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Turkish Journal of COLORECTAL DISEASE

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Aims and Scope

Turkish Journal of Colorectal Disease is an official journal of the Turkish Society of Colon and Rectal Surgery to provide epidemiologic, pathologic, diagnostic and therapeutic studies relevant to the management of small intestine, colon, rectum, anus and pelvic floor diseases. It was launched in 1991. Although there were temporary interruptions in the publication of the journal due to various challenges, the Turkish Journal of Colorectal Disease has been published continually from 2007 to the present. It is published quarterly (March, June, September and December) as hardcopy and an electronic journal at http://www.turkishjcrd.com/

The target audience of Turkish Journal of Colorectal Disease includes surgeons, pathologists, oncologists, gastroenterologists and health professionals caring for patients with a disease of the colon and rectum.

The Turkish name of the journal was formerly Kolon ve Rektum Hastalıkları Dergisi and the English name of the journal was formerly Journal of Diseases of the Colon and Rectum.

Turkish Journal of Colorectal Disease is indexed in **TÜBİTAK/ULAKBİM, Directory of Open Access Journals (DOAJ), British Library, ProQuest, Root Indexing, Idealonline, Gale/Cengage Learning, Index Copernicus, Turkish Citation Index, Hinari, GOALI, ARDI, OARE, J-GATE** and **TürkMedline.**

The aim of Turkish Journal of Colorectal Disease is to publish original research papers of the highest scientific and clinical value at an international level. Furthermore, review articles, case reports, technical notes, letters to the editor, editorial comments, educational contributions and congress/meeting announcements are released.

Turkish Journal of Colorectal Disease is an independent open access peer-reviewed international journal printed in Turkish and English languages. Manuscripts are reviewed in accordance with "double-blind peer review" process for both referees and authors. The Editorial Board of the Turkish Journal of Colorectal Disease endorses the editorial policy statements approved by the WAME Board of Directors. The journal is in compliance with the uniform requirements for manuscripts submitted to biomedical journals published by the International Committee of Medical Journal Editors (NEJM 1997;336:309-315, updated 2001).

Open Access Policy

This journal provides immediate open access to its content on the principle that making research freely available to the public supports a greater global exchange of knowledge. Open Access Policy is based on rules of Budapest Open Access Initiative (BOAI) http://www.budapestopenaccessinitiative.org/.

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Instructions for authors are published in the journal and at www.turkishjcrd.com

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Authors are responsible for the manuscripts they publish in Turkish Journal of Colorectal Disease. The editor, editorial board, and publisher do not accept any responsibility for published manuscripts.

If you use a table or figure (or some data in a table or figure) from another source, cite the source directly in the figure or table legend.

The journal is printed on acid-free paper.

Financial expenses of the journal are covered by Turkish Society of Colon and Rectal Surgery.

Editorial Policy

Following receipt of each manuscript, a checklist is completed by the Editorial Assistant. The Editorial Assistant checks that each manuscript contains all required components and adheres to the author guidelines, after which time it will be forwarded to the Editor in Chief. Following the Editor in Chief's evaluation, each manuscript is forwarded to the Associate Editor, who in turn assigns reviewers. Generally, all manuscripts will be reviewed by at least three reviewers selected by the Associate Editor, based on their relevant expertise. Associate editor could be assigned as a reviewer along with the reviewers. After the reviewing process, all manuscripts are evaluated in the Editorial Board Meeting.

Turkish Journal of Colorectal Disease's editor and Editorial Board members are active researchers. It is possible that they would desire to submit their manuscript to the Turkish Journal of Colorectal Disease. This may be creating a conflict of interest. These manuscripts will not be evaluated by the submitting editor(s). The review process will be managed and decisions made by editor-in-chief who will act independently. In some situation, this process will be overseen by an outside independent expert in reviewing submissions from editors.

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Amaç ve Kapsam

Türk Kolon ve Rektum Hastalıkları Dergisi, Türk Kolon ve Rektum Cerrahi Derneği'nin resmi dergisidir. Bu dernek; ince barsak, kolon, rektum, anüs ve pelvik taban hastalıkları gibi hastalıkların yönetimi ile ilişkili epidemiyoloijk patolojik, tanısal ve tedavi edici çalışmalar yapar. Derneğimiz 1991'de kurulmuştur. Çeşitli zorluklar nedeniyle geçici aksaklıklar olsa da Türk Kolon ve Rektum Hastalıkları Dergisi 2007'den bu yana aralıksız olarak basılmaktadır ve 3 ayda bir olmak üzere (Mart, Haziran, Eylül, Aralık) basılı dergi ve elektronik olarak (http://www.turkishjcrd.com/) yayımlanır.

Derginin hedef kitlesini; cerrahlar, patologlar, onkologlar, gastroenterologlar ve kolorektal hastalarına hizmet veren profesyoneller oluşturur. Derginin amacı; uluslararası düzeyde en yüksek bilimsel ve klinik değeri olan orijinal çalışmaları yayınlamaktır. Bunlara ek olarak derleme (review) makaleleri, olgu sunumları, teknik notlar, editöre mektuplar, editöryal yorumlar, eğitim yazıları ve kongre/toplantı duyuruları yer almaktadır.

Derginin Türkçe eski adı; Kolon ve Rektum Hastalıkları Dergisi ve İngilizce eski adı; Journal of Diseases of the Colon and Rectum'dur.

Kolon ve Rektum Hastalıkları Dergisi, **TÜBİTAK/ULAKBİM, Directory of Open Access Journals (DOAJ), British Library, ProQuest, Root Indexing, Idealonline, Gale/Cengage Learning, Index Copernicus, Türk Atıf Dizini, Hinari, GOALI, ARDI, OARE, J-GATE ve TürkMedline**'de indekslenmektedir.

Türk Kolon ve Rektum Hastalıkları Dergisi, İngilizce ve Türkçe olarak yayımlanan; bağımsız, hakemli, uluslararası bir dergidir. Eserler, hem hakemler hem de otörler tarafından "çift kör hakem denetimi (peer review)" yöntemi ile değerlendirilir. Türk Kolon ve Rektum Hastalıkları Dergisi'nin Editör Kurulu, World Association of Medical Editors (WAME) politikalarına bağlı olarak yürütülmektedir. Bu dergi, Uluslararası Tıp Dergisi Editörler Komitesi (NEJM 1997;336:309-315, updated 2001) tarafından bildirilen, biyomedikal dergilere gönderilen makalelerin uyması gereken standartlara uygunluk göstermektedir.

Açık Erişim Politikası

Bu dergi bilginin yer değiştirmesi ve toplum içinde bilgiye özgürce ulaşma olanağı sağlamak üzere açık erişime imkan vermektedir. Açık Erişim İlkesi "Budapeşte Açık Erişim Girişimi (BOAI)" http://www.budapestopenaccessinitiative.org/ kurallarına dayanmaktadır.

Derginin mali giderleri Türk Kolon ve Rektum Cerrahi Derneği tarafından karşılanmaktadır.

Yazarlar için Kılavuz

Yazarlar için kılavuz hem yayınlanan dergide hem de "http://www.turkishjcrd.com" web sayfasında bulunmaktadır.

Telif Hakkı Devri

Yazarlar Türk Kolon ve Rektum Hastalıkları Dergisi'nde yayınladıkları yazılardan kendileri sorumludurlar. Editör, editör kurulu ve yayıncı hiçbir sorumluluk kabul etmemektedir. Başka bir kaynaktan tablo ya da figür (veya tablo/figürden bir veri) kullandıysanız, direkt olarak tablo ya da figürü kaynak gösteriniz.

Dergi asitsiz kağıda basılmaktadır.

Derginin mali giderleri Türk Kolon ve Rektum Cerrahi Derneği tarafından karşılanmaktadır.

Editöryal Politika

Her yazının alınmasını takiben, bir kontrol listesi Editör Yardımcısı tarafından tamamlanır.

Editör yardımcısı, her yazıyı gerekli öğeleri sağladığı ve yazar kılavuzuna uyumu açısından kontrol eder, ardından editöre iletir. Editör değerlendirmesinin ardından her bir yazı için editör yardımcısı tarafından gözlemciler (reviewers) belirlenir. Genelde, her bir yazıyı ilgili uzmanlıkları göz önüne alınarak atanmış en az 3 gözlemci inceler. Yardımcı editör de diğer gözlemcilerle birlikte gözlemci olarak atanabilir. Gözlemci incelemesinin ardından yazılar editör kurul toplantısında değerlendirilir.

Türk Kolon ve Rektum Hastalıkları Dergisi'nin editör ve editör kurulu üyeleri aktif araştırmacılardır. Kendi araştırmalarının da Türk Kolon ve Rektum Hastalıkları Dergisi'nde yayınlanmasını pek ala arzu edebilirler. Bu durum çıkar sorunları doğurabilir. Bu yazılar, yazıyı yazan editör(ler) tarafından değerlendirilemez. Bu gibi durumlarda bu süreç, (editörlerin yazı başvurularında) yazıların uzman olan bağımsız kişiler tarafından incelenmesiyle aşılabilir.

Abonelik Bilgileri

Türk Kolon ve Rektum Hastalıkları Dergisi, Türk Kolon ve Rektum Cerrahisi Derneği üyelerine, Dünya'da ve Türkiye'deki kütüphanelere ücretsiz dağıtılmaktadır. Yayınlanmış tüm sayılar ücretsiz olarak şu linkte mevcuttur (http://www.turkishjcrd.com/).

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GENERAL INFORMATION

Turkish Journal of Colorectal Disease (TJCD) is the journal of Turkish Society of Colon and Rectal Surgery. The mission of the Journal is to advance knowledge of disorders of the small intestine, colon, rectum, anus and pelvic floor. It publishes invited review articles, research articles, brief reports and letters to the editor, and case reports that are relevant to the scope of the journal, on the condition that they have not been previously published elsewhere. Basic science manuscripts, such as randomized, cohort, cross-sectional, and case control studies, are given preference. Invited reviews will be considered for peer review from known experts in the area.

Manuscripts should be prepared according to ICMJE guidelines (www.icmje.org). All manuscripts are subject to editorial revision to ensure they conform to the style adopted by the journal. There is a double blind kind of reviewing system.

Reviewed and accepted manuscripts are translated from Turkish to English by the Journal through a professional translation service. Prior to printing, the translations are submitted to the authors for approval or correction requests, to be returned within 7 days. If no response is received from the corresponding author within this period, the translation is checked and approved by the editorial board.

Accepted manuscripts are published in both Turkish and English languages.

All manuscripts submitted to the Turkish Journal of Colorectal Disease are screened for plagiarism using the 'iThenticate' software. Results indicating plagiarism may result in manuscripts being returned or rejected.

Turkish Journal of Colorectal Disease does not charge any article submission or processing charges.

The abbreviation of the Turkish Journal of Colorectal Disease is "TJCD", however, it should be denoted as "Turk J Colorectal Dis" when referenced.

EDITORIAL POLICIES

All manuscripts will be evaluated by the scientific board for their scientific contribution, originality and content. Authors are responsible for the accuracy of the data. The journal retains the right to make appropriate changes on the grammar and language of the manuscript. When suitable the manuscript will be sent to the corresponding author for revision. The manuscript, when published, will become the property of the journal and copyright will be taken out in the name of the journal

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In the cover letter the authors should state if any of the material in the manuscript is submitted or planned for publication elsewhere in any form including electronic media. A written statement indicating whether or not "Institutional Review Board" (IRB) approval was obtained or equivalent guidelines followed in accordance with the Helsinki Declaration of 2013 update on human experimentation must be stated; if not, an explanation must be provided. The cover letter must contain address, telephone, fax and the e-mail address of the corresponding author.

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The ORCID (Open Researcher and Contributor ID) number of the correspondence author should be provided while sending the manuscript. A free registration can create at http://orcid.org.

Online Submission

Only online submissions are accepted for rapid peer-review and to prevent delay in publication. Manuscripts should be prepared as word document (*.doc) or rich text format (*.rtf). After logging on to the web www. journalagent.com/krhd double click the "submit an article" icon. All corresponding authors should be provided a password and an username after providing the information needed. After logging on the article submission system with your own password and username please read carefully the directions of the system to provide all needed information in order not to delay the processing of the manuscript. Attach the manuscript, all figures, tables and additional documents. Please also attach the cover letter with "Assignment of Copyright and Financial Disclosure" forms.

Manuscript Preparation Guidelines

Turkish Journal of Colorectal Disease follows the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" (International Committee of Medical Journal Editors: Br Med J 1988;296:401-5).

Upon submission of the manuscript, authors are to indicate the type of trial/research and statistical applications following "Guidelines for statistical reporting in articles for medical journals: amplifications and explanations" (Bailar JC III, Mosteller F. Ann Intern Med 1988;108:266-73).

Preparation of research articles, systematic reviews and meta-analyses must comply with study design guidelines:

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 statement of 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,

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

STROBE statement, a 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).

Text Formatting

Manuscripts should be submitted in Word.

Use a normal, plain font (e.g., 10-point Times Roman) for text.

Use the automatic page numbering function to number the pages.

Do not use field functions.

Use tab stops or other commands for indents, not the space bar.

Use the table function, not spreadsheets, to make tables.

Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

Title Page

All manuscripts, regardless of article type, should start with a title page, containing:

The title of the article;

The short title of the article

The initials, names and qualifications of each author;

The main appointment of each author;

The name(s) of the institution(s) of each author;

The name and email address of the corresponding author;

Full disclosures of potential conflicts of interest on the part of any named author, or a statement confirming that there are no conflicts of interest;

The word count excluding abstract, references, tables, figures and legends;

The place and date of scientific meeting in which the manuscript was presented and it's abstract published in the abstract book, if applicable.

Article Types

Original Articles

This category includes original research including both clinical and basic science submissions. The work must be original and neither published, accepted, or submitted for publication elsewhere. Any related work, either SUBMITTED, in press, or published from any of the authors should be clearly cited and referenced.

All clinical trials must be registered in a public trials registry that is acceptable to the International Committee of Medical Journals Editors (ICMJE). Go to (http://www.icmje.org/faq.html). Authors of randomized controlled trials must adhere to the CONSORT guidelines, available at: www.consort-statement.org, and provide both a CONSORT checklist and flow diagram. We require that you choose the MS Word template at www.consort-statement.org for the flow chart and cite/upload it in the manuscript as a figure. In addition, submitted manuscripts must include the unique registration number in the Abstract as evidence of registration.

All authors are expected to abide by accepted ethical standards for human and animal investigation. In studies that involve human subjects or laboratory animals, authors must provide an explicit statement in Materials and Methods that the experimental protocol was approved by the appropriate institutional review committee and meets the guidelines of their responsible governmental agency. In the case of human subjects, informed consent, in addition to institutional review board approval, is required.

Original Articles should not exceed 3000 words (excluding abstract, references, tables, figures and legends) and four illustrations.

Original Articles should be organized as follows:

Abstract: The abstract must contain fewer than 250 words and should be structured as follows:

Aim: What was the purpose of the study?

Method: A brief description of the materials - patients or subjects (i.e. healthy volunteers) or materials (animals) - and methods used.

Results: What were the main findings?

Conclusion: What are the main conclusions or implications of the study?

Keywords: Below the abstract provide up to 6 key words or short phrases. Do not use abbreviations as keywords.

Introduction: State concisely the purpose and rationale for the study and cite only the most pertinent references as background.

Materials and Methods: Describe your selection of the observational or experimental subjects clearly (patients or experimental animals, including controls). Provide an explicit statement that the experimental protocols were approved by the appropriate institutional review committee and meet the guidelines of the responsible governmental agency. In the case of human subjects, state explicitly those subjects have provided informed consent. Identify the methods, apparatus/product** (with manufacturer's name and address in parentheses), and procedures in sufficient detail to allow other workers to reproduce the results. Give references to established methods, including statistical methods; provide references and brief descriptions of methods that have been published but are not well known, describe substantially modified methods, including statistical methods, give reasons for using them, and evaluate their limitations;

Results: Present the detailed findings supported with statistical methods. Figures and tables should supplement, not duplicate the text; presentation of data in either one or the other will suffice. Emphasize only your important observations; do not compare your observations with those of others. Such comparisons and comments are reserved for the discussion section.

Discussion: State the importance and significance of your findings but do not repeat the details given in the Results section. Limit your opinions to those strictly indicated by the facts in your report. Compare your finding with those of others. No new data are to be presented in this section.

Acknowledgments: Only acknowledge persons who have made substantive contributions to the study. Authors are responsible for obtaining written permission from everyone acknowledged by name because readers may infer their endorsement of the data and conclusions. Begin your text of the acknowledgment with, "The authors thank…".

Authorship Contributions: The journal follows the recommendations of the ICMJE for manuscripts submitted to biomedical journals. According to these, authorship should be based on the following four criteria:

Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; and

Drafting the work or revising it critically for important intellectual content; and

Final approval of the version to be published; and

Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

All other contributors to the paper should be credited in the 'Acknowledgments' section.

References: The author should number the references in Arabic numerals according to the citation order in the text. Put reference numbers in parenthesis in superscript at the end of citation content or after the cited author's name. Use the form of "Uniform Requirements for manuscript abbreviations in Turk Bilim Terimleri" (http:/www.bilimterimleri.com).

Journal titles should conform to the abbreviations used in "Cumulated Index Medicus".

Journals; Last name(s) of the author(s) and initials, article title, publication title and its original abbreviation, publication date, volume, the inclusive page numbers.

Example: 1. Dilaveris P, Batchvarov V, Gialafos J, Malik M. Comparison of different methods for manual P wave duration measurement in 12-lead electrocardiograms. Pacing Clin Electrophysiol 1999;22:1532-1538.

Book chapter; Last name(s) of the author(s) and initials, chapter title, book editors, book title, edition, place of publication, date of publication and inclusive page numbers of the extract cited.

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Example: 1. Schwartz PJ, Priori SG, Napolitano C. The Long QT Syndrome. In: Zipes DP, Jalife J, eds. Cardiac Electrophysiology. From Cell to Bedside. Philadelphia; WB Saunders Co. 2000:597-615.

Tables: All tables are to be numbered using Arabic numerals. Tables should always be cited in text in consecutive numerical order. For each table, please supply a table caption (title) explaining the components of the table. Identify any previously published material by giving the original source in the form of a reference at the end of the table caption. Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body.

Figures: Figures should work under "Windows". Color figures or grayscale images must be at least 300 dpi. Figures using "*.tiff", "*.jpg" or "*.pdf" should be saved separate from the text. All figures should be prepared on separate pages. They should be numbered in Arabic numerals. Each figure must have an accompanying legend defining abbreviations or symbols found in the figure. Figures could be submitted at no additional cost to the author.

Units of Measurement and Abbreviations: Units of measurement should be in Systéme International (SI) units. Abbreviations should be avoided in the title. Use only standard abbreviations. If abbreviations are used in the text, they should be defined in the text when first used.

Permissions: Authors wishing to include figures, tables, or text passages that have already been published elsewhere are required to obtain permission from the copyright owner(s) and to include evidence that such permission has been granted when submitting their papers. Any material received without such evidence will be assumed to originate from the authors.

Invited Review Articles

Abstract length: Not to exceed 250 words.

Article length: Not to exceed 4000 words.

Reference Number: Not to exceed 100 references.

Reviews should include a conclusion, in which a new hypothesis or study about the subject may be posited. Do not publish methods for literature search or level of evidence. Authors who will prepare review articles should already have published research articles on the relevant subject. The study's new and important findings should be highlighted and interpreted in the Conclusion section. There should be a maximum of two authors for review articles.

Case Reports

Abstract length: Not to exceed 100 words.

Article length: Not to exceed 1000 words.

Reference Number: Not to exceed 15 references.

Case Reports should be structured as follows:

Abstract: An unstructured abstract that summarizes the case.

Introduction: A brief introduction (recommended length: 1-2 paragraphs).

Case Report: This section describes the case in detail, including the initial diagnosis and outcome.

Discussion: This section should include a brief review of the relevant literature and how the presented case furthers our understanding to the disease process.

References: See under 'References' above.

Acknowledgments.

Tables and figures.

Technical Notes

Abstract length: Not to exceed 250 words.

Article length: Not to exceed 1200 words.

Reference Number: Not to exceed 15 references.

Technical Notes include description of a new surgical technique and its application on a small number of cases. In case of a technique representing a major breakthrough one case will suffice. Follow-up and outcome need to be clearly stated.

Technical Notes should be organized as follows:

Abstract: Structured "as above mentioned".

Indications

Method

Comparison with other methods: advantages and disadvantages, difficulties and complications.

References, in Vancouver style (see under 'References' above).

Acknowledgments.

Tables and figures: Including legends.

Letters to the Editor

Article length: Not to exceed 500 words.

Reference Number: Not to exceed 10 references

We welcome correspondence and comment on articles published in Turkish Journal of Colorectal Disease. No abstract is required, but please include a brief title. Letters can include 1 figure or table.

Video Article

Article length: Not to exceed 500 words.

Reference Number: Not to exceed 5 references

Briefly summarize the case describing diagnosis, applied surgery technique and outcome. Represent all important aspects, i.e. novel surgery technique, with properly labelled and referred video materials. A standalone video vignette, describing a surgical technique or interesting case encountered by the authors.

Requirements: The data must be uploaded during submission with other files. The video should be no longer than 10 minutes in duration with a maximum file size of 350Mb and 'MOV, MPEG4, AVI, WMV, MPEGPS, FLV, 3GPP, WebM' format should be used. Documents that do not exceed 100 MB can be uploaded within the system. For larger video documents, please contact iletisim@galenos.com.tr All videos must include a narration in English. Reference must be used as it would be for a Figure or a Table. Example: ".....To accomplish this, we developed a novel surgical technique (Video 1)." All names and institutions should be removed from all video materials. Video materials of accepted manuscripts will be published online.

Letters to the Editor

Article length: Not to exceed 500 words.

Reference Number: Not to exceed 10 references

We welcome correspondence and comment on articles published in Turkish Journal of Colorectal Disease. No abstract is required, but please include a brief title. Letters can include 1 figure or table.

Editorial Comments

Article length: Not to exceed 1000 words.

Reference Number: Not to exceed 10 references.

Editorials are exclusively solicited by the Editor. Editorials should express opinions and/or provide comments on papers published elsewhere in the same issue. A single author is preferred. No abstract is required, but please include a brief title. Editorial submissions are subject to review/request for revision, and editors retain the right to alter text style.

Ethics

This journal is committed to upholding the integrity of the scientific record. As a member of the Committee on Publication Ethics (COPE) the journal will follow the COPE guidelines on how to deal with potential acts of misconduct.

Authors should refrain from misrepresenting research results which could damage the trust in the journal, the professionalism of scientific authorship, and ultimately the entire scientific endeavor. Maintaining integrity of the research and its presentation can be achieved by following the rules of good scientific practice, which include:

The manuscript has not been submitted to more than one journal for simultaneous consideration.

The manuscript has not been published previously (partly or in full), unless the new work concerns an expansion of previous work (please provide transparency on the re-use of material to avoid the hint of text-recycling ("self-plagiarism").

A single study is not split up into several parts to increase the quantity of submissions and submitted to various journals or to one journal over time (e.g. "salami-publishing").

No data have been fabricated or manipulated (including images) to support your conclusions.

No data, text, or theories by others are presented as if they were the author's own ("plagiarism"). Proper acknowledgments to other works must be given (this includes material that is closely copied (near verbatim), summarized and/or paraphrased), quotation marks are used for verbatim copying of material, and permissions are secured for material that is copyrighted.

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Consent to submit has been received explicitly from all co-authors, as well as from the responsible authorities - tacitly or explicitly - at the institute/organization where the work has been carried out, before the work is submitted.

Authors whose names appear on the submission have contributed sufficiently to the scientific work and therefore share collective responsibility and accountability for the results.

In addition: Changes of authorship or in the order of authors are not accepted after acceptance of a manuscript.

Requesting to add or delete authors at revision stage, proof stage, or after publication is a serious matter and may be considered when justifiably warranted. Justification for changes in authorship must be compelling and may be considered only after receipt of written approval from all authors and a convincing, detailed explanation about the role/deletion of the new/deleted author. In case of changes at revision stage, a letter must accompany the revised manuscript. In case of changes after acceptance or publication, the request and documentation must be sent via the Publisher to the Editor-in-Chief. In all cases, further documentation may be required to support your request. The decision on accepting the change rests with the Editor-in-Chief of the journal and may be turned down. Therefore authors are strongly advised to ensure the correct author group, corresponding author, and order of authors at submission.

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All individuals have individual rights that are not to be infringed. Individual participants in studies have, for example, the right to decide what happens to the (identifiable) personal data gathered, to what they have said during a study or an interview, as well as to any photograph that was taken. Hence it is important that all participants gave their informed consent in writing prior to inclusion in the study. Identifying details (names, dates of birth, identity numbers and other information) of the participants that were studied should not be published in written descriptions, photographs, and genetic profiles unless the information is essential for scientific purposes and the participant (or parent or guardian if the participant is incapable) gave written informed consent for publication. Complete anonymity is difficult to achieve in some cases, and informed consent should be obtained if there is any doubt. For example, masking the eye region in photographs of participants is inadequate protection of anonymity. If identifying characteristics are altered to protect anonymity, such as in genetic profiles, authors should provide assurance that alterations do not distort scientific meaning.

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Each manuscript submitted to The Turkish Journal of Colorectal Disease is subject to an initial review by the editorial office in order to determine if it is aligned with the journal's aims and scope, and complies with essential requirements. Manuscripts sent for peer review will be assigned to one of the journal's associate editors that has expertise relevant to the manuscript's content. All accepted manuscripts are sent to a statistical and English language editor before publishing. Once papers have been reviewed, the reviewers' comments are sent to the Editor, who will then make a preliminary decision on the paper. At this stage, based on the feedback from reviewers, manuscripts can be accepted, rejected, or revisions can be recommended. Following initial peer-review, articles judged worthy of further consideration often require revision. Revised manuscripts generally must be received within 2 months of the date of the initial decision. Extensions must be requested from the Associate Editor at least 2 weeks before the 2-month revision deadline expires; The Turkish Journal of Colorectal Disease will reject manuscripts that are not received within the 3-month revision deadline. Manuscripts with extensive revision recommendations will be sent for further review (usually by the same reviewers) upon their re-submission. When a manuscript is finally accepted for publication, the Technical Editor undertakes a final edit and a marked-up copy will be e-mailed to the corresponding author for review and to make any final adjustments.

REVISIONS

When submitting a revised version of a paper, the author must submit a detailed "Response to the reviewers" that states point by point how each issue raised by the reviewers has been covered and where it can be found (each reviewer's comment, followed by the author's reply and line numbers where the changes have been made) as well as an annotated copy of the main document. Revised manuscripts must be submitted within 30 days from the date of the decision letter. If the revised version of the manuscript is not submitted within the allocated time, the revision option may be canceled. If the submitting author(s) believe that additional time is required, they should request this extension before the initial 30-day period is over.

ENGLISH LANGUAGE EDITING

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The Turkish Journal of Colorectal Disease publishes abstracts of accepted manuscripts online in advance of their publication in print. Once an accepted manuscript has been edited, the authors have submitted any final corrections, and all changes have been incorporated, the manuscript will be published online. At that time the manuscript will receive a Digital Object Identifier (DOI) number. Both forms can be found at www.journalagent.com/krhd. Authors of accepted manuscripts will receive electronic page proofs directly from the printer, and are responsible for proofreading and checking the entire manuscript, including tables, figures, and references. Page proofs must be returned within 48 hours to avoid delays in publication.

CORRESPONDENCE

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Yazarlara Bilgi

GENEL BİLGİ

Türk Kolon ve Rektum Hastalıkları Dergisi, Türk Kolon ve Rektum Cerrahisi Derneği'nin dergisidir. Derginin misyonu; ince bağırsak, kolon, rektum, anüs ve pelvik taban bozuklukları hakkındaki bilgiye katkı sağlamaktır. Dergi daha önce başka bir yerde yayınlanmamış olması koşuluyla, derginin kapsamı ile ilgili ve talep üzerine yazılan derleme makaleleri, araştırma makaleleri, kısa raporlar ve editöre mektuplar ve olgu sunumlarını yayınlamaktadır. Randomize, kohort, kesitsel ve vaka kontrol çalışmaları gibi temel bilim yazılarına öncelik verilir. Alanında bilinen uzmanlarca talep üzerine yazılan derlemeler dikkate alınacaktır.

Yazılar ICMJE yönergelerine göre (http://www.icmje.org/) hazırlanmalıdır. Tüm yazılar dergi tarafından benimsenen stile uygunluk sağlamak için editöryal kontrol ve düzeltmelere tabi tutulmaktadır. Derginin çift kör bir değerlendirme sistemi vardır. Değerlendirilen ve kabul edilen yayınlar Türkçeden İngilizceye veya İngilizceden Türkçeye derginin profesyonel çeviri hizmeti aracılığıyla tercüme edilir. Yayınlanmadan önce, çeviriler onay veya düzeltme istekleri için yazarlara gönderilir ve 7 gün içinde geri dönüş talep edilir. Bu süre içinde yanıt alınamazsa, çeviri kontrol ve yayın kurulu tarafından onaylanır.

Kabul edilen yayınlar hem Türkçe hem de İngilizce olarak yayınlanır.

Türk Kolon ve Rektum Hastalıkları Dergisi'ne gönderilen tüm yayınlar 'iThenticate' yazılımı kullanılarak intihal açısından taranır. İntihal saptanan durumlarda yayın iade veya reddedilir.

Türk Kolon ve Rektum Hastalıkları Dergisi, makale gönderme veya işlem ücreti adı altında herhangi bir ücret talep etmemektedir.

Türk Kolon ve Rektum Hastalıkları Dergisi'nin kısaltması "TJCD"dir, ancak, refere edildiğinde "Turk J Colorectal Dis" olarak kullanılmalıdır.

YAYIN POLİTİKASI

Tüm makaleler bilimsel katkıları, özgünlük ve içerikleri açısından bilimsel komite tarafından değerlendirilecektir. Yazarlar verilerinin doğruluğundan sorumludurlar. Dergi gerekli gördüğü yerlerde dil ve uygun değişiklik yapma hakkını saklı tutar. Gereğinde makale revizyon için yazara gönderilir. Dergide basılan yayın derginin malı haline gelir ve telif hakkı "Türk Kolon ve Rektum Hastalıkları Dergisi" adına alınmış olur. Daha önce herhangi bir dilde yayınlanmış makaleler dergide yayınlanmak üzere kabul edilmeyecektir. Yazarlar bir başka dergide yayınlanmak üzere olan makaleyi teslim edemez. Tüm değişiklikler, yazar ve yayıncının yazılı izin alındıktan sonra yapılacaktır. Tüm makalelerin tam metinleri derginin www.journalagent.com/krhd web sitesinden indirilebilir.

YAZAR KILAVUZU

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Açıklama bildirimi

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Bilgilendirilmiş Onam

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Üst Yazı

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Makale Yazım Kuralları

Tüm makaleler online başvuru sistemi üzerinden teslim edilmelidir. Yazarlar web sitesi www.journalagent.com/krhd adresinde oturum açtıktan sonra internet üzerinden yazılarını sunmalıdır.

Makale gönderimi yapılırken sorumlu yazarın ORCID (Open Researcher ve Contributor ID) numarası belirtilmelidir. http://orcid.org adresinden ücretsiz olarak kayıt oluşturabilir.

Online Başvuru

Gecikmeyi önlemek ve hızlı hakemlik için sadece çevrim içi gönderimler kabul edilir. Yazılar word belgesi (*.doc) veya zengin metin biçimi (*.rtf) olarak hazırlanmalıdır. www.journalagent.com/krhd adresinde web oturumu açtıktan sonra "Makale gönder" ikonuna tıklayın. Tüm yazarlar, gerekli bilgileri sisteme girdikten sonra bir şifre ve bir kullanıcı adı alır. Kendi şifre ve kullanıcı adınız ile makale gönderme sistemine kayıt olduktan sonra yazının işleme alınmasında bir gecikme olmaması için gerekli tüm bilgileri sağlamak için sistemin yönergelerini dikkatlice okuyunuz. Makaleyi ve tüm şekil, tablo ve ek dökümanları ekleyiniz. Ayrıca üst yazı ve "Telif Hakkı ve Finansal Durum" formunu ve yazının tipine göre aşağıda belirtilen kılavuzların kontrol listesini ekleyiniz.

Makale Hazırlama Kuralları

Türk Kolon ve Rektum Hastalıkları Dergisi "Biyomedikal Dergilere Gönderilen Makaleler için Gerekli Standartları" izler. (International Committee of Medical Journal Editors: Br Med J 1988; 296: 401-5).

Yazarlar yayınlarını gönderirken, çalışmalarının türünü ve uygulanan istatistik yöntemlerini "Tıbbi Dergilere Gönderilen Makaleler için İstatistiksel Raporlama Rehberi"ne uygun olarak belirtmelidir (Bailar JC III, Mosteller F. Ann Intern Med 1988;108:266-73).

Araştırma makalesi, sistematik değerlendirme ve meta-analizin hazırlanması aşağıdaki çalışma tasarımı kurallarına uymak zorundadır; (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 statement of preferred reporting items for systematic reviews and meta-analyses (Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009; 6(7): e1000097.) (http://www.prisma-statement.org/);

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

STROBE statement, a 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).

Metin Biçimlendirme

Yazılar Word programı ile hazırlanarak teslim edilmelidir.

- Metin için normal, düz yazı tipi kullanın (örneğin, 10 punto Times Roman).

- Sayfa numarası için otomatik sayfa numaralandırma işlevini kullanın.

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- Alan fonksiyonları kullanmayın.

- Girintiler için sekme durakları (Tab) kullanın, ara çubuğu ve diğer komutlar kullanmayın.

- Tablo yapmak için diğer işlevleri değil, elektronik tablo fonksiyonunu kullanın.

- Dosyanızı .docx formatında (Word 2007 veya üstü) ya da .doc formatında (eski Word sürüm) kaydedin.

Giriş sayfası

Tüm yazılar, makale türü ne olursa olsun, aşağıdakileri içeren bir başlık sayfası ile başlamalıdır:

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- Makalenin kısa başlığı;

- Yazarların isimleri, isimlerinin baş harfleri ve her yazarın akademik ünvanı;

- Her yazarın görevi;

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- Herhangi bir yazarın olası bir çıkar çatışması olduğunu teyit eden bir ifade, aksi takdirde çatışma olmadığını belirtir bir açıklama;

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- Varsa yayının yayınlanmış olduğu bilimsel toplantının tarihi, yeri ve varsa kongre özet kitabındaki özeti.

Makale Tipleri

Orijinal Makaleler

Bu kategori, klinik ve temel bilimde orijinal araştırmaları içerir. Yayın orijinal olmalı ve başka bir dergide yayınlanmış/gönderilmiş ya da kabul edilmiş olmamalıdır. Yazarlar, herhangi biri tarafından bir dergiye gönderilmiş, baskıda veya basılmış ilgili herhangi bir çalışmaya atıfta bulunmak istiyorlarsa açıkça atıfta bulunulmalı ve kaynak gösterilmelidir.

Tüm klinik çalışmalar, Uluslararası Tıp Dergisi Editörler Komitesince (ICMJE) kabul gören bir kayıt sistemine kayıtlı olmalıdır. Bunun için http://www.icmje.org/faq.html adresine müracaat edin. Randomize kontrollü çalışmaların yazarları da, www.consort-statement.org adresinden başvurulabilen CONSORT kılavuzuna uymalıdır ve yayınlarıyla birlikte CONSORT kontrol listesi ve akış diyagramı tebliğ edilmelidir. Akış şeması olarak www.consort-statement.org adresinde bulunan MS Word şablonunun kullanılması ve bunun yayının içinde bir alıntı veya bir figür olarak yerleştirilmesi gereklidir. Buna ek olarak, sunulan yayınlar her yayına spesifik verilen özel kayıt numarasını içermelidir.

Tüm yazarların, insan üzerindeki çalışmalar ve hayvan deneylerinde etik standartlara uymaları beklenmektedir. İnsan üzerindeki veya laboratuvar hayvanları içeren çalışmalarda, yazarların yayının Gereç ve Yöntem kısmında deney protokolünün ilgili kurumsal inceleme komitesi tarafından onaylandığını ve sorumlu devlet kurumu kurallarına uyduğunu açık bir dille açıklamaları gereklidir. İnsan üzerindeki çalışmalarda kurumsal inceleme kurulu onayına ek olarak, aydınlatılmış onam da bulunmalıdır.

Orijinal Makaleler (özet, kaynaklar, tablolar, rakamlar hariç) 3000 kelime ve dört figürü aşmamalıdır.

Orijinal Makaleler aşağıdaki gibi organize edilmelidir:

Özet: Özet 250 kelimeyi geçmemeli ve şunları içermelidir;

Amaç: Çalışmanın amacı nedir?

Yöntem: Kullanılan yöntem ve materyaller (örneğin hayvanlar) veya hastalar ya da konu (sağlıklı gönüllüler gibi) hakkında kısa bir açıklama içermelidir.

Bulgular: Ana bulgular nelerdir?

Sonuç: Çalışmanın ana sonuçları ve etkileri nelerdir?

Anahtar kelimeler: Özetin altında en az 3 anahtar kelime veriniz. Kısaltmaları anahtar kelime olarak kullanmayınız.

Giriş: Açık bir dille çalışmanın amaç ve gerekçesini belirtin ve çalışmanın arka planını açıklarken sadece en önemli kaynaklardan alıntı yapın.

Gereç ve Yöntem: Gözlemsel veya deneysel deneklerin (hastalar, deney hayvanları veya kontrol grupları dahil) seçim şeklini açıklayın. Deney protokolünün ilgili kurumsal inceleme komitesi tarafından onaylandığını ve ilgili devlet kurumu kurallarına uyduğunu açık bir dille açıklayın. İnsan çalışması durumunda, tüm şahısların aydınlatılmış onamlarının alındığını açık bir dille belirtin. Yöntem, cihaz ve ürünleri tanımlayın (Parantez içinde üretici firma adı ve adresi)** Uygulanmış olan tüm prosedürler, diğer çalışmacıların aynı deneyi tekrar edebilecekleri detay ve netlikte anlatılmalıdır. İstatistiksel yöntemler de dahil olmak üzere yerleşik ve yaygın olarak bilinen çalışma yöntemleri için kaynaklar belirtilmelidir. Yayınlanmış ancak yaygın olarak bilinmeyen yöntemler için ise kaynaklar ve kısa tanımlamalar verilmelidir. Kullanma sebepleri ve limitasyonları belirtilmelidir.

Bulgular: İstatistiksel yöntemlerle desteklenmiş bulgularınızı ayrıntılı olarak sunun. Şekil ve tablolar metni tekrar değil, takviye etmelidir. Verilerin hem metinde hem figür olarak verilmemesi gerekir. Metin veya figürden birisi olarak verilmesi yeterlidir. Sadece kendi önemli izlenimlerinizi belirtin. Kendi izlenimlerinizi diğerlerininkiyle karşılaştırmayın. Bu tür karşılaştırma ve yorumlar tartışma bölümünde yapılmalıdır.

Tartışma: Bulgularınızın önem ve anlamını vurgulayın ancak bulgular kısmında verilenleri tekrarlamayın. Fikirlerinizi yalnızca bulgularınızla kanıtlayabildiklerinizle sınırlı tutun. Bulgularınızı diğerlerininkiyle karşılaştırın. Bu bölümde yeni veriler bulunmamalıdır.

Teşekkür: Sadece çalışmaya ciddi katkılarda bulunmuş kişilere teşekkür edin. Yazarlar ismen teşekkür ettikleri herkesten yazılı izin almak zorundadır. Teşekkür kısmına "Yazarlar ….teşekkür eder" şeklinde başlayın.

Yazarlık ve Katkı Sağlayanlar: Dergi, biyomedikal dergilere gönderilen yayınlara yönelik ICMJE tavsiyelerini izler. Buna göre "yazarlık" aşağıdaki dört kritere dayalı olmalıdır:

Yazar;

- Yayının konsept veya dizaynına, çalışmanın verilerinin elde edilmesine, analizine ve yorumlanmasına önemli katkılar veren; ve

- İşi hazırlayan veya entellektüel içerik açısından eleştirel biçimde gözden geçiren; ve

- Yayınlanacak son şekli onaylayan; ve

- Çalışmanın her bir bölümünün doğruluğu ve bütünlüğü ile ilgili sorunları uygun bir şekilde inceleyen ve çözüm sağlayan sorumlu kişidir.

Bu şartların hepsini sağlamayan diğer tüm katılımcılar yazar değil, "Teşekkür" bölümünde anılması gereken katkı sağlamış kişilerdir.

Kaynaklar: Kaynakları 1'den başlayarak Arap rakamları ve alfabetik sıra ile verin. Kaynak numaraları cümle sonunda noktadan sonra üstte küçük rakamlar şeklinde (superscript) yazılmalıdır. Kısaltmalar için gerekli standartları http:/www.bilimterimleri.com adresinde bulunan Türk Bilim Terimleri Kılavuzu'ndan edinin.

Dergi başlıkları "Cumulated Index Medicus" kısaltmalarına uygun olmalıdır.

Dergiden: Yazar/yazarların soyadı ve adının ilk harfi, makale başlığı, dergi başlığı ve derginin özgün kısaltması, yayın tarihi, baskı, kapsayıcı sayfa numaralarını içermelidir.

Örneğin: 1. Dilaveris P, Batchvarov V, Gialafos J, Malik M. Comparison of different methods for manual P wave duration measurement in 12-lead electrocardiograms. Pacing Clin Electrophysiol 1999;22:1532-1538.

Kitap Bölümü: Yazar/yazarların soyadı ve adının ilk harfi, bölüm başlığı, kitap editörleri, kitap başlığı, basım, yayın yeri, yayın tarihi, kapsadığı sayfa numaralarını içermelidir

Örneğin: 1. Schwartz PJ, Priori SG, Napolitano C. The Long QT Syndrome. In: Zipes DP, Jalife J, eds. Cardiac Electrophysiology. From Cell to Bedside. Philadelphia; WB Saunders Co. 2000:597-615.

