretation: S.A., A.E.A., Ü.K., A.B., Writing: A.E.A.

Conflict of Interest: The authors declare that there is no conflict of interest.

Financial Disclosure: No financial support was received from a person or a company.

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