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Turkish Journal of
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TURKISH JOURNAL OF COLORECTAL DISEASE
Address: Latilokum Sk. Alphan İşhanı No: 3 Kat: 2 Mecidiyeköy Şişli, İstanbul, Turkey
Phone: +90 212 356 01 75-76-77 Gsm: +90 532 300 72 36 Fax: +90 212 356 01 78
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Publisher Contact

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Aims and Scope

Turkish Journal of Colorectal Disease is an international, open access, scientific, peer-reviewed journal in accordance with independent, unbiased, and double-blinded peer-review principles of Turkish Society of Colon and Rectal Surgery. The journal is published quarterly in in March, June, September and December in print and electronically. The publication language of the journal is English.

This journal aims to contribute to science by publishing high quality, peer-reviewed publications of scientific and clinical importance address current issues at both national and international levels. Furthermore, review articles, case reports, technical notes, letters to the editor, editorial comments, educational contributions and congress/meeting announcements are released.

The journal scopes epidemiologic, pathologic, diagnostic and therapeutic studies relevant to the management of small intestine, colon, rectum, anus and pelvic floor diseases.

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.

Turkish Journal of Colorectal Disease is currently indexed in **TÜBİTAK/ULAKBİM, British Library, ProQuest, CINAHL, IdealOnline, EBSCO, Embase, Gale/Cengage Learning, Index Copernicus, Turkish Citation Index, Hinari, GOALI, ARDI, OARE, AGORA J-GATE** and **TürkMedline**.

The editorial and publication processes of the journal are shaped in accordance with the guidelines of the International Committee of Medical Journal Editors (ICMJE), World Association of Medical Editors (WAME), Council of Science Editors (CSE), Committee on Publication Ethics (COPE), European Association of Science Editors (EASE), and National Information Standards Organization (NISO). The journal is in conformity with the Principles of Transparency and Best Practice in Scholarly Publishing.

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Address: Latilokum Sok. Alphan İşhanı No: 3 Kat: 2, Şişli, İstanbul, Türkiye

Telephone: +90 (212) 356 01 75-76-77

Gsm: +90 (532) 300 72 36

Fax: +90 (212) 356 01 78

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• ICMJE Potential Conflict of Interest Disclosure Form which has to be filled in by each author.

Turkish Journal of Colorectal Disease is an international, open access, scientific, peer-reviewed journal in accordance with independent, unbiased, and double-blinded peer-review principles of Turkish Society of Colon and Rectal Surgery. The journal is published quarterly in in March, June, September and December in print and electronically. The publication language of the journal is English.

This journal aims to contribute to science by publishing high quality, peer-reviewed publications of scientific and clinical importance address current issues at both national and international levels. Furthermore, review articles, case reports, technical notes, letters to the editor, editorial comments, educational contributions and congress/meeting announcements are released.

The journal scopes epidemiologic, pathologic, diagnostic and therapeutic studies relevant to the management of small intestine, colon, rectum, anus and pelvic floor diseases.

Reviewed and accepted manuscripts are translated from Turkish to English by the Journal through a professional translation service. Before printing, the translations are submitted to the authors for approval or correction requests, to be returned within 7 days. The editorial board checks and approves the translation if any response is received from the corresponding author within this period.

Accepted manuscripts are published in English.

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.

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As a peer-reviewed journal that is independent, impartial and in compliance with the principles of double-blinded peer review, after checking the compliance of the submitted manuscript with the writing rules and plagiarism control, all articles are reviewed by the editor-in-chief, section editor, at least two reviewers, and statistic editor. All evaluation process except Editor-in-Chief is done double-blinded. After all these processes are completed, the Editor-in-Chief decides whether to publish or reject the article. In the final stage, the plagiarism review is repeated once more

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 "Turkish Journal of Colorectal Disease". Articles previously published in any language will not be considered for publication in the journal. Authors cannot submit the manuscript for publication in another journal. All changes in the manuscript will be made after obtaining written permission of the author and the publisher. Full text of all articles can be downloaded at the web site of the journal www.turkishjcrd.com/archives.

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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 the address, telephone, fax and e-mail address of the corresponding author.

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All manuscripts should be submitted via the online submission system. Authors are encouraged to submit their manuscripts via the internet after logging on to the website www.manuscriptmanager.net/tjcd.

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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);

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.);

STARD checklist for reporting 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.);

STROBE statement, a checklist of items that should be included in reports of observational studies;

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 standard, 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 e-mail 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;

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

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 by any authors, should be clearly cited and referenced.

All clinical trials must be registered in a public trials registry 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 keywords or short phrases. Do not use abbreviations as keywords.

Introduction: State the purpose and rationale for the study concisely 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

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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 essential 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.

Acknowledgements: 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 acknowledgement 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 the 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.

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 of 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 a description of a new surgical technique and its application in 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.

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Tables and figures: Including legends.

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, MPEG-PS, 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 info@galenos.com.tr. All videos must include 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 comments on articles published in the 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.

The Editor exclusively solicits editorials. 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 endeavour. Maintaining integrity of the research and its presentation can be achieved by following the rules of good scientific practise, 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.

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Important note: Turkish Journal of Colorectal Disease uses software (iThenticate) to screen for plagiarism.

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 in authorship or in the order of authors are not accepted after acceptance of a manuscript.

Requesting to add or delete authors at the 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 the 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.

Upon request, authors should be prepared to send relevant documentation or data in order to verify the validity of the results. It could be in the form of raw data, samples, records, etc.

If there is a suspicion of misconduct, the journal will carry out an investigation following the COPE guidelines. If, after investigation, the allegation seems to raise valid concerns, the accused author will be contacted and given an opportunity to address the issue. If misconduct has been established beyond a reasonable doubt, this may result in the Editor-in-Chief's implementation of the following measures, including, but not limited to:

If the article is still under consideration, it may be rejected and returned to the author.

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Peer review of study protocols :

TJCD will consider publishing without peer review protocols with formal ethical approval and funding from a recognized, open Access, supporting research-funding boy (such as those listed by the JULIET Project). Please provide proof that these criteria are met when uploading your protocol. Any protocols that do not meet both these criteria will be sent for open external peer review, with reviewer comments published online upon acceptance, as with research articles. Reviewers will be instructed to review for clarity and sufficient detail. The intention of peer review is not to alter the study design. Reviewers will be required to check that the study is scientifically credible and ethically sound in its scope and methods. There is sufficient detail to instil confidence that the study will be managed and analyzed correctly.

Publishing study protocols enables researchers and funding bodies to stay up to date in their fields by providing exposure to research activity that may not otherwise be widely publicized. This can help prevent unnecessary duplication of work and will hopefully enable collaboration. Publishing protocols in full also makes available more information than is currently by trial registries and increases transparency, making it easier for others (editors, reviewers and readers) to

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see and understand any variations from the protocol that occur during the conduct of the study)

The SPIRIT (Standart Protocol Items for Randomized Trials) statement has now been published. It is an evidence-based tool developed through a systematic review of a wide range of resources and consensus. It closely mirrors the CONSORT statement and also reflects essential ethical considerations.

PRISMA is an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses. PRISMA focuses on reporting reviews evaluating randomized trials but can also be used as a basis for writing systematic reviews of other types of research, particularly evaluations of interventions.

General TJCD policies apply to manuscript formatting, editorial guidelines, licence forms and patient consent.

- Protocol papers should report planned or ongoing studies: Manuscripts that report work already carried out will not be deemed protocols. The dates of the study must be included in the manuscript and cover letter.

Protocol for studies that will require ethical approval, such as trials, is unlikely to be considered without receiving that approval.

- Title: This should include the specific study type, randomized controlled trial

- Abstract: This should be structured with the following sections—introduction; Methods and analysis; Ethics, and dissemination. Registration details should be included as a final section, if appropriate.

- Introduction: describe the rationale for the research and what evidence gay it may fill.

- Methods and analysis:

- Ethics and dissemination: Ethical and safety considerations and any dissemination plan should be covered here

- Full references

- Authors contributions

- Funding Statement

- Competing Interests Statement

- Word Count: Not to exceed 4000 words.

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Statement of human rights: When reporting studies that involve human participants, authors should include a statement that the studies have been approved by the appropriate institutional and/or national research ethics committee and have been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Suppose doubt exists whether the research was conducted in accordance with the 1964 Helsinki Declaration or comparable standards. In that case, the authors must explain the reasons for their approach and demonstrate that the independent ethics committee or institutional review board explicitly approved the doubtful aspects of the study.

The following statements should be included in the text before the References section: Ethical approval: "All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards."

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Statement on the welfare of animals: The welfare of animals used for research must be respected. In experimental animal studies, the authors should indicate that the procedures followed were in accordance with animal rights as per the Guide for the Care and Use of Laboratory Animals, and they should obtain animal ethics committee approval. When reporting experiments on animals, authors should indicate whether the international, national, and/or institutional guidelines for the care and use of animals have been followed, and that the studies have been approved by a research ethics committee at the institution or practise at which the studies were conducted (where such a committee exists).

For studies with animals, the following statement should be included in the text before the References section:

Ethical approval: "All applicable international, national, and/or institutional guidelines for the care and use of animals were followed."

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ed, 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. After their re-submission, manuscripts with extensive revision recommendations will be sent for further review (usually by the same reviewers). 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.

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Turkish Society of Colon and Rectal Surgery

Address: Latilokum Sok. Alphan İşhanı No:3 Kat:2 Mecidiyeköy-Şişli-İstanbul/Turkey

Phone: +90 (212) 356 01 75-76-77

Gsm: +90 (532) 300 72 36

Fax: +90 (212) 356 01 78

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Editor-in-Chief
Fatma Ayca Gultekin, M.D. Zonguldak-Turkey

New Editors on the Journal….

Turkish Journal of Colorectal Disease (TJCD) entered the year 2022 with its new editor-in-chief and editorial group. It was really my great pleasure to be appointed as the successor of our founding editors Prof. Dr. Kemal Alemdaroglu, Prof. Dr. Bulent Mentes, Prof. Dr. Ugur Sungurtekin and Prof. Dr. Tahsin Colak, as the chief editor of the Turkish Journal of Colorectal Disease, the scientific publication of the Turkish Colon and Rectal Surgery Association (TKRCD) and the only and most respected journal in its field in Turkey since its first publication in 1991. I would like to thank TKRCD President Prof. Dr. M. Ayhan Kuzu and the members of the 16th Term Board of Directors for appointing me to this position.

With the efforts of our previous editor-in-chief, Prof. Dr. Tahsin Çolak, and his assistant editors, our journal, which has entered remarkable scientific indexes, and which has a dense flow of articles, has demonstrated a rapid upward trend and has reached the level of accepting articles from all over the world, thanks to its publication language being English. In order to make this intensive article flow process more dynamic, as TJCD, we decided to expand the editorial board in the new period. In this sense, we increased the number of editorial boards from 4-5 in the past to 22 together with the chief editor, assistant editor and section editors (Figure 1). In the new period, the articles sent to TJCD will be gathered under 6 important titles of colorectal surgery, evaluated by specialist department editors and sent to the peers.

As a peer-reviewed Journal, TJCD recognizes its peers and their seemingly unnoticeable contributions. As soon as we took office as the editorial group, we updated our peer list and added new names from colorectal surgery to our peer committee. In this sense, I would like to thank our former peers who have supported us from the past to the present, and I would like to welcome our colleagues who have recently joined the peer board. I strongly recommend our peers to enter their refereeing activities in Publons in order to make their academic activities apparent (https://publons.com/about/reviews/). If you enter Publons as the reviewer for a study submitted to our journal, I receive an e-mail from Publons as the chief editor, and your refereeing becomes visible to other scientific journals upon my approval and evaluation.