Tablolar: Tüm tablolar Arapça sayılarla numaralandırılmalıdır. Tüm tablolardan metin içerisinde numara sırası ile bahsedilmelidir. Her tablo için tablonun içeriği hakkında bilgi veren bir başlık verin. Başka yayından alıntı olan tüm tabloları tablonun alt kısmında kaynak olarak belirtin. Tabloda dipnotlar tablonun altında, üst karakter olarak küçük harflerle verilmelidir. İstatistiksel anlamlı değerler ve diğer önemli istatistiksel değerler yıldız ile işaretlenmelidir.

Şekiller: Şekillerin "Windows" ile açılması gerekir. Renkli şekiller veya gri tonlu görüntüler en az 300 dpi olmalıdır. Şekiller ana metinden ayrı olarak "*.tiff", "*.jpg" veya "*.pdf" formatında kaydedilmelidir. Tüm şekil ayrı bir sayfada hazırlanmalı ve Arap rakamları ile numaralandırılmalıdır. Her şekilde kendisindeki işaret ve sembolleri açıklayan bir alt yazı olmalıdır. Şekil gönderme için yazardan hiçbir ek ücret alınmaz.

Ölçü Birimleri ve Kısaltmalar: Ölçü birimleri System International (SI) birimleri cinsinden olmalıdır. Kısaltmalardan başlıkta kaçınılmalıdır. Sadece standart kısaltmalar kullanın. Metinde kısaltma kullanılırsa ilk kullanıldığı yerde tanımlanmalıdır.

İzinler: Yazarlar yayınlarına önceden başka bir yerde yayınlanmış şekil, tablo, ya da metin bölümleri dahil etmek isterlerse telif hakkı sahiplerinden izin alınması ve bu izin belgelerinin yayınla beraber değerlendirmeye gönderilmesi gerekmektedir. Böyle bir belgenin eşlik etmediği her materyalin yazara ait olduğu kabul edilecektir.

Davetli (Talep üzerine yazılan) Derlemeler

Özet uzunluğu: 250 kelimeyi aşmamalıdır.

Makale uzunluğu: 4000 kelimeyi aşmamalıdır.

Kaynak sayısı: 100 kaynağı aşmamalıdır.

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Derlemeler, üzerine konuyla ilgili yeni bir hipotez ya da çalışma oturtulabilecek bir sonuç içermelidir. Literatür taraması metodlarını veya kanıt düzeyi yöntemlerini yayınlamayın. Derleme makaleleri hazırlayacak yazarların ilgili konuda önceden araştırma makaleleri yayımlamış olması gerekir. Çalışmanın yeni ve önemli bulguları sonuç bölümünde vurgulanır ve yorumlanmalıdır. Derlemelerde maksimum iki yazar olmalıdır.

Olgu Sunumları

Özet uzunluğu: 100 kelimeyi aşmamalıdır.

Makale uzunluğu: 1000 kelimeyi aşmamalıdır.

Kaynak sayısı: 15 kaynağı aşmamalıdır.

Olgu Sunumları aşağıdaki gibi yapılandırılmalıdır:

Özet: Olguyu özetleyen bir yapılandırılmamış özet (gereç ve yöntem, bulgular, tartışma gibi bölümlerin olmadığı).

Giriş: Kısa bir giriş (tavsiye edilen uzunluk: 1-2 paragraf).

Olgu Sunumu: Bu bölümde ilk tanı ve sonuç da dahil olmak üzere olgu ayrıntılı olarak anlatılır.

Tartışma: Bu bölümde ilgili literatür kısaca gözden geçirilir ve sunulan olgunun, hastalığa bakışımızı ve yaklaşımımızı nasıl değiştirebileceği vurgulanır.

Kaynaklar: Vancouver tarzı, (yukarıda 'Kaynaklar' bölümüne bakınız).

Teşekkür

Tablolar ve şekiller

Teknik Notlar

Özet uzunluğu: 250 kelimeyi aşmamalıdır.

Makale uzunluğu: 1200 kelimeyi aşmamalıdır.

Kaynak Sayısı: 15 kaynağı aşmamalıdır.

Teknik Notlar, yeni bir cerrahi tekniğin açıklanmasını ve az sayıda olguda uygulanmasını içermektedir. Büyük bir atılım/değişikliği temsil eden bir tekniğin sunulması durumunda tek bir olgu yeterli olacaktır. Hastanın takip ve sonucu açıkça belirtilmelidir.

Teknik Notlar aşağıdaki gibi organize edilmelidir:

Özet: Aşağıdaki gibi yapılandırılmalıdır:

Amaç: Bu çalışmanın amacı nedir?

Yöntem: Kullanılan yöntemlerin, hastalar ya da sağlıklı gönüllülerin veya hayvanların tanımı, malzemeler hakkında kısa bir açıklama.

Bulgular: Ana bulgular nelerdir?

Sonuç: Bu çalışmanın ana sonuçları ve etkileri nelerdir?

Endikasyonları

Yöntem

Diğer yöntemlerle karşılaştırılması: Avantaj ve dezavantajları, zorluklar ve komplikasyonlar.

Kaynaklar: Vancouver tarzı (yukarıda 'Kaynaklar' bölümüne bakınız)

Teşekkür

Tablolar ve şekiller; alt yazıları dahil

Video Makale

Makale Uzunluğu: 500 kelimeyi aşmamalıdır.

Kaynak Sayısı: 5 kaynağı aşmamalıdır.

Tanıyı, uygulanan cerrahi tekniği ve sonucu açıklayarak olguyu kısaca özetleyiniz. Uygun şekilde adlandırılmış ve referans edilmiş video materyalleri ile tüm önemli noktaları, örn; yeni cerrahi tekniği, belirtiniz. Materyaller, yazarların cerrahi tekniğini anlattıkları veya karşılaştıkları ilginç vakalardan oluşmalıdır.

Teknik Gereklilikler: Veriler, makale yükleme sırasında diğer dosyalarla birlikte eklenmelidir. Video süresinin 10 dakikayı geçmemesi kaydıyla dosya boyutu maksimum 350 MB olmalı ve 'MOV, MPEG4, AVI, WMV, MPEGPS, FLV, 3GPP, WebM' formatlarından biri kullanılmalıdır. 100 MB'yi aşmayan video dokümanları sisteme yüklenebilir. Daha büyük video dokümanları için lütfen iletisim@galenos.com.tr adresinden bizimle iletişime geçiniz. Tüm video seslendirmeleri İngilizce olmalıdır. Video atıfları, Şekil veya Tablo atıfları ile aynı biçimde kullanılmalıdır. Örneğin; "….Bunu gerçekleştirmek için, yeni bir cerrahi teknik geliştirdik (Video 1)." Video materyallerinde isim ve kurumlar yer almamalıdır. Kabul edilen makalelerin video materyalleri online yayınlanacaktır.

Editöre Mektuplar

Makale uzunluğu: 500 kelimeyi aşmamalıdır.

Kaynak Sayısı: 10 kaynağı aşmamalıdır.

Türk Kolon ve Rektum Hastalıkları Dergisi'nde yayınlanan makaleler hakkında yorumlar memnuniyetle kabul edilir. Özet gerekli değildir, ancak lütfen kısa bir başlık ekleyiniz. Mektuplar bir şekil veya tablo içerebilir.

Editöryal Yorumlar

Makale uzunluğu: 1000 kelimeyi aşmamalıdır.

Kaynak Sayısı: 10 kaynağı aşmamalıdır.

Editöryal yorumlar sadece editör tarafından kaleme alınır. Editöryal yorumlarda aynı konu hakkında başka yerlerde yayınlanmış yazılar hakkında fikir veya yorumlar belirtilir. Tek bir yazar tercih edilir. Özet gerekli değildir, ancak lütfen kısa bir başlık ekleyiniz. Editöryal gönderimler revizyon/gözden geçirme talebine tabi tutulabilir. Editörler, metin stilini değiştirme hakkını saklı tutar.

Etik

Bu dergi, bilimsel kayıtların bütünlüğünü korumayı tahhüt etmektedir. Yayın Etik Komitesi (COPE) üyesi olarak, dergi olası olumsuz davranışlarla nasıl başa çıkılacağı konusunda Yayın Etik Komitesi (COPE) kılavuzlarını takip edecektir.

Yazarlar araştırma sonuçlarını yanlış sunmaktan; derginin güvenilirliğine, bilimsel yazarlık profesyonelliğine ve en sonunda tüm bilimsel çabalara zarar verebileceğinden dolayı, sakınmalıdır. Araştırma bütünlüğünün sürdürülmesi ve bunun sunumu, iyi bilimsel uygulama kurallarını takip ederek başarılır. Bu da şunları içerir:

- Yazılı eser değerlendirilmek üzere eş zamanlı birden fazla dergiye gönderilmemelidir.

- Yazılı eser daha önceki bir eserin geliştirilmesi olmadıkça, daha önce (kısmen ya da tamamen) yayınlanmamış olmalıdır. [Metnin yeniden kullanıldığı imasından kaçınmak için tekrar kullanılabilir materyallerde şeffaflık sağlayın ("self-plagiarism""kişinin kendinden intihali")].

- Tek bir çalışma; sunum miktarını arttırmak için birçok parçaya bölünmemeli ve zaman içinde aynı ya da çeşitli dergilere gönderilmemelidir. (örneğin "salam-yayıncılık" "salamizasyon").

- Veriler, sonuçlarınızı desteklemek için fabrikasyon (uydurma) ya da manüple edilmiş olmamalıdır.

- Yazarın kendine ait olmayan hiçbir veri, metin veya teori kendininmiş gibi sunulmamalıdır (intihal). Diğer eserlerin kullanımı, (eserin birebir kopyalanması, özetlenmesi ve/veya başka kelimeler kullanarak açıklanmasını da içeren) ya telif hakkı korunacak şekilde izin alınarak ya da tırnak işareti içinde birebir kopyalanarak uygun onay ile kullanılmalıdır.

Önemli not; Türk Kolon ve Rektum Hastalıkları Dergisi intihal taramak için bir program (iThenticate) kullanmaktadır.

- Eser sunulmadan önce sorumlu makamlardan ve çalışmanın yapıldığı enstitü/kuruluşlardan-zımnen veya açıkça-onay alınmasının yanı sıra tüm yazarlardan açıkça onay alınmış olmalıdır.

- Sunulan eserde yazar olarak ismi olanların, bilimsel çalışmaya yeterince katkısı olmuş olmalıdır ve ortak mesuliyet ve sorumluluğu olmalıdır.

Bununla beraber:

- Yazarlık veya yazarların sıra değişiklikleri eserin kabulünden sonra yapılamaz

- Yazının revizyon aşamasında, yayın öncesi veya yayınlandıktan sonra yazar isim eklenmesi veya çıkarılması istemi; ciddi bir konudur ve geçerli sebepler olduğunda değerlendirilebilir. Yazar değişikliği gerekçesi; haklı gerekçeli, inandırıcı ve sadece tüm yazarların yazılı onayı alındıktan sonra; ve yeni/silinmiş yazarın rolü silme hakkında ikna edici ayrıntılı bir açıklama ile kabul edilebilir. Revizyon aşamasında değişiklik olması halinde, bir mektup revise edilmiş yayına eşlik etmelidir. Yayına kabul edildikten veya yayınlandıktan sonra değişiklik olması halinde, bu istek ve gerekli dökümantasyonun yayıncı yoluyla editöre gönderilmesi gerekmektedir. Gerek görüldüğünde bu isteğin gerçekleşmesi için daha fazla doküman talep edilebilir. Değişikliğin kabul veya red kararı dergi editörü insiyatifindedir. Bu nedenle, yayının gönderilmesi aşamasında yazar/yazarlar; gönderecekleri ilgili yazar grubunun isim doğruluğundan sorumludur.

- Yazarlardan sonuçların geçerliliğini doğrulamak amacıyla verilerin ilgili belgelerinin istenmesi halinde bu verileri göndermek için hazır bulundurulmalıdır. Bunlar, ham veri, örnekler, kayıt vb. şeklinde olabilir.

Görevi kötüye kullanma ya da suistimal şüphesi halinde dergi COPE yönergeleri izleyerek bir soruşturma yürütecektir. Soruşturmanın ardından, iddia geçerli görünüyorsa, yazara sorunu gidermek için bir fırsat verilecektir.

Usulsüzlük, şüphe seviyesinde kaldığında; dergi editörü aşağıdaki yollardan birine başvurabilir;

- Makale halen şüpheli ise, reddedilip yazara iade edilebilir.

- Makele online yayınlanmış ise; hatanın mahiyetine bağlı olarak ya yazım hatası olarak kabul edilecek ya da daha ciddi durumlarda makale geri çekilecektir.

- Hatalı yayın ve geri çekme durumlarında açıklayıcı not yayınlanır ve yazarın kurumu bilgilendirilir.

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İnsan ve Hayvan Araştırmaları

İnsan Hakları Beyannamesi

İnsan katılımlı araştırmalar; 1964 Helsinki Deklarasyonu'na ve sonrasında yayımlanan iyileştirici ilkelere uygun olmalıdır ve yazarlar tarafından kurumsal ve/veya ulusal etik kurul komitelerine başvurulup onay alınmış olduğu beyan edilmelidir.

Araştırmanın 1964 Helsinki Deklarasyonu veya kıyaslanabilir standartlara göre yürütülmesi ile ilgili şüphe durumunda, yazarlar bu durumun nedenlerini açıklamak zorundadır ve bağımsız etik kurulları veya diğer değerlendirme kurulları aracılığıyla şüphelerin giderilmesi gerekmektedir.

Aşağıda belirtilen durumlar yazı içerisinde "Kaynaklar" bölümünden önce yer almalıdır:

Etik Kurul Onayı: "Çalışmada insanlara uygulanan tüm prosedürler kurumsal ve ulusal araştırma kurullarının etik standartlarına, 1964 Helsinki Deklarasyonu'na ve sonrasında yayımlanan iyileştirici ilkelere uygun olmalıdır."

Retrospektif çalışmalarda, aşağıda belirtilen cümle yer almalıdır.

"Bu tür çalışmalarda yazılı onam gerekmemektedir."

Hayvan Hakları Beyannamesi

Araştırmalarda kullanılan hayvanların refahına saygı gösterilmelidir. Hayvan deneylerinde, yazarlar hayvanların bakımında ve kullanımında uluslararası, ulusal ve/veya kurumsal olarak oluşturulmuş kılavuzlara uymalıdır ve çalışmalar için kurumdaki veya çalışmanın yapıldığı veya yürütüldüğü merkezdeki (eğer böyle bir merkez varsa) Klinik Araştırmalar Etik Kurulundan onay alınmalıdır. Deneysel hayvan çalışmalarında "Guide for the care and use of laboratory animals http://oacu.od.nih.gov/regs/guide/guide.pdf doğrultusunda hayvan haklarını koruduklarını belirtmeli ve kurumlarından etik kurul onay raporu almalıdırlar.

Hayvanlar ile yürütülen çalışmalarda, aşağıda belirtilen durumlar yazı içerisinde 'Kaynaklar' bölümünden önce yer almalıdır:

Etik Kurul Onayı: "Hayvanların bakımı ve kullanımı ile ilgili olarak uluslararası, ulusal ve/veya kurumsal olarak oluşturulmuş tüm kılavuzlara uyulmuştur."

Eğer uygun bulunduysa (komitenin bulunduğu merkezde): "Hayvan çalışmalarında yapılan tüm uygulamalar kurumsal veya çalışmanın yürütüldüğü merkez tarafından belirlenmiş etik kurallara uyumludur."

Eğer makale insan ya da hayvan katılımlı bir çalışma değilse, lütfen aşağıda yer alan uygun durumlardan birini seçiniz:

"Bu makalenin yazarları insan katılımlı bir çalışma olmadığını bildirmektedir."

"Bu makalenin yazarları çalışmada hayvan kullanılmadığını bildirmektedir."

"Bu makalenin yazarları insan katılımlı veya hayvan kullanılan bir çalışma olmadığını bildirmektedir."

Bilgilendirilmiş Onam

Bütün bireyler ihlal edilemeyecek kişisel haklara sahiptir. Çalışmada yer alan bireyler, elde edilen kişisel bilgilere, çalışmada geçen görüşmelere ve elde edilen fotoğraflara ne olacağı konusunda karar verebilme hakkına sahiptir. Bundan dolayı, çalışmaya dahil etmeden önce yazılı bilgilendirilmiş onam alınması önemlidir. Bilimsel olarak gerekli değilse ve katılımcılardan (veya katılımcı yetkin değilse ebeveynlerinden veya velilerinden) basılması için yazılı onam alınmadıysa, katılımcılara ait detaylar (isimleri, doğum günleri, kimlik numaraları ve diğer bilgileri) tanımlayıcı bilgilerini, fotoğraflarını ve genetik profillerini içerecek şekilde yazılı formda basılmamalıdır. Tam gizlilik sağlanmasının zor olduğu durumlarda, bilgilendirilmiş onam formu şüpheyi içerecek şekilde düzenlenmelidir. Örneğin fotoğrafta katılımcıların göz kısmının maskelenmesi gizlilik açısından yeterli olmayabilir. Eğer karakteristik özellikler gizlilik açısından değiştirilirse, örneğin genetik profilde, yazar yapılan değişikliğin bilimsel olarak sorun oluşturmadığından emin olmalıdır.

Aşağıdaki ifade belirtilmelidir:

Bilgilendirilmiş Onam: "Çalışmadaki tüm katılımcılardan bilgilendirilmiş onam alınmıştır."

Eğer makalede katılımcıların tanımlayıcı bilgileri yer alacaksa, aşağıdaki ifade belirtilmelidir:

"Makalede kişisel bilgileri kullanılan tüm katılımcılardan ayrıca bilgilendirilmiş onam alınmıştır."

DEĞERLENDİRME SÜRECİ

Türk Kolon ve Rektum Hastalıkları Dergisi'ne gönderilen tüm yazılar, sisteme yüklendikten sonra ilk önce editöryal kurul tarafından derginin amaç ve hedeflerine uygunluk ve temel şartları sağlama yönünden değerlendirilecektir. Yazılar, konusunda uzman dergi hakemlerine değerlendirilmek üzere gönderilecektir. Tüm kabul edilen yazılar yayımlanmadan önce, istatistik ve İngiliz dili konusunda uzman editörler tarafından değerlendirilecektir. Sayfaların ilk gözden geçirilmesinden sonra, hakem yorumları ön karar vermek için Editör'e gönderilecektir. Bu aşamada, ilk değerlendirmede bulunanların düşüncesi doğrultusunda, yazı kabul edilebilir, reddedilebilir veya yazıda düzeltme yapılması istenebilir. İlk değerlendirme sonrasında değerli bulunan makaleler için genellikle düzeltme istenir. Düzeltilen makaleler ilk karardan sonraki 2 ay içerisinde tekrar dergiye gönderilmelidir. Süre uzatmaları yardımcı editörden 2 aylık süre bitmeden en az 2 hafta önce talep edilmelidir. Türk Kolon ve Rektum Hastalıkları Dergisi tarafından, 2 aylık düzeltme süresi sona erdikten sonra, yazı kabul edilmeyecektir. Düzeltme yapılan yazılar sisteme tekrar yüklendikten sonra değerlendirilmek üzere (genellikle ilk değerlendirmeyi yapan hakeme) gönderilecektir. Sonuç olarak yayımlanma kararı verildikten sonra, baskı öncesi Teknik Editör tarafından son kez değerlendirilecektir ve iletişim kurulacak olan yazara gözden geçirme ve son düzenlemeleri yapmak üzere işaretlenmiş bir nüshası elektronik ortamda gönderilecektir.

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Revize edilmiş bir versiyonu gönderirken yazar, yorumcular tarafından ele alınan her konuyu ayrıntılı olarak açıklamalı ve nokta nokta ayrıntılı olarak "yorumlara yanıt" sunmalıdır ve ardından belgenin açıklamalı kopyası bulunmalıdır (her yorumcunun yorumu nerede bulunabilir, yazarın cevap ve satır numaraları gibi yapılan değişiklikler).

Bunun yanı sıra ana revize yazı, kabul mektubu tarihinden itibaren 30 gün içinde teslim edilmelidir. Yazının revize edilmiş versiyonunun tanınan süre içinde verilmemesi durumunda, revizyon seçeneği iptal edilebilir. Yazar(lar) ek sürenin gerekli olduğunu düşünüyorsa, ilk 30 günlük süre bitmeden, uzatmayı talep etmelidir.

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REVIEW

What is the Role of the Neutrophil: Lymphocyte Ratio in Colorectal Cancer?

Kolorektal Kanserde Nötrofil:Lenfosit Oranının Rolü Nedir?

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ABSTRACT

The composition and cell-to-cell interactions of the peripheral immune compartment are known to influence outcomes in multiple disease entities, both neoplastic and otherwise. There is an ongoing search for a reliable biomarker in the peripheral immune compartment that can predict outcomes in colorectal cancer, given its high mortality rates. The neutrophil:lymphocyte ratio (NLR) has been suggested as one such marker, given its accessibility. This review discusses the current evidence behind the use of the NLR in predicting different aspects of colorectal cancer (CRC) behaviour, from survival to recurrence, metastasis, tumour biology, response to therapy and CRC complications. We also discuss the debate in the literature surrounding the use of other peripheral immune compartment biomarkers compared with the NLR for this purpose and ideas for future research.
Keywords: Colorectal cancer, neutrophil: lymphocyte ratio, survival

ÖZ

Periferal immün kompartmanının kompozisyonunun ve hücreler arası etkileşimlerinin, hem neoplastik hem de neoplastik olmayan birçok hastalıkta sonlanımı etkilediği bilinmektedir. Periferik bağışıklık kompartmanında, yüksek mortalite oranı olan kolorektal kanserdeki sonlanımı tahmin edebilen güvenilir bir biyobelirteç için devam eden bir arayış vardır. Nötrofil:lenfosit oranının (NLO) kolay erişilebilirliği göz önüne alındığında, böyle bir belirteç olabileceği öne sürülmüştür. Bu derleme, sağkalım, nüks, metastaz, tümör biyolojisi, tedaviye yanıt ve komplikasyonlar gibi kolorektal kanser davranışının farklı yönlerini tahmin etmede NLO kullanımının arkasındaki mevcut kanıtları tartışmaktadır. Literatürdeki veriler ışığında, NLO'ya kıyasla diğer periferik immün kompartman biyobelirteçlerinin bu amaçla kullanımı tartışılacak ve gelecekteki araştırmalar için fikirler üzerinde durulacaktır.
Anahtar Kelimeler: Kolorektal kanser, nötrofil: lenfosit oranı, sağkalım

Introduction

Colorectal cancer (CRC) is the world's third most common cancer and the fourth most common cause of cancer mortality. Blood-based biomarkers are attractive for the management of this disease, given their ease of access and amenability to repetitive sampling. Low-grade, chronic inflammation has long been associated with a range of diseases and poor outcomes. Many different markers of inflammation have been described over the years; however, apart from the erythrocyte sedimentation rate and plasma viscosity, these are not used in routine clinical assessment. One simple marker that has been widely described, the neutrophil:lymphocyte ratio (NLR), has been generally overlooked in clinical practice. The aim of this review is to discuss its role as a biomarker in CRC, compare its value against other biomarkers and encourage its wider adoption into mainstream clinical practice.

What is the Neutrophil:Lymphocyte Ratio (NLR)?

The NLR is an inexpensive, readily available marker, which is proposed to provide additional risk stratification beyond other more traditional risk scores. Calculation of the NLR simply involves dividing the peripheral blood neutrophil count by the lymphocyte count on a full blood count. The NLR has been suggested as a good marker of systemic low-grade inflammation,[1] which is associated with a poorer outcome in many disease types.

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The role of the NLR in Colorectal Cancer (CRC)

The concept of the influence of the NLR in CRC is not new. Back in 2005, a landmark study by Walsh et al.[2] identified that a NLR >5 (i.e. neutrophils present at 5 times the number of lymphocytes) was correlated with poor overall and cancer-specific survival in univariate analyses. Other studies have set a lower value of 2 or 3 to dichotomise populations, thus increasing the number of individuals in the poorer prognosis group.

This observation has since been replicated by subsequent studies (Table 1) and supported by pooled analysis of a meta-analysis.[3] With respect to single studies, there are many examples where this effect of NLR on CRC survival outcomes has been replicated. In patients undergoing elective resection of colorectal cancer, a lower postoperative NLR was found to correlate with longer cancer-specific and disease-free survival.[4] Similarly, another study[5] found that a high preoperative NLR (>3) in colon cancer patients was associated with worse disease-free survival and cancer-specific death [heart ratio (HR) 1,377 95% confidence interval (CI) 1,104-1,717, p=0.014]. It is of note that this difference was larger in colon cancer than in rectal cancer patients. Consistently, another study investigating patients with early-stage colorectal cancer[6] who were candidates for curative surgery found that there was a statistically significantly poorer outcome in 5-year disease-free survival and cancer-specific survival in those with a high NLR compared with those with a low NLR. Following a similar pattern of findings, a study looking at stage II colon cancer[7] found that an elevated NLR was an independent predictor of poorer overall survival but not disease-free survival when analysed using Cox regression analysis. A study conducted at our institute[8] found that the NLR predicted disease-free and overall survival in our patients with primary colorectal malignancy.

To summarise an overview of the literature, a systematic review[9] identified higher 3-year and 5-year survival rates in patients with a low NLR compared with those with a high NLR (77.8% vs 61.8%), and the range of cut-off values used to define the high- and low-NLR groups varied from 2 to 5.

NLR in Metastatic Colorectal Cancer

Liver metastases develop in up to 40% of patients with a high recurrence rate, even after primary bowel resection. The NLR is suggested to be one such marker in multiple studies (Tables 2, 3).

A systematic review[9] identified multiple studies reporting survival results in patients with CRC and liver metastases. Similar to the pattern observed in non-metastatic disease, the low-NLR group had a better 3-year survival rate compared with the high NLR group (64.74% vs 45.1% respectively). This systematic review identified multiple studies showing a differential 5-year survival rate in this patient group, the 5-year survival being higher in patients with a low NLR than in those with a high NLR (47.6% vs 27%, respectively). A further meta-analysis, including 1,685 patients, found that an elevated pre-treatment NLR was associated with poor overall and recurrence-free survival in patients with colorectal liver metastasis.[10] A significant negative finding of the study was that there was no correlation between NLR and the timing and number of metastases at the time of diagnosis.

Using a cut-off value of 5, Halazun et al.[11] found that an increased NLR decreased the 5-year survival rate and risk of recurrence in patients who underwent resection for colorectal liver metastases. Neal et al.[12] found that in a multivariable analysis, a high NLR was independently associated with major infectious complications after hepatectomy, which may be an explanation for the worse survival rates in this patient group observed in previous studies.

A prospective, multicentre randomised Italian Trial in Advanced Colorectal Cancer[13] randomised patients to receive first-line chemotherapy with or without bevacizumab (an anti-angiogenic monoclonal antibody) and found that NLR was a marker of progression-free survival and overall survival in patients with metastatic colorectal cancer. Moreover, those with a high NLR treated with bevacizumab and chemotherapy had a worse overall survival than those treated with chemotherapy alone, although the pathophysiological explanation for this was unclear.

NLR and the Tumour Recurrence Rate

CRC can recur locally at multiple sites, including intra-abdominal lymph nodes, the peritoneum and the retroperitoneum or anastomosis. Higher NLR values are associated with a higher tumour recurrence rate in patients with stage II and stage III disease.[9] A study based in Leeds[8] found that a NLR >/=5 was correlated with greater disease recurrence. The above finding was in agreement with a previously published paper[14], which found that a NLR >5 was a significant and independent factor predictive of recurrent colorectal cancer, when all stages of CRC were included. In a study population of patients with stage IIA colon cancer undergoing curative resection, an elevated NLR was found to be an independent predictor of worse recurrence-free survival[7], with a 5-year recurrence-free survival of 91.4% in those with a normal NLR and 63.8% for those with an elevated NLR.

NLR and Tumour Biology

A systematic review identified multiple studies showing that poorly differentiated tumours were more likely to be correlated with higher NLR values[9] This same systematic review also identified multiple studies which showed a significant correlation between a high NLR and an advanced tumour stage.

Table 1. A summary of the literature discussing NLR and survival in patients with non-metastatic colorectal cancer

Author	Title	Source	Sample size	NLR cut off	Findings
Li et al.[3]	Prognostic significance of elevated preoperative neutrophil-to-lymphocyte ratio for patients with colorectal cancer undergoing curative surgery: A meta-analysis	Medicine (Baltimore)	5897	2.3-5	An elevated NLR correlates with lower overall survival, disease-free survival, recurrence-free survival and disease-specific survival after treatment.
Kubo et al.[4]	Impact of the perioperative neutrophil-to-lymphocyte ratio on the long-term survival following an elective resection of colorectal carcinoma	International Journal of Colorectal Disease	524	NLR value was calculated prior to curative resection, on the first postoperative day and the third or fourth postoperative day: Patients with low median NLR value at all time points were given a score of 0, whereas those with a high median NLR at all time points were assigned a score of 3. Following the above scoring, those with a score of 0 or 1 were classed as the low perioperative NLR group, whereas the high perioperative NLR group had scores of 2 or 3. The cut-off value for low and high NLR levels are as follows: Median NLR pre-op 2.29 Median NLR postoperative day 1: 7.90 Median NLR: Postoperative day 3: 5.10_	A high perioperative NLR is an independent risk factor for both cancer-specific and disease-free survival.
Chiang et al.[5]	Can neutrophil-to-lymphocyte ratio predict the survival of colorectal cancer patients who have received curative surgery electively?	International Journal of Colorectal Disease	3857	3	A NLR >3 was associated with worse 5 year disease-free survival, with a larger difference in colonic vs rectal cancer. An elevated NLR was also associated with clinicopathological factors related to advanced diseases.
Shin et al.[6]	Preoperative neutrophil-to-lymphocyte ratio predicts survival in patients with T1-2N0 colorectal cancer	Journal of Surgical Oncology	269	3	Preoperative NLR is a prognostic factor for disease-free survival and cancer-specific survival in stage I colorectal cancer patients.
Hung et al.[7]	Effect of preoperative neutrophil-lymphocyte ratio on the surgical outcomes of stage II colon cancer patients who do not receive adjuvant chemotherapy	International Journal of Colorectal Disease	1040	5	Cox regression analysis revealed that an elevated NLR is an independent predictor of overall survival but not disease-free survival.
Pine et al.[8]	Systemic neutrophil-to-lymphocyte ratio in colorectal cancer: the relationship to patient survival, tumour biology and local lymphocytic response to tumour	British Journal of Cancer	358	5	An elevated NLR predicts disease-free and overall survival and more advanced tumour biology. The NLR is not associated with tumour mutation status.

NLR: Neutrophil:lymphocyte ratio

Table 2. A summary of the literature discussing NLR and prognosis in metastatic colorectal cancer patients

Author	Title	Source	Sample size	NLR cut off	Findings
Haram et al.[9]	The prognostic value of neutrophil-to-lymphocyte ratio in colorectal cancer: A systematic review	Journal of Surgical Oncology	10,259	5	A NLR >5 is associated with worse 3- and 5-year survival in CRC patients with liver metastases.
Tang et al.[10]	Prognostic significance of neutrophil-to-lymphocyte ratio in colorectal liver	PLoS One	1,685	2.5-5	An elevated NLR is associated with poor overall survival and recurrence-free survival in colorectal patients with liver metastases.
Halazun et al.[11]	Elevated preoperative neutrophil-to-lymphocyte ratio predicts survival following hepatic resection for colorectal liver metastases	European Journal of Surgical Oncology	440	5	An elevated NLR is associated with a worse 5-year survival and tumour recurrence.
Neal et al.[12]	Preoperative systemic inflammation and infectious complications after resection of colorectal liver metastases	Archives of Surgery	202	5	A high NLR is associated with postoperative infectious morbidity and overall and disease-free survival on univariate analysis.
Passardi et al.[13]	Inflammatory indexes as predictors of prognosis and bevacizumab efficacy in patients with metastatic colorectal cancer	Oncotarget	289	3	The correlation between lower NLR levels and improved overall and progression- free survival was significantly associated with the addition of bevacizumab to first-line chemotherapy.

NLR: Neutrophil:lymphocyte ratio, CRC: Colorectal cancer

Table 3. A summary of the literature discussing the NLR and the response to oncological treatment

Author	Title	Source	Sample size	NLR cut off	Findings
Kaneko et al.[21]	Elevated Neutrophil-to-Lymphocyte Ratio Predicts Poor Prognosis in Advanced Colorectal Cancer Patients Receiving Oxaliplatin-Based Chemotherapy.	Oncology	50	4.0	An elevated NLR is associated with overall survival and the disease response rate in patients with advanced or recurrent CRC receiving oxaliplatin-based combination chemotherapy.
Dell'Aquila et al.[22]	Prognostic and predictive role of neutrophil/lymphocytes ratio in metastatic colorectal cancer: a retrospective analysis of the TRIBE study by GONO.	Annals of Oncology	508	3	The NLR had prognostic value in predicting overall survival, progression-free survival and the response rate in patients treated with FOLFIXIRI and bevacizumab.
Kishi et al.[23]	Blood neutrophil-to-lymphocyte ratio predicts survival in patients with colorectal liver metastases treated with systemic chemotherapy.	Annals of Surgical Oncology	200	5	In patients with colorectal liver metastases treated with chemotherapy and resection, a NLR >5 was an independent predictor of 5-year survival. In this patient group, preoperative chemotherapy normalised the NLR and improved survival. In the non-resection group receiving chemotherapy only, an NLR >5 was an independent predictor of worse 3-year survival.
Botta et al.[24]	1439 POSTER Treatment-related Changes in Systemic Inflammatory Status, Measured by Neutrophil-to-lymphocyte Ratio, is Predictive of Outcome in Metastatic Colorectal Cancer Patients.	European Journal of Cancer	247	3	NLR >3 was a significant prognostic factor for overall and progression-free survival in patients with metastatic colorectal cancer receiving first-line chemotherapy. The reduction to a NLR <3 following treatment was associated with a longer time to event.

Table 3. continued

Chua et al.[25]	Neutrophil/lymphocyte ratio predicts chemotherapy outcomes in patients with advanced colorectal cancer.	British Journal of Cancer	349	5	In patients with unresectable metastatic colorectal cancer undergoing first- line palliative chemotherapy, the NLR was predictive of overall and progression-free survival. Normalisation of NLR following treatment could improve progression-free survival.
Turnbull et al.[26]	Chemotherapy to reverse diminished immune responses (IRs) associated with a raised neutrophil–lymphocyte ratio (NLR) in patients with advanced colorectal cancer (aCRC).	Journal of Clinical Oncology	29	5	A high NLR is associated with reduced overall survival and measured IRs in patients with advanced colorectal cancer. The NLR normalises after 6 weeks of first-line chemotherapy, and their depressed IRs can be reversed by chemotherapy.
Wood et al.[27]	Derived neutrophil-to-lymphocyte ratio as a prognostic factor in patients with advanced colorectal cancer according to RAS and BRAF status: a post-hoc analysis of the MRC COIN study.	Anticancer Drugs	1603	dNLR cut-off was 2.2	In patients with metastatic colorectal cancer, a dNLR <2.2 was associated with better overall survival in patients in all mutation groups, but it did not predict the survival benefit from the addition of cetuximab to oxaliplatin.
Chen et al.[28]	Cytokine profile and prognostic significance of high neutrophil-lymphocyte ratio in colorectal cancer.	British Journal of Cancer	1180	5	The NLR is a prognostic factor across multiple settings of CRC, including surgically resected stage II/III CRC, metastatic colorectal cancer with liver metastases after hepatectomy and previously untreated and refractory metastatic CRC. In a cohort of patients with colorectal cancer, patients with liver metastases who were refractory to standard treatments such 5 fluorouracil, NLR is not associated with tumour mutation status.
Grenader et al.[29]	Derived neutrophil-lymphocyte ratio is predictive of survival from intermittent therapy in advanced colorectal cancer: a post-hoc analysis of the MRC COIN study.	British Journal of Cancer	1630	dNLR >/=2.22	The dNLR can predict survival in patients undergoing both continuous and intermittent chemotherapy in advanced colorectal cancer. However, the dNLR does not add to the platelet count in the selection of patients who would benefit from continuous rather than intermittent therapy.
Shen et al.[32]	Baseline neutrophil-lymphocyte ratio (≥2.8) as a prognostic factor for patients with locally advanced rectal cancer undergoing neoadjuvant chemoradiation.	Radiation Oncology	224	2.8	The baseline NLR can predict overall survival in patients with locally advanced rectal cancer undergoing neoadjuvant chemoradiation, but it did not predict the response to treatment.
Hodek et al.[33]	Neoadjuvant chemoradiotherapy of rectal carcinoma: Baseline haematologic parameters influencing outcomes.	Strahlentherapie und Onkologie	173	2.8	NLR was a prognostic factor for overall survival and primary tumour downstaging (treatment response) in patients with locally advanced rectal cancer treated with neoadjuvant chemoradiotherapy.
Carruther et al.[34]	Systemic inflammatory response is a predictor of outcome in patients undergoing preoperative chemoradiation for locally advanced rectal cancer.	Colorectal Disease	115	5	An NLR >/=5 was associated with decreased overall survival, time to local recurrence and worse disease-free survival in patients with locally advanced rectal cancer who had preoperative chemoradiation.

NLR: Neutrophil:lymphocyte ratio

A study conducted on patients with stage I-III CRC undergoing curative cancer[5] found that an elevated NLR was associated with more aggressive clinicopathological factors such as increased size, tumour stage, elevated CEA, low albumin, the presence of disease complications and non-abdominal morbidity.

Pine et al.[8] found that an elevated NLR was associated with a higher stage, a greater incidence of extramural venous invasion as well as lymph node metastasis. In contrast, a lower NLR was associated with a less aggressive phenotype, for example, they had a pronounced lymphocytic reaction at the invasive margin, associated with a better prognosis.

The NLR and Mismatch Repair Status

Microsatellites are short, repetitive stretches of DNA interspersed within the whole genome and are susceptible to high rates of mutation. A unique, hypermutable phenotype known as microsatellite instability (MSI-H) results from impaired DNA mismatch repair. Tumours displaying high levels of MSI-H have two molecular types: Lynch syndrome, which occurs from germline mutations of *MMR* genes, and sporadic colorectal cancers, which arise from epigenetic alterations of the hMLH1 promoter. Tumours displaying loss of MMR protein are known as MMR deficient (dMMR), whereas those with intact MMR protein expression are known as MMR proficient (pMMR), with dMMR tumours having a better prognosis. We know that dMMR tumours have a more favourable local immune response.[15] Several mechanisms have been suggested to link the systemic inflammatory response and MMR status. Llosa et al.[16] found that dMMR tumours have a high infiltration with CD8+ T lymphocytes and interferon gamma-producing Th1-cells, leading to an immunologically active anti-tumour micro-environment. Counterbalancing this, MSI tumours had differentially high expression of a number of immune checkpoint proteins e.g. PD1, PDL1, CTLA4, LAG3 and IDO, all of which act as a brake on the immune response to the tumour, making this patient group good candidates for immunotherapy. An alternative hypothesis[17] is that chronic inflammation can lead to dMMR colorectal cancers though IL6 production, which may change the localisation of human MutS homolog 3 and induce tumours with the dMMR phenotype. Pine et al.[8] failed to find a correlation between MMR status and NLR, whereas Park et al.[18] found that dMMR patients had higher neutrophil counts. This inconsistency led He et al.[19] to explore the relationship between NLR MMR status and survival. In agreement with Park et al.[18], they found that NLR and C-reactive protein (CRP) were more likely to be raised in dMMR patients with no distant metastases; however, this correlation was stage dependent. With respect to survival data, NLR was not found to be significantly correlated with disease- free and overall survival in dMMR patients, although it did predict survival in pMMR patients. A more recent study[20] found that among an array of markers of systemic inflammatory response, only a preoperative NLR >5 was associated with worse overall survival and greater recurrence in patients with dMMR CRC undergoing surgery. They also found an inversely proportional relationship between NLR and the local inflammatory response in this tumour group. Due to the above-described controversy in the literature on the prognostic effect of NLR in MSI tumours, this area should be a focus of future work.

NLR and the Response to Oncological Treatment in Colorectal Cancer

A study of patients with advanced CRC receiving palliative oxaliplatin-based chemotherapy found that an elevated NLR was independently associated with poorer overall survival in a multivariate analysis.[21] A high NLR was also associated with a lower objective response and disease control rate compared with the low-NLR group. An analysis of NLR levels conducted in patients enrolled into a multicentre phase III TRIBE trial[22], which randomised unresectable metastatic CRC patients to receive the triplet FOLFOXIRI plus bevacizumab or doublet FOLFIRI plus bevacizumab, found that patients with an elevated NLR (>3) had significantly shorter progression-free survival (HR=1.27, 95% CI=1.05-1.55, p=0.017). They also reported a better objective response rate (65% vs 53% p=0.006), progression-free and overall survival in the triplet plus bevacizumab group. These data not only support the choice of FOLFOXIRI plus bevacizumab as a preferable first-line treatment for this patient group but also suggest that NLR measurement may be a useful tool for better patient selection for those who would derive more benefit from this more intense chemotherapy regimen.

Kishi et al.[23] demonstrated that the NLR can be normalised by chemotherapy in 17 out of 25 patients with metastatic colorectal cancer, which also has an impact on survival, suggesting that this biomarker may be useful for predicting the response to chemotherapy. Another retrospective multicentre study[24] was concordant with the above finding that chemotherapy can normalise the NLR in metastatic CRC patients and consequently achieve a longer time to event for these patients when compared with the patient group whose NLR did not normalise following treatment. In a study of 349 patients with advanced colorectal cancer, Chua et al.[25] found that normalisation of the NLR following a single cycle of chemotherapy resulted in improved progression-free survival, leading to the idea that manipulation of the systemic inflammatory response can be of clinical benefit. This observation was supported by Turnbull et al.[26], who

found that depressed immune responses in patients with a high baseline NLR could be reversed after 6 weeks of first-line chemotherapy in patients with advanced colorectal cancer, with increased expression of PD-1 on natural killer cells as well as B cells and monocytes, suggesting the identification of this patient group as candidates for immunotherapy.

If a lymphocyte count has not been undertaken, then the derived NLR can be calculated from the following equation:

dNLR = Absolute neutrophil count/(white blood cell count-absolute neutrophil count)

Wood et al.[27] found that a dNLR <2.2 was associated with better overall survival compared with a dNLR >/=2.2 in patients receiving oxaliplatin-based chemotherapy in patients with metastatic CRC with RAS and BRAF mutations. The wider literature suggests that the association of high NLR with worse survival is more pronounced in patients with metastatic disease, probably reflecting a greater tumour burden and a more significant chronic inflammatory process. In agreement with a previous study[28], the correlation between NLR and survival is independent of the mutation group (with the mutations studied being KRAS, NRAS, BRAF, PIK3CA, PTEN loss and CpG Island Methylator Phenotype testing).

Grenader et al.[29] examined whether the dNLR could predict the effect of intermittent vs continuous chemotherapy in patients with advanced colorectal cancer. They found a strong association between dNLR and overall survival but concluded that it does not add to the prognostic value of the platelet count in selecting patients that would benefit from continuous vs intermittent therapy and therefore cannot be used to select patients for chemotherapy-free breaks. These findings add to the conclusions of the COIN trial[30], which had previously reported that patients with normal baseline platelet counts would be candidates for intermittent chemotherapy without a survival cost, whereas those with thrombocytosis (platelet count >400,000) would have better outcomes without a treatment break. The above suggests that the platelet count is a better predictor than dNLR in this regard.

Extrapolating to other oncological treatments, this time with reference to radiotherapy, a raised pre-treatment NLR was associated with significantly worse overall survival in patients with solid tumours with a pooled hazard ratio of 1.90 (95% CI=1.66-2.17, p<0.001).[31] This suggests that this biomarker may be useful for risk stratification for patient selection for more aggressive radiotherapy.

With respect to patients with locally advanced rectal cancer, an elevated baseline NLR was noted to predict poorer overall survival but failed to predict the response to treatment following neoadjuvant chemoradiation.[32] Hodek et al.[33] evaluated a large group of patients with locally advanced rectal adenocarcinoma who were exposed to neoadjuvant chemoradiation. They found that a NLR range between 2.2 and 2.8 produced a significantly better overall survival and response to treatment; however, the NLR did not have a significant influence on pathologic complete remission. This pattern of observation was replicated by Carruther et al.[34], who observed that an elevated NLR was a useful prognostic marker in patients treated with chemoradiation. It had predictive power for overall survival, time to local recurrence and disease-free survival.

Placing the above findings into the clinical context, we know that a tumour-free circumferential resection margin (CRM) is a key determinant of cancer outcome following rectal cancer surgery[35] Preoperative MRI staging is used to select patients for neoadjuvant chemoradiotherapy once it is established that a clear CRM is unlikely to be achieved with initial surgery. The above findings suggest that apart from radiology, the NLR may be an inexpensive, easily accessible biomarker that may provide further prognostic information regarding outcomes of preoperative chemoradiotherapy.

NLR and Postoperative Complications in Colorectal Cancer

Josse et al.[36] found that a NLR value of 2.3-5 was associated with the incidence of perioperative complications, of which wound infection was the most common (12%). The association between an elevated NLR and postoperative infectious complications was corroborated by Kubo et al.[4] Anastomotic dehiscence is a major postoperative complication of resectional surgery with high morbidity and mortality rates. A case control study[37] found that both CRP and NLR were significant predictors of anastomotic dehiscence. However, the granularity that this study provided was that NLR was not as effective as CRP in predicting anastomotic dehiscence, as it had a smaller area under the curve in receiver operating characteristic analysis.

Paliogiannis et al.[38] found that CRP had a high negative predictive value on postoperative day 4 in identifying patients who were unlikely to develop anastomotic leak and would be suitable for discharge. This study also found that the NLR value on postoperative day 4 was correlated with the incidence of anastomotic dehiscence as well as mortality and morbidity from this complication. However, in agreement with Walker et al.[37], this study also found that the accuracy of NLR based on receiver operating curve analyses had a poorer outcome, suggesting the inferiority of this biomarker in predicting anastomotic leakage compared with CRP.

NLR as a Component of the Wider Systemic Inflammatory Response

The exact understanding of what drives a high NLR remains to be elucidated. However, Motomura et al.[39] have demonstrated a link between the presence of tumour-associated macrophages (derived from splenic monocytes) and IL17-producing T-cells (in both the peritumoral region and the peripheral blood) and a high NLR. The mechanistic explanation behind interleukin (IL)17 and a high NLR may be that IL17 plays a significant role in neutrophil chemotaxis through the release of CCL2 and CXC chemokines. The authors also suggest an interaction between IL17-producing T-cells and tumour-associated macrophages in the production of the same family of chemokines that attract neutrophils.

Considering how NLR affects tumour immunology, an unpublished study at our institution has found a differential cytokine profile in CRC patients with NLR <5 compared with those with a NLR >5. Seven cytokines were found to be preferentially upregulated in the low-NLR group. These are IL-1beta, IL2, IL7, IL13, bFGF, interferon gamma and MIP-1 alpha. The cocktail of cytokine production in the low-NLR group is thought to skew the immune response to an anti-tumour Th1 phenotype in contrast to the pro-tumour environment of the Th2 type immune response in the NLR >5 group. In a separate cohort of patients with metastatic colorectal cancer, Chen et al.[28] found that a high NLR was associated with increased expression of IL-6, IL-8, IL-2Rα, hepatocyte growth factor, granulocyte-macrophage colony-stimulating factor and vascular epidermal growth factor. These functional drivers of an active systemic inflammatory response are associated with angiogenesis, inflammation and tumour growth promotion and found to be specifically linked to the NLR.

The NLR and the Microbiome

Apart from using the systemic inflammatory response in isolation to predict prognosis in colorectal cancer, there is the suggestion that NLR be used in conjunction with other prognostic parameters of CRC such as the gut bacterial landscape (the gut microbiome).

A previous study[40] observed that a more diverse gut microbial landscape, which is associated with a beneficial outcome in several conditions, is associated with a lower NLR, thus lending itself to the idea of manipulating the microbiome to alter the systemic immune response to cancer.

Mechanistic Explanations for the Prognostic Value of NLR in Colorectal Cancer

Tumour-related angiogenesis through vascular endothelial growth factor (VEGF) production has been suggested to be a mechanism through which neutrophils have a pro-tumour effect. Neutrophils can activate cytokines such as IL16, and this is thought to promote cell adhesiveness, invasion and migration.[41] Lymphocytopenia may signify depression of innate cellular immunity with a decrease in T4 helper lymphocytes and increase in T8 suppressor lymphocytes. This overall balance is tipped towards a pro-neoplastic process when the NLR is raised.[2]

The link between NLR and the response to radiotherapy in solid cancers such as CRC may be hypoxia. With neoplastic progression, the supply of oxygen and nutrients does not match the demand, leading to necrosis and subsequent release of inflammatory mediators that recruit inflammatory cells such as neutrophils. This pro-tumour effect of hypoxia may explain the prognostic role of high NLR in predicting the response to radiotherapy.

A Brief Summary of other Peripheral Serum Inflammatory Biomarkers in Colorectal Cancer[42]

C-reactive Protein Level (CRP)

This is an acute-phase protein produced by the liver that plays a role in the systemic inflammatory response. Multiple studies[43,44,45] have found that elevated CRP is correlated with recurrence after surgery for colorectal cancer.

The Glasgow Prognostic Score (GPS)

The GPS calculated from serum CRP and albumin is widely thought to reflect the systemic inflammatory response to cancer. In a cohort of 1,590 patients with primary colorectal adenocarcinoma[46], the authors found a predictive effect of GPS on long-term survival in multivariate analysis.

Platelet-to-lymphocyte Ratio (PLR)

Platelet aggregation and the release of platelet-derived proangiogenic mediators into the vasculature of the tumour micro-environment through degranulation is suggested to influence tumour growth. The findings from a metanalysis[47] indicate that a high PLR can be used as a predictor of overall survival and clinicopathological parameters such as tumour differentiation and depth of infiltration in patients with CRC, but not disease-free survival.

Carcinoembryonic Antigen (CEA)

This is an easily accessible peripheral blood marker whose postoperative level is routinely used as tumour marker for prognostication in colorectal cancer. In rectal cancer patients treated with neoadjuvant radiotherapy and chemotherapy, Toiyama et al.[45] found that elevated CEA was a predictor of poor overall survival. Another study[48] found that the blood CEA level was an independent predictive biomarker in patients with colorectal cancer.

Comparing Biomarkers in Colorectal Cancer

When comparing the superiority of one biomarker over another, Kwon et al.[49] found that PLR was better than

NLR as a prognostic marker in CRC (HR=1.971, p=0.021). Survival curve analysis showed a consistent pattern of progressively poorer survival associated with a larger PLR. Moreover, the PLR was also significantly reported to be related to a positive lymph node ratio, which is known to have prognostic significance in colorectal cancer. Therefore, this study concluded that PLR is the most significant predictor of survival and is related to a more advanced tumour biology, although it is of note that serum CEA also retained significance in this study.

In concordance with the above, a study by Szkandera et al.[50] supported the role of PLR in predicting time to recurrence in CRC patients undergoing curative resection. Bong et al.[51] simultaneously examined the prognostic influence of PLR, NLR and CEA in predicting survival in patients with colorectal peritoneal carcinomatosis treated operatively and with chemotherapy. In a multivariate analysis, only PLR retained significance in predicting 5-year overall survival.

However, the above findings were contradicted by Choi et al.[52] Only a limited number of studies have evaluated both the NLR and PLR in the same population of patients in colorectal cancer. The study found that a high NLR was a negative independent prognostic factor in CRC and predicted a worse recurrence-free and overall survival. Interestingly, this study failed to find a significant association between PLR and survival, although it is of note that Kwon et al.[49] used a different threshold for high PLR than this study. The findings of Choi et al.[52] contradict those of a meta-analysis[53] which found that PLR was a negative predictor of cancer survival (HR=1.60, 95% CI=1.35-1.90), although it is of note that this study included a heterogenous patient population with cancers of different parts of the GI tract and who were exposed to a variety of oncological treatments. In agreement with Choi et al.[52], Zhan et al.[54] found no significant correlations between PLR and clinicopathological characteristics or survival outcomes.

The differential prognostic influence of PLR on CRC is suggested to be due to a variety of factors. Apart from a lack of consensus regarding the optimal cut-off value for PLR, the heterogeneity in tumour specificity and underlying genetic and biological differences between the variety of patient populations used are cited as root causes of these differences, making a fair comparison between studies difficult.

Another study[55] compared NLR and CEA as prognostic biomarkers in colorectal cancer. They found that an NLR <5 was correlated with a better 5-year overall and disease-free survival. A NLR >5 was also associated with more aggressive tumour biology (poorer tumour differentiation and larger tumour size). This study also found that there was a direct correlation between NLR and CEA levels. Pooled results of this meta-analysis found that a NLR >5 was correlated with a CEA >5. Subsequently, it was identified that a CEA <5 was correlated with a better complete pathological response (downstaging and complete regression) after receiving oncological therapy. Overall, this study concluded that NLR and CEA were both independent prognostic factors in CRC and directly correlated with each other. A retrospective study[56] found that in a population of patients with colorectal cancer, that there was no overall correlation between the CEA and NLR, although they retain individual prognostic significance. On the other hand, Kim et al.[57] argue for the combined use of both CEA and NLR as prognostic markers for outcomes in CRC patients with liver metastases. Zhan et al.[54] also advocate for the combined used of CEA and NLR for prognostic assessment of CRC patients as a superior biomarker to the independent use of these prognostic markers alone.

Maeda et al[42] investigated whether combining the GPS and NLR with clinicopathological factors such as performance status and the extent of distant metastasis was useful. They found that the median survival time was significantly shorter at only 5 months in the high-risk group (consisting of patients with three or four prognostic factors) vs 21.5 months in the intermediate risk group (consisting of patients with one or two prognostic factors) and 37 months in the low-risk group (consisting of patients without any prognostic factors). They suggest that this may be a simple risk classification tool for optimising treatments for patients with advanced colorectal cancer.

The Role of NLR for All Cancers

A meta-analysis investigating the prognostic effect of NLR on a range of solid tumours found that it was consistently predictive of survival among a variety of cancers at various stages[58]. There was a differential role of NLR in survival in metastatic vs non-metastatic disease, which may also reflect differences in the underlying pathophysiology of the tumour burden or chronicity of the inflammatory process. There was a consistent effect of the NLR on cancer-specific survival, progression-free survival and disease-free survival across both the primary site of malignancy and the cancer stage.

The Utility of the Neutrophil:Lymphocyte Ratio in Entities Outside of Cancer

Epidemiological studies have demonstrated that chronic low-grade inflammation, measured by the NLR, is linked to a broad range of risk factors for cardiovascular disease such as diabetes mellitus, hypertension, metabolic syndrome, obesity and hyperlipidaemia.[59] The NLR has also been noted to be of prognostic significance in respiratory conditions such as COPD (in acute exacerbations, as a marker of

functional status and mortality)[60], pulmonary embolism (in predicting short- and long-term mortality)[61] and COVID-19 (predicting the likelihood of acute respiratory distress syndrome and the requirement for ventilation).[60,61,62] The NLR also has a role to play in neurological conditions, particularly in acute cerebral haemorrhage.[63] The above evidence suggests that NLR may be a biomarker that can predict outcomes in both neoplastic and non-neoplastic conditions, where the systemic immune response plays a role in the pathophysiology of the disease.

Conclusions, Controversies and Future Ideas

Studies have identified that NLR has a prognostic effect on multiple aspects of the disease course of those with colorectal cancer, both primary and metastatic. The time point of measurement of the NLR and the cut-off value of the NLR for classification of high and low groups was inconsistent between studies. Moreover, there is a differential effect of the NLR on colon vs rectal tumours. It has been suggested that the effect of NLR is more difficult to assess in rectal cancer patients due to the presence of confounding factors such as neoadjuvant or adjuvant radiotherapy, which makes survival analysis more complex. The pathophysiology of rectal cancers may also be different. For example, there is an anatomical difference in lymphatic drainage between colon and rectal cancer. More advanced lymphatic spread in rectal cancer may make curative surgery more challenging. These differences may explain the difference in the effect of elevated NLR in colon and rectal cancers.

It is of interest that tumour mutation status such as dMMR and pMMR may have a link with NLR, although its association with survival in this patient group is controversial.

Moreover, there is debate in the literature regarding the single best peripheral blood biomarker to use in colorectal cancer. There are studies arguing for the use of other biomarkers such as CRP over the NLR, particularly in cases of anastomotic leaks; however, there is a growing consensus for the use of combined use of biomarkers such as NLR, CEA, PLR and GPS.

The idea is that by predicting the poor outcome of patients with CRC, using the NLR, it may be possible to tailor their treatment to improve their outcomes. Some have suggested the use of COX 2 inhibitors, which have an inhibitory effect on VEGF.[23] Other suggestions include the use of preoperative granulocyte-macrophage colony-stimulating factor, which may increase the population of dendritic cells in the liver and support their interaction with CD8+ T-lymphocytes, thus having an anti-tumour effect. Another avenue to explore for CRC patients with liver metastases is the use of cancer vaccines to boost the lymphocytic response to tumours.

Future plans may involve harnessing the role of the systemic inflammatory response with other known prognostic factors of colorectal cancer, such as the gut microbiome. The clinical utility of the use of NLR would be to risk stratify patients who undergo curative surgery or oncological treatment such as chemo and radiotherapy. The normalisation of the NLR could be used as a predictive marker of the response to therapy. Moreover, if the consistency of the prognostic effect of NLR in CRC is established, this might lend itself to the idea of manipulating the NLR though the intravenous use of cytokines or interventions that change the gut microbial diversity and composition to alter the prognosis of CRC patients. We know that the gut microbiota can be influenced by oncological treatments such as radiotherapy, stem cell transplantation and chemotherapy. It would therefore be of interest to investigate the link between the microbiome, the NLR and the above oncological treatments in the context of CRC outcomes and response to treatment. This could yield insights into whether the iatrogenic modulation of these key prognostic factors of CRC could change outcomes.

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RESEARCH ARTICLE

Effects of the COVID-19 Pandemic on General Surgery Training in Turkey

Türkiye'de COVID-19 Pandemisinin Genel Cerrahi Eğitimine Etkileri

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ABSTRACT

Aim: The Coronavirus disease-19 (COVID-19) pandemic has affected all countries in the world and has created a serious burden on the health systems of countries. Although health systems, which have not encountered such a sudden and intense load for many years, had difficulty in responding to this need at first, measures have been taken to meet this sudden demand in a short time. This change in the health system has led to a decrease in the number of elective surgeries in particular. One of the outcomes of the COVID-19 pandemic is interrupted and insufficient surgery training. In this study, we aimed to assess the effects of COVID-19 on general surgery education in Turkey.

Method: In the study, a questionnaire consisting of 22 questions including participants' demographic information, their education level and the average number of cases in the time interval covering the same period of the previous year was used. In the study, the period between January 2019-April 2019 and January 2020-April 2020 was compared, and the operations performed during this period were compared in terms of emergency, elective, laparoscopic and open surgery.

Results: When the number of elective/emergency hernia, upper gastrointestinal-hepatobiliary and colorectal-benign anorectal operations performed primarily by the assistant under the supervision of the responsible lecturer were compared, it was found that the rates were decreased from 9.67 to 0.76, 7.66 to 1.38 and 7.48 to 2.00, respectively, and all these changes were found to be statistically significant. The rate of emergency operations performed primarily by the lecturer decreased from 34.16% to 28.93% (p=0.045), and the rate of elective surgeries performed primarily by the faculty member decreased from 61.09% to 55.93% (p=0.045 and p=0.411).

Conclusion: There has been a significant decrease in the number of elective and emergency surgeries due to the change in the health system. We believe that changes should be made by clinics to their training programmes so that this decrease does not affect the training of surgical residents.

Keywords: COVID-19, general surgery training, laparoscopy, laparotomy

ÖZ

Amaç: Koronavirüs hastalığı-19 (COVID-19) salgını dünyadaki tüm ülkeleri etkilemiş ve ülkelerin sağlık sistemi üzerinde ciddi bir yük oluşturmuştur. Uzun yıllardır bu kadar ani ve yoğun bir yük ile karşılaşmayan sağlık sistemleri, ilk başta bu ihtiyaca cevap vermekte zorlansa da, bu ani ihtiyacı kısa sürede karşılayacak önlemler alınmıştır. Sağlık sistemindeki bu değişiklik, özellikle elektif ameliyatların sayısının azalmasına neden olmuştur. Bu COVID-19 salgınının sonuçlarından biri, kesintiye uğrayan ve yetersiz cerrahi eğitimdir. Bu çalışmada, COVID-19'un Türkiye'deki genel cerrahi eğitimine etkilerini değerlendirmeyi amaçladık.

Yöntem: Çalışmada, katılımcıların demografik bilgileri, eğitim düzeyleri ve bir önceki yılın aynı dönemini kapsayan zaman aralığındaki ortalama olgu sayılarını içeren 22 sorudan oluşan anket kullanıldı. Çalışmada Ocak 2019-Nisan 2019 ile Ocak 2020-Nisan 2020 arasındaki dönem karşılaştırılmış ve bu dönemde yapılan vakalar acil, elektif, laparoskopik ve açık cerrahi açısından karşılaştırılmıştır.

Bulgular: Sorumlu öğretim üyesi gözetiminde asistan tarafından yapılan elektif/acil fıtık (inguinal/insizyonel/umbilikal), üst gastrointestinal-hepatobiliyer ve kolorektal-benign anorektal operasyon sayıları karşılaştırıldığında oranların düştüğü görüldü (sırasıyla 9,67'den 0,76'ya, 7,66'dan 1,38'e ve 7,48'den 2,00'e gerilemiş ve tüm bu değişimler istatistiksel olarak anlamlı bulunmuştur). Öğretim üyesi tarafından elektif olarak yapılan acil ameliyat oranı %34,16'dan %28,93'e (p=0,045), öğretim üyesi tarafından öncelikli olarak yapılan elektif ameliyat oranı %61,09'dan %55,93'e geriledi (p=0,045 ve p=0,411)

Sonuç: Cerrahi eğitimin en önemli adımlarından biri, olguların öncelikle sorumlu öğretim görevlisinin gözetiminde bir asistan tarafından yapılmasıdır. Ancak bu, ameliyatın süresini uzatabilir ve olası komplikasyon riskini artırabilir. Acil olgu sayısındaki azalmaya rağmen, sorumlu

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öğretim üyesi gözetiminde öncelikle cerrahi asistan tarafından yapılan acil olguların oranındaki artış asistan eğitimi üzerinde olumlu bir faktör olarak değerlendirilmektedir. Sağlık sistemindeki değişime bağlı olarak elektif ve acil ameliyat sayısında önemli bir düşüş yaşandı. Bu azalmanın cerrahi asistanlarının eğitimini etkilememesi için kliniklerin eğitim programlarında değişiklik yapması gerektiğini düşünüyoruz.
Anahtar Kelimeler: COVID-19, genel cerrahi eğitimi, laparoskopi, laparotomi

Introduction

With the rapid spread of the new coronavirus starting from China and spreading to the whole world in December 2019, a pandemic has posed serious problems for the economies and health systems of all countries. The first Coronavirus disease-19 (COVID-19) case in Turkey was detected in March of 2020, and the ministry of health and other government agencies have taken precautions to prevent the spread of the disease. Furthermore, it was announced that COVID-19 was no longer an epidemic limited to certain regions and was declared a pandemic in March 2020.

Although health systems, which have not encountered such a sudden and intense load for many years, had difficulty responding to this need at first, measures have been taken to meet this sudden need in a short time. Since COVID-19 primarily affects the respiratory tract, requirements for services such as hospitalisation, intensive care admission and ventilators have increased; therefore, it is certain that a need for new guidelines to help healthcare facilities meet this increased demand has emerged.[1,2,3] Therefore, elective procedures have been postponed, emergency cases have been given priority and non-surgical approaches have been recommended as the first step, even in emergency cases.

This change in the health system has led to a decrease in the number of elective surgeries in particular. Many international professional organisations have advocated that elective surgery should be delayed as much as possible.[4] All these changes have interrupted clinical surgery training and have led to certain new problems. The effects of COVID-19 on surgical residency programmes have only recently been realised, and studies on this subject are limited.

Considering that the COVID-19 pandemic is ongoing, and there is no specific vaccine or treatment method yet, many authors suggest that this prolonged situation will have an increasingly negative effect on resident training.[5,6] Anticipating all these possible effects, clinics need to make changes in their own operations, but few centres have restructured in this direction.[5] In this study, we aimed to determine the effects of COVID-19 on the health system, in particular on general surgery education.

Performing operations under the supervision of the responsible lecturer in surgical sciences resident training constitutes the basis of surgical training. As in all surgical residency programmes, general surgery has a wide range of emergency cases. Elective cases were stopped in many centres during the COVID-19 pandemic, but some hospitals were excluded from the pandemic, and elective surgeries were intended to continue in those hospitals. However, due to the health service requirement of COVID-19, which constitutes a burden on the health systems of countries, such a distinction could not be made in some countries, and the burdens brought by the COVID-19 pandemic disrupted other health services.

Elective surgeries have been postponed as much as possible since COVID-19 requires additional precautions during the surgical and anaesthesia stages to prevent disease transmission. Since COVID-19 has a much more severe course and causes higher mortality and morbidity in patient populations with susceptibility to immunosuppression, such as cancer patients, non-surgical treatments are the priority in these cases. This has also caused a decrease in the number of elective cancer surgeries.

It is inevitable that surgical training will be affected by the COVID-19 pandemic in a clinic where most of the elective cases consist of a high-risk group for COVID-19 such as elderly patients and patients with other comorbidities. Considering that training of an assistant by a responsible lecturer during surgery may prolong the duration of the operation, and this prolonged period will increase the risk of COVID-19 transmission, it can also be argued that during the pandemic, general surgery assistant training will be disrupted in both emergency and elective cases.

In this study, we aimed to assess the effects of COVID-19 on general surgery education in Turkey based on questionnaire data.

Materials and Methods

In this study, a questionnaire consisting of 22 questions, including participants' demographic information, their education level and the average number of cases in the time interval covering the same period of the previous year, was used. Questionnaires were sent to general surgery residents all over the country, and 120 residents completely filled out the form (Table 1).

The questionnaires were sent to the participants via e-mail, and the participants were asked to click on the questionnaire link and fill out the questionnaire through the online system. In the study, the period between January 2019-April

Table 1. The questionnaire used in the study

1. Age	• 20-29 • 30-39 • 40-49 • >50
2. Gender	• Male • Female
3. How long have you been a surgery resident?	• <1 year • 2 years • 3 years • 4 years • 5 years or more
4. Which hospital are you working in?	• Public university hospital • Research and training hospital • Foundation/private university hospital
5. How many emergency cases were done in your hospital per week on average in last year (April 2019)?	
6. How many emergency cases were done in your hospital per week on average in this year (April 2020)?	
7. How many elective cases were done in your hospital per week on average in last year (April 2019)?	
8. How many elective cases were done in your hospital per week on average in this year (April 2020)?	
9. How many elective/emergency hernia (inguinal/incisional/umbilical) surgeries did you primarily perform under the supervision of the responsible faculty member in last year (April 2019)?	
10. How many elective/emergency hernia (inguinal/incisional/umbilical) surgeries did you primarily perform under the supervision of the responsible faculty member in this year (April 2020)?	
11. How many elective/emergency upper gastrointestinal/hepatobiliary surgeries did you primarily perform under the supervision of the responsible faculty member in last year (April 2019)?	
12. How many elective/emergency upper gastrointestinal/hepatobiliary surgeries did you primarily perform under the supervision of the responsible faculty member in this year (April 2020)?	
13. How many elective/emergency colorectal, benign anorectal surgeries did you primarily perform under the supervision of the responsible faculty member in last year (April 2019)?	
14.How many elective/emergency colorectal, benign anorectal surgeries did you primarily perform under the supervision of the responsible faculty member in this year (April 2020)?	
15. As a surgical assistant, in which emergency case did you frequently encounter during the pandemic process and feel better about making a primarily?	• Appendectomy • Ileus • Trauma • Mesentery ischaemia • Upper gastrointestinal system perforation
16. What percentage of hernia (inguinal/umbilical/incisional) cases did you do laparoscopically in last year (2019)?	
17. What percentage of hernia (inguinal/umbilical/incisional) cases did you do laparoscopically in this year (2020)?	

Table 1. continued

18. What percentage of upper gastrointestinal, hepatobiliary cases did you do laparoscopically in last year (2019)?	
19. What percentage of upper gastrointestinal, hepatobiliary cases did you do laparoscopically in this year (2020)?	
20. What percentage of colorectal cases did you do laparoscopically in last year (2019)?	
21. What percentage of colorectal cases did you do laparoscopically in this year (2020)?	
22. What is the reason affecting your laparoscopy or laparotomy choice?	• Laparoscopic surgeries are safer in terms of transmission • Open operations are safer in terms of transmission • Laparoscopy needs shorter operation duration • Laparostomy needs shorter operation duration • I am more experienced in laparoscopic operations • I am more experienced in open operations • Due to hospital policy • Due to defence of the staff • Due to hospital facilities • The choice of lecturers • Due to defence of the anaesthesia
23. How many of the emergency surgeries were performed primarily by the lecturer in last year (2019)?	
24. How many of the emergency surgeries were performed primarily by the lecturer in this year (2020)?	
25. How many of the elective surgeries were performed primarily by the lecturer in last year (2019)?	
26. How many of the elective surgeries were performed primarily by the lecturer in this year (2020)?	

2019 and January 2020-April 2020 was compared, and the operations performed during this period were compared in terms of emergency, elective, laparoscopic and open surgery. In addition, the rates of inguinal, incisional and umbilical hernia; upper gastrointestinal-hepatobiliary surgery and colorectal and benign anorectal surgeries performed in the same period were compared in terms of whether the surgery was performed mainly by the lecturer or the resident.

Statistical Analysis

SPSS Statistics for Windows, Version 20.0. (Armonk, NY: IBM Corp.) was used to evaluate the data. Variables were expressed as mean ± standard deviation, percentage and frequency values. In addition, the normality assumption, one of the prerequisites of parametric tests, was tested with the Shapiro-Wilk test. For evaluation of differences between two groups, when the preconditions of parametric tests were met, the matching t-test was used; otherwise, the Wilcoxon test was applied. The statistical significance level was accepted as $p<0.05$ and $p<0.01$.

Results

A total of 120 general surgery residents participated in the study. Of them, 62 residents (51.7%) were between the ages of 20 and 29, 56 (46.7%) between 30 and 39 and 2 (1.7%) between 40 and 49. In all, 104 (86.7%) of the respondents were male, while the remaining 16 (13.3%) were female. In terms of the surgical experience, 16 residents (13.3%) had less than 1 year, 10 residents (8.3%) had 1 year, 26 residents (21.7%) had 2 years, 24 assistants (20%) had 3 years, 26 assistants (21.7%) had 4 years and 18 residents (15%) had 5 years or more. Eighty of the participants (66.7%) were working in a public university hospital, 36 (30%) in training and research hospitals and the remaining 4 (3.3%) in a foundation or private university hospital (Table 2).

When the admissions were analysed, it was observed that 37.9% of the emergency cases were operated due to appendicitis, 23.3% due to ileus, 8.6% due to trauma, 12.9% due to mesenteric ischaemia, 15.5% due to upper gastrointestinal perforation and approximately 1.7%

due to other surgical emergencies. When the factors that affect surgeons' choice of laparoscopy or laparotomy in emergency cases were examined, it was found that 3.1% of the participants found laparoscopic surgeries safer in terms of contamination, 23.9% found open operations safer in terms of contamination, 18.9% asserted that surgery times were shorter in open operations, 1.3% thought that they were more skilful in laparoscopic operations, 6.9% thought that they were more skilful in open operations, 0.6% stated that laparoscopic surgeries take less time, 13.2% stated that they make their choices due to hospital policy, 6.9% due to defence of the hospital staff and 5% due to the hospital's facilities, 10.7% preferred laparoscopy or laparotomy due to the preference of the lecturer and 9.4% due to the defence of the anaesthesia (Table 3).

When the period between January and April 2019 was examined, the weekly average number of emergency cases was calculated as 28.34, while the weekly average number of elective cases in the same period was 69.27. When the cases under the supervision of a responsible lecturer were examined, it was seen that the average number of elective/emergency inguinal, incisional or umbilical hernia operations performed in the same period of 2019 was 9.67, the average number of upper gastrointestinal/hepatobiliary cases was 7.66 and the average number of colorectal and benign anorectal cases was 7.48. When the period between January and April 2020 was examined, the weekly average number of emergency cases was calculated as 16.07, while the weekly average number of elective cases in the same period was 13.22. When cases under the supervision of a responsible lecturer were examined, it was seen that the average number of elective/emergency inguinal, incisional or umbilical hernia surgeries performed in the same period of 2020 was 0.76, the average number of upper gastrointestinal/hepatobiliary cases was 1.38 and the average number of colorectal and benign anorectal cases was 2.0.

When the distribution of surgeries performed between January and April 2019 in terms of laparoscopy or laparotomy was examined, 23.07% of elective/emergency inguinal, incisional or umbilical hernia surgeries, 40.70% of upper gastrointestinal/hepatobiliary surgeries, and 26.60% of colorectal surgeries were performed laparoscopically. In the same period, it was observed that 34.16% of the emergency surgeries were primarily carried out by the responsible lecturer, while this rate was 61.09% for cases elective cases.

When the distribution of surgeries performed between January and April of 2020, were compared in terms of laparoscopy or laparotomy, 4.55% of elective/emergency inguinal, incisional or umbilical hernia surgeries, 5.91% of upper gastrointestinal/hepatobiliary surgeries, and 4.82% of colorectal surgeries were performed laparoscopically. In the same period, it was observed that 28.93% of emergency surgeries were primarily carried out by the responsible faculty member, and this rate was 55.93% for elective cases.

When the periods between January-April 2019 and January-April 2020 were compared, it was determined that the weekly number of emergency cases decreased from 28.34 to 16.07

Table 2. Demographic characteristics of the participants

Age (years)	%	n
20-29	51.7	62
30-39	46.7	56
40-49	1.7	2
Gender		
Male	86.7	104
Female	13.3	16
Experience (years)		
<1	13.3	16
1	8.3	10
2	21.7	26
3	20.0	24
4	21.7	26
5 or more	15.0	18
Hospital type		
Public university hospital	66.7	80
Training and research hospital	30.0	36
Foundation or private university hospital	3.3	4

Table 3. Factors that affect the choice of surgery type

Reason for laparoscopy or laparotomy choice	%	n
Laparoscopy is safer in terms of disease transmission	3.1%	4
Laparotomy is safer in terms of disease transmission	23.9%	29
Laparotomy takes shorter time	18.9%	23
I am more experienced in laparoscopic surgeries	1.3%	2
I am more experienced in open surgeries	6.9%	8
Laparoscopy takes shorter time	0.6%	1
Due to hospital policy	13.2%	16
Due to defence of hospital staff	6.9%	8
Due to hospital's facilities	5.0%	6
Choice of the lecturer	10.7%	13
Due to defence of the anaesthetist	9.4%	11

on average and there is a statistically significant difference (p=0.002). When the elective cases were compared, it was seen that the weekly average number of cases decreased from 69.27 to 13.22, and there was a statistically significant difference (p=0.001). When the number of elective/emergency hernia (inguinal/incisional/umbilical), upper gastrointestinal-hepatobiliary and colorectal-benign anorectal operations performed primarily by the assistant under the supervision of the responsible lecturer were compared, it was found that the rates were decreased from 9.67 to 0.76, 7.66 to 1.38 and 7.48 to 2.00, respectively, and all these changes were found to be statistically significant (p=0.001, 0.001, 0.001, respectively) (Table 4).

While 23.07% of hernia (inguinal/incisional/umbilical) operations were performed laparoscopically in 2019, this rate decreased to 4.55% in the same period of 2020 (p=0.001). When the same comparison was made for upper gastrointestinal-hepatobiliary and colorectal surgeries, it was observed that these rates decreased from 40.71% to 5.91% and from 27.60% to 4.82%, respectively (p=0.001, p=0.001). When the periods of 2019 and 2020 are compared, it is seen that the rate of emergency operations performed primarily by the lecturer decreased from 34.16% to 28.93% (p=0.045), and the rate of elective surgeries performed primarily by the faculty member decreased from 61.09% to 55.93% (p=0.045 and p=0.411) (Table 5).

Discussion

Although the issue of which method (laparoscopy or laparotomy) is safer in terms of transmission risk in infected patients is controversial, the general opinion is that the open method is safer.[7] Although there is no evidence that COVID-19 causes transmission by vaporisation during the operation, it should be acted on considering the possibility of transmission as it carries a potential risk.[8] In our study, when the rates of laparoscopy were compared, it was found that there was a statistically significant decrease in the laparoscopy rates in all surgeries performed. Considering that the risk of contamination with laparoscopy is higher, a decrease in laparoscopy rates is predictable. Considering that this situation may cause a deficiency in laparoscopic training of residents, it may be recommended to exclude the diagnosis of COVID-19 by performing preoperative polymerase chain reaction test in elective cases and to operate on COVID-19-negative patients laparoscopically as much as possible. In this way, the deficiency in laparoscopic training can be prevented to some extent.

One of the most important steps of surgical training is that operations are performed primarily by an assistant under the supervision of the responsible lecturer. However, this can prolong the duration of the surgery and increase the risk of possible complications.[9,10] All these factors also cause an increase in the risk of COVID-19 transmission. In our study, during the pandemic period, in which 34.6% of emergency surgeries were primarily performed by the lecturer in 2019, it was observed that this rate decreased to 28.3% in 2020, and a statistically low significant difference was observed. Despite the decrease in the number of emergency cases, the increase in the rate of emergency surgeries primarily performed by the surgical assistant under the supervision of the responsible lecturer is considered as a positive factor in resident training. Likewise, it was observed that the rate of elective surgeries performed primarily by residents increased during the pandemic, but this change was not statistically significant (61.09% vs 55.93%, p=0.411).

Table 4. Comparison of emergency and elective cases performed before and after the COVID-19 pandemic

	2019	2020	p
How many emergency cases were done in your hospital per week on average?	28.34	16.07	0.002
How many elective cases were on average per week in your hospital?	69.27	13.22	0.001
On average, how many elective/emergency hernia (inguinal/incisional/umbilical) surgeries have you performed under the supervision of the responsible lecturer?	9.67	0.76	0.001
How many elective/emergency upper GIS-hepatobiliary surgeries have you performed primarily under the supervision of the responsible lecturer?	7.66	1.38	0.001
On average, how many elective/emergency colorectal-benign anorectal operations have you performed under the supervision of the responsible lecturer?	7.48	2.00	0.001

COVID-19: Coronavirus disease-19, GIS: Gastrointestinal system

Table 5. Comparison surgery types before and after the COVID-19 pandemic

	2019	2020	p
What percentage of hernia (inguinal/umbilical/incisional) cases have you performed laparoscopically?	23.07	4.55	0.001
What percentage of upper GIS-hepatobiliary cases have you performed laparoscopically?	40.71	5.91	0.001
What percentage of colorectal cases have you done laparoscopically?	27.60	4.82	0.001
How much of the emergency surgeries primarily performed by lecturers?	34.16	28.93	0.045
How many of the elective surgeries primarily performed by lecturers?	61.09	55.93	0.411

COVID-19: Coronavirus disease-19, GIS: Gastrointestinal system

When the elective cases before and after the pandemic were compared, considering that the weekly average number of cases decreased from 69.27 to 13.22 and that there was a statistically significant difference between these two periods (p=0.001), there was also a significant difference in the number of elective surgeries performed primarily by the surgery resident. Making a primary case under the supervision of responsible lecturer is one of the most important stages of surgical training, and the interruption of this step may cause major deficiencies in surgical training. Since a protective vaccine or a specific therapeutic drug against COVID-19 cannot be developed today and it is not certain how long this situation will continue, it is thought that the rate of operations performed primarily by the surgical resident should increase in order not to interrupt surgical training.[11] We believe that this deficiency can be reduced to some extent by increasing the rate of surgeries primarily performed by the surgery resident insofar as possible according to the experience of the resident.

Conclusion

The COVID-19 pandemic has affected all countries around the world and has created a serious burden on the health systems of countries. There has been a significant decrease in the number of elective and emergency surgeries due to changes in such health systems. It is our opinion that changes should be made by clinics in their training programmes so that this decrease does not affect the training of surgical residents.

Ethics

Ethics Committee Approval: Approval was obtained from Aydın Adnan Menderes University Local Ethics Committee for the study.

Informed Consent: Since the study is a questionnaire form, there is no patient consent form.

Peer-review: Externally and internally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: E.M.Y., U.U.Ş., Concept: E.M.Y., H.Ö., Design: T.Ç., E.M.Y., Data Collection or Processing: U.U.Ç., H.Ö., Analysis or Interpretation: T.Ç., H.Ö., Literature Search: E.M.Y., U.U.Ş., Writing: E.M.Y.

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RESEARCH ARTICLE

Pelvic Exenteration for Recurrent Rectal Cancer: A Single Institution Experience

Rekürren Rektal Kanserlerde Pelvik Ekzantrasyon: Tek Merkez Deneyimi

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ABSTRACT

Aim: Rectal cancer is an important cause of cancer-related deaths worldwide (1-2). Although rectal cancers can be diagnosed earlier nowadays due to the development of screening programmes, 18% of patients have a locally advanced stage at the time of diagnosis (3). Despite the improvements in total mesorectal excision and oncological treatments, the locoregional recurrence rates vary between 6-10% in rectal cancer patients (4-5).
Method: The data of patients who underwent pelvic exenteration for recurrent rectal cancer in our clinic between January 2015 and December 2019 were retrospectively analysed.
Results: It was found that the patients with lymphovascular invasion (LVI) and perineural invasion (PNI) showed statistically poor survival rates (p=0.038/0.022). Two of the patients had a positive surgical margin and two others had a positive radial margin. There was no statistically significant difference between surgical margin positivity and prognosis (p>0.05). The mean number of metastatic lymph nodes was 4.0 (0-12), and the total number of lymph nodes was 12.35 (2-27). There was no statistically significant difference between patients with lymph node metastasis in terms of survival (p=0.079). Seven of the patients (41.1%) received systemic treatment before the surgery. It was statistically determined that the patients who received this treatment showed better survival rates (p=0.045).
Conclusion: It was found that pelvic exenteration had a positive effect on survival and local recurrence in recurrent rectal cancer, and that neoadjuvant therapy increased survival rates.
Keywords: Complication, pelvic exenteration, rectal cancer, recurrence, survival

ÖZ

Amaç: Rektal kanser tüm dünyada kansere bağlı ölümlerin önemli bir nedenidir (1-2). Günümüzde gelişen tarama programları ile birlikte rektal kanserlere daha erken tanı konulabilse de tanı anında hastaların %18'i lokal ileri evrededir (3). Total mezorektal eksizyon ve onkolojik tedavilerdeki gelişmelere rağmen rektum kanserli hastalarada lokorejyonel rekurrens oranları %6-10 arasında değişmektedir (4-5).
Yöntem: Kliniğimizde Ocak 2015-Aralık 2019 tarihleri arasında nüks rektum kanseri nedeniyle pelvik ekzantrasyon yapılan hastaların verileri retrospektif olarak inceledi.
Bulgular: Patoloji raporları incelendiğinde hastaların 10'unda (%58,8) lenfovasküler invazyon, 10'unda (%58,8) perinöral invazyon vardı. lenfovasküler invazyon ve perinöral invazyon olan hastaların istatistiksel olarak kötü sağkalım gösterdikleri saptanmıştır (p=0,038/0,022). Hastaların 2'sinde cerrahi sınır pozitif gelmiş olup, 2'si de radyal sınır pozitifliğiydi. Cerrahi sınır pozitifliği ile prognoz arasında istatistiksel olarak anlamlı fark yoktu (p>0,05). Metastatik lenf nodu sayısı ortalama 4,0 (0-12), toplam lenf nodu sayısı ortalama 12,35 (2-27) olarak bulunmuştur. Lenf nodu metastazı olan hastalarda sağkalım açısından istatistiksel olarak fark bulunmamıştır (p=0,079). Hastaların 7'si (%41,1) operasyon öncesi sistemik tedavi almıştır. Sistemik tedavi alan hastaların daha iyi sağkalım gösterdiği istatistiksel olarak saptanmıştır (p=0,045).
Sonuç: Nüks rektum kanserinde pelvik ekzantrasyon ve neoadjuvan tedavinin sağ kalımı artırdığı lokal nüksü azalttığı gözlenmiştir.
Anahtar Kelimeler: Komplikasyon, pelvik ekzantrasyon, rektum kanser, nüks, sağkalım

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Introduction

Rectal cancer is an important cause of cancer-related deaths worldwide.[1,2] Although rectal cancers can be diagnosed earlier nowadays due to the development of screening programmes, 18% of patients have a locally advanced stage at the time of diagnosis.[3] Despite the improvements in total mesorectal excision and oncological treatments, the locoregional recurrence rates vary between 6%-10% in rectal cancer patients.[4,5] Invasion to the genitourinary organs occurs in some patients with pelvic recurrence.[6,7] Pelvic recurrences may present with symptoms such as pain, tenesmus, dysuria and fistula that cannot be controlled by treatment.[8] The procedure of removing all tumour tissues in order to achieve negative surgical margins in the pelvis is called pelvic exenteration, which significantly contributes to survival in well-selected patient groups with a multidisciplinary approach.