Today, great numbers of respected magazines use social media actively in order to reach the large audiences. As TJCD, we also believe in power of social media. To that end, we have created a sub-editor group under our new editorial group that monitors the social media visibility and activities of the magazine, as well as the department editorships. We will be glad if our readers follow TJCD on social media and share their favourite articles. (Twitter: @turkdiscolrect)

As TJCD's new editorial group, our goal is to deliver up-to-date and of high-quality articles to our readers. We have adopted as a principle optimizing the articles submitted by our authors to TJCD with the constructive criticism of our peers and editors, because we believe that scientific publishing is information sharing. With your trust in us and your help, we can carry TJCD to even higher levels. To this end, we want you to share your valuable studies with us, read our magazine and support us by citing the articles published in our magazine!

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INVITED REVIEW

Endoluminal Surgery: Where are We Headed?

İlker Özgür, Emre Görgün

Department of Colorectal Surgery, Digestive Disease and Surgery Institute, Cleveland Clinic, Cleveland, Ohio, US

ABSTRACT

The expansion of colorectal cancer screening programs predicts a remarkable increase in non-malignant polyps and early-stage colorectal neoplasia. While the majority of these polyps are managed endoscopically, a large number of patients are referred to surgery. Over thirty thousand patients with large colon polyps undergo surgical procedures, such as colectomy or proctectomy, in a given year in the United States of America. Such surgeries lead to organ loss due to benign disease and have significant morbidity and mortality rates. Conversely, endoluminal surgery (ELS) may provide organ preservation with low morbidity and mortality for the majority of these patients. In this review, we aimed to discuss ELS and future directions in this field.

Keywords: Endoluminal surgery, advanced endoscopy, endoscopic submucosal dissection, endorobotic submucosal dissection

Introduction

Colorectal cancer (CRC) is one of the leading causes of cancer death in the United States.[1] Colonoscopy and polypectomy starting at the age of 45 years old is well established in the United States as a screening program and has decreased CRC-related mortality.[2] While most polyps detected during routine colonoscopy are less than 10 mm in size and are treated with simple techniques, such as cold forceps or snaring, advanced endoscopic treatment options can be offered for larger polyps with advanced morphological features that are not amenable to conventional endoscopic removal.[3]

Surgery for non-malignant polyps and CRC has been increasing in the last decade, and 25% of all colorectal resections are performed for non-malignant polyps with a significant annual increase from 5.9 in 2000 to 9.4 in 2014 per 100,000 adults.[4] The performed colectomies have 0.8% in-hospital mortality and 25% morbidity within 30 days of surgery.[5] Surgeons considering surgery for non-malignant polyps should be aware of this potential for morbidity and mortality. Furthermore, in 92% of these resections the final pathology after organ resections does not identify invasive cancer.[6]

Advanced endoscopy techniques had been developed and are well described to treat large colorectal lesions and achieve organ preservation. These were first described in Japan and have gradually become more prevalent all over the world. The procedures were first described for upper gastrointestinal system (GI) lesions and then adapted to the lower GI tract. The significant difference in the anatomy of the lower GI compared to the upper GI and the technically demanding procedures with a long learning curve limited the widespread use of advanced endoscopy in the colon and rectum. Advanced endoscopy has recently increased interest due to its technical advantages and proposed organ preservation despite these limitations.

Advanced endoscopy techniques and the development of endoluminal surgery (ELS) is a rapidly progressing field in the treatment of lower GI lesions. ELS offers organ preservation with less invasive methods compared to surgery and can even be performed in outpatient settings.

Indications for Endoluminal Surgery

Current guidelines recommend resection of all mucosal lesions, reserving advanced endoscopy techniques for larger lesions.[3,7] Endoscopic Mucosal Resection (EMR) is defined as a technique involving submucosal injection and snaring of the lesion. In contrast, Endoscopic Submucosal Dissection (ESD) is defined as submucosal injection followed by mucosal incision and submucosal dissection with a needle-type knife

Address for Correspondence: Emre Görgün, MD, FACS, FASCRS,
Department of Colorectal Surgery, Digestive Disease and Surgery Institute, Cleveland Clinic, Cleveland, Ohio, US
E-mail: gorgune@ccf.org **ORCID ID:** orcid.org/0000-0001-7725-3522
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and complete removal of the lesion in one piece. Precutting EMR is the term used for a technique where snaring is performed without dissecting the submucosal layer after incising the lesion's circumference. If the submucosal layer is dissected and additional snaring is performed to complete the resection of the lesion, the procedure can be defined as hybrid ESD.

The primary aim of polypectomy is the complete removal of the colorectal lesion. Based on current scientific evidence, endoscopists should employ the most favorable, complete, safest, and efficient technique with the most negligible recurrence probability. EMR is a more common technique performed for smaller lesions, whereas ESD is reserved for larger lesions. Compared to EMR, ESD was found to have higher en-bloc resection and lower recurrence rates with comparable complication rates.[8,9] In addition, an en-bloc resection yields increased accuracy on histopathologic evaluation and decreased risk for further surgical interventions.[10]

Preprocedural Management

Endoscopists should evaluate colored images of the previous colonoscopy reports and pathology reports. Such evaluation provides an opportunity to predict planned intervention and additional equipment needed during the procedure. Patients' medical histories and medication use should be questioned in detail. Information about anticoagulant use and dosage is crucial. The anticoagulants are typically stopped 2-7 days prior to the procedure. The decision whether a procedure will be performed in an endoscopy suite or in the operating room is currently made by reviewing all the available data and taking into account patient specific risk factors (Figure 1). Operating room settings may be preferred for patients who have comorbidities and/or high-risk lesions, as well as for planned combined endolaparoscopic (CELS) procedures. The operating room is also recommended if additional endoluminal enabling platforms are planned to be used.

The endoscopists can use advanced endoscopic imaging techniques, such as narrow-band imaging[11] and focal interrogation, Paris classification[12], and Kudo pit pattern[13] to predict the risk of submucosal invasion. Where available, these methods are helpful to evaluate the surface morphology related to submucosal invasion risk. Perioperative evaluation of patients is critical for successful results.

Submucosal Injection

Injection of lifting solution into the submucosal space is the first important step in advanced endoluminal procedures. Common submucosal lifting agents are saline, hyaluronic acid, glycerol, dilute albumin, and brand-name gels. The submucosal saline injection will suffice and provides a lift that lasts approximately three minutes for simple polypectomies. However, advanced endoluminal procedure typically takes longer. ORISE™ Gel Submucosal Lifting Agent (Boston Scientific) and Eleview® are Food and Drug Administration-approved and readily available lifting agents on the market.[9] The pre-prepared form with no need for mixing before the injection facilitates the procedure time by shortening the duration of the preparation step. In addition, longer-lasting solutions in the submucosal space should be preferred to reduce the time loss due to repetitive injections. Thus, saline is not a preferred injectate as its stay in tissue is limited, and it disperses quickly.[14] In addition to these solutions, diluted adrenalin (1 mL of 0.1% adrenalin) and hydroxyethyl starch solution mixed with methylene blue or other dyes can be used.[15]

The injection step aims to achieve an adequate lift of the lesion. The injection needle should be advanced tangentially along the mucosa (Figure 1). If tissue elevation is not observed after starting the injection, this could be due to entry into an incorrect plane, typically into the abdominal cavity. The injection needle should be adjusted slightly

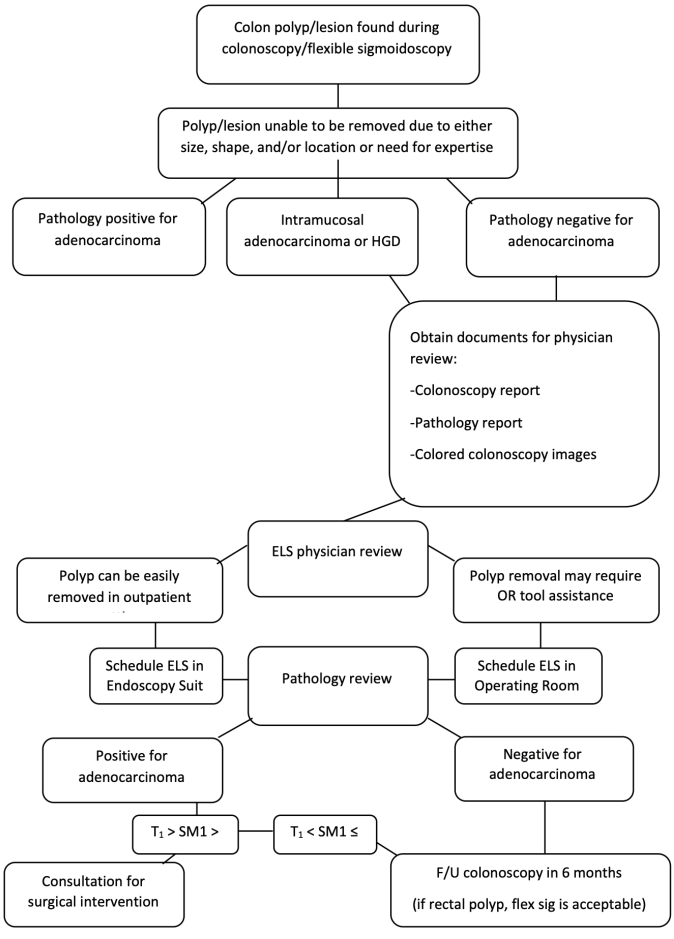

Figure 1. Current ELS Care Path in the management of complex colorectal lesions designed by the Endoluminal Surgery Center, Cleveland Clinic, Ohio, United States of America
ELS: Endoluminal surgery

and realigned before continuing the injection. For lesions located on a fold, it is advantageous to start the injection along the far aspect (oral/proximal side) of the lesion to lift the lesion towards the operative field of view. The lesion may fall away from the view if the injection is started from the distal (anal) side. Despite ensuring the correct plane is injected, there may be no obvious or adequate lift (non-lifting sign). This sign could be due either to deep invasion or fibrosis arising from previous interventions to the lesion. Endoscopists should stop the procedure in case of suspicion of deep invasion.

Endoscopic Mucosal Resection

EMR consists of snaring the lesion after the injection step. The goal should be en-bloc lesion removal, but repeating the snaring as few times as possible is favored when not practical. Increasing the number of pieces snared will decrease the adequacy of the histopathological examination. There are many different shapes and sizes of snares available. The endoscopists should choose the appropriate snare shape and size for the lesion. At least 2-3 mm normal mucosal margin should be targeted while snaring. Although not encouraged, if the resection will be piecemeal, the snare should be aligned at the resected margin edge and be repeated until complete lesion removal.

Endoscopic Submucosal Dissection

ESD applies surgical principles, that is en-bloc resections with clear margins. The dissection is performed with either endoscopic knives or snare tips. There are different knives available, including the FlexKnife Electrosurgical Knife (Olympus, Tokyo, Japan), HookKnife™ (Olympus America Inc., Center Valley, PA, USA), the DualKnife™ (Olympus America Inc., Center Valley, PA, USA), the HybridKnife® (ERBE, Tübingen, Germany) and more recently the ORISE™ ProKnife (Boston Scientific, Marlborough, MA, USA). The combined knives integrate the injection needle and knife functions into one instrument and can decrease the procedure time lost during device placement for each step. The decision about which instrument to use should be based on the availability of the device and the endoscopist's comfort level with it.

Precut EMR and Hybrid ESD

Occasionally, a hybrid method comprising a combination of EMR and ESD can be helpful and time-efficient when pure ESD is not achievable. ESD techniques can be used to define the resection borders, perform the lift, and get the dissection started. Afterward, the remaining central or peripheral resection can be performed with a large snare. The submucosal plane should be visualized clearly during this step, and in case of elevation loss, injections should be repeated as necessary. These steps should be continued until complete resection is achieved. It is essential to clean the field after dissection, visualize the resected area, inspect for any remaining island-like remnants of the lesion, and identify any injury or full-thickness defects. If any submucosal defects are observed, they should be closed with endoscopic hemoclips. Multiple clips can be applied for closure of the defect if necessary.