This study aimed to present the outcomes of our patients who underwent pelvic exenteration for locoregional recurrence and to determine the prognostic factors.

Materials and Methods

Data of patients who underwent pelvic exenteration for recurrent rectal cancer in our clinic between January 2015 and December 2019 were retrospectively analysed. Patients with a pelvic recurrence who developed systemic metastasis were not operated. The site of local recurrence and presence of a distant metastasis in all patients were evaluated by magnetic resonance imaging (MRI) and computed tomography (CT). Preoperative colonoscopy was performed on the patients to locate the tumour site, and cystoscopy was performed on patients with suspected bladder invasion. A total of 17 patients who met these criteria were included in the study. The patients' surgery types and pathology reports, demographic features, length of hospital stay, reasons for re-admission, postoperative complications, postoperative mortality, total and disease-free survival were examined. The radiological examinations (chest X-ray, CT, ultrasonography, endoultrasonography, MRI, positron emission tomography) were reviewed by retrospectively scanning the patients' data. The 8th edition of the TNM classification was used for staging. Ethics committee approval was obtained from our institute. All patients were operated by the same surgical team. Informed consent was obtained from the patients in the preoperative period. The patients underwent bowel cleansing using laxatives and enemas a day before the surgery, and a single-dose prophylactic antibiotic (cefazolin 2 gr) was administered preoperatively. The patients underwent total pelvic exenteration (TPE). TPE is defined as the removal of the genitourinary and reproductive organs including the rectum, distal colon, distal ureters and the lymph nodes draining these, as well as the pelvic peritoneum, and this procedure can be performed in combination with sacrectomy. Afterwards, reconstructions such as lower anastomoses instead of permanent ileostomy, new vagina due to sexual dysfunction, urinary diversion (new bladder or supravesical urinary diversion) and flap-grafts to close the pelvic floor defects can be performed in order to increase the quality of life.

Statistical Analysis

Data analysis was done using SPSS 11.5 software. For descriptive statistics, quantitative variables were presented as mean ± standard deviation and median (minimum-maximum), and qualitative variables were presented as number of patients (percentage). A survival analysis was performed using the Kaplan-Meier method through qualitative and quantitative variables and the log-rank test was used to determine significant differences between the groups. The level of statistical significance was set at 0.05.

Results

Of the patients, 9 (52.9%) were females and 8 (47.1%) were males. The mean age of the patients was 53.4±10.1 years. TPE was performed on all the patients, of whom, 6 (35.3%) had lower, 7 (41.2%) had middle, and 4 (23.5%) had upper rectum localisation, and there was no significant correlation between the survival of the patients and tumour localisation ($p>0.05$). We had performed a low anterior resection for all patient for the initial surgery and all surgical margins were clear. Of the patients, 12 (70.5%) had taken neoadjuvant chemoradiotherapy before the initial surgery. When classified according to T-stage, three patients were T2 (11.7%), five patients were T3 (29.4%), three patients were T4a (11.7%) and six patients were T4b (35.2%). It was observed that survival decreased as the T-stage increased ($p<0.001$). N was positive in 11 (64.7%) and N was negative in 6 (35.3%) patients. Mortality was found to be high in patients with N positive results and was statistically significant ($p<0.05$). There was no statistical significance in terms of overall survival, disease-free survival and deficit conversion ($p>0.05$). The mean follow-up duration was 16 months (1-50 months), and considering overall survival, 8 (47.1%) of 17 patients survived, while 9 (52.9%) died. The mean survival time was 23.8 months. Three of the patients (11.7%) developed recurrence, and all recurrences occurred in the pelvic region as a local recurrence. The mean length of hospital stay was 18.1±11.5 days. The patient characteristics are shown in Table 1.

The surgical indication was vaginal invasion in 5 (29.4%) patients, bladder invasion in 11 (64.7%) patients and uterine

invasion in 1 (5.8%) patient. The mean operative time was 200.8±9.2 min. Of the patients, five developed an infection, one developed an ileal conduit leak and one developed postoperative early bleeding. There was no statistically significant correlation between complication development and survival in the patients (p>0.05). Only the patient who developed an ileal conduit leak required reoperation, while the other patients were treated conservatively. Seven patients were readmitted to the hospital for infection, one patient for acute renal failure and three patients for deterioration of the general condition, and the causes of infection were pyuria[2], intra-abdominal collection[4] and wound infection.[1]

When the pathology reports were examined, 10 (58.8%) of the patients had lymphovascular invasion (LVI) and 10 (58.8%) had perineural invasion (PNI). It was found that the patients with LVI and PNI showed statistically poor survival rates (p=0.038/0.022). Of the patients, two had a positive surgical margin and two had a positive radial margin. There was no statistically significant difference between surgical margin positivity and prognosis (p>0.05). The mean number of metastatic lymph nodes was 4.0 (0-12), and the total number of lymph nodes was 12.35 (2-27). There was no statistically significant difference between patients with lymph node metastasis in terms of survival (p=0.079).

Seven of the patients (41.1%) received chemoradiotherapy before pelvic exenteration. In accordance with the multidisciplinary team decision, 10 (58.9%) of the patient did not receive chemoradiotherapy before pelvic exenteration. It was statistically determined that the patients who received this treatment showed better survival rates (p=0.045).

According to the Kaplan-Meier analysis, the one-year and 2-year survival rate was 74% and 26%, respectively. It was statistically shown that the patients who had 12 months or less between the initial operation and pelvic recurrence had worse survival rates than those who had more than 12 months between the initial operation and pelvic recurrence (p=0.001). Table 2 presents the univariate analysis results that were suggested to affect survival, and the probability of the 1- and 2-year survivals related to these results.

Table 1. Patient characteristics

Age	**53.47±10.16**	
Total number of lymph nodes removed	12.35±1.77	
Number of metastatic lymph nodes	4.00±0.94	
Survival time (months)	23.83±5.07	
Lymphovascular invasion	Yes	10 (58.8)
	No	7 (41.2)
Perineural invasion	Yes	10 (58.8)
	No	7 (41.2)
Recurrence	Yes	3 (17.6)
	No	14 (82.4)
Operative time (min)	200.88±9.27	
Preoperative systemic treatment	Yes	7 (41.2)
	No	10 (58.8)
Length of hospital stay (days)	18.12±2.80	
Reason for re-admission	Infection	7 (63.8)
	ARF	1 (9)
	Deterioration of general condition	3 (27.2)

Min: Minimum, ARF: Acute rheumatic fever

Table 2. Survival analyses

		1 year (%)	2 years (%)	Survival time	p
Overall		74.0	26.9	23.83±5.07	-
Neoadjuvant therapy	No	63.5	19.5	14.06±2.77	0.045
	Yes	85.7	64.3	36.64±7.74	
LVI	No	80.0	80.0	41.20±7.87	0.038
	Yes	70.0	16.7	14.70±2.55	
PNI	No	83.3	83.3	42.66±6.69	0.022
	Yes	57.1	15.2	14.32±2.56	
Metastatic lymph node	No	75.0	50.0	39.00±9.52	0.079
	Yes	72.7	13.6	17.18±3.15	
Sex	Female	55.6	27.8	21.52±6.52	0.507
	Male	27.8	0	20.66±2.37	

PNI: Perineural invasion, LVI: Lymphovascular invasion

Discussion

Pelvic exenteration was first described in 1948 in Brunschwig pelvic malignancies as the en bloc resection of pelvic organs.[9] Although the mortality rates have been shown to be 20-30% for many years, this rate has dropped to <10% due to the improvements in the surgical technique, intensive care and anaesthesiology.[10,11,12,13]

Rectal cancer surgery is particularly challenging in lower rectal tumours and in patients having a narrow pelvis. Despite all the advances in the surgical technique, the locoregional recurrence rates in colorectal cancer vary between 6%-10%.[4,5] The vast majority of recurrences occur within the first three years after surgery, and when these patients are left untreated, the prognosis varies between 6-8 months.[14] Patients whose tumour is limited to the pelvis and who do not have distant metastasis are eligible for pelvic exenteration. However, pelvic exenteration can be performed in combination with metastasectomy in a group of patients with resectable distant liver and lung metastases.[7,15,16] Resectability should be determined by preoperative imaging, including CT, MRI and positron emission tomography. Siatic nerve invasion, external iliac artery invasion, paraaortic lymph node involvement and lymphoedema as a finding of venous or lymphatic infiltration in the lower extremity are considered contraindications for pelvic exenteration.[17] TPE is defined as the removal of the genitourinary and reproductive organs including the rectum, distal colon, distal ureters and the lymph nodes draining them as well as the pelvic peritoneum and can be performed in combination with sacrectomy. Anterior pelvic exenteration is the resection of the reproductive organs, upper rectum and bladder by preserving the lower part of the rectum. Posterior pelvic exenteration is defined as the resection of the rectum and reproductive organs by preserving the bladder. In our study, all of the patients underwent TPE.

Despite the high mortality and morbidity rates, pelvic exenteration is associated with increased survival in recurrent rectum tumours. In their systemic review, Heriot et al.[18] showed that pelvic exenteration increased survival with an acceptable morbidity rate and found that the cancer-specific survival rate was increased and local recurrence was significantly reduced by neoadjuvant or adjuvant chemoradiotherapy. Domests et al.[19] found a 30-day mortality rate of 3.6%, 3-year disease-free survival rate of 52.2% and 3-year overall survival rate of 75.1%. In our study, the 30-day mortality rate was 5.8%, 1- and 2-year overall survival rates were 74% and 26.4%, respectively. Our 1- and 2-year disease-free survival rates were 67.3% and 40.4%, respectively. We think that the reason for the lower survival time in our study is due to the inclusion of only patients who developed recurrences, the short follow-up period and small number of patients.

In the literature, many factors such as positive surgical margin, neoadjuvant therapy, number of metastatic lymph nodes, lymphovascular invasion and perineural invasion have been identified to be effective in determining survival after pelvic exenteration, and among these, R0 resection has been shown to be the most important prognostic factor.[19,20,21,22,23] However, in their study, Kakuda et al.[24] found no difference between patients who underwent R1 resection and those who underwent R0 resection in terms of overall survival rates (23-18 months p=0.67). In our study, the radial surgical margin was positive in two patients and the effect of surgical margin positivity on survival could not be demonstrated (p>0.05). While the effect of lymph node positivity on survival has been demonstrated in many studies[22,23,24,25], the effect of lymph node positivity on survival could not be demonstrated in the present study. We think that the reason for this is our small number of patients and short follow-up time. In our study, the factors affecting survival rates were found to be the time from the initial operation to pelvic recurrence, lymphovascular invasion, perineural invasion and neoadjuvant therapy (p=0.001, p=0.038, p=0.022, p=0.045).

In patients undergoing pelvic exenteration, a second surgery may be required for reasons such as adhesion due to primary surgery and fibrosis due to radiotherapy, resulting in the prolongation of the operative time, increase in postoperative complications and prolonged length of hospital stay. In a systemic review including 23 studies, the researchers found the complication rates after pelvic exenteration as 37%-100%.[26] In our study, the complication rate was 41.1%, and most of these patients developed wound infection. Reoperation was performed on one patient for postoperative bleeding and in one patient for ileal conduit leak. In the literature, there are prolonged operative times.[20] In our study, the mean operative time was recorded as 200.88±9.27 min. We think that the operative time in this study is shorter than those reported in the literature because all the surgical interventions were performed by the same team of experienced professionals.

Radiological studies are unable to determine whether invasion to the genitourinary organs is due to inflammation or tumour invasion in 20%-56% of patients undergoing pelvic exenteration.[27,28] In our series, 29.4% of the patients did not show tumour invasion to the genitourinary organs.

Although pelvic exenteration provides a high level of local control in recurrent rectal cancers, the rate of recurrence after pelvic exenteration ranges from 4.8%-61% (average 22%) in the literature.[26] In our study, three of all patients developed local recurrence (11.7%), which is consistent with the literature.

Conclusion

In conclusion, it was found that pelvic exenteration had a positive effect on survival and local recurrence in recurrent rectal cancer, and that neoadjuvant therapy increased survival rates.

Ethics

Ethics Committee Approval: University of Health Sciences Turkey, approval was obtained from the Ethics Committee of Ankara Dr. Abdurrahman Yurtaslan Oncology Health Application and Research Center (decision no: 95, date: 27.05.2020).

Informed Consent: Obtained.

Peer-review: Externally and internally peer reviewed.

Authorship Contributions

Concept: S.C., C.Y., M.O.K., F.G., E.G., B.A., L.D., Design: S.C., C.Y., M.O.K., F.G., E.G., B.A., L.D., Data Collection or Processing: S.C., C.Y., M.O.K., F.G., E.G., B.A., L.D., Analysis or Interpretation: S.C., C.Y., M.O.K., F.G., E.G., B.A., L.D., Literature Search: S.C., C.Y., M.O.K., F.G., E.G., B.A., L.D., Writing: S.C., C.Y., M.O.K., F.G., E.G., B.A., L.D.

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RESEARCH ARTICLE

Our Surgical Experience and Clinical Results in Non-traumatic Small Bowel Perforations

Non-travmatik İnce Bağırsak Perforasyonlarında Cerrahi Deneyimlerimiz ve Klinik Sonuçlarımız

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ABSTRACT

Aim: In this study, we aimed to share our surgical experiences and clinical results in non-traumatic small bowel perforations.

Method: Patients who underwent surgical treatment for non-traumatic small bowel perforation between 2009-2019 were included in the study. Patients were divided into two groups according to postoperative 90-day mortality status: Group 1 (no mortality), Group 2 (mortality). The demographic, clinical features, treatment methods and results of the patients were compared between the groups.

Results: Forty-two patients participated in our study. Group 1 consisted of 25, and Group 2 consisted of 17 patients. Male sex was dominant in Group 2 (48% vs 76.5%, p=0.062). Mean age was higher in Group 2 (54 vs 61, p=0.218). American Anesthesiology Association score (ASA) was statistically significantly higher in Group 2 (12% vs 58.8%). Forty-two percent of patients had abdominal surgery and 30% had a history of malignancy. The presence of electrolyte imbalance was similar in the groups (56% vs 76.5%, p=0.049). The days between the first complaint and laparotomy were similar between the groups (6.40 vs. 5.70 p=0.699). In perforated areas, jejunum was dominant in Group 2 with 64.7%, and ileum in Group 1 with 68%. The multiple perforation rate was higher in Group 2, but was not statistically significant (12% vs 23.5%, p=0.284). From postoperative complications, anastomosis leakage was higher in Group 1, but it was not statistically significant (12% vs 5.9%, p=0.501).

Conclusion: Morbidity and mortality of non-traumatic small bowel perforations is high. While the ASA score and hypoalbuminemia were associated with postoperative mortality in non-traumatic small bowel perforations, we did not find the localization of the perforation and the time between the first complaint and laparotomy to be related to mortality.

Keywords: Hypoalbuminemia, mortality, resection, small bowel perforation, stoma

ÖZ

Amaç: Bu çalışmada non-travmatik ince bağırsak perforasyonlarındaki cerrahi deneyimlerimizi ve klinik sonuçlarımızı paylaşmayı amaçladık.

Yöntem: 2009-2019 yılları arasında non-travmatik ince bağırsak perforasyonu nedeniyle cerrahi tedavi uyguladığımız hastalar çalışmaya dahil edildi. Hastalar postoperatif 90 günlük mortalite durumuna göre iki gruba ayrıldı: Grup 1 (mortalite yok), Grup 2 (mortalite var). Gruplarda hastaların demografik, klinik özellikleri, labarotuvar parametreleri, uygulanan tedavi yöntemleri ve sonuçları karşılaştırıldı.

Bulgular: Çalışmamıza 42 hasta dahil edildi. Grup 1: 25, Grup 2: 17 hastadan oluşuyordu. Grup 2'de erkek cinsiyet baskındı (%48 vs %76,5 p=0,062). Grup 2'de yaş daha büyük (54 vs 61 p=0,218). Grup 2'de Amerikan Anesteziyoloji Derneği sınıflandırması, sınıflandırması (ASA) istatistiksel olarak anlamlı ölçüde daha yüksekti (%12 vs %58,8). Hastaların %42'sinde geçirilmiş batın cerrahisi, %30'unda malignite öyküsü vardı. Elektrolit imbalansı varlığı gruplarda benzerdi (%56 vs %76,5 p=0,049). İlk şikayet ile laparotomi arasındaki süre gruplar arasında benzerdi (6,40 vs 5,70 p=0,699). Perforasyon alanı açısından Grup 2'de jejunum %64,7 Grup 1'de ileum %68 ağırlıktaydı. Multiple perforasyon oranı Grup 2'de daha fazla idi fakat istatistiksel olarak anlamlı değildi (%12 vs %23,5 p=0,284). Postoperatif komplikasyonlardan anastomoz kaçağı Grup1'de daha fazla ancak istatistiksel olarak anlamlı değildi (%12 vs %5,9 p=0,501).

Sonuç: Non-travmatik ince bağırsak perforasyonlarının morbidite ve mortalitesi yüksektir. Travmatik olmayan ince barsak perfosyonlarında ASA skoru ve hipoalbunemi postoperatif moratalite ile ilişkili iken perforasyonun lokalizasyonu ve ilk şikayet ile laparotomi arası süreyi mortalite ile ilişkili bulmadık.

Anahtar Kelimeler: Hipoalbunemi, mortalite, rezeksiyon, ince bağırsak perfosyonu, stoma

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Introduction

Although small bowel perforations, which are generally caused by non-traumatic reasons, are considered spontaneous, some call this condition as non-traumatic small bowel perforations. Non-traumatic perforation of the small intestine is an emergency that surgeons often encounter in developing countries.[1]

The most common causes include various malignancies, infections, non-specific inflammation and, in children, necrotising enterocolitis.[2,3] The causes of non-traumatic perforation of the small intestine in developing countries are different from those observed in developed countries. While malignancies and inflammatory bowel disease are the most common aetiological factors in western populations, infections and typhoid fever are the leading causes in developing countries.[4,5]

Rapid diagnosis is vital in these patients to achieve the best possible outcome. Unfortunately, non-specific clinical and laboratory findings associated with the underlying disease cause a delay in diagnosis. Patients often apply to the hospital late with purulent peritonitis and poor general condition.[2,6] Although radiological imaging procedures help diagnosis, early diagnosis is low, and most cases are diagnosed during laparotomy.[7]

Primary repair or resection-anastomosis is surgical procedures performed with or without ileostomy depending on the disease's cause and the degree of peritoneal contamination. Despite advances in surgical techniques and improved intensive care conditions, non-traumatic small bowel perforation mortality remains high, and some report a mortality rate of up to 42%.[8,9]

In this study, we aimed to group patients who underwent surgical treatment in our clinic for non-traumatic small bowel perforation according to mortality and presented our own experiences in light of the literature.

Materials and Methods

Patients who underwent surgical treatment due to small bowel perforation between 2009 and 2019 were included in the study. Patients with duodenal ulcer perforations, traumatic small bowel perforations and missing medical records were excluded. A common database was created by examining patient files and hospital information system records. Patients were analysed retrospectively using this database.

Patients were divided into two groups according to their postoperative 90-day mortality status: Group 1 (no mortality) and Group 2 (mortality).

Demographic and clinical features of patients, their presenting complaints, the time between the first complaint and the laparotomy, American Anesthesiology Association score (ASA), laboratory findings, presence of electrolyte imbalance, immunosuppression history, history of abdominal surgery, presence of malignancy, inflammatory bowel disease, the location and number of the perforated areas, the type of surgery and anastomosis performed, additional organ resection, length of hospital stay and postoperative complications were compared between the groups.

The surgical procedure was decided according to the patient's haemodynamic parameters and the findings during the operation.

Anastomosis leak was defined as a disruption in the integrity of the anastomosis documented by the combination of clinical, radiological and operative tools. Wound infection was defined as a superficial or deep incisional surgical site infection occurring in the surgical wound, according to the definition of the Centers for Disease Control.[10]

Statistical Analysis

SPSS 23.0 package programme was used for statistical analysis of the data. Categorical measurements were summarised as numbers and percentages, and continuous measurements as mean and standard deviation (median and minimum-maximum, where necessary). Pearson's chi-square test was used to compare categorical variables. In comparing the groups' continuous measurements, the distributions were checked, and an independent Student t-test was used for binary variables. The statistical significance level was accepted as 0.05 in all tests.

Results

Forty-two patients participated in our study. Group 1 consisted of 25, and Group 2 consisted of 17 patients. The male sex was dominant in Group 2 (48% vs 76.5%, p=0.062). The mean age was higher in Group 2 (54 vs 61 years, p=0.218). Patients with ASA 3 score was statistically significantly higher in Group 2 (12% vs 58.8%). A history of immune suppression (p=0.433), previous abdominal surgery (p=0.310), history of malignancy (p=0.065) and type (p=0.0320), number of comorbid diseases (p=0.883), presenting complaint (p=0.448) and inflammatory bowel disease (p=0.200) between the groups. Demographic and clinical characteristics are shown in Table 1.

The albumin value was lower in Group 2 (3.05 vs 2.53, p=0.049). The presence of electrolyte imbalance was similar in the groups (56% vs 76.5%, p=0.049). Other laboratory parameters were similar. Laboratory parameters are shown in Table 2.

The days between the first complaint and laparotomy were similar between the groups (6.40 vs 5.70 days, p=0.699). In

the perforated areas, the jejunum was dominant in Group 2 with 64.7%, and the ileum in Group 1 with 68%. The multiple perforation rate was higher in Group 2 but was not statistically significant (12% vs 23.5%, p=0.284). The surgical techniques (p=0.366) and anastomosis techniques (p=0.635) applied were similar. From postoperative complications, anastomosis leakage was higher in Group 1, but it was not statistically significant (12% vs 5.9%, p=0.501). Intraoperative and postoperative outcomes are shown in Table 3.

Discussion

Spontaneous small bowel perforations are rare but essential because of their high morbidity and mortality rates. Currently, it remains an important problem in clinical, surgical practice.

Today, treatment results of non-traumatic small bowel perforation cases are better than in the last decade, due to improvements in imaging methods, surgical techniques and intensive care conditions. Although the mortality rate of small bowel perforation has decreased from 40% to 20%, it remains high.[8,9,10,11] The most commonly blamed

Table 1. Demographic and clinical characteristics

Mean ± SD		Group 1 (n=25) Mean ± SD	Group 2 (n=17)	p
Sex	Male	12 (48.0)	13 (76.5)	0.062
	Female	13 (52.0)	4 (23.5)	
Age (years)		54.08±21.24	61.47±14.30	0.218
ASA	1	11 (44.0)	4 (23.5)	0.005*
	2	11 (44.0)	3 (17.6)	
	3	3 (12.0)	10 (58.8)	
Immunosuppression history		7 (28.0)	6 (35.3)	0.433
Previous abdominal surgery		12 (48.0)	6 (35.3)	0.310
History of malignancy		5 (20.0)	8 (47.1)	0.065
Type of malignity	Lung	1 (4.0)	2 (11.8)	0.320
	Colon	2 (8.0)	4 (23.5)	
	Stomach	0 (0.0)	1 (5.9)	
	Ovary	1 (4.0)	0 (0.0)	
	Rectum	1 (4.0)	1 (5.9)	
	None	20 (80.0)	9 (52.9)	
Comorbid disease	Multiple	6 (24.0)	5 (29.4)	0.883
	Single	9 (36.0)	5 (29.4)	
	None	10 (40.0)	7 (41.2)	
Presenting complaint	Diarrhoea	0 (0.0)	1 (5.9)	0.448
	Abdominal pain	13 (52.0)	11 (64.7)	
	Abdominal pain and constipation	7 (28.0)	2 (11.8)	
	Abdominal pain and vomiting	4 (16.0)	3 (17.6)	
	Abdominal pain and nausea	1 (4.0)	0 (0.0)	
Inflammatory bowel disease history		3 (12.0)	0 (0.0)	0.200

ASA: American Anesthesiology Association score, SD: Standard deviation

reason for the poor outcomes is the late presentation to the hospital.[9,12] Early diagnosis is a critical factor in morbidity and mortality. The delay in surgical treatment worsens electrolyte imbalance and systemic toxaemia due to the rapid progression of peritonitis.[13] The study of Ben-Baruch et al.[14] found that mortality rates were as low as 7.1%. It should be considered that 78.5% of the patients in the study were operated on within the first 24 hours after the onset of their symptoms. In our study, admission time to the hospital was not related to mortality.[14]

In the Uzunoglu et al.[2] study series of spontaneous small bowel perforations, the most common admission types were

Table 2. Laboratory parameters

	Group 1 (n=25) Mean ± SD	Group 2 (n=17) Mean ± SD	p
WBC (mm^3/L)	13.03±4.73	12.55±10.21	0.840
Neutrophil (mm^3/L)	10.80±4.85	10.96±9.48	0.943
Lymphocyte (mm^3/L)	1130.40±637.19	978.23±753.60	0.485
Platelet (mm^3/L)	339.08±123.81	282.41±191.42	0.250
Haemoglobin (g/dL)	11.99±2.66	12.61±2.94	0.482
Albumin (g/dL)	3.05±0.84	2.53±0.79	0.049*
Electrolyte imbalance	14 (56.0)	13 (76.5)	0.151

WBC: White blood cell, SD: Standard deviation

Table 3. Intraoperative and postoperative outcomes

		Group 1 (n=25) Mean ± SD	Group 2 (n=17) Mean ± SD	p
Days between first complaint and laparotomy		6.40±6.44	5.70±4.26	0.699
Hospital stay (days)		33.41±41.74	11.94±9.71	0.045*
Perforated area localisation	Ileum	17 (68.0)	6 (35.3)	0.054
	Ileum + colon	1 (4.0)	0 (0.0)	
	Jejunum	7 (28.0)	11 (64.7)	
Perforation	Single	22 (88.0)	13 (76.5)	0.284
	Multiple	3 (12.0)	4 (23.5)	
Performed surgery	Resection + anastomosis	5 (20.0)	5 (29.4)	0.366
	Resection + stoma	20 (80.0)	12 (70.6)	
Anastomosis technique	Hand-sewn	2 (8.0)	3 (17.6)	0.635
	Stapler	3 (12.0)	2 (11.8)	
	None	20 (80.0)	12 (70.6)	
Additional organ resection	Colon	4 (16.0)	1 (5.9)	0.315
	None	21 (84.0)	16 (94.1)	
Postoperative complication	Anastomosis leakage	3 (12.0)	1 (5.9)	0.501
	Acute kidney failure	1 (4.0)	1 (5.9)	
	Wound site infection	5 (20.0)	1 (5.9)	
	None	16 (64.0)	14 (82.4)	

SD: Standard deviation

abdominal pain (100%), vomiting (76%) and constipation (31%). In their series, 28% of patients had a history of abdominal surgery, and 42% had comorbid diseases. In 88% of patients, there was a perforation in one area, and ileal perforation rate was higher (71%). In their series, the primary repair rate was 11%, resection-anastomosis rate was 62% and resection stoma rate was 26%.[2] The rate of abdominal surgery in our series was similar to that in the literature. In our series, 60% of patients had another disease. Almost all our patients presented with abdominal pain, typically accompanied by constipation and vomiting, similar to the literature. Perforated areas were dominated by the ileum, similar to the literature; however, the jejunum was predominant in patients with mortality. Our perforations frequently developed from a single region. In the decision of the surgical procedure, we considered the aetiology and degree of peritoneal contamination. We did not perform anastomosis on many patients after resection. We associated this with the degree of peritonitis due to patients' admission to the hospital with an average delay of six days. We also attributed the high rate of anastomosis leakage to patients' late admission, low albumin values, comorbid diseases and electrolyte imbalance. The development of postoperative complications did not increase patient mortality. We linked our low hospital stay in the mortality group to the mortalities developing due to early term sepsis.

Albumin is known as a nutritional marker, representing malnutrition in patients. It is also known that albumin is a negative acute phase protein. Therefore, hypoalbuminaemia represents the patient's increased inflammatory state.[15] In a series of 204,819 cases, 25.4% of whom had major cardiovascular surgery, 19.0% had orthopaedic surgery and 55.6% had oncological surgery, mortality rates were approximately four times higher (3.81% vs 0.87%; p<0.001) in the hypoalbuminaemia cohort.[16] Our series supported the literature, and the albumin level was lower in the mortality group.

Inflammatory bowel diseases, such as Crohn's disease and ulcerative colitis, can lead to a perforation in the gastrointestinal tract. Crohn's disease is typically a chronic disease that involves transmural inflammation of the intestinal wall. As a result of Crohn's disease, intestinal perforation usually occurs during an acute exacerbation. Perforation in Crohn's disease continues to be an ongoing cause of acute surgical intervention. Perforation of the small or large intestine secondary to Crohn's disease requires resection, primary anastomosis, or stoma.[17] In our series, three patients had a history of Crohn's disease.

Tan et al.[11] found that ASA 3-4 scores were associated with postoperative poor results and mortality in a far-east study. They evaluated the factors related to morbidity and mortality in small bowel perforations.[11] It was expected that mortality would be more common in patients with various comorbid diseases, immunosuppression and malignancy and high ASA scores.

Study Limitations

Our study's most important limitations were that it was a single centre study and had a retrospective design. However, considering the low incidence of spontaneous small bowel perforations, our series was more extensive.

Conclusion

Patient mortality from spontaneous small bowel perforations was due to the other diseases of the primary patient and the albumin level before the operation. The surgical technique, the perforation location and the time of admission to the hospital did not increase mortality.

Ethics

Ethics Committee Approval: We did not receive an ethics committee approval because the study is retrospective.

Informed Consent: Because the study was retrospective, we could not get informed consent.

Peer-review: Externally and internally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: F.D., E.M.S., T.B.A., G.K.B., M.A., Concept: F.D., U.T., E.M.S., T.B.A., M.A., Design: F.D., U.T., E.M.S., T.B.A., M.A., Data Collection or Processing: E.M.S., G.K.B., Analysis or Interpretation: E.M.S., G.K.B., M.A., Literature Search: F.D., U.T., E.M.S., Writing: F.D., U.T., E.M.S., M.A.

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RESEARCH ARTICLE

Laser Hemorrhoidoplasty of a Single Surgical Centre

Tek Cerrahi Merkezin Lazer Hemoroidoplasti Deneyimleri

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ABSTRACT

Aim: The aim of our study was to assess the outcome of hemorrhoidal dearterialization, achieved by a dedicated laser energy device.
Method: From February 2013 to December 2017, 441 patients with second- or third-degree hemor-rhoids were studied. The primary end point was a reduction in the bleeding rate; secondary end points were; reduction in pain and recurrence of the symptoms which patients complaint. The procedure was carried out as 1-day surgery. A 1,470 nm diode laser device was employed to seal the terminal branch-es of the hemorrhoidal arteries. Follow-up was scheduled at 1 and 4 weeks, 3 and 6 months.
Results: Two early postoperative bleeding (2/441) which recquired surgical intervention, Late com-plications were Eight (8/441) thrombosed hemorrhoids that resolved medically and recurrence of the symptoms which patients suffer in 10 patients (10/441). Postoperative pain was recorded by using a 10-point visual analog scale (VAS) on which 0 represents no pain and 10 represents the worst pain imaginable. VAS protocol was followed up after 1 week, 1 month. Mean pain score was 0.65 in postoperative 1 week and decreased gradually. All patients were discharged on the day of surgery.
Conclusion: The hemorrhoid laser procedure was effective in improving bleeding and pain symp-toms in patients with Grade II and III hemorrhoids, but prospective randomized controlled studies are needed for evidence based conclusions.
Keywords: Dearterialization, hemorrhoidal disease, laser

ÖZ

Amaç: Çalışmamızın amacı, özel bir lazer enerji cihazı ile gerçekleştirilen hemoroidal arteri kapatma işleminin sonucunu değerlendirmekti.
Yöntem: Şubat 2013'ten Aralık 2017'ye kadar 441 Grade 2-3 hemoroid hastası çaşılmaya dahil edildi. Birincil hedef kanamanın azalması; ikincil hedefler ağrının ve hasta şikayetlerinin nüksünün azalması idi. İşlem 1 günlük cerrahi girişim olarak uygulandı. Hemoroidal arterlerin terminal uçlarını kapatmak için 1470 nm diod lazer cihazı kullanıldı. Hastalar 1. hafta, 4. hafta 3 ve 6. aylarda takip edildi.
Bulgular: İki olguda postoperatif erken kanama (2/441) oldu ve bunlar cerrahi girişim gerektirdi. Geç komplikasyon olarak Sekiz olguda (8/441) tromboze hemoroid gelişti, bunlar medikal tedavi ile düzeldi. On olguda (10/441) ameliyat öncesi şikayetleri tekrarladı (nüks). Postoperatif ağrı 10 üzerinden görsel analog ölçek (VAS) ile kaydedildi. 0: hiç ağrı yok, 10: en kötü ağrı olarak değerlendirildi. VAS skoru 1 hafta ve 1 ay sonra da tekrarlandı. Ağrı skoru postoperatif 1. haftada 0.65 idi ve giderek azaldı. Tüm hastalar ameliyat günü taburcu edildiler.
Sonuç: Hemoroidal laser girişimi Grade 2 ve 3 hemoroidlerde kanama ve ağrıyı tedavi etmede etkili bir yöntemdir, fakat kanıta dayalı sonuçlar elde etmek için prospektif randomize kontrollü çalışmalara gereksinim vardır.
Anahtar Kelimeler: Dearterialization, hemoroidal hastalık, lazer

Introduction

Haemorrhoidal disease (HD) is a common disorder that affects millions of people worldwide and causes significant disability. Further, rectal bleeding, pain, anal irritation and prolapse, which can lead to an altered quality of life, are the most common symptoms.[1] Despite the fact that there are multiple techniques used to treat HD, there are still contradictory views about the ideal procedure, i.e. the most effective and without causing discomfort to the patient.[2,3] Conventional excisional haemorrhoidectomy[4,5] is an

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effective treatment for HD, but, severe postoperative pain is commonly experienced.[6] Morinaga et al.[7] first identified a non-excisional technique, known as haemorrhoidal artery ligation, in the 1990s. This approach is based on reducing the supply of blood to the terminal branches of the haemorrhoidal arteries using Doppler-guided identification and surgical ligation of the vessels. Further, the subsequent decrease in the blood supply results in a reduction in the volume of the haemorrhoidal plexus, resulting in shrinkage of the haemorrhoidal cushions.[8,9] Giamundo et al.[10,11] have also recently suggested a Doppler-guided laser dearterialization of the terminal branches of the superior haemorrhoidal arteries (HeLP procedure). Thus, the goal of our single-centre retrospective study was to report the results of HeLP in patients with symptomatic second- and third-degree haemorrhoids.

Materials and Methods

In this study, 441 patients suffering from Grades II and III HD were included. Furthermore, the criteria for exclusion were fourth-degree and prolapsed haemorrhoids and any coexisting anal conditions such as anal fissure or fistula. In addition, all those procedures were done by three surgeons. Preoperatively, a thorough medical history was taken, and patients underwent routine blood tests and physical examination (inspection, palpation and digital rectal examination). Anoscopy was routinely conducted, but colonoscopy was only performed in selected patients.

Two enemas (135 mL) were administered preoperatively (on the evening before surgery and early on the morning of the procedure). Antibiotic prophylaxis with 500 mg metronidazole was regularly administered 30 minutes before the procedure.

Mask anaesthesia was administered to the patients in lithotomy position. Following anal retractor insertion, a 2-mm skin incision close to the anal verge was performed. Up to the apex of haemorrhoidal cushion, the laser probe was promoted. Moreover, four to six beams per pack were applied in 3 seconds (6W 1470 nm diode laser) during proximal and distal retraction of the probe form (Figure 1). After the procedure, an anal spongostan was inserted into the anal canal, and 10 cc of local anaesthetic was injected around the anus. The mean procedure time was 7 (5-12) minutes. After 4-8 hours of surgery, the patients were discharged.

Data and procedure-related data of the patients, rates of peri- and postoperative complications, and pre- and postoperative symptoms were collected. A 10-point visual analogue scale (VAS) was used to record postoperative pain, where 0 represents no pain and 10 represents the worst pain imaginable. After 1 week and 1 month, the VAS protocol was followed up.

Recurrence was defined as any symptom that resolved after the surgical procedure but recurred during follow-up and caused discomfort.

All patients were informed about the procedure, and certificate of consent was taken for every patient.

Statistical Analysis

The t-test for continuous variables and x2 test for categorical values were used to compare preoperative and postoperative outcomes. A p value below 0.05 was considered statistically significant. Moreover, the analysis was conducted using standard statistical software for biomedical research (SPSS for MAC advanced statistical software, release 20.0, SPSS Inc., Chicago, IL, USA).

Figure 1. 6W 1470 nm diode laser application

Table 1. Pain presentation by VAS score

VAS score	Day 1 (patient%)	Day 7 (patient%)	1 month (patient%)
0-1	110/441 (25%)	419/441 (95%)	441/441 (100%)
2-5	331/441 (75%)	22/441 (5%)	0/441 (0%)
>5	0/441 (0%)	0/441 (0%)	0/441 (0%)

VAS: Visual analogue scale

Results

Between 2013 and 2017, 441 patients [251 (57%) male and 190 (43%) female] were operated on with laser coagulation at our facility. Moreover, 10 patients had Grade II (3%) while 431 had Grade III (97%) disease, with a mean age of 43.1 (22-71).

The hemorrhoid laser procedure (HLP) was performed on 441 patients who had symptomatic Grades II and III haemorrhoids with a mean age of 43.1±11.3 (range: 22-71) years. The mean surgical time was 7.36±3.7 min. In two cases, early postoperative bleeding was observed and surgical haemostasis was required. Postoperative nonsteroid analgesics were administered on demand for 2-5 days. There was no major pain reported that required narcotic medication. In any of the cases, no blood transfusions were needed. Over the first year, ten patients' symptoms recurred (2.3%).

Discussion

Our single-centre study confirms the safety and efficacy of the HLP procedure for the treatment of haemorrhoids. Moreover, it showed that the good results are maintained in the long term and that patients thought there was a good level of improvement after surgery.

Over the past few decades, several non-excisional techniques for treating HD were developed. These surgical approaches are focused on the replacement of haemorrhoidal cushions within the anal canal, such as in Longo's procedure[12,13] or in the reduction in the arterial inflow in the haemorrhoidal plexus obtained by ligation of the terminal branches of the haemorrhoidal arteries under Doppler guidance.[14] The most effective surgical procedure for HD, namely, excisional haemorrhoidectomy, is associated with moderate to severe postoperative pain that is difficult to manage at home. Unfortunately, an efficient and painless procedure has not yet been identified. Dearterialization techniques have demonstrated good results in the treatment of second- and third-degree haemorrhoids.[15] However, when evaluated in randomized trials, the postoperative course was not significantly different from that after the excisional procedures.[16,17] Recently, the HLP technique was introduced as a new minimally invasive dearterialization procedure, where sealing of the arterial flow to the haemorrhoidal plexus was obtained by laser photocoagulation of the terminal branches of the superior rectal artery. The literature demonstrated that this procedure is effective, with low intraoperative and postoperative morbidity and little postoperative pain expected.[18] Postoperatively, preoperative bleeding and pain were greatly improved, and the benefit observed after 3 months was maintained over the long term.[19] In this study, we included Grades II and III haemorrhoid patients, but from our previous studies, we observed minimal retraction effect on mucosal prolapse with HLP. We also reported recurrence of symptoms in ten patients (2.3%), all during the first year. This is comparable with short-term results of other non-excisional procedures.[20] The reasons for recurrences are not known. In this procedure, we applied four to six beams (in 3 seconds) to each haemorrhoid. This is up to the expertise of the surgeon. This aspect, we assume, is the lack of this technique. Finally, it could be argued that the HLP kit is rather expensive (300 dollars). However, HLP is associated with a shorter operating period and hospital stay than other non-excisional procedures, and little postoperative care is required. Moreover, as regards the social cost of the treatment, patients resumed normal habits and work practices earlier. In the short term, the present study showed a good resolution of symptoms. However, to evaluate the accuracy of this procedure, studies with longer follow-up as well as randomized controlled trials are needed.

Conclusion

This single-centre study has shown that the HLP procedure in patients with second- and third-degree haemorrhoids is effective and is associated with a short operative and recovery time, can be carried out in a day surgery setting with minor intra- and postoperative pain, and provides a significant improvement in symptoms. Since this is not a prospective randomized controlled study, the evidence value is low. The initial results of the study are maintained in the long term; therefore, as an author recommendation, this procedure could be regarded as an alternative to more invasive interventions in early-stage HD.

Ethics

Ethics Committee Approval: Since it is a retrospective study, ethics committee approval is not required.

Informed Consent: All patients were informed about the procedure, and certificate of consent was taken for every patient.