Novel Endoluminal Platforms

Although ESD offers a way to avoid unnecessary surgery and provides better results compared to piecemeal resections, it is not widely applicable and adapted due to technical challenges including poor stabilization and visualization. Additionally, the required technical skills are very hard to acquire with a steep learning curve. New endoluminal devices are being developed to facilitate the process and increase procedural success rates. They aim to help the endoscopist stabilize the procedure field and incorporate surgical principles, such as traction-counter traction.

ORISE Tissue Retractor System (ORISE TRS; Boston Scientific, Marlborough, MA, USA) consists of a cage-like structure with two instrument channels and can be inserted over a standard colonoscope. This platform stabilizes the intraluminal space, and endoscopic instruments can be introduced to retract the lesion. After starting the dissection, this platform can be introduced with the colonoscope, positioned on the lesion, and the cage-like structure is then opened. Like other platforms, this provides stability of the dissection field, and separate instrument channels allow forceps to be introduced for precise and active real-time retraction.

DiLumen C^{2}™ Endolumenal Interventional Platform is a novel endoscopic stabilization and tissue manipulation device facilitating traction and en-bloc complete removal of complex colorectal lesions. The DiLumen platform consists of a soft, flexible sheath that fits over standard and small-diameter endoscopes. The device employs two balloons, one behind the bending section of the endoscope and the second in front of the tip. When both balloons are deployed and inflated, the area in between is stabilized. In addition, the platform employs two 6 mm working channels at the 3 and 9 o'clock position of the endoscope for graspers and scissors. These instruments can be used for retraction and cutting.

Endorobotic Submucosal Disection

The DaVinci Single Port robotic platform can be used to perform rectal submucosal dissections (Figure 2). This platform is a semi-flexible robot that can reach up to 20-25 cm from the anal verge. We have performed more than ten submucosal dissections in the rectum with the platform.

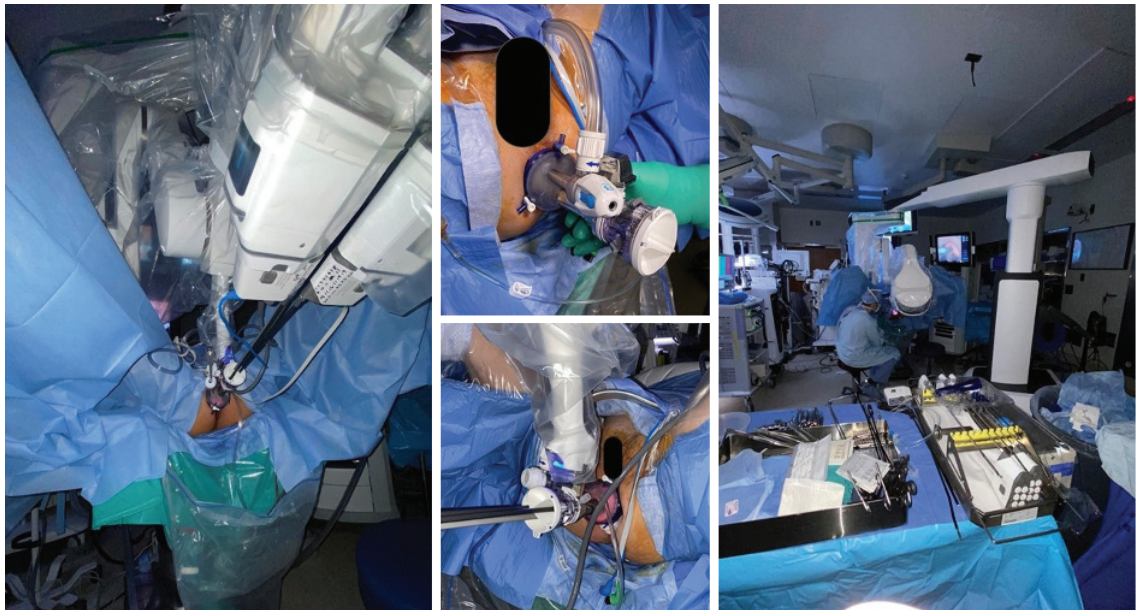

Figure 2. Single port robot (SP DaVinci Robot) and use of Endorobotics

With the development of novel, fully flexible, robot-assisted surgical systems, there may soon be significant progress in the current understanding of ELS. These platforms might enable surgeons to perform incisionless surgeries through the gastrointestinal wall, that previously could only be performed via transabdominal surgery.

However, the identification of specific biomarkers that detect genetic aneuploidy/instability will further help in assessing the invasiveness of the tumor, level of invasiveness, and even detecting metastatic lymph nodes. More accurate preoperative or intraoperative evaluation may enable resection of just the tumor and involved lymph nodes or surveillance.

Surveillance

After ELS every patient should undergo periodic follow-up colonoscopy (sigmoidoscopy is acceptable for rectal lesions). This follow-up colonoscopy aims to detect local recurrence and/or metachronous lesions. There is no consensus on the timing of surveillance after mucosal resection, but it is generally accepted that follow-up colonoscopy should be performed depending on individual pathology results and quality of the specimen with proximity to en-bloc resection technique. In addition, individual risk factors play a role: for more than one lesion or carcinoma and accompanying comorbidities should be considered when proposing the frequency of surveillance. Eastern and Western guidelines propose different periods but, in general, follow-up endoscopy is recommended on the sixth month after the index procedure.[7,16,17] Subsequent colonoscopies after this first follow-up are recommended to occur at the first and third year, in case of no recurrence.

Conclusion

ELS is a promising, minimally invasive approach for organ preservation for the GI tract and a potential major advance for GI surgery. Endoscopists may overcome the challenges of advanced endoscopic tissue resections with the help of new instruments and platforms where traction and counter-tractions can be applied intraluminally. These procedures can be assisted with CELS surgery. Thus surgeons can quickly and naturally adapt these endoluminal techniques. Although ELS is considered challenging, it will continue to progress and potentially gain popularity in the near future. Increased education, research, and availability of the tools to perform these procedures will help more surgeon endoscopists become adept over time. As ELS means there is less need for intra-abdominal surgery, ELS could be the next big step for minimally invasive surgery. Fully flexible endorobotic platforms with stable camera positioning, increased dexterity, and precision will become a reality and this will push the field of ELS forward.

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Surgical and Medical Practices: İ.Ö., E.G., Concept: İ.Ö., E.G., Design: İ.Ö., E.G., Data Collection or Processing: İ.Ö., E.G., Analysis or Interpretation: İ.Ö., E.G., Literature Search: İ.Ö., E.G., Writing: İ.Ö., E.G.

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References

1. White A, Joseph D, Rim SH, Johnson CJ, Coleman MP, Allemani C. Colon cancer survival in the United States by race and stage (2001-2009): Findings from the CONCORD-2 study. Cancer 2017;123(Suppl 24):5014-5036.
2. Zauber AG, Winawer SJ, O'Brien MJ, Lansdorp-Vogelaar I, van Ballegooijen M, Hankey BF, Shi W, Bond JH, Schapiro M, Panish JF, Stewart ET, Waye JD. Colonoscopic Polypectomy and Long-Term Prevention of Colorectal-Cancer Deaths. N Engl J Med 2012;366:687-696.
3. Kaltenbach T, Anderson JC, Burke CA, Dominitz JA, Gupta S, Lieberman D, Robertson DJ, Shaukat A, Syngal S, Rex DK. Endoscopic Removal of Colorectal Lesions-Recommendations by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2020;158:1095-1129.
4. Peery AF, Cools KS, Strassle PD, McGill SK, Crockett SD, Barker A, Koruda M, Grimm IS. Increasing Rates of Surgery for Patients with Nonmalignant Colorectal Polyps in the United States. Gastroenterology 2018;154:1352-1360.
5. Ma C, Teriaky A, Sheh S, Forbes N, Heitman SJ, Jue TL, Munroe CA, Jairath V, Corley DA, Lee JK. Morbidity and Mortality After Surgery for Nonmalignant Colorectal Polyps: A 10-Year Nationwide Analysis. Am J Gastroenterol 2019;114:1802-1810.
6. Gorgun E, Benlice C, Abbas MA, Steele S. Experience in colon sparing surgery in North America: advanced endoscopic approaches for complex colorectal lesions. Surg Endosc 2018;32:3114-3121.
7. Tanaka S, Kashida H, Saito Y, Yahagi N, Yamano H, Saito S, Hisabe T, Yao T, Watanabe M, Yoshida M, Saitoh Y, Tsuruta O, Sugihara KI, Igarashi M, Toyonaga T, Ajioka Y, Kusunoki M, Koike K, Fujimoto K, Tajiri H. Japan Gastroenterological Endoscopy Society guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. Dig Endosc 2020;32:219-239.
8. Klein A, Bourke MJ. Advanced polypectomy and resection techniques. Gastrointest Endosc Clin N Am 2015;25:303-333.
9. Repici A, Hassan C, De Paula Pessoa D, Pagano N, Arezzo A, Zullo A, Lorenzetti R, Marmo R. Efficacy and safety of endoscopic submucosal dissection for colorectal neoplasia: A systematic review. Endoscopy 2012;44:137-150.
10. Saito Y, Uraoka T, Yamaguchi Y, Hotta K, Sakamoto N, Ikematsu H, Fukuzawa M, Kobayashi N, Nasu J, Michida T, Yoshida S, Ikehara H, Otake Y, Nakajima T, Matsuda T, Saito D. A prospective, multicenter study of 1111 colorectal endoscopic submucosal dissections (with video). Gastrointest Endosc 2010;72:1217-1225.
11. Hayashi N, Tanaka S, Hewett DG, Kaltenbach TR, Sano Y, Ponchon T, Saunders BP, Rex DK, Soetikno RM. Endoscopic prediction of deep submucosal invasive carcinoma: Validation of the Narrow-Band Imaging International Colorectal Endoscopic (NICE) classification. Gastrointest Endosc 2013;78:625-632.
12. No authors listed. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002. Gastrointest Endosc 2003;58(6 Suppl):3-43.
13. Kudo S, Tamura S, Nakajima T, Yamano H, Kusaka H, Watanabe H. Diagnosis of colorectal tumorous lesions by magnifying endoscopy. Gastrointest Endosc 1996;44:8-14.
14. Sanchez-Yague A, Kaltenbach T, Raju G, Soetikno R. Advanced endoscopic resection of colorectal lesions. Gastroenterol Clin North Am 2013;42:459-477.
15. Sapci I, Gorgun E. Endoscopic Submucosal Dissection. In: Bardakcioglu O, ed. Advanced Techniques in Minimally Invasive and Robotic Colorectal Surgery. Springer; 2019:9-16.
16. Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T, Repici A, Vieth M, De Ceglie A, Amato A, Berr F, Bhandari P, Bialek A, Conio M, Haringsma J, Langner C, Meisner S, Messmann H, Morino M, Neuhaus H, Piessevaux H, Rugge M, Saunders BP, Robaszkiewicz M, Seewald S, Kashin S, Dumonceau JM, Hassan C, Deprez PH. Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2015;47:829-854.
17. Gupta S, Lieberman D, Anderson JC, Burke CA, Dominitz JA, Kaltenbach T, Robertson DJ, Shaukat A, Syngal S, Rex DK. Recommendations for Follow-Up After Colonoscopy and Polypectomy: A Consensus Update by the US Multi-Society Task Force on Colorectal Cancer. Am J Gastroenterol 2020;115:415-434.

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INVITED REVIEW

Role of Neoadjuvant Chemotherapy in Locally Advanced Colon Cancer

Erdinç Kamer[1], Tahsin Çolak[2]

[1]University of Health Sciences Turkey, İzmir Faculty of Medicine, Department of General Surgery, İzmir, Turkey
[2]Mersin University Faculty of Medicine, Department of General Surgery, Division of Surgical Oncology, Mersin, Turkey

ABSTRACT

Stage II and stage III (T1-4/N1-2/M0) colon cancers are known as locally advanced colon cancer (LACC). About 15% of colon cancers present as LACC without signs of metastasis. Standard treatment of LACC is based on complete oncologic resection followed by adjuvant chemotherapy (AC). In the surgical treatment of LACC, multivisceral resections are applied to obtain R0 resection. Despite such aggressive resections, the rate of obtaining R0 in LACC varies between 40% and 90%, and 5-year survival is between 28% and 73%. Neoadjuvant chemotherapy (NAC) is widely used in the treatment of gastrointestinal system malignancies, such as locally advanced gastric, esophageal and rectal cancers and locally advanced breast cancer. In the literature, there has been an increase in studies on the use of NAC in LACC. These show that NAC appears to be safe and provides similar overall survival compared to adjuvant CT in LACC, that the R0 resection rate is increased in patients who have undergone NAC, that there is no significant increase in postoperative complications or mortality, and that there is also significant downstaging of tumor and lymph node stages in patients who have undergone NAC.

Keywords: Locally advanced, colon cancer, neoadjuvant therapy

Introduction

Stage II and Stage III (T1-4/N1-2/M0) colon cancers are known as locally advanced colon cancer (LACC). Approximately 15% of colon cancers present as LACC without signs of metastasis.[1] Standard treatment for LACC is based on complete oncologic resection followed by adjuvant chemotherapy (AC).[2,3] Current European guidelines suggest surgery of the primary tumor in high-risk stage II or III tumors.[4] This recommendation has been shown to be effective in adenocarcinoma, and similarly improved survival has been demonstrated in both mucinous and signet-ring cell tumors.[1]

In this context, multivisceral resections are applied to obtain complete resection (R0) in the surgical treatment of LACC. Despite such aggressive resections, the rate of obtaining R0 in LACC is variable, ranging from 40% to 90%, and 5-year survival ranges from 28% to 73%. Having a 20-30% risk of local or distant recurrence, this treatment strategy has been shown to fail to prevent the risk of locoregional spread of the tumor.[5,6] A number of factors have been suggested for this failure. These include delayed onset of chemotherapy (later than four months after the initial diagnosis), accelerated duplication of colorectal metastases during this chemotherapy-free period, stimulation of growth factors causing tumor progression with surgery, and the growth and advance of micrometastases at the surgical site because of induced immunosuppression in the postoperative period. Therefore, initiating neoadjuvant chemotherapy (NAC) in these patients provides an improvement in prognosis by eliminating the circulating micrometases through control of the putative failure factors mentioned above, and improving the integrity and quality of tumor surgery with local downstaging. The response of the primary tumor to chemotherapy and the preoperative imaging of these patients should be carefully evaluated, the tumor stage should be performed correctly, and NAC should be well tolerated and should not increase the risk of complications before and after surgery.[6] Computed tomography (CT) is the generally preferred method in the staging of colon cancer. With CT,

Address for Correspondence: Erdinç Kamer, University of Health Sciences Turkey, İzmir Faculty of Medicine, Department of General Surgery, İzmir, Turkey
E-mail: erdinc.kamer@gmail.com **ORCID ID:** orcid.org/0000-0002-5084-5867
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the depth of tumor spread along the colon wall (T-stage) can be measured, and metastatic spread to regional lymph nodes (stage-N) and distant metastases (stage-M) can be detected. The quality of CT used for colon cancer depends on the quality of bowel preparation, oral and rectal administration of contrast agent, amount of air in the colon, and intravenous (i.v.) contrast administration. Combining the venous and arterial phases during CT scanning provides a better evaluation of the T and N-phases.[7] Dighe et al.[8] compared CT and pathological staging in 94 patients and reported a sensitivity of 87% and specificity of 49% for high-risk tumors. The sensitivity to predict any tumor suitable for chemotherapy (T3 or T4) was 95% and specificity was 50%. For node-positive disease, the sensitivity was 68% and the specificity was 42.8%. The management of LACC requires expertise. In CT, T-stage can be reported more accurately than N-stage. Thus, it is difficult to distinguish stage II patients from stage III patients in the preoperative period.

NAC is widely used for the treatment of gastrointestinal system malignancies, such as locally advanced gastric, esophageal and rectal cancers, and locally advanced breast cancer.[1,9] There has been an increase in the number of studies published about the use of NAC in LACC. The first of the potential benefits of NAC is downstaging. That is, it induces tumor regression with a decrease in tumor volume/mass, seen on both imaging and pathological examinations. Since the tissues are intact, preoperative chemotherapy reduces the number and viability of tumor cells that have spread to lymph and blood vessels, thereby reducing the possible rate of micrometastasis.[10] NAC can reduce the risk of distant relapse and increase overall survival. It can help facilitate a laparoscopic procedure and so minimizing the delay in starting AC. In addition, NAC reduces the rate of multivisceral resection and the rate of tumor cell shedding during surgery, and increases the rate of R0 resection.[10,11] The failure of the tumor to respond to NAC can provide valuable information about the biology of the tumor. In patients who respond well to NAC, the effect of postoperative AC may be questionable, with a tendency to reduce AC.[10,12] In their study in 2020, de Gooyer et al.[1] achieved R0 in 77.2% of patients in the NAC group (n=115). In 19 (12.8%) patients, the resection margins were macroscopically disease-free but microscopically positive for tumor invasion (R1).[1] Six (4%) patients had macroscopically visible residual disease (R2) in which complete resection of the tumor was not possible. In the control group, 86.2% (n=225) R0 resection rate, 6% (n=18) R1 resection rate, and 1.7% (n=5) R2 resection rate were achieved. Data on complications were available in 92% (n=137) of patients in the NAC group and 93% (n=275) of patients in the control group, with no significant difference between the two groups in terms of surgical complications, such as anastomotic leak and abscess formation (p=0.854).[1] Concerns about tumor growth and inability to perform surgical treatment during NAC, incorrect selection of high-risk patients with incorrect radiological staging, and the possibility of incorrect radiological staging that may lead to overtreatment of low-risk patients have limited the use of NAC in LACC. However, with more effective chemotherapy regimens and advances in radiological staging, NAC is now seen as a promising National Comprehensive Cancer Network (NCCN)-supported option for patients with LACC.[13]

The NCCN Guideline Colon Cancer, version 2.2021, recommends that neoadjuvant treatment with folinic acid, fluorouracil, and oxaliplatin (FOLFOX) or capecitabine plus oxaliplatin (CAPEOX) can be applied before surgery in bulky nodal disease or clinical T4b colon cancer (Figure 1).[3,14] There are small series describing the feasibility of NAC or chemoradiation. These studies demonstrated safety, high R0 resection rates, and excellent local control rates. The most compelling evidence to date was published by the Fluoropyrimidine Oxaliplatin and Targeted Receptor Preoperative Therapy (FOxTROT) Collaborative group. In this study, the results of a pilot phase randomized clinical trial comparing NAC with AC were published.[12] The FOxTROT trial was the first randomized controlled trial to evaluate preoperative chemotherapy in primary colon cancer. The FOxTROT trial was designed to evaluate whether an effective 6-week combination chemotherapy regimen given preoperatively to patients with radiologically-staged, locally advanced but potentially resectable colon cancer improved disease-free survival. In this study, patients with locally advanced T4 or colon adenocarcinoma with an extramural depth ≥5 mm were included in the study. In the pilot phase, it provided clear evidence of downstaging with only six weeks of preoperative treatment.[12] In the FOxTROT trial which was performed in 1,052 patients and published in 2019, 59% of patients treated with NAC had histological regression and 4% had pathological complete response. It was reported that NAC was well tolerated, there was no increase in perioperative morbidity and there was a decrease in serious complications. It was also shown that there was a half reduction in histological downstaging and incomplete resection rates. FOxTROT concluded that NAC for colon cancer improved surgical outcomes and that NAC could now be considered as a treatment option, but longer follow-up and further studies were needed to confirm the long-term benefits of NAC, examine its use, and optimize patient selection.[14]

In the 2018 study of Dehal et al.[5], a total of 27,575 patients with non-metastatic and clinically T3 and T4 primary colon cancer were included, with 97% treated with surgery

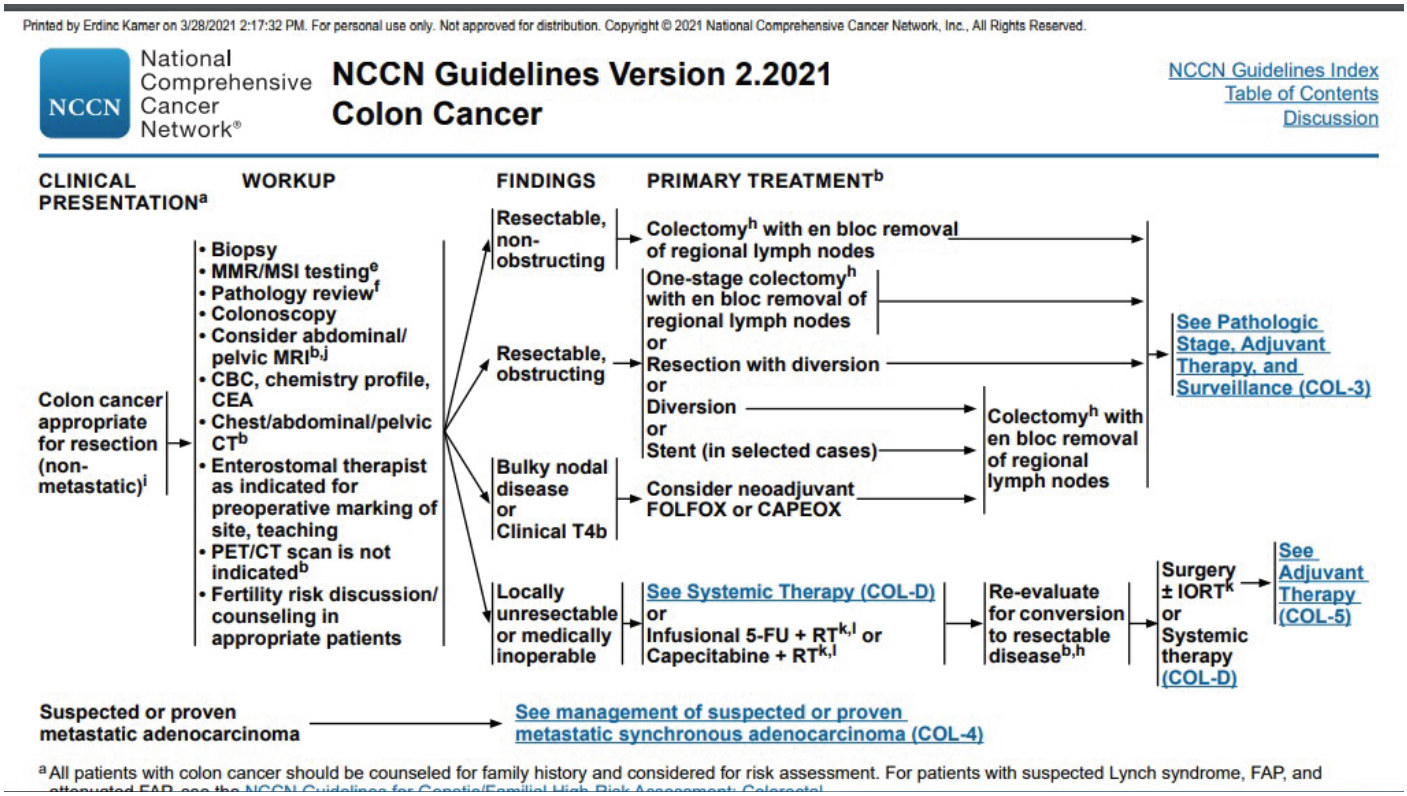

Figure 1. NCCN Guidelines Version 2.2021 Colon Cancer[3]
NCCN: National Comprehensive Cancer Network, MMR: Mismatch repair, MSI: Microsatellite instability, CBC: Complete blood count, CEA: Carcinoembryonic antigen, CT: Computed tomography, PET: Positron emission tomography, 5-FU: 5-Fluorouracil, RT: Radiation therapy, IORT: Intra Operative radiation therapy, FOLFOX: Folinic acid, fluorouracil, and oxaliplatin, CAPEOX: Capecitabine plus oxaliplatin, MRI: Magnetic resonance imaging

followed by AC, and 3% treated with NAC followed by surgery. It was the first study on the long-term outcomes of NAC and reported that patients with T4b colon cancer who underwent NAC and subsequently underwent surgery had a better survival than patients who received AC after surgery. It was also reported that the majority of patients with LACC still underwent surgical resection and subsequently received AC, and that NAC had been used at an increased rate in patients with T4b colon cancer in the last 10 years. In this study, it was shown that the risk of death within 3 years was reduced by 23% in the NAC group.[5] In the study of de Gooyer et al.[1], the median follow-up time was 44 (4-133) months in the NAC group and 44 (0-133) months in the control group. The 5-year overall survival was 67% in the NAC group and 65% in the control group, and the difference between the two groups was not statistically significant (p=0.867). The postoperative 30-day mortality in the NAC group was 0.5%.