Peer-review: Internally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: Ü.S., T.O., E.U., Concept: Ü.S., Design: ÜS., Analysis or Interpretation: Ü.S., Literature Search: Ü.S., Writing: Ü.S.

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

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RESEARCH ARTICLE

C-Reactive Protein to Albumin Ratio: A Reliable Marker in Colorectal Cancer

Kolorektal Kanser Cerrahisinde Güvenilir Bir Belirteç: C-reaktif Proteinin Albümine Oranı

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ABSTRACT

Aim: Postoperative complications after colorectal cancer surgery result in increased treatment costs, prolonged hospital stays and poor prognosis and reduce quality of life of the patients. Here, we aim to contribute to the literature in terms of being a reliable marker of postoperative C-reactive protein (CRP) to albumin ratio (CAR) after colorectal cancer surgery.

Method: A total of 213 patients undergoing colorectal cancer surgery between 2013 and 2018 were analyzed in this study. Risk factors for the development of postoperative complications were analyzed using univariate and multiple logistic regression models. A receiver operating characteristic (ROC) curve analysis was used to analyze the association with the CRP and CAR variables, with the aim being to differentiate postoperative complications.

Results: Postoperative complications occurred in 87 (40.8%) patients. Based on the Clavien-Dindo classification, 25 (18.7%) patients developed major complications. Perioperative blood transfusion [odds ratio (OR)=1.3; 95% confidence interval (CI)=1.08-1.55] and postoperative CAR (OR=1.2; 95% CI=1.05-1.35) were independent risk factors for postoperative complications (p=0.005 for each). The cut-off value for CAR was 4.3 (sensitivity: 51.72; specificity: 71.43; and area under the curve: 0.642), meaning that CAR was found to be statistically significantly effective in differentiating postoperative complications (p<0.001). The (median) length of hospital stay was statistically significantly longer in the high CAR (>4.3) group (p=0.001), while the laparoscopic surgery rate was statistically significantly lower in the high CAR group (p=0.039).

Conclusion: CAR is a novel, reliable and independent marker. Moreover the ratio is useful for clinicians and provides the determination of early postoperative complications after colorectal cancer surgery.

Keywords: C-reactive protein to albumin ratio, colorectal cancer, postoperative complication

ÖZ

Amaç: Kolorektal kanser cerrahisi sonrası postoperatif komplikasyonlar, tedavi maliyetlerinin artmasına, hastanede kalış sürelerinin uzamasına ve kötü prognoza neden olur ve hastaların yaşam kalitesini düşürür. Burada kolorektal kanser cerrahisi sonrası postoperatif C-reaktif protein (CRP)/albümin oranının (CAR) güvenilir bir belirteci olması açısından literatüre katkıda bulunmayı hedefliyoruz.

Yöntem: Bu çalışmada 2013-2018 yılları arasında kolorektal kanser cerrahisi geçiren toplam 213 hasta analiz edildi. Postoperatif komplikasyonların gelişimi için risk faktörleri, tek değişkenli ve çoklu lojistik regresyon modelleri kullanılarak analiz edildi. Postoperatif komplikasyonları ayırt etmek amacıyla CRP ve CAR değişkenleri ile ilişkiyi analiz etmek için bir alıcı çalışma özelliği (ROC) eğri analizi kullanıldı.

Bulgular: Seksen yedi (%40,8) hastada ameliyat sonrası komplikasyon gelişti. Clavien-Dindo sınıflandırmasına göre 25 (%18,7) hastada majör komplikasyonlar gelişti. Perioperatif kan transfüzyonu [olasılık oranı (OO)= 1,3; %95 güven aralığı (GA)= 1,08-1,55] ve postoperatif CAR (OO= 1,2; %95 GA= 1,05-1,35) postoperatif komplikasyonlar için bağımsız risk faktörleriydi (her biri için p=0,005). CAR için cut-off değeri 4,3 idi (duyarlılık:

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51,72; özgüllük: 71,43; ve eğri altındaki alan: 0,642), yani CAR'nin postoperatif komplikasyonları ayırt etmede istatistiksel olarak anlamlı derecede etkili olduğu bulundu (p<0,001). Hastanede kalış süresi (ortanca) yüksek CAR (>4,3) grubunda istatistiksel olarak anlamlı derecede daha uzun iken (p=0,001), yüksek CAR grubunda laparoskopik cerrahi oranı istatistiksel olarak anlamlı derecede düşüktü (p=0,039).

Sonuç: CAR, yeni, güvenilir ve bağımsız bir belirteçtir. Ayrıca oran klinisyenler için yararlıdır ve kolorektal kanser cerrahisi sonrası erken postoperatif komplikasyonların belirlenmesini sağlar.

Anahtar Kelimeler: C-reaktif albümin oranı, kolorektal kanser, postoperatif komplikasyon

Introduction

Colorectal cancer is the third most commonly diagnosed form of cancer and the fourth leading cause of cancer-related death around the world.[1] The current curative treatment approach is still surgical resection, despite the improvements in colonoscopic interventions and chemotherapy.[2] Several complications occur after a surgical resection for colorectal cancer.[3,4] Such complications result in increased treatment costs, infections, prolonged hospital stays, delayed recovery times and poor prognosis.[5,6] Accordingly, early identification and the appropriate management of postoperative complications can improve clinical outcomes.

Many factors have been closely linked to cancer, including inflammation and wound healing.[7,8] Inflammation induces the release of cytokines, inhibits apoptosis and causes DNA injury, contributing to the growth, proliferation, invasion and metastasis of cancer cells.[9,10] Proinflammatory cytokines increase due to surgical trauma, resulting in changes in the acute phase reactants in the blood, such as albumin and the C-reactive protein (CRP).[11]

Systemic inflammatory response plays an important role in carcinogenesis and tumor progression, and a number of systemic inflammatory markers have been used for its identification, such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), Glasgow Prognostic Score (GPS), hemoglobin and albumin levels and lymphocyte and platelet count(HALP) and CRP. Recently, the preoperative CRP/albumin ratio (CAR) has come into use as a new inflammatory marker for various cancer types.[12,13,14,15] Literature contains several studies in which preoperative CAR has been used to determine complications following colorectal surgery, although researches investigating postoperative CAR are limited. Among these, the study by Ge et al.[11] demonstrated that the association between postoperative CAR after colorectal surgery with postoperative complications had a high diagnostic accurac.[11]

The present study contributes to literature by establishing the association of postoperative CAR with postoperative complications among patients who had undergone a curative resection due to colorectal cancer.

Methods

A retrospective examination was made of 213 patients who had been histopathologically diagnosed with colorectal cancer in a gastrointestinal surgery clinic between 2013 and 2018. The ethics committee of the hospital granted approval for the study (No: 2019.7/06-220), which was conducted in accordance with the principles of the Declaration of Helsinki (revised in 2013). All surgeries were performed by the same group of surgeons. The laboratory results of the preoperative period and the postoperative day 3 were evaluated. The study included patients aged 18 years and older who had been histopathologically diagnosed with colorectal adenocarcinoma, and who underwent curative surgical resection. The study excluded patients who had undergone an R1/R2 resection, and those with liver cirrhosis, those who had perioperatively received an intravenous albumin infusion, those with preoperative systemic infections, those who underwent an additional organ resection and those who underwent repeat surgery within postoperative three days. Data were acquired through demographic characteristics, laboratory tests and surgical characteristics. The demographic characteristics included gender, age, body mass index (BMI), comorbidities (diabetes mellitus [DM], hypertension [HT], coronary artery disease [CAD], chronic obstructive pulmonary disease [COPD]), smoking, American Society of Anesthesiologists (ASA) scores, laparoscopic or open technique, surgery type and sarcopenia. The laboratory tests included preoperative hemoglobin, hematocrit, serum albumin and CRP levels, and postoperative third day levels of CRP and serum albumin.

A recent review has demonstrated that perioperative immunonutrition prevents postoperative complications[16], and so patients who were administered perioperative immunonutrition in our clinic were also recorded according to the current guidelines.[17]

Furthermore, all patients who received a perioperative blood transfusion, as a possible cause of postoperative complications, were also recorded. The lengths of intensive care unit and hospital stay were recorded to evaluate clinical outcomes.

Definition of Postoperative Complications

Complications occurring within 30 days of surgery were defined as postoperative complications. All complications were categorized according to the Clavien-Dindo classification system.[18] Accordingly, grade I and II complications were classified as minor complications, and grade III and higher grade complications were classified as major complications. CAR was calculated by dividing the postoperative third day CRP value by the serum albumin value. A Receiver Operating Characteristics (ROC) curve analysis was used to determine the cut-off value for CAR.

Furthermore, the widely-accepted Charlson Comorbidity Index (CCI) was used to assess the effects of patient comorbidities. CCI is mostly used to estimate survival in cancer patients, although a number of researchers have found it to be useful also for estimating the clinical outcomes of colon cancer patients.[19,20]

Statistical Analysis

The study data were summarized as tabular descriptive statistics and expressed as mean ± standard deviation or median (IQR) for continuous variables. Categorical variables were expressed as numbers and percentages. Numerical variables were tested for normality using a Kolmogorov-Smirnov test. An Independent Samples t-test and a Mann-Whitney U test were used for the comparison of two independent groups for normally and non-normally distributed numerical variables, respectively. Pearson's Chi-Square or Fisher's Exact Tests were used to compare categorical variables for differences. Risk factors for the development of postoperative complications were analyzed using univariate and multiple logistic regression models, and the results were presented as odds ratio and at a 95% confidence interval.

A ROC curve analysis was used to analyze the association with the CRP and CAR variables, with the aim being to differentiate postoperative complications. The optimal cut-off values, 95% confidence interval and area under the curve (AUC) were calculated based on Youden's index using DeLong's method in the MedCalc Statistical Software Trial version (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2015) program. Statistical analyses were carried out using Jamovi (Version 1.0.7) and JASP (version 0.11.1) software, and a p-value of 0.05 was considered significant in the statistical analyses.

Results

The mean age of study participants was 61.3±13.2 years. Among study participants, there were 119 male and 94 female patients. Postoperative complications occurred in 87 (40.8%) patients. Based on the Clavien-Dindo classification, 25 (18.7%) patients developed major complications. Additionally, 42 (19.7%) patients developed surgical site infections. The median length of hospital stay was 8 days.

Table 1 presents a comparison of certain demographic and clinical characteristics and the development of postoperative complications. A univariate analysis revealed that the development of complications was statistically significantly associated with length of stay in the intensive care unit, the length of hospital stay, perioperative blood transfusion and laparoscopic surgery. Patients with postoperative complications had longer stays in both intensive care and hospital. Furthermore, postoperative complications were statistically significantly associated with lower postoperative albumin levels and higher postoperative third day CRP and CAR levels (p=0.032, p=0.001, respectively). None of the other comparisons revealed any statistically significant differences (p>0.05 for each, Table 1).

Table 2 presents the cut-off values, calculated using a ROC analysis based on the CRP and CAR variables and the influence on postoperative complication development. Accordingly, the cut-off value for CRP was 7.9 (sensitivity: 86.21; specificity: 36.51; and AUC: 0.646), meaning that CRP was statistically significantly effective in differentiating postoperative complications (p<0.001) (Figure 1). Furthermore, the cut-off value for CAR was 4.3 (sensitivity: 51.72; specificity: 71.43; and AUC: 0.642), meaning that CAR was found to be statistically significantly effective in differentiating postoperative complications (p<0.001). The comparison of the AUC values for CPR and CAR revealed no superiority between the two (p=0.769).

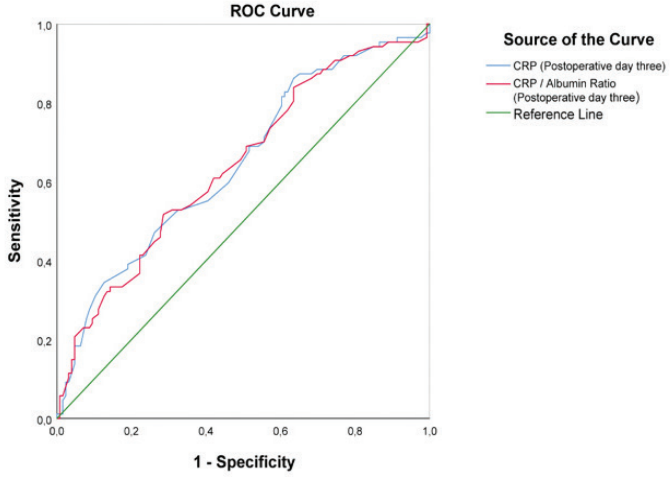

Figure 1. ROC curve analysis of postoperative 3rd day CRP and CAR values

CRP: C-reactive protein, CAR: C-reactive protein to albumin ratio

Table 1. Comparison of certain demographic and clinical characteristics and the development of postoperative complications

		Postoperative complication		
	All (n=213)	**No (n=126)**	**Yes (n=87)**	**p-value**
Age	61.3±13.2	60.2±12.3	62.9±14.3	0.158*
Gender (%)				
Male	119 (55.9)	71 (56.3)	48 (55.2)	0.976**
Female	94 (44.1)	55 (43.7)	39 (44.8)	
BMI (%)				
<25	69 (32.4)	45 (35.7)	24 (27.6)	0.273**
≥25	144 (67.6)	81 (64.3)	63 (72.4)	
Smoking (%)	56 (26.4)	37 (29.6)	19 (21.8)	0.270**
Perioperative immunonutrition (%)	103 (48.4)	65 (51.6)	38 (43.7)	0.319**
Sarcopenia (%)	82 (42.7)	47 (41.2)	35 (44.9)	0.724**
HT (%)	69 (32.4)	37 (29.4)	32 (36.8)	0.323**
DM (%)	45 (21.1)	27 (21.4)	18 (20.7)	0.999**
COPD (%)	14 (6.6)	5 (4.0)	9 (10.3)	0.118**
CAD (%)	42 (19.7)	24 (19.0)	18 (20.7)	0.904**
Intensive care unit stay (day), (median)	1.0 [1.0- 1.0]	1.0 [1.0- 1.0]	1.0 [1.0- 1.0]	**0.001****
Length of hospital stay (day), (median)	8.0 [7.0- 14.0]	7.0 [6.0- 8.0]	15.0 [12.0- 20.0]	**0.001****
Operation time (min), (median)	210.0 [160.0- 250.0]	220.0 [166.2- 250.0]	210.0 [160.0- 260.0]	0.931***
Perioperative blood transfusion (median)	0.0 [0.0- 2.0]	0.0 [0.0- 2.0]	1.0 [0.0- 2.5]	**0.003****
Anterior resection (%)	42 (19.7)	24 (19.0)	18 (20.7)	0.904**
Low anterior resection (%)	74 (34.7)	43 (34.1)	31 (35.6)	0.936**
Right hemicolectomy (%)	57 (26.8)	32 (25.4)	25 (28.7)	0.701**
Left hemicolectomy (%)	19 (8.9)	13 (10.3)	6 (6.9)	0.538**
Subtotal colectomy (%)	5 (2.3)	2 (1.6)	3 (3.4)	0.401**
Total colectomy (%)	1 (0.5)	1 (0.8)	0 (0.0)	0.999**
Transverse colectomy (%)	3 (1.4)	3 (2.4)	0 (0.0)	0.272**
Loop ileostomy (%)	45 (21.1)	23 (18.3)	22 (25.3)	0.287**
Miles (%)	12 (5.6)	8 (6.3)	4 (4.6)	0.765**
Harttman (%)	2 (0.9)	1 (0.8)	1 (1.1)	0.999**
Laparoscopic (%)	52 (24.4)	39 (31.0)	13 (14.9)	**0.012****
ASA ≥3 (%)	141 (66.2)	81 (64.3)	60 (69.0)	0.574**
Charlson Comorbidity Index (median)	3.0 [2.0- 4.0]	3.0 [2.0- 4.0]	4.0 [2.0- 5.0]	0.057***
Charlson Comorbidity Index (%)				
≥2	174 (81.7)	101 (80.2)	73 (83.9)	0.606**
<2	39 (18.3)	25 (19.8)	14 (16.1)	0.606**
Preoperative hematocrit	34.9±5.6	35.4±5.8	34.3±5.3	0.188*
Preoperative albumin (mg/dL)	4.1±0.5	4.1±0.5	4.1±0.4	0.580*
Preoperative CRP (mg/dL), (median)	0.7 [0.3- 1.7]	0.6 [0.3- 1.4]	0.8 [0.3- 1.9]	0.252***
Albumin (Postoperative 3rd day)	3.0±0.4	3.1±0.4	3.0±0.4	**0.032***
CRP (Postoperative 3rd day), (median)	11.0 [7.8- 16.0]	10.0 [6.0- 14.0]	13.0 [9.0- 19.5]	**0.001*****
CAR (Postoperative 3rd day), (median)	3.6 [2.4- 5.3]	3.2 [1.9- 4.8]	4.4 [2.8- 6.2]	**0.001*****

BMI: Body mass index, HT: Hypertension, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, CAD: Coronary artery disease, CRP: C-reactive protein

Based on the CAR cut-off value, 132 patients were classified as low CAR (≤4.3) and 81 patients as high CAR (>4.3) groups. Table 3 presents a comparison of certain clinical parameters by CAR. Accordingly, the (median) length of hospital stay was statistically significantly longer in the high CAR (>4.3) group (p=0.001), while the laparoscopic surgery rate was statistically significantly lower in the high CAR group (p=0.039).

A multivariate analysis model was then applied to determine the risk factors from the univariate analysis that were independently associated with postoperative complications (Table 4). First, a univariate logistic regression model was analyzed, and all variables included in the model were found to be statistically significant (p<0.05 for each, Table 4). An analysis of the multiple logistic regression model revealed that perioperative blood transfusion (OR=1.3; 95% CI=1.08-1.55) and CAR (OR=1.2; 95% CI=1.05-1.35) were independent risk factors for postoperative complications (p=0.005 for each).

Discussion

The present study demonstrated postoperative CAR to be an independent and a significant risk factor for postoperative complications among 213 patients who underwent curative

Table 2. ROC analysis results of postoperative complication based on CRP and CAR variables

	AUC	Sensitivity	Specificity	Cut-Off	95% CI	p-value	Pairwise comparison of ROC curves p-value
CRP	0.646	86.21	36.51	>7.9	0.578–0.710	**<0.001**	0.769
CAR	0.642	51.72	71.43	>4.3	0.574- 0.706	**<0.001**	

CRP: C-reactive protein, CAR: C-reactive protein to albumin ratio, CI: Confidence interval, ROC: Receiver operating characteristic, AUC: Area under the curve

Table 3. Comparison of certain clinical parameters based on CAR levels of patients

		CAR		
	All (n=213)	**≤4.3 (n=132)**	**>4.3 (n=81)**	**p**
BMI (%)				
<25	69 (32.4)	45 (34.1)	24 (29.6)	0.600*
≥25	144 (67.6)	87 (65.9)	57 (70.4)	
Smoking (%)	56 (26.4)	35 (26.7)	21 (25.9)	0.999*
Perioperative immunonutrition (%)	103 (48.4)	64 (48.5)	39 (48.1)	0.999*
Sarcopenia (%)	82 (42.7)	50 (42.4)	32 (43.2)	0.999*
6th month survival (%)	6 (2.8)	3 (2.3)	3 (3.7)	0.676*
HT (%)	69 (32.4)	41 (31.1)	28 (34.6)	0.704*
DM (%)	45 (21.1)	28 (21.2)	17 (21.0)	0.999*
COPD (%)	14 (6.6)	10 (7.6)	4 (4.9)	0.639*
CAD (%)	42 (19.7)	24 (18.2)	18 (22.2)	0.588*
Intensive care unite (day), (median)	1.0 [1.0- 1.0]	1.0 [1.0- 1.0]	1.0 [1.0- 1.0]	0.775**
Length hospital stay (day), (median)	8.0 [7.0- 14.0]	8.0 [7.0- 11.0]	10.0 [7.0- 16.0]	**0.001****
Laparoscopic (%)	52 (24.4)	39 (29.5)	13 (16.0)	**0.039***
Charlson Comorbiditiy Index (%)				
≥2	174 (81.7)	103 (78.0)	71 (87.7)	0.114*
<2	39 (18.3)	29 (22.0)	10 (12.3)	
Clavian dindo (%)				
<3	109 (81.3)	65 (86.7)	44 (74.6)	0.119*
≥3	25 (18.7)	10 (13.3)	15 (25.4)	

BMI: Body mass index, HT: Hypertension, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, CAD: Coronary artery disease,

Table 4. Univariate and multiple logistic regression analyses of the factors affecting postoperative complication development

	Univariate LR		Multiple LR	
	OR. (95%CI)	p-value	OR. (95%CI)	p-value
Perioperative blood tx	1.35 [1.13-1.62]	**0.001**	1.3 [1.08-1.55]	**0.005**
Laparoscopic: Yes vs. No	0.39 [0.19-0.79]	**0.009**	0.48 [0.23-1.01]	0.055
Albumin (postoperative 3rd day)	0.47 [0.23-0.96]	**0.038**	1.18 [0.51-2.76]	0.698
CRP (postoperative 3rd day)	1.08 [1.03-1.12]	**< 0.001**	-	-
CAR (postoperative 3rd day)	1.21 [1.08-1.35]	**< 0.001**	1.2 [1.05-1.35]	**0.005**

Dependent variable: Presence of Post-op complication. Bold p values were considered statistically significant (p<0.05). OR: Odds ratio, LR: Logistic regression, CI: Confidence interval, CRP was not included in the multiple model due to multicollinearity problems.

CRP: C-reavtive protein

surgical resection due to colorectal cancer. Furthermore, the ROC analysis revealed that high CAR values prolonged the hospital stays, and that postoperative CAR was higher in patients who had not undergone laparoscopic surgery.

CRP is an acute phase reactant that is synthesized by the liver. Elevated CRP serum levels induce the release of the inflammatory cytokines associated with cancer. In addition, serum albumin level is a commonly used marker for nutritional status, and is associated with the chronic inflammatory process that activates cytokines like IL-1 and TNF-α.[21,22] Recent studies have demonstrated that a systemic inflammatory response after surgical trauma is associated with poor outcomes, which was established with serum levels of CRP and albumin.[23,24] A recent study reported that CRP alone was not a sufficient determining factor indicating inflammation in the early postoperative period.[25]

Ge et al. conducted a study to determine postoperative complications in the early period after colorectal surgery, and established a ratio using CRP and albumin together. They found that the postoperative third day CAR value had a higher diagnostically accurate association with postoperative complications than CRP (predictive value [PPV] for CRP: 79.1%; PPV for CAR: 81.4%). Additionally, the CAR cut-off value was found to be 2.2, and an independent risk factor for postoperative complications (AUC of CAR was 0.779, sensitivity was 0.748, specificity was 0.695).[11] A recent study by Man et al., in turn, compared modified GPS, CAR, postoperative GPS and CRP values to determine postoperative complications after colorectal cancer surgery. The authors reported that the postoperative third day CAR value was more useful than the other markers among all of these scoring systems (AUC: 0.711, PPV: 83.2%); the cut-off value was 2.6 (sensitivity: 51.3%, specificity: 87.8%); and the postoperative complication rate was higher in those with high CAR (≥2.6) values.[26]

Our study had a larger sample size than the two similar studies identified, but established a postoperative complication rate that was lower than those two studies (40.8%).[11,26] Different to these studies, we found the CAR cut-off value to be 4.3 (sensitivity: 51.72, specificity: 71.43, and AUC: 0.642). Despite the lower specificity and AUC values, the multiple logistic regression analysis revealed CAR to be an independent risk factor for postoperative complications, which was consistent with other studies. Furthermore, an AUC value of >0.5 is statistically a good predictor of postoperative complications. Other studies.[11,26] found major and minor postoperative complications, based on the Clavien-Dindo classification, to be statistically significantly lower in the low CAR group, whereas no statistically significant association was identified between patients with postoperative minor and major complications, and CAR in the present study. On the other hand, our study reported longer hospital stays and lower laparoscopic surgery rates in the high CAR group.

Once again, the studies by Man et al.[26], and Ge et al.[11] failed to identify any statistically significant association between laparoscopic surgery and postoperative complications, while the present study identified a lower postoperative complication rate among patients undergoing laparoscopic surgery. In a similar vein, literature contains a number of studies reporting reduced postoperative complication rates and shortened hospital stays with laparoscopic surgery when compared to open surgery.[27,28]

Another point to emphasize about the present study is the identification of a perioperative blood transfusion as an independent risk factor for postoperative complications. In a recent meta-analysis it was indicated that transfusions can lead to infections, and pulmonary, cardiac, anastomotic and overall complications among patients undergoing colorectal cancer surgery.[29]

Although there was no statistically significant association between CCI and postoperative complications (p=0.057), postoperative complications were found to be more common among patients with a higher median CCI value (>3). Similar to the present study, Huang et al.[20] reported more postoperative complications in the group with CCI ≥3 among elderly colorectal cancer patients who had undergone laparoscopic surgery.[20]

Additionally, two recent meta-analyses reported high preoperative CAR to be associated with poor prognosis and disease-free survival in colorectal cancer patients.[30,31] Our study made no investigation of the link with survival, although further studies may analyze the relationship between postoperative CAR and prognosis and disease-free survival in colorectal cancer patients.

Study Limitations

There are some limitations in the present study, first and foremost among which is its retrospective, single-center design. Second, CAR was not compared with other inflammatory scoring systems, and so it could not be established whether or not it was superior to other markers. As such, there is a need for prospective, multi-center and large-scale studies with a larger sample size for the comparison of other markers.

Conclusion

Despite the lack of comparison with other inflammatory markers, CAR is an easy to use and independent ratio for clinicians that allows the early postoperative determination of complications. Especially today, when there are still high postoperative complication rates after colorectal surgery, it is of vital importance to identify and manage postoperative complications in the early period with a view to shortening hospital stays, decreasing hospital costs and improving the quality of life of patients.

Ethics

Ethics Committee Approval: The ethics committee of the hospital granted approval for the study (no: 2019.7/06-220), which was conducted in accordance with the principles of the Declaration of Helsinki (revised in 2013).

Informed Consent: The informed consent was given by all the participated patients.

Peer-review: Externally and internally peer reviewed.

Authorship Contributions

Design: Ö.Z.S., E.P., M.D., Data Collection or Processing: H.B., T.Ö., E.A., O.U., Analysis or Interpretation: S.G., A.S.Z., Writing: Ö.Z.S.

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RESEARCH ARTICLE

Seasonal Pattern of Diverticular Disease Admissions in Central Anatolia

Orta Anadolu'da Divertiküler Hastalık Başvurularının Mevsimsel Paterni

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ABSTRACT

Aim: In the present study, we aimed to investigate the seasonal characteristics of presentations to the hospital due to diverticular disease.
Method: The patients who were admitted to the hospital between January 1st, 2015 and January 1st, 2020 due to diverticular disease were included in the study. The study was designed retrospectively. The patients were divided into groups according to the treatment method, namely Group 1: patients who received surgical treatment, and Group 2: patients who received medical treatment. Age, sex and seasonal periods were compared. Also, the patients were separated into three groups according to age: those between 18 and 40 years of age, those between 40 and 60 of age and those over 60 years of age. The sex and the treatment methods of the patients were also examined in the season groups
Results: One hundred fifty seven patients participated in our study. Group 1 consisted of 39 patients and Group2 consisted of 118 patients. Presentations to the hospital with acute diverticulitis occurred most frequently in the winter (39.5%). The average age was higher in Group 1 (60.61 vs 54.42, p=0.030). The sex distribution was similar in the groups (p=0.152). Winter was dominant in treatment groups (30.8% vs 42.4% p=0.060). In winter, the average age of the patients who received surgical treatment was higher than those who received medical treatment (68 vs 50 p=0.001). In winter, all patients who received surgical treatment were over 60 years of age. In summer, the ratio of patients who received medical treatment was highest for the group over 60 years of age (p=0.040).
Conclusion: In our study, we displayed the seasonal change in hospital admissions due to diverticular disease. We detected an increased rate of presentations to the hospital in winter. Selection of the treatment method did not display a seasonal variation. However, when we made an additional evaluation according to the age groups, it was seen that greater number of patients who were older than 60 years received surgical treatment in winter whereas the greater number of them received medical treatment in summer. Pathophysiological mechanism of this change could not be fully revealed.
Keywords: Diverticular disease, seasonal change, surgical treatment

ÖZ

Amaç: Bu çalışmada divertiküler hastalık sebebiyle hastaneye başvurunun mevsimsel eğilimlerini araştırmayı amaçladık.
Yöntem: 1 Ocak 2015 ile 1 Ocak 2020 yılları arasında divertiküler hastalık nedeniyle hastaneye yatırılan hastalar çalışmaya dahil edildi. Çalışma retrospektif olarak dizayn edildi. Hastalar tedavi yöntemine göre Grup 1: cerrahi ve Grup 2: medikal olmak üzere iki gruba ayrıldı. Yaş, cinsiyet ve mevsimsel dönem karşılaştırıldı. Ayrıca hastalar yaşa göre 18-40, 40-60, 60 üstü olmak üzere üç gruba ayrıldı. Hastaların cinsiyeti ve tedavi yöntemi de mevsim gruplarında incelendi.
Bulgular: Çalışmamıza 157 hasta katıldı. Grup 1 cerrahi: 39, Grup 2 medikal: 119 hastadan oluşuyordu. Akut divertikülit nedeniyle başvuru en sık kış mevsiminde olmuştu (%39,5). Grup 1'de yaş ortalaması daha yüksekti (60,61 vs 54,42 p=0,030). Gruplarda cinsiyet dağılımı benzerdi (p=0,152). Her iki grupta da kış mevsimi ağırlıktaydı (%30,8 vs %42,4 p=0,060). Kış mevsiminde cerrahi tedavi uygulanan hastaların yaş ortalaması medikal tedavi alanlardan fazlaydı (68 vs 50 p=0,001). Kış mevsiminde cerrahi tedavi uygulanan hastaların hepsi 60 yaşın üstündeydi. Yaz mevsiminde ise medikal tedavi uygulanan hasta oranı 60 yaş üstü grupta en fazlaydı (p=0,040).
Sonuç: Çalışmamızda divertiküler hastalık sebebiyle hastaneye yatışın mevsimsel değişimini gösterdik. Kış mevsiminde artmış bir başvuru oranı saptadık. Tedavi yöntemi seçimi mevsimsel varyasyon göstermiyordu. Fakat yaş gruplarına göre ayrıca değerlendirdiğimizde kış aylarında 60 yaş üstü daha çok cerrahi tedavi alırken yaz aylarında 60 yaş üstü daha çok medikal tedavi almıştı. Bu değişimin patofizyolojik mekanizması tam olarak ortaya koyulamamıştır.
Anahtar Kelimeler: Divertiküler hastalık, mevsimsel değişim, cerrahi tedavi

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Introduction

Diverticular disease consists of various pathologies associated with diverticula in the colon. Diverticular disease of the colon is prevalent in industrialised countries. It has an important influence on patient health and healthcare costs.[1] The prevalence of colonic diverticulosis has a tendency to increase worldwide probably due to lifestyle changes in various populations.[2] The pathophysiology of diverticulosis and/or diverticulitis is challenging to describe. Diverticulitis may be caused by a combination of triggering factors or a single factor.[1]

The concept of seasonal change is well known in medical literature. The seasonal patterns of some gastrointestinal diseases such as inflammatory bowel disease, acute infective gastroenteritis, upper gastrointestinal tract bleeding, peptic ulcer, acute pancreatitis, acute cholecystitis and acute appendicitis have been demonstrated.[3,4,5]

The seasonal pattern of diverticular disease has not been fully revealed. Studies have shown that the number of patients who present to the hospital with acute diverticulitis increases in summer months.[6,7] The aetiology of this seasonal variation is uncertain. Diet changes according to seasons, dehydration, alterations in colon motility, changes in infectious diseases and seasonal fluctuations in vitamin D levels may play a role in the aetiology.[8] In the literature, these seasonal differences have mostly been associated with exposure to ultraviolet (UV) light, which makes an important contribution to serum vitamin D levels. Given the geographical and seasonal differences, the number of cases presenting with diverticulitis were considerably higher in geographical regions with low UV light level.[6]

In this study, considering evidence in literature as baseline, we aimed to investigate whether there was a difference between hospital admission ratios and treatment methods and to explore the relation of these differences in different age groups.

Materials and Methods

Patients admitted to the General Surgery Department of Erciyes University Faculty of Medicine with a pre-diagnosis of acute diverticulitis between 1 January 2015 and 1 January 2020 was included in the study. Patients who had missing clinical data or who were <18 years old were excluded from the study. Patients were diagnosed as having acute diverticulitis based on their clinical history and imaging methods. By examining patient files and hospital information system records, a common database was created. Patient information retrieved from this database was evaluated retrospectively.

The study was performed in accordance with the ethical rules based on the principles of the Declaration of Helsinki.

Patients were grouped according to the seasons of their admission to the hospital and were compared in terms of age, sex and treatment. Patients were divided into two groups in terms of the treatment method, i.e. surgical group and medical group. Percutaneous drainage was considered a medical treatment. Moreover, the patients were divided into three groups according to age: 18-40, 40-60 and >60 years. Sex and treatment methods were also examined according to seasonal groups.

This study was carried out in a university hospital, which is a tertiary hospital that provides services to five million people in Kayseri, located in the Middle Kızılırmak region of Turkey, near Central Anatolia and Taurus Mountains. It is located between latitudes 37°45′ north and 38°18′ north and longitudes 34°56′ east and 36°58′ east. The city centre of Kayseri has an altitude of 1054 m. Kayseri has predominantly steppe climate. The summers are hot and dry, and the winters are cold and snowy. We obtained weather data of cities from the Turkish state meteorological service (http://www.mgm.gov.tr/veridegerlendirme/ilveilceler-ista- tistik.aspx). In the Northern Hemisphere, the seasons are described as winter (December-February), spring (March-May), summer (June-August) and autumn (September-November).

Statistical Analysis

In the statistical analysis, SPSS 23.0 software program (IBM Corp., Armonk, NY, USA) was used. Categorical measurements were summarised as numbers and percentages, and continuous measurements were summarised as average, standard deviation and minimum-maximum. The compliance of variables to normal distribution was examined using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). In the comparison of categorical variables, chi-square test and Fisher's exact test were employed. In variables that did not comply with a normal distribution, Mann-Whitney U test was used. Statistical significance level was taken as 0.05 in all tests.

Results

In this study, 157 patients participated in our study. The surgical and medical groups consisted of 39 and 118 patients, respectively. Of the patients who received surgical treatment, 21 underwent colon resection with or without faecal diversion and anastomosis and 18 patients underwent Hartmann's procedure. The average patient age was 55.96. The sex distribution was comparable. The most frequent age group was 40-60 years (40.8%). The predominant season of

hospital admission due to acute diverticulitis was the winter (39.5%). Data are shown in Table 1 and Graphic 1.

On average, the surgical group was older than the medical group (60.61 vs 54.42 p=0.030). The sex distribution were comparable in both groups (p=0.152). The winter season was dominant in the treatment groups (30.8% vs 42.4%, p=0.060). Seasonal variation of diverticular disease between the treatment groups is shown in Table 2.

In autumn, a higher number of female patients received medical treatment (50% vs 80%, p=0.049). In winter, on average, the patients in the surgical group were older than those in the medical group (68 vs 50, p=0.001), and all patients who underwent surgical treatment were >60 years old. In summer, the ratio of those who received medical treatment was the highest in the group aged >60 years (p=0.040). Case distribution of age groups and sex by seasons is shown in Table 3.

Table 1. Seasonal variations of diverticular disease

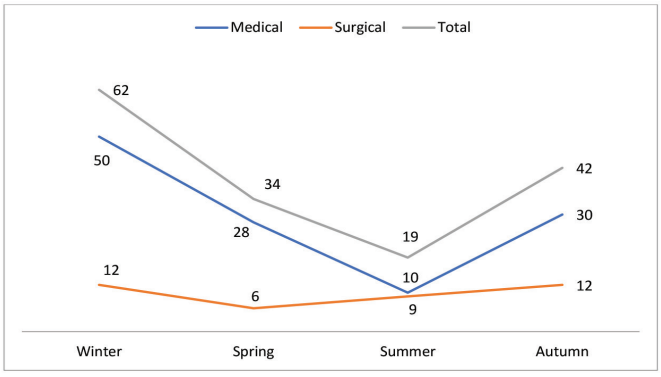
Measurements		Diverticular disease admissions n (%)
Age [(mean ± SD) (min-max)]		55.96±15.51 (21-90)
Sex	Male	77 (49.0)
	Female	80 (51.0)
Season	Winter	62 (39.5)
	Spring	34 (21.7)
	Summer	19 (12.1)
	Autumn	42 (26.8)
Age groups, years	18-39	30 (19.1)
	40-60	64 (40.8)
	≥61	63 (40.1)

max: Maximum, min: Minimum, SD: Standard deviation

Discussion

In this study, where hospital admissions due to diverticular disease and treatment methods were examined, the number of hospital admissions due to diverticular disease increased in the winter and the treatment methods were not associated with seasons.

The prevalence of diverticular disease is comparable for male and female patients. However, diverticular disease occurs in <10% of patients aged <40 years and in 50%-70% of patients aged 80 years, and prevalence increases considerably with age. Studies conducted within the last 10 years have also



Graphic 1. Distribution of diverticular disease admissions according to seasons and the numbers indicate the number of patients

Table 2. Seasonal variation of diverticular disease according to treatment groups

Measurements		Surgical n (%)	Medical n (%)	p*
Age [(mean + SD) (min-max)]		60.61±11.91 (36-80)	54.42±16.29 (21-90)	**0.030**
Sex	Male	23 (59.0)	54 (45.8)	0.152
	Female	16 (41.0)	64 (54.2)	
Season	Winter	12 (30.8)	50 (42.4)	0.060
	Spring	6 (15.4)	28 (23.7)	
	Summer	9 (23.1)	10 (8.5)	
	Autumn	12 (30.8)	30 (25.4)	
Age groups, years	18-39	4 (10.3)	26 (22.0)	**0.018**
	40-60	12 (30.8)	52 (44.1)	
	≥61	23 (59.0)	40 (33.9)	

max: Maximum, min: Minimum, SD: Standard deviation

Table 3. Case distribution of age groups and sex according to seasons

Measurements		Surgical n (%)	Medical n (%)	p*
Winter	Male	10 (83.3)	28 (56.0)	0.081
	Female	2 (16.7)	22 (44.0)	
Spring	Male	4 (66.7)	14 (50.0)	0.458
	Female	2 (33.3)	14 (50.0)	
Summer	Male	3 (33.3)	6 (60.0)	0.245
	Female	6 (66.7)	4 (40.0)	
Autumn	Male	6 (50.0)	6 (20.0)	**0.049**
	Female	6 (50.0)	24 (80.0)	
Seasons and age	Winter	68.33±5.58	50.28±17.28	0.001
	Spring	62.33±14.03	52.21±11.40	0.067
	Summer	58.88±8.82	67.20±13.75	0.140
	Autumn	53.33±13.64	59.13±16.51	0.288
Winter	18-39	0 (0.0)	16 (32.0)	**0.000**
	40-60	0 (0.0)	20 (40.0)	
	>61	12 (100.0)	14 (28.0)	
Spring	18-39	0 (0.0)	6 (21.4)	0.436
	40-60	4 (66.7)	16 (57.1)	
	≥61	2 (33.3)	6 (21.4)	
Summer	18-39	0 (0.0)	0 (0.0)	**0.040**
	40-60	6 (66.7)	2 (20.0)	
	≥61	3 (33.3)	8 (80.0)	
Autumn	18-39	4 (33.3)	4 (13.3)	0.134
	40-60	2 (16.7)	14 (46.7)	
	≥61	6 (50.0)	12 (40.0)	

investigated the incidence and disease progression in young patients with diverticulitis.[1,9] In a population study that analysed 267,000 patients presenting with acute diverticulitis between 1998 and 2005, an increase of 26% in the total was seen in the number of admissions due to diverticulitis from 1998 until 2005. The increase rate was higher in patients aged 18-44 years than in older patients (82% vs 36%, respectively). In that study, diverticulitis dominantly occurred in young male patients, and the disease had a more aggressive course with high rates of complication and recurrence.[10] In the present study, sex distribution was consistent with the literature, and the incidence was higher in patients aged >40 years.

Acute diverticulitis is accompanied by diverse clinical scenarios ranging from pericolonic inflammation to faecal peritonitis. Planning for patients with purulent peritonitis and faecal peritonitis is more inclined to operative treatment.[11,12] Traditional treatment of mild acute diverticulitis has focused on antibiotics, pain control and bowel rest. These treatment principles have been examined recently. In the latest guidelines issued by the American Gastroenterology Society Institute, the recommendation for acute diverticulitis without abscess is the administration of selective antibiotics according to the characteristics of the patient, instead of the routine use of antibiotics.[13] In 1923, Hartmann's resection was described as an alternative to abdominoperineal resection for patients with rectal cancer. This procedure has rapidly become the most frequently applied procedure for patients with perforated diverticulitis over time. In selected emergent cases, loop ileostomy with sigmoid resection and primary anastomosis may be performed.[14] In our series, the treatment method was planned according to the patient's

clinical status and disease severity. Our medical treatment consisted of bowel rest and antibiotherapy as recommended in the literature. While planning the surgical treatment method, we considered the degree of peritonitis and the general status of the patient. Patients for whom we planned surgical treatment had advanced age. Especially, for patients aged >60 years, our surgical treatment ratio was higher, and this could be associated with the deteriorated clinical status due to increasing age.