Conclusion

Some studies have shown that NAC appears to be safe in LACC and provides similar overall survival compared to AC, the R0 resection rate is increased in patients who have undergone NAC, and there is no significant increase in postoperative complications or mortality. In addition, it has been shown that tumor and lymph node stages exhibit significant downstaging in patients undergoing NAC. In the NCCN Guideline Colon Cancer version 2.2021, the feasibility of NAC with FOLFOX or CAPEOX before surgery in bulky nodal disease or clinical T4b colon cancers is suggested, which means that NAC is now included in the guidelines for the treatment of LACC, but it seems that larger randomized studies are still needed.

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Authorship Contributions

Surgical and Medical Practices: E.K., T.Ç., Concept: E.K., Design: E.K., Data Collection or Processing: E.K., Analysis or Interpretation: E.K., T.Ç., Literature Search: E.K., Writing: E.K., T.Ç.

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

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References

1. de Gooyer JM, Verstegen MG, 't Lam-Boer J, Radema SA, Verhoeven RHA, Verhoef C, Schreinemakers JMJ, de Wilt JHW. Neoadjuvant chemotherapy

for locally advanced T4 colon cancer: a nationwide propensity-score matched cohort analysis. Dig Surg 2020;37:292-301.

2. Arredondo J, Pastor E, Simó V, Beltrán M, Castañón C, Magdaleno MC, Matanza I, Notarnicola M, Ielpo B. Neoadjuvant chemotherapy in locally advanced colon cancer: a systematic review. Tech Coloproctol 2020;24:1001-1015.
3. Benson AB, Venook AP, Al-Hawary MM, Arain MA, Chen YJ, Ciombor KK, Cohen S, Cooper HS, Deming D, Farkas L, Garrido-Laguna I, Grem JL, Gunn A, Hecht JR, Hoffe S, Hubbard J, Hunt S, Johung KL, Kirilcuk N, Krishnamurthi S, Messersmith WA, Meyerhardt J, Miller ED, Mulcahy MF, Nurkin S, Overman MJ, Parikh A, Patel H, Pedersen K, Saltz L, Schneider C, Shibata D, Skibber JM, Sofocleous CT, Stoffel EM, Stotsky-Himelfarb E, Willett CG, Gregory KM, Gurski LA. Colon Cancer, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2021;19:329-359
4. Schmoll HJ, Van Cutsem E, Stein A, Valentini V, Glimelius B, Haustermans K, Nordlinger B, van de Velde CJ, Balmana J, Regula J, Nagtegaal ID, Beets-Tan RG, Arnold D, Ciardiello F, Hoff P, Kerr D, Köhne CH, Labianca R, Price T, Scheithauer W, Sobrero A, Tabernero J, Aderka D, Barroso S, Bodoky G, Douillard JY, El Ghazaly H, Gallardo J, Garin A, Glynne-Jones R, Jordan K, Meshcheryakov A, Papamichail D, Pfeiffer P, Souglakos I, Turhal S, Cervantes A. ESMO Consensus Guidelines for management of patients with colon and rectal cancer. a personalized approach to clinical decision making. Ann Oncol 2012;23:2479-2516.
5. Dehal A, Graff-Baker AN, Vuong B, Fischer T, Klempner SJ, Chang SC, Grunkemeier GL, Bilchik AJ, Goldfarb M. Neoadjuvant Chemotherapy Improves Survival in Patients with Clinical T4b Colon Cancer. J Gastrointest Surg 2018;22:242-249.
6. Karoui M, Rullier A, Luciani A, Bonnetain F, Auriault ML, Sarran A, Monges G, Trillaud H, Le Malicot K, Leroy K, Sobhani I, Bardier A, Moreau M, Brindel I, Seitz JF, Taieb J. Neoadjuvant FOLFOX 4 versus FOLFOX 4 with Cetuximab versus immediate surgery for high-risk stage II and III colon cancers: a multicentre randomised controlled phase II trial--the PRODIGE 22--ECKINOXE trial. BMC Cancer 2015;15:511.
7. Leufkens AM, van den Bosch MA, van Leeuwen MS, Siersema PD. Diagnostic accuracy of computed tomography for colon cancer staging: a systematic review. Scand J Gastroenterol 2011;46:887-894.
8. Dighe S, Swift I, Magill L, Handley K, Gray R, Quirke P, Morton D, Seymour M, Warren B, Brown G. Accuracy of radiological staging in identifying high-risk colon cancer patients suitable for neoadjuvant chemotherapy: a multicentre experience. Colorectal Dis 2012;14:438-444.
9. Roth MT, Eng C. Neoadjuvant Chemotherapy for Colon Cancer. Cancers (Basel) 2020;12:2368.
10. Body A, Prenen H, Latham S, Lam M, Tipping-Smith S, Raghunath A, Segelov E. The Role of Neoadjuvant Chemotherapy in Locally Advanced Colon Cancer. Cancer Manag Res 2021;13:2567-2579
11. Nelson H, Petrelli N, Carlin A, Couture J, Fleshman J, Guillem J, Miedema B, Ota D, Sargent D; National Cancer Institute Expert Pane. Guidelines 2000 for colon and rectal cancer surgery. J Natl Cancer Inst 2001;93:583-596.
12. Foxtrot Collaborative Group. Feasibility of preoperative chemotherapy for locally advanced, operable colon cancer: The pilot phase of a randomised controlled trial. Lancet Oncol 2012;13:1152-1160.
13. Jakobsen A, Andersen F, Fischer A, Jensen LH, Jørgensen JC, Larsen O, Lindebjerg J, Pløen J, Rafaelsen SR, Vilandt J. Neoadjuvant chemotherapy in locally advanced colon cancer. A phase II trial. Acta Oncol 2015;54:1747-1753.
14. Seymour MT, Morton D. FOxTROT: an international randomised controlled trial in 1052 patients (pts) evaluating neoadjuvant chemotherapy (NAC) for colon cancer. J Clin Oncol 2019;37(15 Suppl):3504.

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Turk J Colorectal Dis 2022;32:10-15

RESEARCH ARTICLE

Comparison of Anorectal Functional Outcome Following Low Anterior Resection Versus Intersphincteric Resection for Rectal Cancer

Suprabhat Giri, Sridhar Sundaram, Harish Darak, Sanjay Kumar, Megha Meshram, Shobna Bhatia

Seth GS Medical College and King Edward Memorial Hospital, Department of Gastroenterology, Mumbai, India

ABSTRACT

Aim: Low anterior resection (LAR) and intersphincteric resection (ISR) are the standard surgical options for low and very low rectal cancers, respectively. Unlike LAR, dissection in between the internal and external sphincter in ISR may functionally compromise sphincter integrity post-surgery. The aim was to compare anal sphincter function using anorectal manometry (ARM) in patients undergoing LAR and ISR, prior to stoma closure.

Method: Retrospective review of 50 cases of rectal cancer operated between January 2017 to October 2019 and referred for ARM before stoma closure. Patients with anorectal dysfunction were referred for physiotherapy and reassessed.

Results: Of the 50 patients, 25 patients had undergone LAR and 25 patients had undergone ISR. No difference was seen between the groups with relation to mean Cleveland Clinic Florida Fecal Incontinence Score [(CCFFIS); 4.76±2.93 vs. 5.28±3.57], mean resting pressure (56.22±15.48 vs. 51.10±19.83 mmHg), mean squeeze pressure (128.68±47.15 vs. 126.09±41.90 mmHg) and mean squeeze duration (25.98±10.90 vs. 24.55±13.12 seconds). In the LAR and ISR groups 8/25 (32%) and 11/25 (44%) had inadequate sphincter function on manometry ($p>0.05$). Significantly lower squeeze pressure (145.36±43.30 vs. 114.37±40.70 mmHg) and higher CCFFIS score was seen in those patients who underwent ARM a year after surgery.

Conclusion: Both ISR and LAR had similar losses in anal sphincter function, with greater degree of dysfunction in patients having stoma for a prolonged period.

Keywords: Intersphincteric resection, low anterior resection, rectal cancer, anorectal manometry, pelvic floor muscle training

Introduction

The rectum is the most common site for colorectal cancer in India, accounting for around 42% of cases.[1] Low anterior resection (LAR) with total mesorectal excision (TME) is the standard treatment for patients with proximal rectal cancer, wherein tumors in the lower rectum above the level of the sphincters, extending below the peritoneal reflection, are resected with colorectal anastomosis. Intersphincteric resection (ISR) has been introduced as an alternative to abdomino-perineal resection for very low rectal cancer (tumor within 10-50 mm of the anorectal ring)[2] with the advantage of preserving the sphincter and thus avoiding a permanent colostomy. ISR has evolved from an open procedure to a laparoscopic procedure, followed by robotic ISR, with the advantage of reducing blood loss and morbidity. Presently ISR with TME and partial or complete excision of the internal anal sphincter, with coloanal anastomosis is the ultimate anal preserving surgery through both abdominal and anal approaches. However, dissection between the internal and external sphincter in ISR may functionally compromise sphincter integrity post-surgery, which is not the case with LAR. So, postoperative anorectal function is an important outcome following these surgeries.

Previous studies have compared the postoperative anorectal function using standardized patient questionnaires.[3] There are very few studies that have compared the functional outcome by manometry when assessing anorectal function following surgeries for rectal cancer. The aim of this study

Address for Correspondence: Sridhar Sundaram, MD, Seth GS Medical College and King Edward Memorial Hospital, Department of Gastroenterology, Mumbai, India
E-mail: drsridharsundaram@gmail.com **ORCID ID:** orcid.org/0000-0002-9626-5243
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was to analyze the difference in anal sphincter function objectively by manometry in patients who had undergone LAR or ISR prior to stoma closure.

Materials and Methods

In this retrospective analysis, prospectively maintained data of patients who were operated because of rectal cancer and were referred to our department of Gastroenterology in a tertiary care center for anorectal manometry before stoma closure from September 2017 to October 2019 were analyzed. Patients had undergone either ISR (laparoscopic or robotic) or LAR according to the site of the tumor and the clinical choice of the operating surgeon. All patients had received neoadjuvant chemoradiation (with capecitabine as chemotherapy). Ileostomy was done in all patients for temporary fecal diversion to protect the anastomotic site from complications like anastomotic dehiscence. Patients were referred for ARM prior to stoma closure. All patients had undergone flexible sigmoidoscopy prior to the ARM procedure and those who were found to have stricture beyond which the scope could not be negotiated, underwent dilatation and were excluded from the study. A baseline Cleveland Clinic Florida Fecal Incontinence Score (CCFFIS) at referral for manometry was also recorded for all patients (Table 1) with a score ranging from 0 to 20.[4]

ARM was performed using a 20-channel water perfused anorectal catheter with length of 164 cm and a balloon at its tip. Manometry was performed with the patient being in the left lateral position. A digital rectal examination was performed before placing the catheter. Patients with rectal stricture on digital examination were excluded from the study and were referred for stricture dilatation and were considered for manometry after adequate dilatation. However these patients were not included in the present analysis. A catheter lubricated using lignocaine jelly was inserted such that the pressure sensors are located across the anal canal. After taking a baseline reading for two minutes, subjects were instructed to squeeze the anal canal as tightly as possible and for as long as possible, three times in succession with a resting period of 60 seconds in between two readings. The maximal endurance squeeze pressure and the maximal duration were recorded. Data were analyzed by MMS database software, version 9.5 h (Medical Measurement Systems B.V.). Although data regarding normal anorectal function (Figure 1) in a healthy Indian population is lacking, adequate sphincter function was defined by resting pressure ≥40 mmHg, maximal squeeze pressure ≥80 mmHg and squeeze duration ≥30 seconds.