In the latest studies published in the literature, geographical and seasonal changes were observed in hospital admissions for diverticulitis.[6,7,8,11] Based on this observation, diverticulitis risk was associated with UV radiation exposure and vitamin D serum levels. Some observational retrospective studies have argued that the diverticulitis rate was lower in the winter, the admission rate was higher in low UV regions than in high UV regions, and there was an inverse ratio between 25-hydroxyvitamin D serum levels and hospital admission for diverticulitis.[6,12]

Based on the literature, the seasonal distribution of hospital admissions due to diverticular disease has not been established. In their study conducted in Denmark, Hupfeld et al.[13] found that hospital admissions due to diverticular disease were most frequent in autumn, with a rate of 26.1%. In Canada, Warner et al.[14] could not find a seasonal relation in the rates of hospital admissions due to diverticular disease. In the United States, Ricciardi et al.[7] demonstrated a seasonal cyclic fluctuation where the highest incidence was noted in the summer months for hospital admissions due to acute diverticulitis. They explained that infectious conditions increase in summer and related with diet changes, which was associated with greater consumption of fruits and vegetables in the summer and indigestible food materials that affect the lumen of the diverticulum caused by diet variations. Another probable factor that could be associated with the seasonal variation in the incidence of diverticulitis was changes in the intake of food-containing fibre.[7]

In their study, Adler et al.[8] included countries from different hemispheres and showed that hospital admissions due to diverticulitis increased in summer, and this finding was valid internationally and in both hemispheres. They attributed this situation to the argument that seasonal changes in diet, physical activity and medicine intake could trigger diverticulitis and to the probable increase in sensitivity to diverticulitis by stool stasis associated with slowing of the colonic passage caused by relative dehydration in the summer.[8]

In Italy, Manfredini et al.[4] demonstrated a cyclic pattern with two phases in hospital admissions due to acute diverticulitis peaking in autumn and spring. Moreover, they showed that winter could represent as a low-frequency but high-risk season and that mortality cases peaked only in winter.[4]

In the United States, Maguire et al.[6] observed a higher rate of geographical and lower rate of seasonal variation among young patients. Moreover, seasonal change was more prominent among Caucasian patients than among African-American patients. In the same study, the seasonality rates were higher among rural hospitals and the source of these differences could be related to vitamin D levels.[6]

Unlike previous studies, we detected an increased rate of hospital admissions in winter. The selection of treatment method did not demonstrate seasonal variation. However, on evaluation according to age groups, a high number of patients aged >60 years received surgical treatment in winter and a high number received medical treatment in summer. The finding that a high number of older patients received surgical treatment in winter may be related to the delay in presenting to the hospital due to winter conditions. Similarly, this situation can be explained by the low-fibre diet in winter. In another study in our region, we found an increase in hospital admissions due to appendicitis in winter.[3]

The reason for this tendency is uncertain. The pathogenesis of diverticular disease is probably multifactorial. Seasonal changes in different geographical zones and diet and lifestyle changes in similar geographical regions may cause this seasonal pattern.

The most important limitations of this study were its retrospective design, small sample size and single-centre setting. However, given the limited number of studies on this subject, we believe that our study makes a contribution to the literature.

Conclusion

In this study, we showed the seasonal change in hospital admissions due to diverticular disease, but the pathophysiological mechanism of this change could not be fully revealed. Thus, there is a need for multicentre studies on this subject. Our results suggest that there exists a seasonal risk factor shared in international populations and that this situation warrant further research to explain the pathophysiology of this common disease.

Ethics

Ethics Committee Approval: We did not receive an ethics committee approval because the study is retrospective.

Informed Consent: Because the study was retrospective, we could not get informed consent.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: F.D., E.M.S., M.A., T.T., İ.B., Concept: F.D., U.T., E.M.S., M.A., T.T., İ.B., Design: F.D., U.T., E.M.S., M.A., T.T., İ.B., Data Collection or Processing: F.D., U.T., E.M.S., M.A., İ.B., Analysis or Interpretation: F.D., Literature Search: U.T., Writing: F.D., U.T., M.A.

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RESEARCH ARTICLE

How Can We Manage the Therapeutic Approach of Acute Diverticulitis Regarding the Number of Attacks?

Akut Divertikülit Tedavisi; Atak Sayısına Göre Yaklaşım Nasıl Olmalıdır?

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ABSTRACT

Aim: The risk of acute diverticulitis (AD) increases with each attack and the decision of therapeutic management is getting more complicated. We aimed to investigate the effective features of the number of attacks.

Method: Two hundred thirty six patients with AD defined by computerized tomography were retrospectively analyzed according to the number of attacks (1, 2, and ≥3).

Results: 45.8% patients were female. The mean age was 58.3±12.7 years old, mean body mass index was 28.8±6.5 kg/m^2. Elective colonoscopy of AD was mostly localized in the left colon (p<0.05). The majority of the patients had a conservative treatment regardless of several attacks (81.4%). The percentage of patients received a conservative treatment (83.6% vs 81.1% and 75.5%) and radiological abscess drainage (10.5% vs 5.7% vs 6.1%) were higher in the patients with first attack (p=0.012). The percentage of patients undergone abscess drainage by open surgery (0.7% vs, 5.7% vs 12.2%) was higher in the patients with ≥3 attacks, while the number of segmental colon resection (7.5% vs 61% vs 5.2%) was higher in the patients with 2 attacks (p=0.012). The increase in Hinchey classification had an impact on the invasive interventions regarding the clinical parameters of AD [odds ratio (OR): 0.052; 95% confidence interval (CI): 0.022-0.126; p<0.001]. The patients with older age were more likely to be treated with surgical interventions (OR: 0.960; 95% CI: 0.918-1.003; p=0.07).

Conclusion: The increases in Hinchey classification with older age has a potential impact among the invasive abscess drainage and surgical intervention regarding the severity of each attack of AD.

Keywords: Abdominal abscesses, acute diverticulitis, colonoscopy

ÖZ

Amaç: Akut divertikülit (AD) riski her atakta artmakta ve tedavi yönteminin kararı daha karmaşık hale gelebilmektedir. Çalışmamızda atak sayısını etkileyen faktörleri araştırmayı amaçladık.

Yöntem: Bilgisayarlı tomografi ile tanımlanmış 236 AD hastası retrospektif olarak atak sayısına (1, 2 ve ≥3) göre değerlendirildi.

Bulgular: Hastaların %45,8'i kadındı. Ortalama yaş 58,3±12,7, ortalama vücut kitle indeksi 28,8±6,5 kg/m^2 idi. Yapılan elektif kolonoskopilerde hastalık, çoğunlukla solda (sol kolon %60,2 ile sağ kolon %10,6) solda lokalize idi. Hastaların büyük bir kısmına, atak sayısından bağımsız olarak konservatif tedavi (%81,4) verildi. Hastalara ilk ataklarında %83,6 oranında konservatif tedavi ve %10,5 oranında radyolojik apse drenajı uygulandı (p=0,012). Üç ve daha fazla atak geçirenlerde sıklıkla açık cerrahi ile apse drenajı yapıldı (%12,2). İki atak geçiren hastalarda ise segmental kolon rezeksiyonu sayısı (%7,5) daha yüksek oranda izlendi (p=0,012). Hinchey sınıflamasına göre evre, AD tedavisinde invaziv yöntemlerin kullanılmasında anlamlı derecede etkilidir [odds ratio (OR): 0,052; %95 güven aralığı (GA): 0,022-0,126; p<0,001]. İleri yaşlarda hastalara daha çok cerrahi tedavi uygulanmıştır (OR: 0,960; %95 CI: 0,918-1,003; p=0,07).

Sonuç: Hinchey sınıflamasına göre ileri evre ve yaşla birlikte, geçirilen AD atağının şiddetine bağlı olarak hastalarda cerrahi apse drenajı veya cerrahi müdahale ihtiyacında potansiyel bir artış izlenmiştir.

Anahtar Kelimeler: Abdominal apse, kolonik divertikülit, kolonoskopi

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Introduction

Acute diverticulitis (AD) is a serious inflammatory disease that occurs in 25% of patients with diverticulosis, involving the colon. AD is frequently encountered in the emergency room of general surgery due to the severity of its consequences. Up to 20% of patients hospitalised for AD need surgery for septic, haemorrhagic and/or obstructive complications.[1] The diagnosis of AD is performed by a clinical examination and abdominal tomography. In general, AD occurs in attacks, and its characterisation is based on the patient's presentation at the time of the initial attack of AD and on the appearance of disease on computerised tomography imaging during the initial visit.[2,3,4]

Approximately 10% of patients with diverticulitis develop complications, such as an abscess or free perforation, which require close observation and further treatment with antibiotics, percutaneous drainage or open surgery.[2,5] The risk of complications increases with each attack of AD. As a result of radiological imaging performed in each attack or during follow-up, the choice of conservative or elective or surgical intervention is made according to the Hinchey stage, a widely used classification of the degree of intraperitoneal contamination.[6,7] Elective surgery is generally delayed at least 6 weeks after the first episode so that the inflammation and infection resolve considerably. Unfortunately, emergency surgery cannot be postponed in some situations, and in these cases, the magnitude of intraperitoneal contamination dictates the choice of reconstruction. Generally, with localised contamination, observed in grades I and II, a primary anastomosis without a protective ostomy can be performed, while with more diffuse contamination, observed in grades III and IV, a two-stage procedure is generally preferred; either a Hartmann's procedure or a primary anastomosis with a protective proximal diverting stoma.[8]

Recurrent diverticulitis can occur in 20%-35% of patients after a first acute attack of AD treated non-surgically.[9] Rarely, it can also present in patients after resection for sigmoid diverticulitis despite complete remission. Moreover, 36% of people have ongoing abdominal symptoms after the first episode of diverticulitis.[10] As the incidence of diverticulitis increases, the risk of recurrent attacks is expected to increase with each attack. There is insufficient literature to determine the management of AD in each admission of a patient who has never undergone surgical intervention for AD before the primary attack. Historically, surgery was advised after two attacks of AD and after the first attack in patients younger than 40 years.[11] This has been challenged recently by a new approach to individualise treatment depending on the rates of previous AD events and frequency of attacks as well as the patient's immune status and the presence of complications such as chronic pain.[4,8] In this study, we aimed to investigate the effect of the number of attacks on the follow-up of patients with a surgical or conservative approach, as well as the decision to perform emergency surgery in AD cases.

Materials and Methods

The study protocol was approved by the Clinical Research Ethics Committee of the Bağcılar Training and Research Hospital of Health Science University (no: 2020.01.2.02.012). All procedures performed in this study involving human participants followed the ethical standards of the institutional research committee and the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Study Population

Patients (236) who applied to University of Health Sciences Turkey, Bağcılar Training and Research Hospital between June 2016 and January 2020 and were diagnosed with AD according to a clinical examination, radiological imaging and elective colonoscopy were included in the study and analysed retrospectively. The medical records were evaluated. All readmissions to the emergency unit and medical care received after discharge at our facility were captured to documents. Patients older than 18 years who underwent elective colonoscopy for a primary diagnosis of diverticulitis were included in the final analysis and divided into three groups according to the number of diverticulitis attacks as Attack 1 (applied for only 1 attack), Attack 2 (applied for 2 attacks) and Attack ≥3 (applied for 3 or more attacks). Patients younger than 18 years and those who underwent colectomy with a diagnosis of colon or rectal cancer or inflammatory bowel diseases or benign diseases were excluded from the study. We performed a colonoscopy during the follow-up period on patients who had been previously diagnosed with diverticulitis clinically and radiologically. If the patient had a colonoscopy without an accurate diagnosis of diverticulitis, it was excluded.

Variables and Outcomes

The demographic, radiological and per-operative clinical findings and haematological parameters at admission were recorded and categorised retrospectively. Demographic characteristics included age, sex, body mass index (BMI, kg/m^2), smoking and alcohol usage status, comorbidities [hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD)], functional health status and history of colorectal cancer (CRC). Clinical outcomes were Hinchey classification, laboratory parameters, localisation of diverticulitis according to CT imaging and colonoscopy and treatment management, namely either by conservative

treatment or by abscess drainage or by segmental colon resection such as the Hartman procedure. We did not include any elective surgery, which was very limited in our clinic. We evaluated radiological or surgical drainage and segmental colon resection at the onset of emergency settings following their clinical assessments and examinations regarding their emergency admissions.

Clinically, diverticulitis was separated into complicated and uncomplicated disease, based on the Hinchey system.[4] Among the laboratory parameters routinely measured during admission, only white blood cell count (WBC), haematocrit (HTC) and albumin (ALB) concentration were analysed. The reference ranges of WBC, HTC and ALB levels were 3.8-10.8x103/μL, 35%-50% and 3.4-5.4 g/dL, respectively.

Statistical Analysis

Descriptive statistics were reported as percentages for categorical variables and as means with standard deviations for continuous variables. The normality of the distribution of variables was examined by using the Kolmogorov-Smirnov test. The comparisons of the variables between groups were performed either by one-way ANOVA or by the Kruskal-Wallis test (non-parametric ANOVA). Univariate analysis comparing patients according to selective therapeutic management of AD cases were performed using the chi-square test for categorical variables and the t-test for continuous variables. Multivariate analyses with logistic regression were performed to identify the impact of risk factors on invasive therapeutic management to control potential confounders. $p<0.05$ was considered to indicate statistical significance. The analysis was performed with IBM SPSS Statistics, Version 23 (Armonk, NY: IBM Corp.).

Results

Of the 236 patients diagnosed with AD, 108 (45.8%) were female and 128 (54.2%) were male. The mean age of all patients was 58.3±12.7 years, and the mean BMI was 28.8±6.5. It was determined that the mean age, sex distribution, number of patients with COPD or hypertension, CRC history, rate of alcohol usage and smoking status did not differ among patients according to the number of attacks (Table 1). On the other hand, patients with 2 attacks were more likely to have a higher BMI (28.7±5.8 vs 30.3±9.0 vs 27.3±4.3, p=0.08). In addition, patients who had 3 or more attacks showed a significantly higher incidence of DM disease (1.5% vs.7.5% vs, 10.2% p=0.03).

According to the patients' functional health status, the majority of patients (88.1%) were functionally independent (Table 1). However, the percentage of partially dependent

Table 1. Demographic characteristics of patients compared with the number of attacks of acute diverticulitis

Characteristics	Total (n=236)	Attack 1 (n=134)	Attack 2 (n=53)	Attack ≥3 (n=49)	p value
Age (X ± SD) (min-max)	58.3±12.7 [27-89]	58.4±12.7 [27-89]	57.6±13.5 [32-85]	58.5±11.8 [34-81]	0.92
Sex n (%)					
Male	128 (54.2)	76 (56.7)	29 (54.7)	23 (46.9)	0.50
Female	108 (45.8)	58 (43.3)	24 (45.3)	26 (53.1)	
BMI (X ± SD) (min-max)	28.8±6.5 [18.2-82.2]	28.7±5.8 [18.4-43.6]	30.3±9.0 [18.2-82.2]	27.3±4.3 [19.4-43.6]	0.08
Comorbidities, n (%)					
DM	11 (4.7)	2 (1.5)	4 (7.5)	5 (10.2)	**0.03**
COPD	16 (6.8)	9 (6.7)	5 (9.4)	2 (4.1)	0.56
Hypertension	74 (31.4)	45 (33.6)	18 (33.96)	11 (22.5)	0.32
Functional health status, n (%)					
Independent	208 (88.1)	121 (90.3)	42 (79.2)	45 (91.8)	
Partially dependent	19 (8.1)	6 (4.5)	10 (18.9)	3 (6.1)	**0.02**
Totally dependent	9 (3.8)	7 (5.2)	1 (1.9)	1 (2.0)	
Alcohol usage, n (%)	6 (2.5)	2 (1.5)	3 (5.7)	1 (2.0)	0.26
Smoking, n (%)	33 (14.0)	20 (14.9)	8 (15.1)	5 (10.2)	0.69
CRC history, n (%)	8 (3.4)	5 (3.7)	1 (1.9)	2 (4.1)	0.79

X ± SD: Mean ± standard deviation, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, CRC: Colorectal cancer, min: Minimum, max: Maximum

patients was significantly higher in patients with 2 attacks (4.5% vs 18.9% vs 6.1%) while the percentage of totally dependent patients was considerably higher in patients with one attack (5.2% vs 1.9% vs 2.0%, p=0.02) (Table 1).

The evaluated clinical characteristics of patients, such as WBC, HTC and ALB; localisation of diverticulitis and Hinchey stage did not differ statistically with respect to the number of AD attacks (Table 2). However, clinically, simple AD (Hinchey stage 0 and I) was observed mostly in patients with one attack (19.4% and 44.0%, respectively) and two attacks (18.9% and 49.1%, respectively) (p=0.49). Patients with ≥3 attacks were more likely to be diagnosed with complicated AD, which was correlated with the higher stages of the Hinchey classification (Hinchey II, III and IV), (26.5%, 10.2% and 10.2%, respectively) (p=0.49). Moreover, elective colonoscopy examination showed AD mostly localised in the left colon and less frequently in bilateral localisation (60.2% vs 7.2%, p=0.006). The percentage of patients who had a first attack also had AD mostly in the left colon (61.9% vs 54.7% vs 61.2%, p=0.006) (Table 2).

Comparing treatment management, the majority of patients received a conservative treatment (81.4%) regardless of the number of attacks (Table 2). The percentage of patients who received conservative treatment (83.6% vs 81.1% vs 75.5%, respectively) and radiological percutaneous abscess drainage (10.5% vs 5.7% vs 6.1%, respectively) was significantly higher in patients with a first attack (p=0.012).

Segmental colon resection such as the Hartman procedure was a less likely option in the first attack (5.2% vs 7.5% and 6.1%, p=0.012). Percutaneous abscess drainage was performed more than open surgical drainage in patients with one attack (10.5% vs 0.7%, p=0.012). The percentage of patients who underwent abscess drainage by open surgery (0.7% vs 5.7% vs 12.2%) was highest in patients with ≥3 attacks, while the percentage of segmental colon resection (5.2% and 7.5% vs 6.1%) was higher in patients with 2 attacks, respectively (p=0.012) (Table 2).

Univariate regression analysis of all variables showed that older age [odds ratio (OR): 1.038; 95% confidence interval (CI): 1.009-1.068; p=0.01] and increased Hinchey stage of

Table 2. Clinical characteristics and intraoperative findings of patients compared with the number of attacks of acute diverticulitis

	Total (n=236)	Attack 1 (n=134)	Attack 2 (n=53)	Attack ≥ 3 (n=49)	p value
Laboratory data	**X ± SD**				
WBC	8.3±3.5	8.3±3.5	8.6±3.2	8.4±3.9	0.46
HTC	39.5±5.4	39.9±5.4	38.5±5.4	39.5±5.5	0.26
ALB	3.72±0.7	3.7±0.7	3.6 0.7	3.8±0.7	0.21
CT localization, n (%)					
Right	36 (15.3)	14 (19.5)	10 (18.9)	12 (24.5)	
Left	183 (77.5)	111 (82.8)	37 (69.8)	35 (71.4)	0.08
Bilateral	17 (7.2)	9 (6.7)	6 (11.3)	2 (4.1)	
Hinchey stage, n (%)					
0	44 (18.6)	26 (19.4)	10 (18.9)	8 (16.3)	
I	103 (43.6)	59 (44.0)	26 (49.1)	18 (36.7)	
II	49 (20.8)	25 (18.7)	11 (20.8)	13 (26.5)	0.49
III	29 (12.3)	19 (14.2)	5 (9.4)	5 (10.2)	
IV	11 (4.7)	5 (3.7)	1 (1.9)	5 (10.2)	
Colonoscopic localization, n (%)					
None	52 (22.0)	30 (22.4)	17 (32.1)	5 (10.2)	
Right	25 (10.6)	10 (7.5)	3 (5.7)	12 (24.5)	0.006
Left	142 (60.2)	83 (61.9)	29 (54.7)	30 (61.2)	
Bilateral	17 (7.2)	11 (8.2)	4 (7.5)	2 (4.1)	
Management, n (%)					
Conservative treatment	192(81.4)	112 (83.6)	43 (81.1)	37 (75.5)	
Percutaneous abscess drainage	20 (8.5)	14 (10.5)	3 (5.7)	3 (6.1)	0.012
Abscess drainage by open surgery	10 (4.2)	1 (0.7)	3 (5.7)	6 (12.2)	
Segmental colon resection	14 (5.9)	7 (5.2)	4 (7.5)	3 (6.1)	

X ± SD: Mean ± standard deviation, CT: Computerized tomography, WBC: White blood cell, HTC: Hematocrit, ALB: Albumin

AD (OR: 19.65; 95% CI: 8.212-47.01; p<0.001) primarily affected the surgical therapeutic approach (Table 3). However, other demographic characteristics and clinical parameters did not affect the therapeutic approach, regardless of the increase in the number of attacks (Table 3). The increase in Hinchey classification had an impact on invasive interventions with respect to clinical parameters of AD (OR: 0.052; 95% CI: 0.022-0.126; p<0.001) (Table 4). Multivariate analysis adjusted for age showed that older patients were more likely to be treated with surgical intervention (OR: 0.960; 95% CI: 0.918-1.003; p=0.07).

Discussion

Various attack numbers, which have an impact on the progress of AD, have been reported in 10%–25% of diverticulitis patients.[12] The role of prophylactic surgery following conservatively treated AD is controversial in numerous studies.[12,13,14] Prevention of recurrent acute attacks and the need for urgent surgery are some of the important inconveniences with the assessment of AD during elective follow-up.[15] In this single-centre, retrospective study, we focused on the attack number in patients with AD and its effect on clinical outcomes and decision making regarding conservative management of the disease.

In previous studies based on identification of predictors of persistent, complicated diverticular disease, it was found that the number of attacks did not increase the patient's risk of persistent complexity.[4] However, Nizri et al.[16] reported that the first attack of complicated diverticulitis was the main risk factor associated with eventual complications compared with the number of recurrent attacks. In contrast, Van de Wall et al.[10] reported that a major effect of previous attacks of diverticulitis could not be found based on the severity of diverticulitis since patients with uncomplicated diverticulitis had a higher number of previous attacks than

Table 3. Unadjusted covariates for the management of the acute diverticulitis

Characteristics	Odds ratio	95% CI	p value
Number of attacks	1.184	0.518-2.704	0.69
Age	1.038	1.009-1.068	0.01
Sex	0.536	0.271-1.061	0.07
BMI	1.007	0.958-1.059	0.79
Comorbidities			
DM	0.198	0.038-1.018	0.05
COPD	3.094	0.395-24.21	0.28
Hypertension	0.583	0.291-1.167	0.13
Functional health status	0.313	0.071-1.371	0.12
Smoking	1.616	0.536-4.876	0.39
CRC history	1.489	0.178-12.44	0.71
Laboratory data			
WBC	1.040	0.950-1.138	0.40
HTC	1.001	0.939-1.066	0.99
ALB	1.122	0.651-1.935	0.68
Hinchey stage	19.65	8.212-47.01	<0.001
CT Localization	3.20	0.354-28.95	0.30
Colonoscopic localization	2.25	0.45-11.26	0.32

DM: Diabetes Mellitus, COPD: Chronic obstructive pulmonary disease, CRC: Colorectal cancer, CT: Computerized tomography, WBC: White blood cell, HTC: Hematocrit, ALB: Albumin, BMI: Body mass index, CI: Confidence interval

Table 4. Adjusted covariates for the management of the acute diverticulitis

Management of treatment	Odds ratio	95% CI	p value
Hinchey	0.052	0.022-0.126	<0.001
Age	0.960	0.918-1.003	0.07

CI: Confidence interval

patients with complicated diverticulitis. In the present study, an increasing number of attacks were detected in higher stages of the Hinchey classification, considering that AD could be more complicated in Hinchey II, III and IV.

Considering the variable factors in AD, some studies underscored the fact that patients presenting with complicated diverticulitis frequently have a more complex clinical presentation. Many of these factors have been studied from different clinical perspectives.[4,9,17,18,19,20,21] Patients prone to comorbidities may also carry an increased risk of AD due to the pathophysiology of diseases such as diabetes mellitus. Moreover, ageing, alcohol use, obesity and smoking may also enhance both the immune system and the tissue-healing pathways of the intestinal system.[17,18,19,20,21,22] In some previous studies, it was reported that complicated diverticulitis was more likely to present with a lower functional status and be associated with increasing age and alcohol use.[4]

Consistently in our study, the number of patients with diabetes mellitus was significantly higher in patients with ≥3 attacks. According to functional health status, the percentage of partial dependence was significantly higher among patients with 2 attacks. This may be related to the limited number of patients included in the analysis, based on the data and the observational study. Still, our findings suggest that the risk for AD may increase with the increasing number of attacks regarding the severity of attacks, especially in patients with a lower functional status.

Today, the indications for emergency surgery in the management of AD at the first attack of the disease are becoming more controversial. For AD cases, an optional sigmoid colectomy has only been suggested following the urgent Hinchey evaluation and the clinical view on the individual patient's condition such as age, functional health status, number and severity of attacks and severity of symptoms.[11] However, there are some reports stating that elective surgery is indicated more frequently in patients with recurrent attacks and the presence of persistent symptoms.[15] This statement may have been affected by various reported clinical parameters about an elective resection after two attacks of AD.[23] In our study comparing the surgical and conservative management of treatment, the majority of patients received conservative treatment regardless of the number of attacks. Moreover, segmental colon resection such as the Hartman procedure was less likely to be an option at the first attack. Percutaneous abscess drainage with radiological intervention was performed more often in patients with one attack than abscess drainage with open surgery. Open surgical drainage was mostly performed in patients who had ≥3 attacks, suggesting that each attack might cause a change among individual patterns of disease severity.

An early focus on the diagnosis of diverticulitis might give a clue to designing a successful treatment algorithm according to the degree of disease and other demographic parameters. To support disease management, CT evaluations, hospitalisation at the time of the first attack, longer courses of antibiotic treatment and closer radiological imaging may be needed in follow-up.[4,17,18,19,20,21] Moreover, if a patient presents with several factors that may increase the risk of complicated diverticulitis resulting in poor prognosis, a colonic resection may be indicated rather than after multiple percutaneous drainage procedures and long-term application of antibiotics.[4,17,18,19,20,21] A primary crucial indication for surgery is the Hinchey classification.[6,7] In our study, the Hinchey classification of each attack of AD was more likely to impact on invasive interventions regarding attack numbers and the clinical parameters of AD in our population. Suarez Alecha et al.[15] evaluated the safety of conservative management and the risk factors for emergency surgery after the first episode of AD.[15] They concluded that after an attack of AD, the nonoperative approach is safe because fewer number of patients, less than 5%, will need an emergent procedure in a subsequent attack of AD. They also add that the first attack of complicated AD can be a risk factor for emergency surgery in conservatively treated patients.[15] The Hinchey classification should be considered to decide the need for urgent surgery or elective surgery following each attack of AD to decrease further attacks.[8]

The need for surgery after recovery from AD in patients younger than 50 years of age remains controversial.[15,19,24] Some reports showed that ageing has no differences in attacks of AD compared to older patients regarding surgical procedures.[15,24] Our regression analysis showed that aging patients were often treated with invasive radiological and surgical interventions regarding the complexity of AD and an increase in attacks.

Study Limitations

The limitations of our study are that a small number of patients were analysed retrospectively from the data from a single centre without comparison with elective cases and AD groups from a restricted region (Bağcılar area), which may limit generalisation to other regions and groups. Our study was limited by its retrospective nature, which may have induced measurement, observational and recall biases. Despite these limitations, this study is the first report that evaluated the predictive factors for urgent therapeutic management for AD in the Bağcılar region of Istanbul, suggesting a prediction model for the therapeutic management of AD at the time of diagnosis based on attack number.

Conclusion

In conclusion, an increase in the number of AD attacks should be considered during clinical follow-up regarding disease severity. Our prediction model might be a helpful clinical tool to select the proper therapeutic approach for the management of AD patients depending on the number of attacks. Treatment of AD should be patient-oriented with special attention to the number of attacks and the severity of the disease. Invasive procedures must be chosen carefully, considering the risks of surgical intervention, to improve postoperative outcomes. The early recognition of complicated diverticulitis before urgent surgery and optional therapy based on disease progression in frail patients are warranted. Further multi-institutional, prospective, randomised control studies on a large sample size are needed to validate our model.

Ethics

Ethics Committee Approval: University of Health Sciences Turkey, Bağcılar Training and Research Hospital Clinical Research Ethics Committee (decision number: 2020.01.2.02.012)

Informed Consent: For this type of study formal consent is not required.

Peer-review: Externally and internally peer review.

Authorship Contributions

Surgical and Medical Practices: Y.A., N.A.H., S.M., Concept: Y.A., N.A.H., Design: Y.A., Data Collection or Processing: N.A.H., M.T., Analysis or Interpretation: S.M., A.A., Literature Search: N.A.H., M.T., Writing: Y.A., A..A.

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RESEARCH ARTICLE

Evaluation of the Modified Systemic Inflammation Score and Inflammatory Markers According to Stage in Colorectal Cancer

Kolon Kanserinde Evreye Göre Modifiye Sistemik Enflamasyon Skoru ve Enflamatuvar Belirteçlerin Değerlendirilmesi

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ABSTRACT

Aim: There is recent increasing evidence of an association between inflammation and cancer. There are many studies showing that inflammatory markers can be used as prognostic markers in many types of cancer. The aim of this study was to retrospectively evaluate the effect of tumour stage on inflammatory markers and the modified systemic inflammation score (mSIS).

Method: The study included 218 of 376 patients identified as having undergone curative surgery in Ankara Training and Research Hospital general surgery clinic with the diagnosis of colorectal cancer (CRC) between February 2015 and February 2020. A retrospective evaluation was made of clinical and pathological data, including age, gender, tumor type, histological tumour grade, localization of the tumor, lymph node involvement, hemogram results, albumin, carcinoembryonic antigen, and carbohydrate antigen 19-9 (CA-19-9). Laboratory data of neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR)and mSIS were analyzed according to the tumor-node-metastasis stage.

Results: When the cases were evaluated in terms of stage, there was a statistically significant difference in terms of Hb, albumin, neutrophil and platelet value ($p<0.05$). When the cases were evaluated in terms of NLR, PLR and mSIS, there was a statistically significant difference between stage I and stage II ($p<0.05$).

Conclusion: NLR, PLR and mSIS may be predictive factors that can be used to differentiate stage 1 from other stages. Determining the pre-treatment levels of NLR, PLR and mSIS can provide useful information in early diagnosis or the evaluation of treatment options in CRC patients.

Keywords: Colorectal cancer, mSIS, NLR, PLR, stage

ÖZ

Amaç: Enflamasyon ve kanser arasındaki ilişki uzun zamandır gündemde olan konulardan biridir. Enflamatuvar belirteçlerin birçok kanser türünde prognostik belirteç olarak kullanılabileceğini gösteren çok sayıda çalışma mevcuttur. Bu çalışmada enflamatuvar belirteçler ve modifiye enflamatuvar sistemik skorunun (mSIS) tümör evresine etkisini retrospektif olarak değerlendirmeyi amaçladık.

Yöntem: Şubat 2015 ile Şubat 2020 arasında Ankara Eğitim ve Araştırma Hastanesi Genel Cerrahi Kliniği'ne başvuran ve kolorektal kanser (KK) tanısı ile küratif cerrahi yapılan 376 hastanın 218'i çalışmaya dahil edildi. Olgular yaş, cinsiyet, tümör tipi, tümörün histolojik derecesi, tümörün lokalizasyonu, lenf nodu tutulumu, tam kan sonuçları, albumin, karsinoembriyojenik antijen, karbonhidrat antijeni 19-9 (CA 19-9) gibi klinikopatolojik verilerine veri sistemi üzerinden retrospektif olarak ulaşıldı. Nötrofil lenfosit oranı (NLR), trombosit lenfosit oranı (PLR), lenfosit monosit oranı ve mSIS laboratuvar verileri tümör-nod-metastaz evresine göre analiz edildi.

Bulgular: Olgular evre açısından değerlendirildiğinde hemoglobin, albümin, nötrofil ve trombosit değerleri açısından istatistiksel olarak anlamlı farklılık vardı ($p<0,05$). Olgular NLR, PLR ve mSIS açısından değerlendirildiğinde ise evre 1 ile evre 2 arasında istatistiksel olarak anlamlı fark vardı ($p<0,05$).

Sonuç: NLR, PLR ve mSIS, evre 1'i diğer evrelerden ayırt etmek için kullanılabilecek öngörücü faktörler olabilir. NLR, PLR ve mSIS'nin tedavi öncesi düzeylerinin belirlenmesi, KK hastalarında erken tanı veya tedavi seçeneklerinin değerlendirilmesinde faydalı bilgiler sağlayabilir.

Anahtar Kelimeler: Kolorektal kanser, mSIS, NLR, PLR, evre

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Introduction

Colorectal cancers (CRCs) are one of the most commonly observed cancers, with morbidity and mortality rates placing it as the third most common cancer worldwide in 2018.[1] The relationship between inflammation and cancer was discovered by Rudolf Virchow for the first time in the 19th century. There is abundant evidence that the neutrophil-to-lymphocyte ratio (NLR) can be used as a prognostic factor in many cancer types from studies conducted to predict postoperative survival and classify patients before surgery.[2] Cancer progression and metastasis are considered to be increased by systemic inflammation.[3] NLR and platelet-to-lymphocyte ratio (PLR) have recently been used in studies to identify systemic inflammation.[4,5]

This study aimed to retrospectively evaluate the effect of tumour stage on inflammatory markers and modified systemic inflammation score (mSIS).

Materials and Methods

Patients who underwent curative surgery in Ankara Training and Research Hospital General Surgery Clinic and had a diagnosis of CRC between February 2015 and February 2020 were identified. Patients were excluded from the study for various reasons, including (1) perforation or obstruction, (2) known inflammatory disease (rheumatoid arthritis, ankylosing spondylitis, etc.), (3) recurrent tumour, (4) other known malignancies and (5) incomplete data. We included patients who had a neoadjuvant or complementary treatment for their disease. A retrospective examination of the clinicopathological data of the remaining 218 patients was made, including age, gender, tumour type, histological tumour grade, localisation of the tumour, lymph node involvement, haemogram results, albumin, carcinoembryonic antigen (CEA) and CA19-9. All blood samples were taken a week before the surgery. The NLR, PLR and lymphocyte-to-monocyte ratio (LMR) were calculated using the simple proportioning method in the electronic system.

mSIS is a scoring system based on serum albumin and LMR. The patients are categorised as 0 points with albumin value ≥4.0 g/dL, one point with albumin <4.0 g/dL and LMR ≥3.4 and two points with albumin <4.0 g/dL and LMR <3.4.[5]

Tumour staging was applied according to the tumour, node and metastasis (TNM) staging system approved by AJCC 8th edition, published in 2018.

Statistical Analysis

Data were analysed using SPSS version 21.0 software. Values showing a parametric distribution were expressed as mean ± standard deviation, and variables not showing a normal distribution were expressed as median and interquartile range values. In the comparisons of groups of multiple data, ANOVA was used to determine whether there was a significant difference. A value of $p<0.05$ was considered statistically significant.

Results

Clinical and Pathological Features of Patients

A total of 376 patients were included in the study: 158 patients were excluded and 218 patients were included. The study included 137 (62.8%) males and 81 (37.2%) females with a mean age of 23.91 years (range: 23-91 years). In 81 (37.1%) patients, the primary tumour was located in the right colon, in 42 (19.2%) patients, the left colon, in 34 (15.5%) patients, the sigmoid colon and in 52 (23.8%) patients, the rectum. Nine cases (4.1%) had synchronous tumours in the right and left colon. According to histological grade, 62 (28.4%) lesions were well differentiated, 92 (42.2%) were moderately differentiated and 61 (27.9%) were poorly differentiated (Table 1). No significant difference was determined between the cancer stages regarding age, gender, tumour localisation and histological type (adenocarcinoma, mucinous adenocarcinoma, stone ring cell carcinoma, etc.).

Tumour and Inflammatory Markers

The study results showed that NLR, which is one of the inflammatory markers, was statistically significantly higher in stage II (3.6±1.7) than in stage I (2.5±1.5) cancers ($p=0.037$). PLR was found to be statistically significantly higher in stage II (213.1±97.8) than in stage I (159.8±69.9) cancers ($p=0.004$) (Figure 1). Neutrophil and platelet counts were significantly higher in stage II than in stage I ($p=0.003$; $p=0.009$, respectively). No statistically significant difference was determined between the groups in terms of lymphocyte, monocyte and red cell distribution width (Rdw) values ($p>0.05$). There was no statistically significant difference between the groups in terms of LMR (Table 1).

According to the mSIS, two points were scored by 26.8% of stage I tumours and by 59.4% of stage II tumours, and the difference was determined to be statistically significant ($p=0.012$) (Table 2) (Figure 2). The CEA and CA 19-9 values were higher in patients at stage 4 than in the other groups, but the difference was not statistically significant.

A statistically significant difference was determined between stage I and stage II cancers in terms of haemoglobin, albumin, neutrophil, platelet, NLR, PLR and mSİS values ($p=0.001$, $p=0.01$, $p=0.003$, $p=0.009$, $p=0.004$, $p=0.037$ and $p=0.012$, respectively) (Table 3). Neutrophil, platelet, NLR, PLR, and mSİS values were higher in stage II than stage I, and haemoglobin and albumin values were lower in stage II than stage I.

Table 1. Clinical and pathological features of cases

Clinicopathological features	Stage I Mean/ N (± SD)	Stage II Mean/ N (± SD)	Stage III Mean/ N (± SD)	Stage IV Mean/ N (± SD)
Age	68.3±12.6	66.75±12.4	64.5±11.9	59.2±10.3
Sex				
Male	26	57	45	9
Female	15	27	30	9
Differentiation				
Unidentified	2	0	1	0
Well Diff.	17	18	23	4
Mod. Diff.	14	39	30	9
Poor. Diff.	8	27	21	5
Tumour localization				
Right colon	13	40	22	6
Left colon	6	16	16	4
Sigmoid colon	8	10	12	4
Rectum	13	16	21	2
Both	1	2	4	2
Hb (g/dL)[a]	13.02±2.83 [a]	11.33±2.34[a]	12.05±0.27	12.26±2.35
Albumin (mg/dL)[b]	4.12±0.58[b]	3.79±0.59[b]	4.02±0.53	4.02±0.52
Neutrophil (10^9/L) [c]	4.62±1.62[c]	5.75±1.69[c]	4.95±1.95	5.88±2.74
Lymphocyte (10^9/L)	1.96±0.81	1.79±0.68	1.81±0.92	1.86±0.69
Monocyte (10^9/L)	0.57±0.18	0.74±0.71	0.59±0.2	0.64±0.04
Platelet (10^9/L)[d]	277±94[d]	344±121[d]	299±100	342±108
Rdw	15.26±2.92	16.35±3.30	16.09±4.07	15.12±2.46
NLR[e]	2.77±1.55[e]	3.64±1.77[e]	3.87±1.98	3.54±2.36
PLR[f]	159.8±69.9[f]	213.1±97.8[f]	216.1±172.1	196.9±65.0
LMR	3.59±1.65	2.87±1.27	3.25±1.59	3.01±1.19
CEA (ng/mL)*	3.28 (3.31)	3.91 (7.75)	7.12 (13.65)	9.89 (171.54)
CA 19-9 (U/mL)*	12.60 (9.69)	20.15 (24.61)	13.7 (24.20)	27.25 (128.28)

[a]Significantly different stage I versus stage II (p=0.001), [b]Significantly different stage I versus stage II (p=0.01), [c]Significantly different stage I versus stage II (p=0.003), [d]Significantly different stage I versus stage II (p=0.009), [e]Significantly different stage I versus stage II (p=0.037), [f]Significantly different stage I versus stage II (p=0.004).

*Variables not showing normal distribution were stated as median and interquartile range (IQR) values

Hb: Hemoglobin, Rdw: Red cell distribution width, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, LMR: Lymphocyte-to-monocyte ratio, CEA: Carcinoembryonic antigen, CA: Carbohydrate antigen

Table 2. Modified inflamatory systemic score (mSIS) of the cases

	MSIS		
Stage	**Albumin ≥4.0 (score 0)**	**Albumin <4.0; LMR ≥3.4 (score 1)**	**Albumin <4.0; LMR <3.4 (score 2)**
I	26 (63.4%)	4 (9.75%)	11 (26.8%)[x]
II	30 (40.5%)	10 (13.5%)	44 (59.4%)[x]
III	44 (58.6%)	12 (16%)	19 (25.3%)
IV	10 (55.5%)	4 (22.2%)	4 (22.2%)

[x]Stage I vs stage II sig. diff. (p=0.012), MSIS: Modified systemic inflammation score, LMR: Lymphocyte-to-monocyte ratio

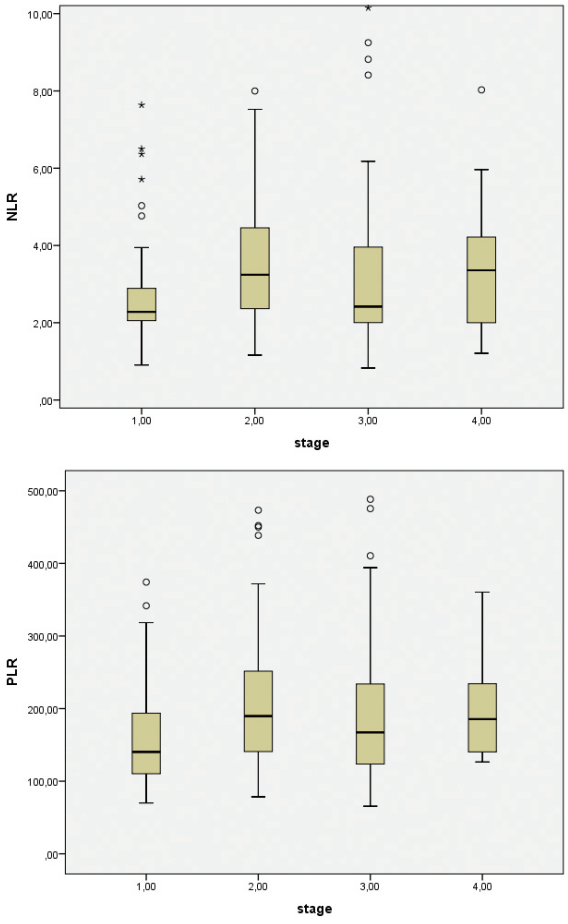

Figure 1. Distribution of NLR (A) and PLR (B) by TNM staging system
NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio

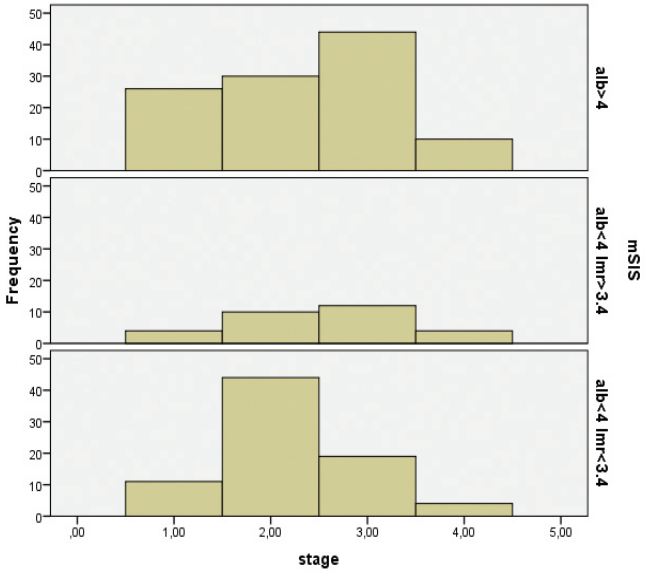

Figure 2. Distribution of modified inflammatory systemic scoring system according to TNM staging system

Discussion

Many definitions are related to the association between elevated NLR and poor oncological outcomes.[6] According to a study by Ding et al.[7], the host response to the tumour is lymphocyte-dependent. Although tumour infiltrating lymphocytes in the primary tumour are initially an indicator of good prognosis, increased neutrophils later increase the potent proangiogenic factors that cause the tumour to develop and progress. Therefore, NLR is the balance between protumour inflammatory status and antitumour immune status.[6] Rashtak et al.[8] stated that NLR is an important marker of prognosis in colon cancer, and Galizia et al.[9] also showed that preoperative NLR is an important predictor showing the probability of recurrence. Guo et al.[10] stated that the right and left colon cancers are different from each other, and while NLR can be considered a predictive factor in the right colon cancer, it cannot be a predictive factor in the left colon cancer. In this study, it was concluded that NLR was higher in stage II than in stage I. This result shows that the low NLR in early stages before surgery may also contribute to patient's treatment plan.