All the patients who had anorectal dysfunction/inadequate sphincter function as defined by either resting pressure <40 mmHg or maximal squeeze pressure <80 mmHg (Figure 2) or maximum squeeze duration <30 seconds (Figure 3) or a combination of these, were referred for physiotherapy. Patients were taught pelvic floor muscle exercises, which included tightening and pulling up the pelvic floor muscles and anal sphincter muscles for as long as they could. Patients were asked to rest for four seconds and then repeat the contractions, gradually increasing up to 10 slow contractions at a time, holding them for 10 seconds each with a rest of four seconds in between. Patients were asked to practice three sets of these exercises 3-4 times each day for three months. They were then asked to return for repeat manometry prior to surgery with recalculation of CCFFIS

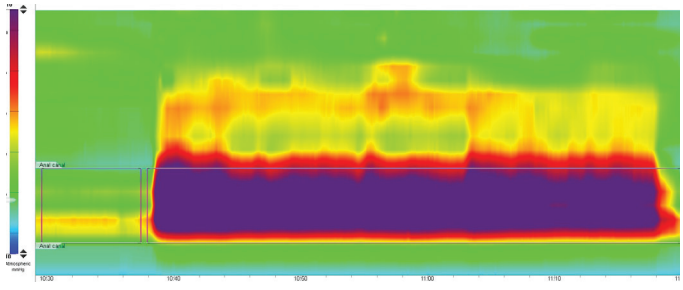

Figure 1. Normal anorectal manometry

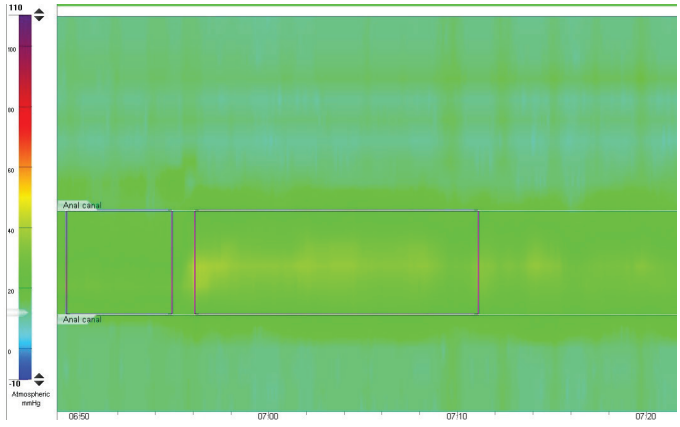

Figure 2. Inadequate endurance squeeze pressure of 35 mmHg

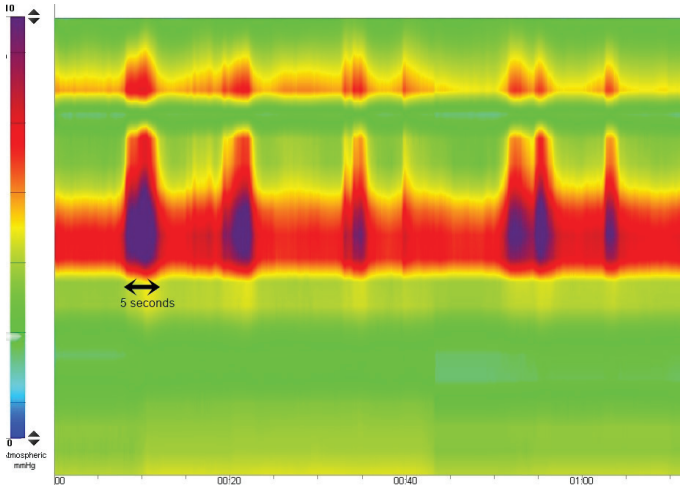

Figure 3. Poorly sustained squeeze pressure of 5 seconds

score. Stoma closure was deferred in patients with anorectal dysfunction.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation and were analyzed with the chi-square test. Pearson chi-square test was used to compare the prevalence of anorectal dysfunction between the two groups. Paired data before and after physiotherapy were compared using a paired t-test. A p-value ≤0.05 was taken to be significant. All statistical analyses were performed using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA).

Results

Out of 94 patients who underwent surgery during this period, manometry data for 26 patients were not available and 18 patients were excluded due to the presence of strictures. Of the patients with strictures, 11 (61%) were associated with ISR while seven (38.9%) were associated with LAR.

So, a total of 50 patients with a mean age 45.82±12.98 years, of whom 27 were males (54%), were included in the study. All patients had received perioperative CRT. Abnormality in at least one parameter of anorectal function was seen in 19 (38%) patients. Reduced squeeze duration was the most common dysfunction present in all patients (100%) while eight (16%) patients had combination of two or more abnormal parameters (Figure 4). Patients who had abnormal parameters on manometry had a higher CCFFIS (8.63±1.67) compared to patients with normal manometry (2.80±1.49) (p<0.001).

Of the 50 patients, 25 (50%) had undergone LAR (laparoscopic=15, robotic=10) while 25 (50%) had ISR (laparoscopic=20, robotic=5). There was no difference between the groups in terms of age, CCFFIS, mean resting pressure, maximal squeeze pressure and mean squeeze duration. In the two treatment groups 8/25 (32%) in the LAR and 11/25 (44%) in the ISR group had inadequate sphincter function as assessed by manometry [odds ratio (OR): 1.66, 95% confidence interval (CI): 0.527 to 5.28; p=0.560] (Table 2).

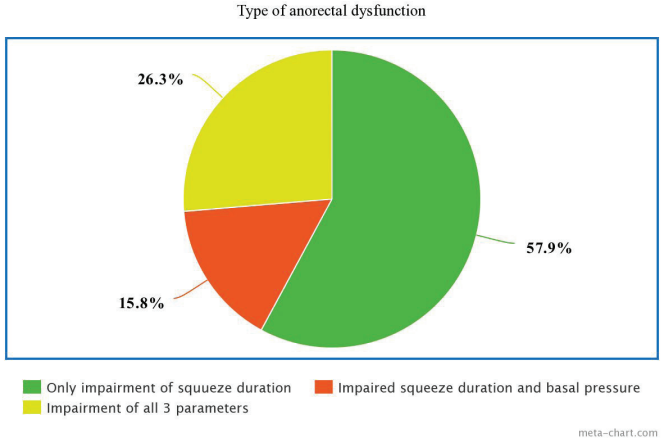

Figure 4. Pie-chart showing type of anorectal dysfunction

Patients underwent ARM after a median duration of 10 months (2-28 months) after the primary surgery. To assess whether duration of ileostomy affected the anal sphincter function, patients were divided into two groups: those patients who underwent ARM within a year of surgery and those after more than one year of surgery. Patients who underwent ARM within a year had lower CCFFIS score. Average squeeze pressure was lower in those patients who underwent ARM after a year of surgery (p=0.014) while there was no difference in basal pressure and squeeze duration. Of the 29 patients who underwent ARM within a year, only five patients had dysfunction while 14/21 (66.7%) who underwent ARM after 1 year had dysfunction (OR=9.6, 95% CI: 2.18 to 45.11; p=0.0008) (Table 3).

Table 1. Cleveland clinic florida fecal incontinence score

Type of incontinence	Frequency				
	Never	Rarely	Sometimes	Usually	Always
Solid	0	1	2	3	4
Liquid	0	1	2	3	4
Gas	0	1	2	3	4
Wears pad	0	1	2	3	4
Lifestyle alteration	0	1	2	3	4

Rarely: Less than 1 per month, Sometimes: Less than 1 per week and 1 or more per month, Usually: less than 1 per day and 1 or more per week, Always: 1 or more per day

Table 2. Comparison of anorectal function between LAR and ISR groups

	LAR (n=25)	ISR (n=25)	p value
Age (years)	48.4±15.25	43.24±9.89	0.163
CCFFIS (mean ± SD)	4.76±2.93	5.28±3.57	0.577
Basal pressure (mmHg)	56.22±15.48	51.10±19.83	0.315
Squeeze pressure (mmHg)	128.68±47.15	126.09±41.90	0.838
Duration of squeeze (seconds)	25.98±10.90	24.55±13.12	0.678
Impaired anorectal function (n)	8	11	0.560

LAR: Low anterior resection, ISR: Intersphincteric resection, CCFFIS: Cleveland Clinic Florida Fecal Incontinence Score, SD: Standard deviation

Out of the 19 patients who had dysfunction, only 10 patients came for follow-up and repeat manometry showed improvement in CCFFIS and all manometric parameters above the baseline value (Table 4) but complete resolution with respect to maximal squeeze pressure and maximal squeeze duration was seen in 6 of the 10 patients.

Table 3. Comparison of anorectal function with respect to interval between surgery and anorectal manometry

	Early (<12 months) (n=29)	Late (>12 months) (n=21)	p value
CCFFIS (mean ± SD)	3.85±3.26	5.86±3.02	**0.030**
Mean basal pressure (mmHg)	59.06±18.58	49.75±16.43	0.074
Mean squeeze pressure (mmHg)	145.36±43.30	114.37±40.70	**0.014**
Mean duration of squeeze (seconds)	28.63±10.80	22.83±12.35	0.084
Impaired anorectal function (n)	5	14	**0.0008**

CCFFIS: Cleveland Clinic Florida Fecal Incontinence Score, SD: Standard deviation

Table 4. Change in anorectal function after physiotherapy

	Before physiotherapy (n=10)	After physiotherapy (n=10)
CCFFIS	9.20±1.81	6.60±1.17
Mean basal pressure (mmHg)	40.85±16.00	49.25±15.95
Mean squeeze pressure (mmHg)	90.47±34.45	120.68±31.81
Mean duration of squeeze (seconds)	13.18±5.66	27.32±7.26

CCFFIS: Cleveland Clinic Florida Fecal Incontinence Score

Discussion

Anorectal dysfunction was seen in 38% of the patients undergoing surgery for rectal cancer. Reduced squeeze duration was the most common dysfunction. There was no difference in anorectal function between the patients undergoing LAR or ISR. Patients who underwent ARM after 12 months of surgery were more likely to have anorectal dysfunction. Around two thirds of the patients with dysfunction improved after physiotherapy.

The mean age in the presented cohort was 45.8 years, which is similar to the mean age of presentation of patients with colorectal cancer in other studies from India.[1,5] This is in contrast to Western data where 90% of new cases of colorectal cancer are above 50 years at diagnosis and 58% of all new cases are above 65 years of age.[6] This difference can be attributed to the younger aged population in India compared to Western countries, which have a larger elderly population or a biologically different type of disease.

The complex interaction of motor and sensory function between the rectum and anus maintains normal continence. The pathophysiology of sphincter dysfunction after surgery for rectal cancer is multifactorial and includes direct trauma to the sphincter during surgery[7], injury of pelvic nerves[8], chemo-radiotherapy[9] and disuse-atrophy of sphincter muscles.

Sailer et al.[10] studied the morphological changes in anal sphincter muscles during and after temporary diverting stoma by using endoscopic ultrasound (EUS). They observed that from the time of primary operation to stoma closure, the puborectalis and components of the external anal sphincter (EAS) underwent significant reduction in diameter, which normalized three months after stoma closure without any change in the internal anal sphincter (IAS).[10] These changes were ascribed to the involutional atrophy of the muscles during the resting period and this highlights the importance of initiating PFMT immediately postoperatively in preventing these changes.

In our study, we objectively compared anorectal functional parameters using manometry after a median duration of 10 months after surgery and found no difference between the two groups. Other methods for post-operative assessment of anorectal function include functional questionnaires, such as the Wexner score and GIFO score. Kawada et al.[3] compared anorectal function using questionnaire in patients who underwent laparoscopic ISR or LAR, before and at 6, 12, and 24 months after surgery. They observed that the mean Wexner score (CCFFIS) was significantly higher in the ISR group than the LAR group at 6 months postoperatively (11.9±5.6 vs 5.2±4.2). The return of anorectal function to that of the preoperative level took around 24 months in the ISR group while patients in the LAR group achieved the same by 12 months after stoma closure.[3]

Previous studies have reported that pre/peri-operative cardiac resynchronization therapy (CRT) was a risk factor for deterioration in continence function following surgery which was ascribed to neural degeneration.[11,12] In a study from Italy, manometric data from patients with rectal cancer were studied before and after CRT and it was reported that 23% of patients developed new-onset anorectal dysfunction with a significant reduction in resting anal sphincter pressure.[13] In our study, all the patients received CRT so that there is no confounding effect in our data although

we could not assess the effect of CRT in the induction of anorectal dysfunction as compared to surgery.

Pelvic floor muscle training (PFMT), which includes exercises for anal sphincters, is aimed at increasing the strength and improving endurance and coordination. In a RCT of patients treated for rectal cancer who were given biofeedback therapy (BFT) during the period of temporary stoma, Kye et al.[14] found that BFT was helpful in maintaining resting anal sphincter tone but had no effect on preventing anorectal dysfunction after stoma closure. In contrast, a similar study from China reported that BFT combined with PFMT significantly improved anorectal function.[15] In our study there was objective evidence of improvement in all parameters after PFMT, but complete improvement was seen in only 6 out of the 10 patients. Although knowledge regarding the ideal timing of starting PFMT is limited, various small studies have concluded that early initiation of PMFT will help in preventing fecal incontinence after surgery for rectal cancers.

Study Limitations

The limitations of our study are the lack of baseline pressure values prior to surgery, the retrospective nature of analysis and the small sample size. Due to the small sample size, the study is underpowered to detect a statistical significance. A larger sample size with additional BFT and a longer follow up period would have helped in confirming the findings of our study. There is the possibility of selection bias as this is a retrospective study. Although there are a few limitations, the study provided an objective assessment and comparison of sphincter function using manometry, which has not been previous performed or published.

Conclusion

To conclude, both ISR and LAR have a high rate of anal dysfunction in more than one-third of patients undergoing surgery in our cohort of patients. The rate of anal sphincter dysfunction in both surgeries is the same, based on manometry data, despite ISR being a surgery associated with sphincter manipulation. Anorectal manometry may be a useful tool for monitoring continence problems after surgery for rectal cancer so that adequate physiotherapy could be given to accelerate the recovery of the sphincter function.

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Ethics

Ethics Committee Approval: Received and approved by the IEC at King Edward Memorial Hospital, Mumbai.

Informed Consent: Consent waiver received as it was retrospective study.

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Authorship Contributions

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

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References

1. Patil PS, Saklani A, Gambhire P, Mehta S, Engineer R, De'Souza A, Chopra S, Bal M. Colorectal Cancer in India: An Audit from a Tertiary Center in a Low Prevalence Area. Indian J Surg Oncol 2017;8:484-490.
2. Shirouzu K, Murakami N, Akagi Y. Intersphincteric resection for very low rectal cancer: A review of the updated literature. Ann Gastroenterol Surg 2017;1:24-32.
3. Kawada K, Hida K, Hasegawa S, Sakai Y. A comparison of the long-term anorectal function between laparoscopic intersphincteric resection and low anterior resection for low rectal cancer. Surg Today 2018;48:921-927.
4. Jorge JM, Wexner SD. Etiology and management of fecal incontinence. Dis Colon Rectum 1993;36:77-97.
5. Sarkar S, Mukherjee R, Paira SK, Roy B, Banerjee S, Mukherjee SK. Profile of colorectal cancer in Eastern India. J Indian Med Assoc 2012;110:901-903.
6. Siegel R, Desantis C, Jemal A. Colorectal cancer statistics, 2014. CA Cancer J Clin 2014;64:104-117.
7. Ho YH, Tsang C, Tang CL, Nyam D, Eu KW, Seow-Choen F. Anal sphincter injuries from stapling instruments introduced transanally: randomized, controlled study with endoanal ultrasound and anorectal manometry. Dis Colon Rectum 2000;43:169-173.
8. Williamson ME, Lewis WG, Finan PJ, Miller AS, Holdsworth PJ, Johnston D. Recovery of physiologic and clinical function after low anterior resection of the rectum for carcinoma: myth or reality? Dis Colon Rectum 1995;38:411-418.
9. Canda AE, Terzi C, Gorken IB, Oztop I, Sokmen S, Fuzun M. Effects of preoperative chemoradiotherapy on anal sphincter functions and quality of life in rectal cancer patients. Int J Colorectal Dis 2010;25:197-204.
10. Sailer M, Fein M, Fuchs KH, Bussen D, Grun C, Thiede A. Morphologic changes of the anal sphincter musculature during and after temporary stool deviation. Langenbecks Arch Surg 2001;386:183-187.
11. Kienle P, Abend F, Dueck M, Abel U, Treiber M, Riedl S. Influence of intraoperative and postoperative radiotherapy on functional outcome in patients undergoing standard and deep anterior resection for rectal cancer. Dis Colon Rectum 2006;49:557-567.
12. Lim JF, Tjandra JJ, Hiscock R, Chao MW, Gibbs. Preoperative chemoradiation for rectal cancer causes prolonged pudendal nerve terminal motor latency. Dis Colon Rectum 2006;49:12-19

13. De Nardi P, Testoni SG, Corsetti M, Andreoletti H, Giollo P, Passaretti S, Testoni PA. Manometric evaluation of anorectal function in patients treated with neoadjuvant chemoradiotherapy and total mesorectal excision for rectal cancer. Dig and Liv Dis 2017;49:91-97.
14. Kye BH, Kim HJ, Kim G, Yoo RN, Cho HM. The Effect of Biofeedback Therapy on Anorectal Function After the Reversal of Temporary Stoma When Administered During the Temporary Stoma Period in Rectal Cancer Patients With Sphincter-Saving Surgery: The Interim Report of a Prospective Randomized Controlled Trial. Medicine (Baltimore) 2016;95:3611.
15. Wu XD, Fu CF, Chen YL, Kong LH, Pan ZZ, Zheng MC. Intervention effect of biofeedback combined with pelvic floor muscle exercise on low anterior resection syndrome in patients with low anus-preserving rectal cancer. Zhonghua Yi Xue Za Zhi 2019;99:2337-2343.

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RESEARCH ARTICLE

Clinical Outcomes of Salvage Surgery in Locally Advanced Distal Rectal Cancer Patients with Local Regrowth Following Non-operative Management

İlker Özgür[1], Cemil Burak Kulle[1], Metin Keskin[1], Halil Alper Bozkurt[1], Melek Bayram[2], Yersu Kapran[3], Bülent Acunaş[4], Bengi Gürses[5], Dursun Buğra[6], Emre Balık[6], Mehmet Türker Bulut[1]

[1]İstanbul University Faculty of Medicine, Department of General Surgery, İstanbul, Turkey
[2]İstanbul University Faculty of Medicine, Department of Pathology, İstanbul, Turkey
[3]Koç University Hospital, Clinic of Pathology, İstanbul, Turkey
[4]İstanbul University Faculty of Medicine, Department of Radiology, İstanbul, Turkey
[5]Koç University Hospital, Clinic of Radiology, İstanbul, Turkey
[6]Koç University Hospital, Clinic of General Surgery, İstanbul, Turkey

ABSTRACT

Aim: Locally advanced distal rectal cancer (LADRC) patients managed with non-operative management (NOM) with complete clinical response following neoadjuvant treatment will experience local regrowth in about 25% of cases. The long-term risks of this strategy or local regrowth treatment have not been well established, and the main concern is the probability of impaired oncological outcomes after salvage surgery. This study aimed to evaluate the feasibility and clinical outcomes of salvage surgery in LADRC patients with local regrowth following NOM.

Method: All locally advanced, distal rectal cancer patients managed with NOM after neoadjuvant therapy with clinical complete response, who developed local regrowth during surveillance, between May 2016 and November 2018, were enrolled in the study. Patients were analyzed for the rate of salvage surgery, disease-free survival and overall survival.

Results: Eleven out of 63 (17.5%) patients developed local regrowth after a mean of 8.4 (3-15) months. The mean surveillance period was 31.8 (14-50) months. Eleven (100%) patients underwent salvage surgery due to the principles of total mesorectal excision. LE was not performed. No patients experienced local recurrence and three out of eleven (27.3%) developed carcinomatosis peritonei and/or distant metastasis after a mean surveillance period of 12.2 (3-26) months. At 30 months, the local and/or systemic recurrence rate, disease-free survival, and overall survival in the patients undergoing surgical treatment were 100%, 73%, 73% and 91%, respectively.

Conclusion: The vast majority of patients with regrowth following NOM were suitable for salvage surgery with curative intent and justifiable pelvic tumor control.

Keywords: Rectal cancer, non-operative management, local regrowth, salvage surgery

Introduction

The introduction and ubiquitous establishment of neoadjuvant treatment strategies, such as the standard trimodal treatment, consolidation, or induction chemotherapy has increased the rate of clinical complete response (cCR) and the rate of the clinically favorable pathologic complete response (pCR). Patients with a pCR have improved oncological outcomes, with local recurrence rates of <1% and a 5-year survival rate of more than 95%.[1,2] Despite dramatic improvements in oncological outcomes in locally advanced distal rectal cancer (LADRC) patients, there has been an increasing interest and focus in organ-preserving approaches, such as local excision (LE) or non-operative management (NOM), which is also known as the "watch and wait" (W&W) strategy. This is mainly because resection surgery based on the principles of total mesorectal excision (TME) is associated with 1-2% preoperative mortality, temporary or permanent colostomy,

Address for Correspondence: Cemil Burak Kulle, MD, İstanbul University Faculty of Medicine, Department of General Surgery, İstanbul, Turkey
E-mail: cemilburakkulle@gmail.com **ORCID ID:** orcid.org/0000-0003-2956-4486
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disturbed bowel function and long-term morbidity, such as urinary and sexual dysfunction in more than 60% of patients, which significantly reduces the quality of life.[3,4,5]

Since the pioneering publication reporting W&W among LADRC patients with cCR following neoadjuvant treatment by Habr-Gama et al.[6] in 2004, multiple observational case series have confirmed the feasibility of W&W with nearly equal and acceptable short- and long-term clinical outcomes compared to patients undergoing TME.[7,8,9,10,11] Despite these achievements, there are still concerning and unsolved issues. There is currently no advanced imaging modality, such as magnetic resonance imaging (MRI), capable of detecting small remnants of viable tumor cells in the tumor bed or mesorectal lymph nodes with an accuracy of 100%. That is why 15% to 30% of all LADRC patients managed with NOM will experience local regrowth during frequent surveillance. The only option for treatment with no alternative is salvage surgery.[9,10,11,12]

However, there are risks and concerns related to the deferral of surgery compared to immediate surgery without the delay of NOM. These are: missing the opportunity of "*salvage surgery*" due to increased invasiveness; technical difficulty due to pelvic fibrosis leading to increased intraoperative and postoperative complications; increased postoperative morbidity and mortality; and impaired short- and long-term clinical outcomes in terms of disease-free and overall survival. These issues have not yet been fully clarified and have led to increased and considerable uncertainty regarding NOM.