Platelets facilitate the proliferation of tumours by detaching the tumour from its primary site and masking the tumour cells from immune surveillance. Platelets also help metastasis, thus causing distant metastasis. When the number of platelets in patients with colon cancer was examined, a relationship was found between the primary tumour and high platelet count.[11] Li et al.[12] demonstrated that PLR is a predictive factor indicating the prognosis in colon cancer and concluded that as PLR increases, patient's survival decreases. Hu et al.[13] showed that PLR can be used to differentiate benign colon tumours from malignant colon tumours. In this study, it was determined that PLR was higher in stage II than stage I. Accordingly, PLR value may play an important role in patient's treatment plan, platelet-dependent drug selection, and evaluation of the response to treatment.

A low lymphocyte count is considered to cause a weak and inadequate immunological reaction to the tumour. Tumour infiltrating leukocytes, including neutrophils and monocytes, play an important role in tumour development and progression.[14] Ozawa et al.[15] showed that LMR is a prognostic indicator in stage II colon cancer undergoing curative resection, and survival increases with increasing LMR. Peng et al.[16] reported that LMR is a superior predictor in terms of survival compared with NLR and PLR in patients with colon cancer who have liver metastasis. In this study, no statistically significant difference was found when LMR was evaluated in terms of tumour stage.

Table 3. Clinical and pathological features of stages I and II

	Stage I Median/N	Stage II Median/N	p
Age	**68.3±12.6**	**66.75±12.4**	**1**
Sex			
Male	26	57	1
Female	15	27	
Differentiation			
Unidentified	2	0	0.028
Well diff.	17	18	
Mod. diff.	14	39	
Poor diff	8	27	
Tumour localisation			
Right colon	13	40	0.15
Left colon	6	16	
Sigmoid colon	8	10	
Rectum	13	16	
Both	1	2	
Hb (g/dL)	13.02±2.83[a]	11.33±2.34[a]	0.001
Albumin (mg/dL)	4.12±0.58[b]	3.79±0.59[b]	0.01
Neutrophil (10^9/L)	4.62±1.62[c]	5.75±1.69[c]	0.003
Lymphocyte (10^9/L)	1.96±0.81	1.79±0.68	0.84
Monocyte (10^9/L)	0.57±0.18	0.74±0.71	0.42
Platelet (10^9/L)	277±94[d]	344±121[d]	0.09
Rdw	15.26±2.92	16.35±3.30	0.61
NLR	2.77±1.55[e]	3.64±1.77[e]	0.037
PLR	159.8±69.9[f]	213.1±97.8[f]	0.004
LMR	3.59±1.65	2.87±1.27	0.063
CEA (ng/mL)	3.28 (3.31)	3.91 (7.75)	0.40
CA 19-9 (U/mL)	12.60 (9.69)	20.15 (24.61)	0.32

Hb: Hemoglobin, Rdw: Red cell distribution width, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, LMR: Lymphocyte-to-monocyte ratio, CEA: Carcinoembryonic antigen, CA: Carbohydrate antigen

Systemic inflammation plays a critical role in cancer pathogenesis and progression. Increased C-reactive protein and low serum albumin levels are biomarkers of systemic inflammation.[17] The systemic inflammation score is based on the preoperative serum albumin level, and LMR is a strong prognostic marker in clear-cell renal cell carcinoma.[18] Lin et al.[19] concluded that mSIS is a useful predictive factor for postoperative survival in stomach cancer. Suzuki et al.[17] reported that SIS is a novel prognostic factor in patients with CRC and is an alternative inflammation-based biomarker, which may improve the prediction of clinical outcomes. According to the hypothesis of Mariani et al.[20], inflammatory reactions play an important role in the early stages of CRC development. Similarly, in this study, there was a significant difference in mSIS between stages I and II. Although LMR was not significant when evaluated according to stage alone, it was significant when used with albumin in mSIS. According to our study, the mSIS value can also be used in treatment planning and evaluation of response to treatment.

Study Limitations

This study has some limitations. First, it was a retrospective study in a single centre, and the statistical power was decreased due to the small number of stage IV patients compared with other stages.

Conclusion

In conclusion, the results of this study showed that NLR, PLR and mSIS may be predictive factors that can be used to differentiate stage I CRC from stage II. Determining the pretreatment levels of NLR, PLR and mSIS can provide useful information in early diagnosis or evaluation of treatment options in patients with CRC.

Ethics

Ethics Committee Approval: Ethics committee approval was obtained on 17.09.2020 as the study numbered 364.

Informed Consent: Retrospective study.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: A.D., K.K., M.S., Concept: A.D., K.K., Design: A.D., A.Ş., T.Y., Data Collection or Processing: K.K., A.Ş., T.Y., Analysis or Interpretation: A.D., T.Y., M.S., Literature Search: A.D., T.Y., M.S., Writing: A.D., A.Ş.

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RESEARCH ARTICLE

Identifying Pathological Pneumoperitoneum After Laparoscopic Surgery

Laparoskopik Cerrahi Sonrası Patolojik Pnömoperitoneumun Belirlenmesi

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ABSTRACT

Aim: The study aims to analyze the frequency and extent of pneumoperitoneum after laparoscopic surgery and to differentiate routine post laparoscopy pneumoperitoneum from pneumoperitoneum due to possible bowel perforation.
Method: Pneumoperitoneum after laparoscopic surgery persists for a variable number of days and can mask pathological pneumoperitoneum due to the complication of bowel perforation at laparoscopic surgery. This study aims to find a simple radiological solution to this issue, so that pathological bowel perforation can be detected at the earliest and corrective action taken.
Results: We had four cases of bowel perforation after laparoscopic surgery, and, the clinical signs were subtle and not clearly indicating any peritonitis. Radiological tests on post operative day 1were inconclusive, as free gas was attributed to persisting carbon dioxide pneumoperitoneum. Hence a relook laparoscopy was delayed for 48 hrs ,when clinical signs were obvious. This scenario presented a challenge to distinguish persisting carbon dioxide pneumoperitoneum post laparoscopy from pathological pneumoperitoneum.
Conclusion: We decided to measure by X-ray chest the width of gas under diaphragm in the usual laparoscopic procedures, on the first post operative day and compare this with the width of gas under diaphragm in the four cases of iatrogenic bowel perforation post laparoscopic surgery. It was found that iatrogenic bowel perforation at laparoscopy is characterized by a wider gas under diaphragm, with the width at widest point ranging from 1.5 cms to 2.0 cms. Hence a simple xray chest could raise suspicion of a bowel perforation complication , and dictate further investigations like computed tomography scan or relook laparoscopy at the earliest post operative period.
Keywords: Pneumoperitoneum post laparoscopy surgery, bowel perforation at laparoscopy diagnosis, radiology for post laparoscopy complication

ÖZ

Amaç: Bu çalışma, laparoskopik cerrahi sonrası pnömoperitoneum sıklığını ve şiddetini analiz etmeyi ve olası bağırsak perforasyonuna bağlı pnömoperitoneumu rutin laparoskopi sonrası gelişen pnömoperitoneumdan ayırt etmeyi amaçlamaktadır.
Yöntem: Laparoskopik cerrahiden sonra pnömoperitoneum birkaç gün devam eder ve laparoskopik cerrahinin bağırsak perforasyonu komplikasyonuna bağlı patolojik pnömoperitoneumu maskeleyebilir. Bu çalışma, bu konuya basit bir radyolojik çözüm bulmayı, böylece patolojik bağırsak perforasyonunun en erken dönemde tespit edilerek düzeltici önlemler alınabilmesini amaçlamaktadır.
Bulgular: Laparoskopik cerrahiden sonra bağırsak perforasyonu gelişen 4 hastamız vardı. Tamamında klinik bulgular belirsizdi ve net olarak peritoniti düşündürmüyordu. Serbest gaz, devam eden karbondioksit pnömoperitoneuma atfedildiği için ameliyat sonrası 1. gündeki radyolojik testler sonuçsuz kaldı. Bu nedenle, klinik belirtiler bariz olana kadar, yeniden laparoskopi 48 saat ertelendi. Bu senaryo, laparoskopi sonrası devam eden karbon dioksit pnömoperitoneumu patolojik pnömoperitoneumdan ayırt etmek için zorluk oluşturmuştur.
Sonuç: Ameliyattan sonraki ilk günde, olağan laparoskopik prosedürlerde, diyafram altındaki hava miktarını göğüs grafisi ile ölçmeye ve bunu laparoskopik cerrahi sonrası iyatrojenik bağırsak perforasyonu gelişen 4 hastamızdaki diyafram altındaki hava miktarı ile karşılaştırmaya karar verdik. Laparoskopi sonrası iyatrojenik barsak perforasyonu diyafram altında daha geniş bir hava görünümü ile karakterizedir ve en geniş noktada genişliği 1,5-2 cm arasında değişmektedir. Bu nedenle, basit bir göğüs röntgeni, bağırsak perforasyonu komplikasyonunu düşündürebilir ve ameliyat sonrası en erken dönemde bilgisayarlı tomografi görüntülemesi veya yeniden laparoskopi gibi daha ileri araştırmaların gerekliliğine işaret edebilir.
Anahtar Kelimeler: Laparoskopi sonrası pnömoperitoneum, laparoskopiyi takiben gelişen bağırsak perforasyonunun tanısı, laparoskopi sonrası komplikasyon için radyolojik inceleme

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Introduction

Pneumoperitoneum is an essential component of laparoscopic procedures, with carbon dioxide (CO_2) as the preferred gas, mainly because it does not support combustion and is easily excreted via the lungs. CO_2 is absorbed 32 times quicker than room air when used in double-contrast barium enemas. Studies have identified the frequency and duration of pneumoperitoneum, with 46% of the patients confirmed to have signs of post-laparoscopic pneumoperitoneum that resolves within 1 week in most cases.[1] This study aimed to quantify the extent of post-laparoscopic pneumoperitoneum and identify which level of pneumoperitoneum is likely to be pathological considering the size of the pneumoperitoneum and level of C-reactive protein (CRP). To our knowledge, no such study has focused on this issue. This information will help identify early (postoperative day 1) and occasional pathological pneumoperitoneum caused by iatrogenic bowel perforation.

Iatrogenic bowel perforation after laparoscopic surgery has an incidence of 0.13%[2] and is known for the paucity of clinical signs. Any patient who develops unexplained abdominal pain, fever or an elevated white cell count and/or an increase in CRP levels after a laparoscopic procedure should undergo early contrast-enhanced computed tomography (CT), and there should be a low threshold for repeat laparoscopy or laparotomy.[3] A high level of suspicion and free gas finding can help arrive at an early diagnosis. On postoperative day 1, plain X-ray chest findings and clinical signs are key elements that dictate further investigations such as CT and helps in the decision to perform a relook laparoscopy.

Materials and Methods

This prospective study enrolled a total of 60 patients who underwent laparoscopic surgery from 1 February 2012 to 30 November 2012 in our hospital. Cases were randomly chosen from the procedures performed by four surgeons. In this study, procedures were limited to laparoscopic cholecystectomy, laparoscopic appendectomy and laparoscopic hernia by transabdominal preperitoneal technique (Table 1).

The study population was composed of 48 male and 12 female patients, and 58% of the patients were 20-40 years old (Table 2). Patients aged <20 years and pregnant women were excluded from the study.

Laparoscopic surgery was performed by one of four specialist general surgeons in our institute. For all the selected cases, pneumoperitoneum was achieved by a 1-cm periumbilical incision using an optical trocar or a blunt-tipped metallic trocar. The total number of ports varied from 3 to 4 ports. None of the surgeons used Veress needle technique. After initial entry, CO_2 was inflated to achieve a pressure of 10-12 mmHg. The duration and difficulty of surgery were not taken into consideration for this study. At the end of the surgery, CO_2 was expelled through the ports by opening the cannulas. The telescope was removed at the last moment after checking other port sites after cannula removal. Once the telescope cannula is removed, the abdomen is normally flat. No intra-abdominal suction of gas or other special method was used to expel the gas.

On postoperative day 1, the patient was sent to the radiology room for a standing chest X-ray on the postero-anterior view. Any free gas under the diaphragm on either side was noted. The size of the pneumoperitoneum was quantified by measuring the diameter of the gas shadow at the widest spot.

Gaseous areas under the diaphragm of four cases of iatrogenic laparoscopic perforation, which occurred between 2004 and 2012, were analysed.

Results

The study population was composed of 48 male and 12 female patients, who were mostly in their 20s and 30s (Tables 1 and 2).

Various types of laparoscopic procedures were performed (Table 3).

Of the 60 patients, 20 (33.33%) had pneumoperitoneum on postoperative day 1, and most patients had only trace or

Table 1. Control patients

Age (years)	Patients (n=60)
20-30	15
31-40	20
41-50	17
51-60	6
>60	2

Table 2. Sex distribution

Sex	Number of patients (n=60)
Male	48
Female	12

Table 3. Laparoscopic procedures analysed

Laparoscopic appendectomy 20 cases
Laparoscopic cholecystectomy 21 cases
Laparoscopic hernia 19 cases

mild amounts, with only one each in the moderate and large category. In 13 (21%) patients, the pneumoperitoneum was unilateral under the right dome of the diaphragm, and in 7 cases (11.67%), there was gas under both domes of the diaphragm (Table 4, 5).

During the period from January 2005 to December 2012, we identified four cases of post-laparoscopic bowel perforation.

Cases with laparoscopic iatrogenic bowel perforation

Post-laparoscopic cholecystectomy

Post-laparoscopic varicocoelectomy

Post-laparoscopic hernia repair by TAPP technique

Post-laparoscopic appendectomy

Three laparoscopic procedures were performed by different surgeons in our hospital, and one case was referred to us from an external hospital. In all cases, X-ray of the abdomen and chest was carried out, but free gas was attributed to residual CO_2 after laparoscopic surgery, and all cases had limited clinical signs on postoperative day 1. Hence, a relook laparoscopy was performed only after 48 h in all four patients as there were more evident signs of peritonitis at that time and at CT (Table 6).

Table 4. Cases with gas under the diaphragm

Total number of cases: 60
Gas under diaphragm: 20 (33.33%)
Unilateral gas: 13 (65.0%)
Bilateral gas: 7 (35%)

Table 5. Measurements of gas areas under the diaphragm

Width of gas at the widest point number of cases	
0.4 to 7 mm (trace)	14
7.1 to 14 mm (mild)	4
14.1 to 30 mm (moderate)	1
>30 mm (large)	1

Table 6. Iatrogenic post-laparoscopic bowel perforations

Procedures first X-ray	Width of gaseous area at the widest point reop timing
Laparoscopic cholecystectomy	24 h 1.5 cm 48 h
Laparoscopic varicocoelectomy	24 h 1.7 cm 72 h
Laparoscopic hernia repair	24 h 2 cm 24 h
Laparoscopic appendectomy	24 h 1.5 cm 48 h

Conclusion

This study shows that despite the absence of special efforts to evacuate CO_2 pneumoperitoneum after laparoscopic surgery, X-ray chest imaging on postoperative day 1 (24 h after surgery) shows free gas only in 33.33% of the cases, which is slightly below that reported in literature at 46%. Moreover, in most cases, the amount of gas was small, with the vertical diameter of the gaseous area usually between 0.4 mm and 7 mm.

Cases of iatrogenic perforations however were all characterised by the presence of free gas under the diaphragm with the widest diameter ranging from 1.5 cm to 2.0 cm. Although it is not uncommon to see free gas under the diaphragm after laparoscopic surgery, a broad gas shadow is a cause for concern and dictates the need for CT and possible relook laparoscopy.

However, further studies are needed to analyse the implication of the width of the free gas under the diaphragm so that under appropriate clinical situations, prompt relook laparoscopy can be done to identify and rectify a possible iatrogenic bowel perforation.

Peer-review: Externally and internally peer reviewed.

Authorship Contributions

Concept: K.G.M., Design: K.G.M., Data Collection or Processing: K.G.M., F.A., S.I.P., Analysis or Interpretation: K.G.M., F.A., S.I.P., Literature Search: K.G.M., F.A., S.I.P., Writing: K.G.M., F.A., S.I.P.

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

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RESEARCH ARTICLE

Predictive Value of Red Cell Distribution Width and Mean Platelet Volume in the Diagnosis and Determination of Severity in Acute Appendicitis Cases

Akut Apandisit Olgularında Eritrosit Dağılım Genişliği ve Ortalama Trombosit Hacminin Tanıda ve Hastalığın Şiddetini Belirlemedeki Prediktif Değeri

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ABSTRACT

Aim: We aimed to determine the clinical value of erythrocyte distribution width (RDW) and mean platelet volume (MPV) in the diagnosis of acute appendicitis (AA) and in determining the severity of the disease.

Method: Patients who were operated between January 2013 and January 2020 with a preliminary diagnosis of AA were included in the study. The patients were divided into two groups as Group 1 negative appendectomy and Group 2 acute appendicitis. In addition, Group 2 is divided into subgroups as a:perforated and b: non-perforated. RDW and MPV were compared between the groups and subgroups.

Results: A total of 861 patients participated in our study. Group 1 consisted of 144 patients and Group 2 consisted of 717 patients. The mean age was similar in both groups (33.02 vs 35.34, p=0.088), female sex was higher in Group 1 (52.8% vs 42.9, p=0.019), RDW was higher in Group 1 (14.03 vs 13.67, p=0.007), MPV was similar between the groups (8.81 vs 8.95, p=0.363). RDW was an independent risk factor in the diagnosis of AA in multivariate analysis (odds ratio 0.604, 95% confidence interval (minimum-maximum) 0.420-0.868, p=0.006). RDW and MPV were independent variables in the diagnosis of perforated appendicitis in multivariate logistic regression analysis.

Conclusion: RDW is a useful parameter in the diagnosis of AA and in determining the severity of the disease. However, MPV value does not have sufficient diagnostic value.

Keywords: Acute appendicitis, MPV, RDW, sensitivity, specificity

ÖZ

Amaç: Eritrosit dağılım genişliğinin (RDW) ve ortalama trombosit hacminin (MPV) akut apandisit tanısındaki ve hastalığın şiddetini belirlemedeki klinik değerini saptamayı amaçladık.

Yöntem: Ocak 2013 ile ocak 2020 tarihleri arasında akut appendisit ön tanısı ile opere edilen hastalar çalışmaya dahil edildi. Hastalar Grup 1 negatif appendektomi; Grup 2 akut apandisit olmak üzere iki gruba ayrıldı. Ayrıca Grup 2a: Perfore ve 2b: nonperfore olmak üzere subgruplara ayrıldı. Nötrofil sayısı, RDW ve MPV oranları gruplarda ve subgruplarda karşılaştırıldı.

Bulgular: Çalışmamıza 861 hasta dahil edildi. Grup 1: 144, Grup 2: 717 hastadan oluşuyordu. Yaş ortalaması (33,02 vs 35,34 p=0,088) ve MPV oranları (8,81 vs 8,95 p=0,363) açısından her iki grup arasında anlamlı farklılık yoktu. Grup 1'de kadın cinsiyet oranı daha yüksekti (%52,8 vs 42,9 p=0,019). Ayrıca RDW oranları Grup 1'de daha yüksekti (14,03% vs 13,67% p=0,007) ve RDW oranları multivaryant analizde akut appendisit tanısında bağımsız bir göstergeydi (odds ratio: 0,604 %95 confidence interval: (minimum-maksimum) 0,420-0,868 p=0,006). RDW ve MPV oranları çok değişkenli lojistik regresyon analizinde perfore appendisit tanısında bağımsız değişkenlerdi.

Sonuç: Akut appendisit tanısında ve hastalığın şiddetinin belirlemesinde RDW yararlı bir parametredir. Fakat MPV değerinin yeterli tanısal değeri yoktur.

Anahtar Kelimeler: Akut appendisit, MPV, RDW, sensivite, spesivite

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Introduction

Acute appendicitis (AA) is the most common cause of acute surgical abdominal pain and is usually seen in patients in their 20s and 30s.[1] In the literature, the lifetime prevalence of this disease is approximately 7%, and its perforation rate is between 17% and 20%.[2,3]

Timely diagnosis is very important, since a diagnostic delay is associated with increased risk of perforation and potentially peritonitis, sepsis and death. On the contrary, negative appendectomy is associated with unnecessary risks and costs. Although advanced diagnostic tests and imaging methods have been developed, the rate of false diagnosis is still high.[4,5]

Complete blood count is used as part of the routine testing for AA. Based on this, many parameters in complete blood count and the combination of these parameters in the diagnosis of AA were investigated.[6,7]

The red blood cell distribution width (RDW) is a well-known erythrocyte parameter that shows variations in the diameter of red blood cells. At present, the erythrocyte index, which has been used in haematology practice, is accepted as a biological marker related to inflammation. A high RDW is associated with an increase in erythrocyte sedimentation rate and interleukin-6 levels.[8]

The mean platelet volume (MPV) is reported to be related to platelet function. The platelet size is closely related to platelet activity and function. Large platelets are more active than small platelets, and the MPV has been shown to reflect inflammatory burden.[9]

Recent studies have investigated on whether RDW and MPV can be used as an early predictor in AA.[10,11,12] In this study, we aimed to determine the clinical value of RDW and mean MPV in the diagnosis of AA and in determining its severity.

Materials and Methods

Patients who underwent surgery with a preliminary diagnosis of AA between January 2013 and January 2020 in the Erciyes University Faculty of Medicine General Surgery Clinic were included in the study. This retrospective study was approved by the Erciyes University Institutional Review Board (no: 2020/251, dated: 20.05.2020). Files and hospital information system records were examined, and the cases were analysed retrospectively.

While patients who underwent appendectomy (both open and laparoscopic appendectomy) were included, patients aged <18 years; pregnant patients; patients with heart failure, haematological disease, cancer, chronic infectious disease, liver disease, vascular disease, infection or inflammatory disease; patients who had missing data; or patients taking drugs that may affect the platelet count and volume were excluded from the study.

Patients were divided into two groups according to the histopathological evaluation. The first group included patients with a normal appendix (negative appendectomy group), and the second group was composed of patients with AA (AA group), which was further subdivided into perforated and non-perforated appendicitis groups. Demographic data of patients such as age and sex and preoperative laboratory findings on admission [neutrophil count/mm^3, RDW (%) and MPV (fL)] were compared between the negative appendectomy group and AA group. The same parameters were compared within the subgroups.

The complete blood count was measured by an automated haematology analyser (Roche Hitachi Cobas® 8000 Roche Diagnostics, Indianapolis, IN, USA). Reference values were 2-7x10^9/L for neutrophils, 7.4-10.4 femtoliter (fL) for MPV and 11.6%-14% for RDW.

Statistical Analysis

SPSS (Statistical Package for the Social Sciences) 23.0 package programme was used in the statistical analysis of data. Categorical measurements were summarised as numbers and percentages and continuous measurements as mean and standard deviation (median and minimum-maximum where necessary). Pearson chi-square test statistics were used to compare categorical variables. Shapiro-Wilk test was used to determine whether the study parameters showed normal distribution. In comparing continuous measurements between groups, distributions were checked; independent Student's t-test was used for parameters with normal distribution, and the Mann-Whitney U test was used for parameters without normal distribution. In this study, the cut-off value was determined by calculating the sensitivity and specificity values based on the neutrophil count, RDW and MPV and by examining the area under the receiver operating characteristics (ROC) curve. Logistic regression analysis was employed to determine the independent variables that affect the dependent variables. Statistical significance level was taken as 0.05 in all tests.

Results

A total of 861 patients participated in our study. The negative appendectomy group consisted of 144 patients, and the AA group consisted of 717 patients. The mean age was similar in both groups (33.02 vs 35.34, p=0.088), female patients comprised most the negative appendectomy group (52.8% vs 42.9, p=0.019), the neutrophil count was higher in the AA group (8.20 vs 10.31, p=0.00), RDW was higher in the negative appendectomy group (14.03% vs 13.67%, p=0.007) and MPV was similar between the two groups (8.81 vs 8.95, p=0.363). In the multivariate logistic regression analysis, neutrophil count and RDW were independent variables

in the diagnosis of AA. Comparison results between the negative appendectomy and AA groups are detailed in Table 1. The ROC curve analyses of these independent variables are shown in Figure 1. The recommended cut-off and diagnostic values for these variables are shown in Table 2.

The perforated and non-perforated subgroups were composed of 65 and 652 patients, respectively. While the mean age was higher in the perforated subgroup (42.63 vs 34.62, p=0.00), sex distributions were similar (p=0.33). No significant difference was found between the groups in terms of neutrophil count (11.12 vs 10.23, p=0.143), RDW (13.98% vs 13.64%, p=0.056) and MPV (8.74 vs 8.97, p=0.301). In the multivariate logistic regression analysis, neutrophil count, RDW and MPV were independent variables in the diagnosis of perforated appendicitis. The comparison between the perforated and non-perforated subgroups is detailed in Table 3. The ROC curve analyses of these independent variables are shown in Figure 2. The recommended cut-off and diagnostic values for these variables are shown in Table 4.

Discussion

Appendicitis is still the most common indication of emergency surgery. Traditionally, appendectomies are performed immediately after diagnosis was made to prevent the progression of inflammation and potential complications.[13]

Although leukocyte count generally increases in patients with AA, it is not a specific marker of AA and can increase in many diseases accompanied with inflammation during differential diagnosis. In AA, neutrophilia and left shift on the haemogram are often associated with lymphopaenia.[14,15] Anderson reported a sensitivity of 71%-89% and specificity of 48%-80% in his meta-analysis (neutrophil count >6,500/mm^3).[14]

Table 1. Comparison of the two groups

Parameters		Univariate analysis			Multivariate analysis			ROC curve analysis		
Negative appendectomy		Acute appendicitis	p	OR	95% CI (min-max)	p	AUC	95%CI (min-max)	p	
Patient number		144 (16.7)	717 (83.3)							
Age		33.02±13.87 (18-85)	35.34±15.10 (13-87)	0.088						
Sex	Male	68 (47.2)	409 (57.1)	**0.019**						
	Female	76 (52.8)	307 (42.9)		1.489	1.040-2.132	**0.030**			
Neutrophil (x10^3/mm^3)		8.20±4.59 (1.31-29.16)	10.31±4.70 (1.75-78)	**0.000**	3.846	2.652-5.576	**0.000**	0.654	0.622-0.686	**0.001**
RDW (%)		14.03±1.80 (11.5-24.4)	13.67±1.36 (11.5-20.7)	**0.007**	0.604	0.420-0.868	**0.006**	0.560	0.526-0.594	**0.028**
MPV (Fl)		8.81±1.64 (6.2-13.9)	8.95±1.71 (4.8-13.5)	0.363	1.365	0.954-1.954	0.089	0.527	0.493-0.561	0.291

RDW: Red blood cell distribution width, MPV: Mean platelet volume, AUC: Area under the curve, OR: Odds ratio

Table 2. Proposed cut-off values for significant parameters in the diagnosis of acute appendicitis

	Cut-off value	Sensitivity (%)	Specificity (%)	PPV	NPV	OR	AUC
Neutrophil (x10^3/mm^3)	<7.04	52.08	77.96	32.2	89.0	5.716	0.654
RDW (%)	>13.9	43.75	69.32	22.3	86	2.194	0.560
MPV (Fl)	<8.4	50.69	57.04	19.2	85.2	1.055	0.527

RDW: Red blood cell distribution width, MPV: Mean platelet volume, AUC: Area under the curve, PPV: Positive predictive value, NPV: Negative predictive value, OR: Odds ratio

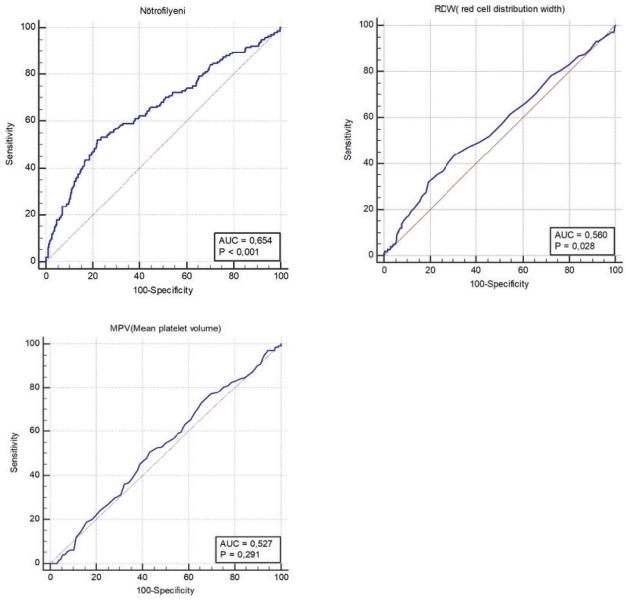

Figure 1. Receiver operating characteristic curve analyses of significant parameters for the diagnosis of acute appendicitis: (a) neutrophil count, (b) red blood cell distribution width and (c) mean platelet volume

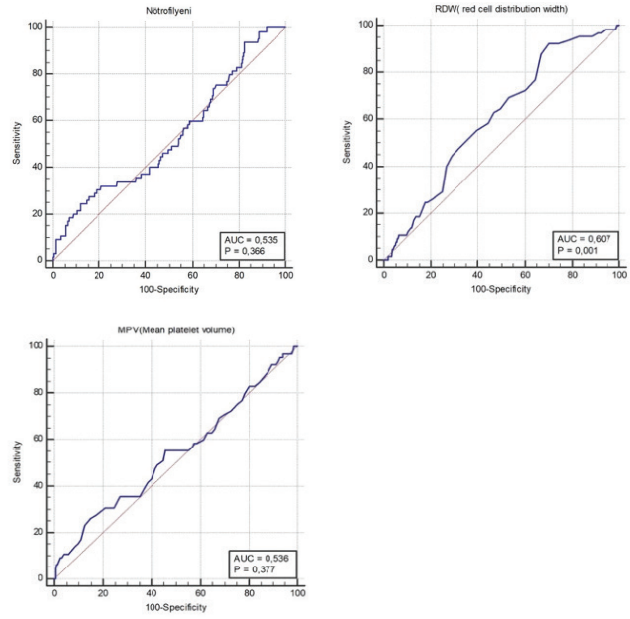

Figure 2. Receiver operating characteristic curve analyses of significant parameters for the diagnosis of perforated appendicitis: (a) neutrophil count, (b) red blood cell distribution width and (c) mean platelet volume

Table 3. Comparison of the subgroups of the acute appendicitis group

Parameters	Multivariate analysis			ROC curve analysis					
Perforated	Non-perforated	p	OR	95% CI (min-max)	p	AUC	95% CI (min-max)	p	
Patient number	65 (9.1)	652 (90.9)							
Age	42.63±18.26 (19-85)	34.62±14.57 (13-87)	**0.000**						
Sex Male	35 (53.8)	374 (57.5)							
Sex Female	30 (46.2)	277 (42.5)	0.333	1.157	0.694-1.931	0.576			
Neutrophil (×10³/mm³)	11.12±4.74 (4.63-27.78)	10.23±4.69 (1.75-78)	0.143	0.416	0.226-0.767	**0.005**	0.535	0.498-0.572	0.366
RDW (%)	13.98±1.22 (11.8-17.9)	13.64±1.37 (11.5-20.7)	0.056	0.197	0.078-0.497	**0.001**	0.607	0.570-0.642	**0.001**
MPV (Fl)	8.74±1.83 (5.6-12.3)	8.97±1.7 (4.8-13.5)	0.301	2.026	1.119-3.669	**0.020**	0.536	0.498-0.573	0.377

RDW: Red blood distribution width, MPV: Mean platelet volume, AUC: Area under the curve, OR: Odds ratio, min: Minimum, max: Maximum, CI: Confidence interval

Table 4. Proposed cut-off values for significant parameters in prediction of perforation

	Cut-off value	Sensitivity (%)	Specificity (%)	p	PPV	NPV	AUC
Neutrophil (x10³/mm³)	>14.57	24.62	88.04	0.366	17.0	92.1	0.535
RDW (%)	>12.8	92.31	29.75	**0.001**	11.6	97.5	0.607
MPV (Fl)	<7.1	26.15	85.12	0.377	14.9	92.0	0.536

RDW: Red blood cell distribution width, MPV: Mean platelet volume, AUC: Area under the curve, PPV: Positive predictive value, NPV: Negative predictive value, OR: Odds ratio

In our study, the neutrophil count was higher in the AA group (p=0.000). For the cut-off value [area under the curve (AUC) 0.654; 95% confidence interval (CI) 622-0.684, p=0.001] determined according to the ROC curve, the sensitivity and specificity were 52% and 77%, respectively.

RDW is frequently used in haematology practice to distinguish iron deficiency anaemia from other microcytic anaemias. Increased RDW is associated with erythropoiesis disorder or erythrocyte destruction. RDW has also been investigated in inflammatory and infectious pathologies such as rheumatoid arthritis, inflammatory bowel disease, colon cancer and celiac disease. RDW elevations have been shown to be associated with increased levels of inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation rate and interleukin-6. Pro-inflammatory cytokines in sepsis negatively affect the life span of circulating erythrocytes and suppress erythrocyte maturation.[12,16]

In the study by Narci et al.[10], RDW was significantly lower in the AA group than in the control group (15.4±1.5 vs 15.9±1.4, p=0.001). In the ROC analysis, the diagnosis of AA with 15.6% cut-off for RDW had sensitivity of 47% and specificity of 67% (AUC 0.62).[11] Günay et al.[17] compared complicated and non-complicated AA cases and reported that the RDW was higher in the complicated appendicitis group (16.97±4.48 vs 14.28±2.73, p=0.001). In the same study, RDW was determined as an independent diagnostic factor for complicated appendicitis in the logistic regression analysis (OR: 1.412, 95% CI: 1.01-1.98, p=0.046).[17] In the study by Boshnak et al.[18], unlike the literature, no difference was found in the RDW of the negative and positive appendectomy groups (13.13±0.36 vs 13.06±0.43, p>0.05). However, in their study, RDW was higher in complicated AA cases (13.02±0.40 vs 13.30±0.58, p=0.006).[18] Tanrikulu et al.[19] reported no significant relationship between RDW and AA, similar to the finding of Boshnak et al.[18]

Bozlu et al.[20] reported that RDW was elevated in children with AA, but they did not find a significant difference in complicated cases. In this study, the diagnostic value of RDW in children with AA was not higher than that of white blood cells or CRP. They concluded that a high RDW is valuable in the diagnosis of AA in children, but it is not a useful marker for complicated appendicitis.[20]

In our series, RDW was higher in the negative appendectomy group (14.03% vs 13.67%, p=0.007). RDW was an independent risk factor for AA in the multivariate analysis. When the cut-off value was 13.9, RDW showed 43% sensitivity and 69% specificity in the diagnosis of AA. RDW was similar in the perforated and non-perforated appendicitis subgroups. In the multivariate analysis, it was an independent risk factor for perforated appendicitis. When the cut-off value was 12.8, RDW demonstrated 92% sensitivity and 29% specificity.

During the development of sepsis, platelets are thought to be one of the first responding anuclear cells. Gurler and Aktas[21] suggested that the increase or decrease in MPV in inflammatory conditions results from the effects of inflammatory cytokines in the bone marrow. Active platelets grow in infectious conditions and cause an increase in MPV in haemogram tests. However, after the use of larger activated platelets in inflammatory processes, smaller platelets lead to a decrease in MPV in blood count tests.[21] Increases in MPV are associated with chronic diseases, and decreases are associated with acute diseases. While increased MPV were observed in chronic disease conditions, decreased MPVs were observed in acute disease environments. In the literature, low MPVs during an attack increased to normal levels in patients with ankylosing spondylitis and rheumatoid arthritis. In addition, in some inflammatory bowel diseases, MPV decreased in parallel with increased disease activity.[22,23] However, the pathophysiological mechanisms for decreased MPV in patients with AA is not yet clear.[24]

Discussions are on-going in studies that have investigated the diagnostic value of MPV. Erdem et al.[5] reported MPVs for the AA group and control group as 7.4±0.9 (5.6-10.6) fL vs 9.1±1.6 (5.1-13.1) fL, respectively (p<0.001). In their ROC analysis, the AUC was 82.4% for the MPV. When the cut-off MPV value was below 7.95 fL, the test's sensitivity and specificity were 74% and 75%, respectively.[25] In the study by Narci et al., the median MPV was 7.92±1.68 fL in the AA group and 7.43±1.34 fL in the control group. The MPV was significantly higher in the AA group than in the control group (p<0.001). In their ROC analysis, the AUC was 62%, and with a cut-off value of 7.87, the sensitivity and specificity were 66% and 51%, respectively.[10] Uyanik et al.[26] concluded that MPV in the paediatric age group was similar in the AA and control groups (7.9±0.9 vs 7.7±0.8, p>0.05) and had no diagnostic value for AA.[26] Similarly, Dinc et al. found a sensitivity of 29.5%, specificity of 49.0% and diagnostic accuracy of 34.0% for MPV, but with limited diagnostic value.[24] However, on separate evaluation, these studies have heterogeneous characteristics. In the most recent meta-analysis for the diagnostic value of MPV in AA, MPV decreased significantly in patients with AA compared with the control group (weighted mean difference, -0.64; 95% CI, -0.74 to -0.54; p=0.037). The analysis showed that MPV can be used as a biomarker for AA, but it does not have sufficient diagnostic value.[27]

Yardımcı et al.[28] found higher MPV values in patients with AA than in healthy controls (9.3±8 vs 9.3±8, p=0.0005). In the same study, according to the pathologies in the patient group, the MPV was 8.8±5.8 (6-96) for phlegmonous

appendicitis, 8.9±5.8 (6.1-74) for localised peritonitis and 12.8±9.7 (6.7-87) for perforation and/or gangrenous appendicitis. They found a statistically significant difference between patient groups (95% CI 8.5-10.1; p=0.005). Another outcome of this study was to identify the role of MPV in predicting more severe forms of AA, such as perforation and/or gangrenous appendicitis. According to the ROC analysis, when the cut-off value was 8.92 in the differential diagnosis of AA, it has 73% sensitivity and 57% specificity (AUC 0.57; 95% CI 0.49-0.62; p=0.0005).[28]

In our series, MPV did not differ significantly between the negative appendectomy group and AA group or between perforated and non-perforated groups. Moreover, MPV has no diagnostic value for either AA or perforated appendicitis.

Study Limitations

The most important limitation of this study was its retrospective nature. In addition, only patients who underwent appendectomy were included in the study, as patients suspected of AA who did not undergo surgery were excluded.

Conclusion

RDW is helpful in the diagnosis of AA and detection of perforated appendicitis, but it has no sufficient diagnostic value when used alone. Normal RDW values cannot exclude AA alone. MPV has a low clinical value in the diagnosis of AA and in the detection of perforated appendicitis.

Ethics

Ethics Committee Approval: After obtaining permission from the Ethics Committee of Erciyes university Faculty of Medicine dated 20.05.2020 and numbered 2020/251.

Informed Consent: Because the study was retrospective, we could not get informed consent.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: M.A., U.T., E.M.S., Ş.Y.İ., M.G., T.B.A., Concept: M.A., U.T., Ş.Y.İ., Design: M.A., U.T., Data Collection or Processing: U.T., Ş.Y.İ, M.G., T.B.A., Analysis or Interpretation: M.A., U.T., E.M.S., Literature Search: U.T., M.G., T.B.A., Writing: M.A., U.T., E.M.S.

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

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CASE REPORT

A Rare Cause of Bowel Obstruction in a 100-year-old Patient: Gallstone Ileus

100 Yaşındaki Bir Hastada Nadir Rastlanılan Bağırsak Tıkanıklığı Nedeni: Safra Taşı İleusu

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ABSTRACT

Gallstone ileus occurs when a gallstone passes into the intestinal system through a fistula between the gallbladder or biliary tract, and the duodenum, stomach or colon, and causes an obstruction. Although it is usually seen in advanced ages, it has rarely been reported in patients who are 100 years old. A 100-year-old female patient, without significant medical or surgical history, was admitted to the emergency department for diffuse abdominal pain, nausea, vomiting, and constipation. Abdominal computed tomography showed air in the biliary tract and obstruction in the small intestine. Patient was operated under emergency conditions. Enterolithotomy was performed and the stone was extracted. Postoperative recovery was uneventful. Bilioenteric fistulas, a major complication of chronic gallbladder diseases, usually develop secondary to intense inflammation. Patients' age, concomitant disease, clinical condition and intraoperative findings should be taken into consideration while planning the treatment. The data in the literature generally supports the employment of enterolithotomy in high-risk patients and reserves cholecystectomy and resection of the fistula for less comorbid patients with feasible anatomy.

Keywords: Cholecystoduodenal fistula, enterolithotomy, gallstone

ÖZ

Safra taşı ileusu safra kesesi veya safra yolları ile duodenum, mide ya da kolon arasında meydana gelen fistüle bağlı olarak safra taşlarının intestinal sisteme geçmesi ve obstrüksiyona neden olması ile oluşur. Genellikle ileri yaşlarda görülmesine rağmen litaratürde 100 yaşındaki hastalarda nadiren bildirilmiştir. Özgeçmişinde önemli bir dahili ya da cerrahi problemi olmayan 100 yaşındaki kadın hasta; acil servise yaygın karın ağrısı, bulantı, kusma ve kabızlık nedeniyle başvurdu. Abdominal bilgisayarlı tomografisinde safra yollarında hava ve ince bağırsak düzeyinde obstrüksiyon vardı. Acil şartlarda opere edildi. Enrolitotomi yapıldı taş eksaktre edildi, postoperatif dönemi sorunsuz geçti. Kronik safra kesesi hastalıklarının önemli bir komplikasyonu olan biliyoenterik fistüller ortalama yoğun inflamasyona sekonder olarak gelişirler. Tedavi planlanmasında, yaşı, yandaş hastalıkları, klinik durumu ve intraoperatif bulgular göz önünde bulundurulmaktadır. Literatürde genel olarak yüksek riskli hastalarda enterolitotomi istihdamını ve daha az komorbid olan hastalar için kolesistektomiyi fistül rezeksiyonunu desteklemektedir.

Anahtar Kelimeler: Kolesistoduodanal fistül, enterolitotomi, safra taşı

Introduction

Bartholin first described by gallstone ileus in 1654, which is a rare cause of small intestinal obstruction. It happens when a gallstone passes through the intestinal system along a fistula between the gallbladder or biliary tract and the duodenum, stomach or colon and causes obstruction.[1]

In patients under 65 years of age, gallstone ileus is the cause of less than 4% of intestinal obstruction, and this incidence increases to 25% in patients over 65 years of age. The proportion of women to men is 3.5-3.6:1, and patients are typically over 65 years of age.[2]

The gallstone ileus-related mortality rate ranges from 12% to 27%, and the morbidity rate reaches 50%.[3] Patients present

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with nonspecific symptoms, such as abdominal pain and vomiting. Typically, laboratory tests are nonspecific. Even though 30-40% of patients can be diagnosed radiologically preoperatively, it is mostly done during the surgery.[4] Radiology shows the pathognomonic triad of pneumobilia, small bowel obstruction and ectopic gallstone. Thus, the ideal treatment of gallstone ileus remains controversial.[2]

In this case, we evaluated our approach to a 100-year-old patient with preoperative diagnosis of gallstone ileus.

Case Report

With abdominal pain, nausea, vomiting and abdominal distention, a 100-year-old Middle Eastern female patient was admitted to the emergency room. Her complaints began 2 days earlier, and for the last 2 days, she hadn't passed gas/stool. Her medical history revealed that she had primary hypertension. In addition, she did not have a history of previous abdominal surgery but had a history of hospitalization due to acute cholecystitis. Additionally, previous ultrasound examination had revealed gallstones in the gallbladder.

The patient had no contributing family or psychosocial history or history of smoking or other metabolic diseases. Physical examination showed abdominal distention and diffuse sensitivity with palpation. During auscultation, no intestinal sounds could be obtained in four quadrants of the abdomen, and tympanism was observed on all four quadrants of the abdomen with percussion. Further, during rectal examination, the rectal ampulla was empty, and no palpable mass was detected. The body temperature of the patient was 38 °C, blood pressure was 100/60 mmHg, pulse was 115/minute, and body mass index was 28. The following values were obtained in laboratory analysis: white blood cell count= 1/4,900/mm^3, aspartate transaminase= 116.7 u/L, alanine transaminase= 112.9u/L, glucose= 77 mg/dL, chloride= 101.4 mmol/L, blood urea nitrogen= 25.4 mg/dL, creatinine= 1.45 mg/dL, sodium= 130 mmol/L, potassium= 3.05 mmol/L, total bilirubin= 0.10 mg/dL, direct bilirubin= 0.10 mg/dL, amylase= 43U/L, gamma-glutamyl transpeptidase= 243u/L, alkaline phosphatase= 285 u/L, lactate dehydrogenase= 429 u/L, and C-reactive protein= 18 mg/L. On the other hand, other parameters were normal.

In abdominal ultrasonography, the integrity of the stone wall inside the gallbladder was impaired. Further, oral and IV contrast computed tomography revealed air in the gallbladder and intrahepatic bile ducts, and there were signs of obstruction of the ileus in the small bowel level (Figure 1).

The patient was admitted to the intensive care unit. Before surgery, intravenous fluid and antibiotics (piperacillin/tazobactam) were administered. The patient also underwent nasogastric intubation and correction of electrolyte disturbances.

The patient then underwent emergency surgery. After anaesthetic clearance, an emergency laparotomy was performed under general anaesthesia with a diagnosis of gallstone ileus. A large 4-cm palpable gallstone was found in the 60th cm of the terminal ileum. The technique of choice was the removal of the stone via enterotomy, then a longitudinal incision was performed on the antimesenteric border proximal to the site of impaction, and the gallstone was milked proximally and removed (Figure 2).

During enterotomy, a general survey of the abdomen was conducted where no signs of malignancy were identified, and it was closed in two layers because the patient's tissues

Figure 1. CT scan showed air in the gallbladder and intrahepatic bile ducts

CT: Computed tomography

Figure 2. The gallstone was removed and the enterotomy was repaired in two layers

in the upper right quadrant were oedematous and fragile, which appeared to be inflamed and compatible with a cholecystoduodenal fistula. Considering the age of the patient and comorbid factors, no attempt was made on the cholecystoduodenal fistula and gallbladder. The final pathology of the specimen was reported as a gallstone: 12.5 gr, olive green-yellow coloured, and ovoid shaped, which measured 4x3.2x2.5 cm (Figure 3).

The duration of the surgery was 1 hour and 45 minutes, with a blood loss of 100 mL. Moreover, the patient was followed up in the postoperative intensive care unit. Postoperative follow-up was followed by antibiotic therapy (piperacillin/tazobactam), intravenous fluid, analgesics (paracetamol) and enoxaparin sodium for thrombosis prophylaxis. Antiemetics were administered, and after gastrointestinal passage was achieved, the oral intake was started.

On the 8th postoperative day, the patient had an uneventful postoperative course and was discharged home. The patient had no specific postoperative complications, and there was no development of wound complications. Therefore, we did not need a rediscovery/revision surgery. We have not experienced postoperative 30-day and long-term morbidity/mortality. Further, 10 days after discharge, the patient was followed up as an outpatient, and an infection was discovered at the incision site, so wound care was administered. During the 1-month follow-up, no recurring complaints were observed. After 6 months, another follow-up was conducted. Moreover, in terms of biliary complications, the patient should be closely monitored.

Figure 3. The appearance of the gallstone after removal by enterotomy

Discussion

Bilioenteric fistulas, a significant complication of chronic gallbladder diseases, usually develop secondary to intense inflammation. The key mechanism is the development of abnormal epithelial connections between two hollow organs by mass effect and secondary inflammation.[5]

Gallstone ileus is observed in 0.3-0.5% of all cases of cholelithiasis. In gallstone ileus, the gallbladder stone enters the intestinal tract through a fistula.[1] When we look at the literature, the localization of the fistula is most often cholecystoduodenal with 68%, while it is 5% cholecystocolonic and 2.5% cholecystoduodenocholic. In addition, the localization of the gallstone has been reported as 64% terminal ileum, 23% proximal ileum and jejunum, 4% colon and 1% stomach.[6]

In our case, a cholecystoduodenal fistula was present, and the gallstone was found in the terminal ileum. With the imaging methods used in diagnosis, the accuracy rates can be increased for preoperative diagnosis. The imaging diagnostic criteria for gallstone ileus are called "Rigler's triad" and consist of the presence of a radiopaque stone (presenting in less than 10% of cases), pneumobilia (Gotta-Mentschler sign) and bowel loop distention. Moreover, two of these three signs are diagnostic.[2,7] The use of X-rays in conjunction with abdominal ultrasound increases sensitivity to 74% for a gallstone diagnosis.[8] The contrast computed tomography (CT) scan is recognized as the gold standard method for the diagnosis of gallstone ileus and is reported to have a sensitivity over 90% in the literature.[9] In the literature, a study comparing direct abdominal X-ray, abdominal ultrasonography and abdominal CT for gallstone ileus found that Rigler's triad is present in 14.8% of plain abdominal film, in 11.11% of abdominal US and in 77.78% of abdominal CT.[9]

Treatment options include enterolithotomy (stone extraction, cholecystectomy, fistula tract excision) or two-stage surgical enterolithotomy and biliary tract surgery.[10,11] Because of the age and comorbidities of the patient, we decided to perform enterolithotomy as the treatment option. In the literature, in a series comparing single-stage surgery with enterolithotomy, the mortality rate of enterolithotomy was found to be lower (11.7%) compared to single-stage surgery (16.9%).[3]

Enterolithotomy can be applied easily and rapidly in patients with an advanced age and in the presence of comorbid disease. However, recurrent gallstone ileus, acute cholecystitis, recurrent cholangitis and the persistence of the risk of gallbladder cancer are the disadvantages of this technique.[10]

Laparoscopic procedures can be an alternative method, but it would be necessary to have a surgeon with specialist expertise in advanced laparoscopic surgery. Moreover, the potential advantages are a shorter hospital stay and reduced laparotomy-associated morbidity.[12] A valid alternative approach is the endoscopic treatment of gallstone ileus. In the literature, endoscopic mechanical lithotripsy and transrectal endoscopic treatment without lithotripsy have been successfully applied. In addition, ultrasound-guided extracorporeal shock wave lithotripsy has also been proposed as a noninvasive alternative to surgery to fragment the stone and solve the sub-occlusion.[13,14,15]

Management of gallstone ileus is mainly surgical. Gallstones should be considered in the differential diagnosis of elderly women with a diagnosis of mechanical intestinal obstruction. The age, concomitant disease, clinical condition and intraoperative findings of patients should be taken into consideration in treatment planning.

Informed Consent: Informed consents was obtained from the patient.

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Surgical and Medical Practices: M.G., U.T., E.M.S., B.Ö., M.A., Concept: M.G., U.T., B.Ö.,

Design: M.G., U.T., Data Collection or Processing: U.T., B.Ö., M.A., Analysis or Interpretation: M.G., U.T., M.S., Literature Search: U.T., M.A., Writing: M.G., U.T., E.M.S.

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CASE REPORT

An Unusual Cause of Rectal Pressure and Difficult Defecation: Giant Pelvic Myelolipoma

Rektum Basısı ve Defekasyon Zorluğunun Alışılmadık Nedeni: Dev Pelvik Miyelolipom

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ABSTRACT

Myelolipoma is a rare benign neoplasm consisting of mature adipose and haematopoietic tissues and usually found in the adrenal gland. However, myelolipoma can be rarely detected in extra-adrenal regions but often detected incidentally in imaging studies performed for other reasons or at autopsy. While adrenal myelolipomas are easily recognised given its typical imaging features, the diagnosis of extra-adrenal myelolipomas may be challenging. Herein, we aimed to present computed tomography and magnetic resonance imaging findings of pelvic extra-adrenal myelolipoma in a 77-year-old woman with hepatocellular carcinoma and to describe the differential diagnoses.

Keywords: Magnetic resonance imaging, computed tomography, pelvis, myelolipoma, lipomatous tumour

ÖZ

Miyelolipom, olgun adipöz ve hematopoietik dokudan oluşan ve genellikle adrenal bezde bulunan nadir benign bir neoplazmdır. Bununla birlikte, miyelolipom adrenal dışı bölgelerde nadiren tespit edilebilir ve sıklıkla başka nedenlerle yapılan görüntülemelerde veya otopside tesadüfen tespit edilir. Adrenal miyelolipomlar, tipik görüntüleme özellikleri nedeniyle kolayca tanınırken, adrenal dışı miyelolipomların teşhisi zor olabilir. Burada hepatoselüler karsinom tanılı 77 yaşındaki bir kadında pelvik ekstra-adrenal miyelolipomun bilgisayarlı tomografi ve manyetik rezonans görüntüleme bulgularını göstermeyi ve ayırıcı tanıları tanımlamayı amaçladık.

Anahtar Kelimeler: Manyetik rezonans görüntüleme, bilgisayarlı tomografi, pelvis, miyelolipom, lipomatöz tümör

Introduction

Myelolipomas are rare and benign tumours composed of variable amounts of haematopoietic elements and fatty tissue and usually located in the suprarenal glands.[1] Moreover, cases have been reported in non-adrenal locations such as the presacral space, retroperitoneum, thoracic cavity, liver and stomach.[2,3,4,5] Myelolipomas are usually small, grow slowly and asymptomatic. Most of them are detected incidentally at autopsy or in imaging examinations performed for other reasons. While adrenal myelolipomas are easily recognised due to the typical imaging features, the diagnosis of extra-adrenal myelolipomas (EAMs) may be challenging, and EAMs can be misdiagnosed as malignant tumours.[1,2,3,4] Therefore, imaging features of EAMs should be well known to avoid aggressive surgical interventions.

Case Report

A 77-year-old woman, who was diagnosed with hepatitis B-related liver cirrhosis 6 years ago, presented with abdominal pain, but she was lost to follow-up for several years. She had a history of constipation and urinary incontinence for several years. Laboratory results revealed low haemoglobin level (12.8 g/dL; normal range, 14-16 g/dL) and platelet count (134,000; normal range: 150,000-400,000) and high alanine aminotransferase (65 IU/L; normal values, <41 IU/L) and alpha-fetoprotein level (344 ng/mL; normal values, <5 ng/

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mL). Other laboratory test results were within normal limits. Abdominal ultrasonography (US) revealed heterogeneity and nodularity of the liver parenchyma, hypertrophy in the left lobe and atrophy in the right lobe, which were compatible with cirrhosis. Moreover, ascites and a heterogeneous, hypoechoic mass with a diameter of 4 cm at segment 5 of the liver were detected. Compared with abdominal US examination performed 3 years ago in an external centre, the lesion had newly appeared. Dynamic contrast-enhanced computed tomography (CT) of the abdomen was performed, which revealed mild ascites and additional focus on segment 6 of the liver compatible with hepatocellular carcinoma (HCC). No metastasis was found on abdominal CT images, but a heterogeneous, well-defined fatty mass with solid components was detected in the presacral space (Figure 1). US-guided liver biopsy was performed with a preliminary diagnosis of HCC, and HCC was confirmed on histopathological examination. For further evaluation of the pelvic mass, magnetic resonance imaging (MRI) of the lower abdomen was performed, which showed a heterogeneous, well-defined, fatty mass with a pseudocapsule in the presacral space. The pelvic mass exhibited mild diffusion restriction with an apparent diffusion coefficient value of 0.92x10-3 mm^2/s and heterogeneous contrast enhancement (Figure 2). In the differential diagnosis of the lesion, EAM was primarily considered. A CT-guided tru-cut biopsy was performed considering the well-differentiated liposarcoma in the outer centre, and the pathological diagnosis was myelolipoma. Surgery was recommended, but the patient declined. Therefore, symptomatic treatment was started. In the control abdominal CT examination obtained 16 months later, the size and imaging features of the pelvic lesion were stable.

Discussion

Myelolipomas are benign and rare tumours composed of haematopoietic cells and adipocytes.[1] The aetiology of myelolipomas is not well elucidated. Still, some theories suggest that myelolipomas result from a metaplastic change in response to infection, inflammation or stress.[1,2,3] Although myelolipomas often present as an isolated adrenal myelolipoma, it could also appear in other locations such as the presacral space, retroperitoneum, thoracic cavity, liver and stomach. The presacral area is the most frequent location of extra-adrenal lesions.[2,3,4,5] En bloc excision of the lesion with careful dissection is recommended in patients without symptoms.[6,7] However, in the presented case, the patient refused surgery.

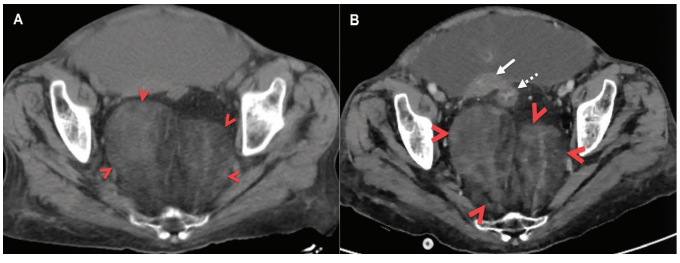

Figure 1. Axial unenhanced and (B) contrast-enhanced computed tomography image of the pelvis demonstrate a heterogeneous, well-defined and contrast-enhanced fatty mass with solid components in the presacral space

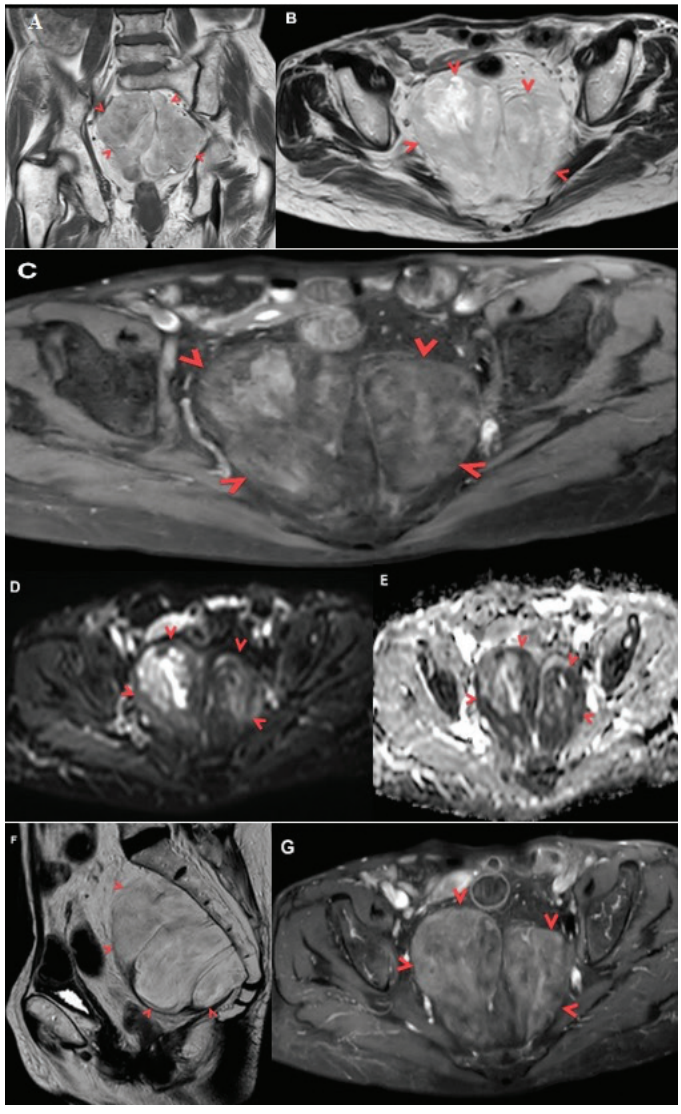

Figure 2. (A) Coronal T1-weighted and (B) Axial T2-weighted magnetic resonance (MR) images show well-defined, encapsulated and mildly hyperintense mass in the presacral space (arrowheads). Note the anteriorly displaced rectum (dashed arrow) and uterus (arrow). (C) Axial T1-weighted fat-suppressed MR image shows signal dropout in the lesion due to the fat component (arrowheads). (D) Axial diffusion-weighted and (E) apparent diffusion coefficient (ADC) map image demonstrates mild diffusion restriction with an ADC value of 0.92x10-3 mm^2/sec (arrowheads). (F) Sagittal T2-weighted MR image shows a hypointense capsule of the presacral lesion (arrowheads). (G) Axial contrast-enhanced T1-weighted fat-suppressed MR image shows heterogeneous contrast enhancement in the lesion (arrowheads)

EAMs are almost always seen as a well-defined, round or oval fatty mass, as in the present case. EAMs are usually asymptomatic and detected incidentally. Rarely, EAMs may cause symptoms due to haemorrhage or mass effect when it reaches massive sizes.[2,3] On abdominal CT, myelolipomas are usually seen as an encapsulated, well-defined, macroscopic fatty mass with regular septa or solid components. After intravenous administration of contrast medium, contrast enhancement is frequently seen in solid components of myelolipomas. On MRI, myelolipomas are detected as masses with mixed-signal intensities and partial hyperintense signal on T2-weighted (T2-W) and T1-W images due to the fat component of the masses, which show as signal dropout on fat-suppressed images, as in the present case.[2,3,4,5]

The differential diagnoses of fatty pelvic masses include liposarcoma, myelolipoma, pelvic lipomatosis and extramedullary haematopoiesis (EH) (Table 1).[6,7]

EH is a benign lesion of haematopoietic cells outside the medulla of the bone. While EH is usually found in the thoracic paravertebral space, presacral involvement is not unusual.[2] On CT, EH usually presents as a heterogeneous lesion close to the sacrum without bone erosion. On MRI, EH can be seen as a fatty mass with high-signal intensity on T1-W and T2-W images and as signal dropout on fat-suppressed images. Although the imaging features are generally similar to EAM, EH is often seen with multiple foci that usually hold the mediastinum and/or the paravertebral space.[2,6,7]

Liposarcomas are seen at any age and more often in male patients than in female patients. In liposarcomas, aggressiveness increases as fat content decreases. Unlike myelolipomas, the well-defined capsule in liposarcomas is not an expected imaging finding. Moreover, liposarcomas could show signs of invasion and may metastasise.[3,4,6] When an ill-defined fatty mass without capsule (or pseudocapsule) and/or invasion features are seen on imaging, liposarcoma should be considered first in the differential diagnosis.

Pelvic lipomatosis is an uncommon entity characterised by excessive fat deposition in perirectal and perivesical spaces. Abdominal CT typically shows a non-encapsulated, symmetric and homogeneous excessive fatty tissue growth surrounding the pelvic organs. MRI shows similar features with CT.[6,8] In myelolipoma, a solid component or septa is often seen, but not in pelvic lipomatosis.

In conclusion, EAM is a rare and benign entity that is generally found incidentally, as in the present case. It is essential to differentiate EAMs from aggressive tumours like liposarcomas. Differentiation of presacral myelolipoma from other presacral fatty masses could be challenging because imaging features may overlap. Well-defined, encapsulated and heterogeneous fatty presacral mass, without any haematologic disease, favours presacral myelolipoma than the others. Moreover, clinical, laboratory and descriptive

Table 1. Main differential diagnosis of presacral fatty masses and imaging features.

Lesion	Imaging features	Clinical findings	Contrast enhancement
Myelolipoma	Encapsulated, well-defined mass with macroscopic fatty tissue and solid areas; calcification may be present.	Usually asymptomatic and may cause symptoms due to haemorrhage or mass effect.	Yes*
Extramedullary haematopoiesis	Heterogeneous mass does not contain calcification, usually seen in multiple foci that frequently hold the mediastinum, and/or the paravertebral space.	Chronic anaemia and haematological disorders.	Yes*
Liposarcoma	Ill-defined fatty mass without capsule, invasion features or metastasis.	Usually asymptomatic at the early stage, may be presented by mass effect or metastasis.	Yes*
Pelvic lipomatosis	Non-encapsulated, symmetric and homogeneous excessive fatty tissue growth surrounding the pelvic organs. Pear-shaped bladder and stretched sigmoid colon can be seen.	Usually asymptomatic, it may cause dysuria, urgency incontinence and constipation due to mass effect.	No
Lipoma	May contain a capsule; the mass effect is asymmetrical.	Almost always asymptomatic.	No

*; in solid components

features of patients such as age and medical history should also be taken into consideration.

Informed Consent: Obtained.

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Surgical and Medical Practices: B.S., H.G.Y., F.U., Concept: H.G.Y., Design: H.G.Y., Data Collection or Processing: B.S., H.G.Y., F.U., Analysis or Interpretation: H.G.Y., F.U., Literature Search: B.S., Writing: B.S., F.U.,

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LETTER TO THE EDITOR

Social Media and its Impact on the General and Colorectal Surgery Communities

Sosyal Medyanın Genel ve Kolorektal Cerrahi Topluluğuna Etkisi

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Keywords: Colorectal surgery, social media, some4surgery
Anahtar Kelimeler: Kolorektal cerrahi, sosyal media, ameliyat

Dear Editor,

Since early in the year 2020, the Coronavirus disease-19 (COVID-19) pandemic has evolved and is affecting every aspect of life, including surgical healthcare worldwide. Surgical practice and surgery have been affected mostly due to their dependency on practical education.[1] Social media, which is increasingly being used nowadays, has been supporting surgical education through free educational contents, video platforms, easy to communicate mentorship facilities and international collaborations without borders. Therefore, on the popular social media site twitter, surgical experts formed "SoMe4Surgery" and embedded twitter communities like "SoMe4Proctology". They use hashtags (#) and tweet with hashtags like "#SoMe4Surgery, #SoMe4ColorectalSurgery", etc.[2] One of this popular online educational platforms was created by young academic surgeons and handled by residents from El Bosque University, Bogota, Colombia. These young surgeons have as primary aim to support the free share of surgical learning by tagging well-known surgical experts to the daily surgical cases and educational materials that are sent by tweeting the related literature, studies and surgical illustrations. Great incorporation has been seen by responses to daily surgical cases when many surgeons have been reported their own comments, and a tremendous educational era has been seen inter-continentally.[3]

Since 2016, colorectal surgeons have been among the leaders in social media use, especially twitter, due to the creation of the hashtag "colorectal surgery", and a growing impact was created by 100,000 tweet impressions. Colorectal surgeons who had been attending and live tweeting colorectal surgery specific meetings had been sharing scientific contents with colorectal surgery hashtag; therefore, this has enabled many surgeons globally to learn the most up-to-date data from experts.[4]

One of the benefits of social media use by surgeons is to facilitate research collaborations, in which high-quality peer-reviewed research protocols are developed through easy and fast communication among young medical students, residents and surgeons with minimal costs. One of these groups have developed the Global Surg network, which later has been published as one of the most essential COVID-19 surgical study to date; from "COVIDSurg" initiative on this background.[5]

Another positive effect of the articles shared on social media was analysed by Korean surgeons and their study was found that article exposure on Twitter leads to a high citation impact.[6]

However, there are also growing concerns about social media use and sharing of information among surgeons, which can be summarised into four main categories as misrepresentation of non-peer-reviewed data, sharing of copyright-protected content, the spread of biased information and damage to professional image.[4] Therefore, creators of surgical education platforms try to form restricted groups that only enable to

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access surgeons, residents and medical students. Another ethical debate about sharing patient's data by imaging and videos even without any special identification of that person is still ongoing.

Additionally, surgeons should be aware that not every surgical content is feasible or optimal to be accepted as a learning material.[7] Therefore some surgical communities create guidelines for members who want to use social media for training purposes. According to these principles, it is strongly recommended that trainers and trainees of social media should comply with the local laws protecting patient privacy. It is also recommended that surgical associations educate and inform especially trainers in social media to weigh the costs and odds of it. Therefore, the society of gastrointestinal and endoscopic surgeons made taskforce recommendations for closed-content Facebook groups, stating that obtaining the patients' informed consent is still one of the physicians' responsibilities on social media.[8]

In conclusion, professional and ethical use of social media can help the surgical community in all aspects like surgical education, collaboration and dissemination lasted up-to-date scientific evidence-based materials. Considering all of its benefits, surgeons should also be aware of the potential risks and should act and behave according to local and universal regulations as mentioned above.

Peer-review: Internally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: A.C.Y., Concept: A.C.Y., Design: A.C.Y., Data Collection or Processing: M.F.E, Analysis or Interpretation: M.F.E., Literature Search: M.F.E., Writing: A.C.Y., M.F.E

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

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VİDEO ARTİCLE

Seton Application in Complex Perianal Fistula: Video Presentation

Kompleks Perianal Fistülde Seton Uygulaması: Video Sunum

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ABSTRACT

Anal fistulas are non-physiological tract-like structures that open into the perianal skin starting from the distal rectum or anal canal and arise from abscesses on the basis of infection in the rudimentary glands around the dentate line. Recurrence rates vary between 10%-50% and this disease affects 2% of the society. Anal fistulas are classified as ischioanal, subanodermal, intersphincteric, transsphincteric, suprasphincteric, and extrasphincteric, and spontaneous remission is not possible in this disease. Physical examination, contrast enhanced pelvic magnetic resonance imaging and endoanal ultrasonography are used in the diagnosis of this disease, which presents with symptoms such as fever, fatigue, soiling and pain. In this clinical picture, which may also be associated with Crohn's disease, the ultimate treatment is surgery, and in this video presentation, we aimed to demonstrate a seton revision and tract curettage treatment in a patient who had previously undergone seton placement procedure for an extrasphincteric fistula.
Keywords: Complex perianal fistula, curettage, seton

ÖZ

Anal fistüller distal rektum veya anal kanaldan başlayan perianal deride açılan fizyolojik olmayan trakt benzeri yapılardır ve dentate çizgideki rudimenter glandların enfeksiyonu zemininde gelişen apselerden kaynaklanırlar. Rekürrens oranları %10-%50 arasında değişmekte olup toplumun %2'sini etkilemektedir. Anal fistüller iskioanal, subanodermal, intersfinkterik, transsfinkterik, suprasfinkterik ve ekstrasfinkterik olarak sınıflandırılmakta olup spontan remisyon bu hastalıkta söz konusu değildir. Ateş, genel durum bozukluğu, perianal akıntı gibi semptomlarla prezente olan bu hastalıkta tanıda fizik muayene, pelvik kontrastlı manyetik rezonans ve endoanal ultrasonografi kullanılmaktadır. Özellikle Crohn hastalığı ile de ilişkili olabilen bu klinik tabloda nihai tedavi cerrahi olup bu video prezentasyonda ekstrasfinkterik fistül nedeni ile daha önceden seton tedavisi uygulanmış bir hastada seton revizyonu ve trakt küretajı tedavisinin gösterilmesi amaçlanmıştır.
Anahtar Kelimeler: Karmaşık perianal fistül, küretaj, seton

Introduction

It has been shown in various sources that perianal fistula disease affects one out of every fifty people in the community. This disease usually has a chronic course despite treatment and causes recurrent hospital admissions due to recurrence. Because of the serious complications such as perianal abscess and sepsis, the negativities in the quality of life of the patient and the cost of treatment, clinicians have tried to optimize the treatment for various fistula types.[1] Another type of fistula that is often associated with difficulties in treatment is extra-sphincteric fistula that usually requires more than one surgery. The long healing process is one of the most important morbidities in this disease, and various surgical interventions have been tried in order to accelerate the recovery and keep the patient's quality of life at the highest level.[2] In this video presentation, it was aimed to demonstrate seton revision and fistula tract curettage in a patient who had previously undergone loose seton therapy due to extrasphincteric fistula.

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Written informed consent was obtained from the patient. Preoperative preparation was not made for the patient, except for a preoperative 6-hour fasting. Prophylactic antibiotic or enema was not administered. The patient was operated under general anesthesia in the gynecological dorsolithotomy position. The outer mouth of the extrasphincteric fistula at the 5 o'clock position was visualized. The inner mouth was found with the help of a stylet. The old seton was removed. The skin structure with pathological appearance in the outer mouth was excised up to the external anal sphincter and sent to pathology. The tract was curetted with gas soaked with oxygenated water and the operation was terminated by placing loose seton.

In conclusion, we think that loose seton application, especially internal curettage of the tract is a simple, comfortable surgical method that has a positive effect on healing, especially in sphincter-related or extrasphincteric fistula disease which has a chronic course and requires repeated surgical interventions.

* This video presentation was recorded at the proctology course held at University of Health Sciences Turkey, Ümraniye Training and Research Hospital on 17.10.2020.

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Authorship Contributions

Surgical and Medical Practices: A.T., M.T.D, Concept: M.K.Y., Design: H.S.O., Data Collection or Processing: A.T., M.K.Y., Analysis or Interpretation: M.K.Y, A.T., H.S.U., Literature Search: M.T.D., M.K.Y. A.T., Writing: M.K.Y., A.T.

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

Financial Disclosure: The authors declared that this study received no financial support.

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Video 1.

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VİDEO ARTİCLE

Perianal Methylene Blue Injection in Patient With Pruritus Ani Unresponsive To Medical Treatment: Video Presentation

Medikal Tedaviye Yanıtsız Pruritus Ani'li Hastada Perianal Metilen Mavisi Enjeksiyonu: Video Prezentasyon

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ABSTRACT

Pruritus Ani is one of the common dermatological diseases of the perianal skin in the general population. This disease affects 1%-5% of the society. It presents as itching and burning in the perianal area. Men are affected four times more than women, and it is diagnosed most commonly in the fourth to sixth decades of life. This disease, which is most commonly seen as idiopathic, may develop secondary to infectious factors such as staph. aureus, candida albicans, thinning of the perianal skin due to the long-time use of topical steroids, dermatological diseases such as psoriasis or malignancies. The treatment of the underlying disease constitutes the main treatment for the secondary disease, and in the idiopathic disease, a wide range of treatment methods are used, from conservative treatments to various medical treatments and injection of various substances into the perianal area. In this video presentation, it is aimed to present the application of methylene blue injection to the perianal skin in a patient with idiopathic pruritus ani unresponsive to medical treatment.
Keywords: Methylene blue injection, perianal itching, pruritus ani

ÖZ

Pruritus ani toplumda sık karşılaşılan perianal bölgenin dermatolojik hastalıklarındandır. Bu hastalık toplumun %1-%5'ini etkilemektedir. Perianal bölgede kaşıntı ve yanma olarak prezente olur. Erkeklerde kadınlara oranla dört kat fazla görülür ve en sık görülme yaşı dördüncü ve altıncı dekatlar arasındadır. En sık idiopatik olarak görülen bu hastalık staf. aureus, candida albicans gibi enfeksiyöz etkenlere, uzun süre steroidli topikal ajanların kullanımına bağlı perianal bölge cildinin incelmesine, psoriasis gibi dermatolojik hastalıklara veya malignitelere sekonder olarak gelişebilmektedir. Sekonder hastalıkta altta yatan hastalığın tedavisi esas tedaviyi teşkil etmekte olup idiopatik hastalıkta ise konservatif tedavilerden çeşitli medikal tedavilere ve çeşitli maddelerin perianal bölgeye enjeksiyonuna kadar geniş bir yelpazede bir çok tedavi yöntemi uygulanmaktadır. Bu video prezentasyonda medikal tedaviye yantısız idiopatik pruritus anili bir hastada perianal bölgeye metilen mavisi enjeksiyonu uygulamasının sunulması amaçlanmıştır.
Anahtar Kelimeler: Metilen mavisi enjeksiyonu, perianal kaşıntı, pruritus ani

Introduction

Pruritus ani is one of the most common diseases among benign anorectal disease group encountered in the society. The men/women incidence of this disease which affects one out of every twenty people in the society is 4.[1] Various factors such as personal hygiene, obesity, wearing tight clothing and psychogenic causes play a role in the etiology of idiopathic pruritus ani. Skin biopsy should be done first for diagnosis.

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After the secondary causes are ruled out, the initial treatment should be administered to the patient for 2-4 weeks. In this treatment, first of all, topical irritants (stool contamination, soap, perfume, etc.) should be eliminated and excessive anal hygiene habits should be avoided. The consumption of food products such as coffee, soda and alcohol should be reduced. Afterwards, topical steroids and oral antipruritic agents should be used in decreasing doses for 4-8 weeks. A method that has been used with increasing frequency recently is methylene blue injection into the perianal skin. In this method, 8 ml of 2% methylene blue is mixed with 0.5% lidocaine in the same volume and injected into the perianal dermis with a 22 gauge needle and it has been shown that the possibility of complications such as skin necrosis is low, when the method is applied correctly.[2] In this video presentation, a patient with pruritus ani, who was unresponsive to medical treatment, was administered methylene blue injection treatment with the described technique.

No preoperative preparation was made for the patient. Prophylactic antibiotherapy or enema was not applied in the preoperative period. The patient underwent surgery in the prone jack-knife position. Eight cc of 2% methylene blue was mixed with 8 cc 0.5% lidocaine and injected intradermally to the entire perianal area using a 22 gauge needle and the procedure was terminated.

In conclusion, we think that in patients with pruritus ani refractory to conservative treatment, injection of methylene blue into the perianal region is a cheap, easy-to-apply and satisfying method for patients.

* This video presentation was recorded at the proctology course held at University of Health Sciences Turkey, Ümraniye Training and Research Hospital on 17.10.2020.

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Authorship Contributions

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Video 2.

https://www.doi.org/10.4274/tjcd.galenos.2020.2020-11-2.video2

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VİDEO ARTİCLE

Robotic Low Anterior Resection and TAH+BSO with Transvaginal NOSE

Robotik Low Anterior Rezeksiyon'la Birlikte TAH+BSO ve Vaginal Yoldan NOSE

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ABSTRACT

In the last century, laparoscopic interventions have been developed to minimize the somatic and phsiological effects of surgery. Laparoscopic approaches have become frequently used in colorectal surgery as well. In recent years, robotic surgery has become a recommended practice in rectum surgeries, especially due to better visualisation of the pelvis. In addition to providing a comfortable view in the pelvis, robotic surgery also provides the surgeon with the ability to perform the surgery under three-dimensional view and superior maneuverability in the narrow pelvis. Additionally removing of the specimen via natural ways, that is, transanal, transvaginal, or transgastric, without creating an incision in the abdomen during laparoscopic procedures has gained attention. This approach is called natural orifice specimen extraction (NOSE) and it has been used with increasing frequency in recent years as a preferred method in experienced centers. However, data on NOSE application in robotic rectum surgery is limited, and in this video presentation, we aimed to present a patient who underwent robotic low anterior resection and total hysterectomy for rectum cancer, in which the entire specimen was removed transvaginally (NOSE).
Keywords: NOSE, rectum cancer, robotic LAR

ÖZ

Cerrahinin somatik ve fizyolojik etkilerini minimalize etmek için son yüzyılda laparoskopik girişimler çok fazla ön plana çıkmıştır. Kolorektal cerrahidede laparoskopik yaklaşımlar sıklıkla tercih edilir hale gelmiştir. Son yıllarda ise robotik cerrahide özellikle pelviste daha iyi görüş sağlaması nedeniyle rektum ameliyatlarında önerilen bir uygulama haline gelmiştir. Robotik cerrahinin pelviste konforlu bir görüş sağlaması dışında, cerrah açısındanda üç boyutlu görüntü altında ameliyatı gerçekleştirmesi ve robotun dar pelviste manevra kabiliyetide diğer avantajlarıdır. Bunun dışında laparoskopik cerrahi uygulamalarında spesimenin çıkarılması için abdomende kesi oluşturmak yerine doğal yollar yani spesimenin transanal, transvajinal veya transgastrik olarak çıkarılması gündeme gelmiştir. Bu uygulama natural orifice specimen extraction (NOSE) olarak adlandırılmakla birlikte deneyimli merkezlerede tercih edilen bir yöntem olarak son yıllarda artan sıklıkla kullanılmaktadır. Ancak Robotik rektum cerrahisi ile beraber NOSE uygulaması ile ilgili veriler kısıtlı olup, bu video sunumda rektum kanseri için robotik low anterior rezeksiyon birlikte total histerektomi uygulanan hastada tüm speswimenin trans vajinal olarak çıkarıldığı (NOSE) olgunun video görüntüsü eşliğinde sunulması amaçlanmıştır.
Anahtar Kelimeler: NOSE, rektum kanseri, robotik LAR

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Introduction

There have been serious developments in the treatment of rectal cancer in the last century. In this process, both neoadjuvant use of radiotherapy and chemotherapeutics played an important role in addition to the definition of total mesorectal excision. In the last 20 years, although minimally invasive surgery has become widespread in the surgical treatment of benign and malignant diseases of the colon and rectum, controversies continue about the use of laparoscopic surgery in rectum cancer. There are studies showing that robotic surgery is superior to conventional laparoscopy in the surgery of rectum cancer with the developing technology. Robotic surgery has some advantages: The robotic arms can manipulate the pelvis more easily, the operation can be performed with three-dimensional images, the surgeon sits and does not reflect possible tremors to the surgery. It has some disadvantages: It can not be performed in every center and it has a high cost. Another development is the methods defined for the removal of the resected specimen. At this point, the specimen is removed via transanal or transvaginal route, that is, without making a new incision in the abdomen. It is reported that this method, called NOSE, provides benefits to the patient in terms of postoperative pain and wound healing.[1,2]

In the colonoscopy of a 60-year-old female patient, a polyp with a size of 1.5 cm was detected in the middle rectum, and polypectomy was performed. After histopathological examination showed the presence of adenocarcinoma, an magnetic resonance imaging was performed and no additional pathology was detected in the uterus, except for a myoma uteri with a size of 6.5 cm. The patient was discussed in the multidisciplinary council and the surgical decision was made. After obtaining the consent form, she was taken to surgery. The ports were placed in accordance with the Da Vinci Xi robotic system in a standard way and the hysterectomy procedure following docking was completed robotically by the obstetrics team and the specimen was taken out of the vagina. The low anterior resection procedure was completed robotically by placing a tampon in the vagina. The tampon was removed from the vagina and the rectum specimen was taken out of the abdomen from the vagina. Following the control of the anastomosis with indocyanine green, an ileostomy was opened in the right lower quadrant and the surgery was terminated. Histopathological examination of the specimen was reported as T1N1.

As a result, although it has a disadvantage in terms of cost, the robotic method and the NOSE method in appropriate patients are the preferred method for the patient and the surgeon.

Informed Consent: After obtaining the consent form, she was taken to surgery.

Peer-review: Externally and internally peer reviewed.

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Video 3.

https://www.doi.org/10.4274/tjcd.galenos.2020.2020-10-9.video3