This study's primary objective was to analyze the clinical and oncological outcomes of "*salvage surgery*" among LADRC patients, who developed local regrowth during follow-up managed with NOM.

Materials and Methods

Study Design

All LADRC patients with a local regrowth, after an initial NOM approach revealing cCR following neoadjuvant treatment, who underwent "*salvage surgery*" between May 2016 and November 2018 in two comprehensive cancer centers, were enrolled in the retrospective observational case series study. Only patients with biopsy-proven distal rectal adenocarcinoma without initial metastasis, neoadjuvant treatment (long-course chemoradiotherapy, consolidation or induction chemoradiotherapy), cCR following neoadjuvant therapy, frequent surveillance according to an adequate predefined and established NOM protocol and radiologically and/or biopsy-proven local intra- or extra-mural regrowth were included.

Patients were primarily analyzed for local recurrence-free rate, distant metastasis-free rate, disease-free survival, and overall survival. The second aim was assessment of the feasibility of "*salvage surgery*" and associated morbidity and mortality. Every patient signed an infomred consent previous to NOM or surgery. They also allowed us to use their information for research.

cCR Assessment and Surveillance

Neoadjuvant treatment response was evaluated with the combination of the digital rectal examination (DRE), sigmoidoscopy and pelvic MRI with the addition of contrast and advanced functional sequences such as diffusion-weighted MRI (DW-MRI) and dynamic contrast-enhanced MRI. The response was defined as: the absence of the primary tumor on DRE; replacement flat white scar tissue and/or telangiectasia without nodularity and ulcer of the mucosa on sigmoidoscopy; and complete normalization of the rectal wall or dense fibrotic lesion with low signal intensity without intermediate tumor signal intensity and no evidence of diffusion restriction within the tumor or lymph nodes on MRI.[13,14]

After confirming a cCR and approving NOM by the institutional tumor board, all patients were followed-up with carcinoembryonic antigen measurements, DRE, sigmoidoscopy, and pelvic MRI in the first three years at an interval of three months and then every six months up to five years. Additional standard rectal cancer surveillance according to international guidelines, was performed, including annual colonoscopy and imaging of the thorax and abdomen with computer tomography (CT) or MRI every six or twelve months for five years.

Local Regrowth and Treatment

Local regrowth was defined as any sign of tumor regrowth in the rectal wall on DRE, new mucosal abnormalities on sigmoidoscopy or concerning imaging findings on MRI, such as an isointense mass or wall thickening of the fibrotic scar on T2W-MRI, new focal high signal intensity on DW-MRI or an enlarging mass in the mesorectum. In some instances, there were no endoscopy changes suggesting endoluminal local regrowth due to an intramural regrowth pattern defined as a new mass with intermediate signal intensity or wall thickening of the fibrotic scar on T2W-MRI first without initial changes on endoscopy. Patients suspected of endoluminal or intramural regrowth patterns were histologically confirmed with an endoscopic biopsy.

Regardless of the growing pattern, endoluminal or extraluminal regrowth was an indication for "*salvage surgery*" based on the principles of TME, which is the only proven rationale and curative treatment option. As part of clinical staging, thorax and abdomen CT was performed

for all patients with local regrowth to determine the local extent of the tumor and to exclude the presence of distant metastasis prior to radical resection surgery. In both centers, LE was not performed due to the potential risk of recurrence compared to TME.

Statistical Analysis

All statistical analyses were performed with SPSS, version 26.0 (IBM Corp., Armonk, NY, USA) and only descriptive statistics were calculated for the entire case series without comparisons. Categorical data were calculated using the number (n) and percentage (%), while continuous variables were analyzed using mean, standard deviation, median and minimum-maximum. We considered the date of diagnosis as the baseline starting point for survival analysis. We calculated the time to diagnosis of local recurrence after salvage surgery from the date of surgery. Local recurrence-free rate, disease-free survival, distant metastasis-free rate, and overall survival were estimated with Kaplan-Meier.

Results

Baseline Characteristics

Eleven of the 63 (17.5%) LARC patients, initially managed with a NOM strategy after cCR following neoadjuvant treatment, who developed local regrowth between May 2016 and November 2018, were included in the study. Mean age, gender distribution and mean tumor distance from the dentate line at initial diagnosis was 60.2 (43-71) years, 81% male and 2.9 (0-5) cm, respectively. At initial diagnosis, all patients were staged as LADRC (T3≤, any N or any T, N+) with pelvic MRI and all patients received long-course chemoradiotherapy (100%). The mean follow-up was 31.8 (14-50) months. Median time from the end of neoadjuvant radiotherapy to local regrowth diagnosis was 15.2 (9-26) months. Further baseline characteristics are depicted in Table 1.

Salvage Surgery and Pathologic Assessment

All patients with local regrowth underwent salvage surgery based on the principles of TME, of which eight (73%) patients underwent low anterior resection (LAR), two (18%) patients underwent abdominoperineal resection (APR), and one (9%) underwent intersphincteric resection (ISR). Minimal invasive surgery, either laparoscopic or robotic surgery, was performed in all (100%) regrowth patients with only rare and minor complications (see below). LE was not performed as a treatment option for local regrowth.

In our study, in all patients (100%) local regrowth was confined to the bowel wall and were classified as endoluminal local regrowth. None of the patients had an extraluminal growing pattern of the primary tumor. Most of the patients (73%) had a local regrowth at an early stage and in three (27%) patients diagnosed for local regrowth, no viable malignant tumor cells were detected on histopathological examination of the TME specimen. These patients were staged as ypT0N0. The R0 rate after TME was 100% and the TME specimen was also inspected and graded as complete, nearly complete, or incomplete mesorectum. Nine out of eleven (82%) TME revealed a complete mesorectum, one patient (9%) had a nearly complete mesorectum and one patient (9%) had an incomplete mesorectum. All patients' histopathological findings are outlined in Table 2.

Intraoperative and Postoperative Outcomes

The mean hospital stay was 7 (4-20) days, the operating time for salvage surgery was 180 (155-212) minutes and the amount of intraoperative blood loss was 90 (30-200) milliliters (Table 3). Intraoperative and postoperative complications were observed at about 9% and were not related to pelvic fibrosis or local regrowth. One (9%) patient received a grade I laceration of the spleen that was managed

Table 1. Baseline features of patients after salvage surgery for local regrowth after initial NOM

	n=11
Age, mean (range), years	60.2 (43-71)
Gender	
Female, n (%)	2 (19)
Male, n (%)	9 (81)
Body mass index, median (range), kg/m^2	29.5 (22.3-43.8)
ASA score	
I, n (%)	4 (36)
II, n (%)	6 (55)
III, n (%)	1 (9)
Height from dentate line, median (range), cm	2.9 (0-5)
Clinical tumor (T) stage	
cT2, n (%)	1 (9)
cT3, n (%)	9 (82)
cT4, n (%)	1 (9)
Clinical nodal (N) stage	
Negative, n (%)	0
Positive, n (%)	11 (100)
Neoadjuvant treatment	
Induction chemotherapy, n (%)	2 (18)
Consolidation chemotherapy, n (%)	9 (82)

NOM: Non-operative management, ASA: American Society of Anesthesiologists

Table 2. Salvage surgery and histopathologic results

	(n=11)
Type of regrowth	
Extraluminal, n (%)	0
Endoluminal, n (%)	11 (100)
Type of salvage surgery	
Low anterior resection, n (%)	8 (73)
Interspincteric resectio, n (%)	1 (9)
Abdominoperineal resection, n (%)	2 (18)
Type of TME approach	
Open surgery, n (%)	0
Minimal invasive, n (%)	11 (100)
Conversion, n (%)	0
ypT-stage	
T0, n (%)	3 (27)
T1, n (%)	3 (27)
T2, n (%)	4 (36)
T3, n (%)	1 (9)
T4, n (%)	0
ypN-stage	
N0, n (%)	7 (64)
n1, n (%)	3 (27)
N2, n (%)	0
Nx, n (%)	1 (9)
Type of salvage surgery resection margin	
R0, n (%)	11 (100)
R1, n (%)	0
TME specimen grading	
Complete, n (%)	
Near complete, n (%)	
Incomplete, n (%)	

TME: Total mesorectal excision

with laparoscopic electrocauterization and concomitant serosal injury of the small bowel managed with laparoscopic primary repair suture. After salvaging, another patient (9%) had an endoscopic decompression due to pseudo-obstruction and underwent an exploration because of bleeding (Table 3).

Clinical Outcome

After salvage surgery, the local recurrence-free rate and pelvic tumor control was 100% and no patient developed local recurrence. However, during surveillance three

Table 3. Perioperative outcomes

	(n=11)
Length of hospital stay, mean (range), days	7 (4-20)
Postoperative complication (Clavien-Dindo grade), n of patients	
II	0
IIIa	0
IIIb	2
IV	0
V	0
Operating time, mean (range), minutes	180 (155-212)
Intraoperative blood loss, mean (range), milliliters	90 (30-200)
Intraoperative complication	
Yes, n (%)	0
No, n (%)	11 (100)

out of eleven (27%) developed distant metastases with dissemination predominantly to the lung. Two patients underwent video-assisted thoracic surgery for pulmonary metastasis, but one of these patients passed away due to disease progression after surgery while under chemotherapy treatment. The third patient with distant metastasis after surgery was advised to receive third-line chemotherapy because of widespread metastatic disease.

The 30-month local recurrence-free rate, distant metastasis-free rate, disease-free survival and overall survival were 100%, 73%, 73% and 91%. The reason why distant metastasis-free rate and disease-free survival have the same value is that the patients in the study only developed distant metastasis and died as a result of this disease state. The oncological outcomes of patients undergoing salvage surgery due to local regrowth are given in Table 4.

Discussion

Before approving and enrolling a patient in a NOM protocol, deteriorating outcomes and impacts during surveillance, such as local regrowth or distant metastasis, most probably associated with the deferral of surgery, must be discussed in detail with the patient. This is because approximately 25% of LADRC patients initially managed with NOM, with cCR following neoadjuvant treatment, will experience local regrowth.[9,10,11,12] In our study 17.5% of NOM patients developed local regrowth and all (100%) patients were suitable for "salvage surgery" based on the principles of TME. Compared to other studies, our "salvage surgery" rate was similar to previously reported large scale NOM case-series by Habr-Gama et al.[7] (93%), Dossa et al.[11] (95%), van der Sande et al.[15] (97%) and Smith et al.[13] (100%). Despite

Table 4. Clinical characteristics of NOM patients with local regrowth

Patient	Local regrowth	Salvage surgery	Mesorectum	CRM	Pathologicstaging	Time to local regrowth (months)	Distant metastasis	Surgery for distant metastasis	Survival
1	Endoluminal	LAR	Complete	Negative	ypT1N0	5	None	None	Alive
2	Endoluminal	LAR	Complete	Negative	ypT0N0	13	None	None	Alive
3	Endoluminal	LAR	Complete	Negative	ypT2N1c	5	None	None	Alive
4	Endoluminal	LAR	Complete	Negative	ypT2N0	10	Lung	Metastasectomy	Alive
5	Endoluminal	LAR	Complete	Negative	ypT1N0	5	None	None	Alive
6	Endoluminal	APR	Near complete	Negative	ypT0N0	10	None	None	Alive
7	Endoluminal	LAR	Complete	Negative	ypT2N0	15	None	None	Alive
8	Endoluminal	ISR	Complete	Negative	ypT1N1c	14	None	None	Alive
9	Endoluminal	LAR	Complete	Negative	ypT3N1b	6	Lung	Metastasectomy	Died
10	Endoluminal	APR	Complete	Negative	ypT2N0	6	None	None	Alive
11	Endoluminal	LAR	Incomplete	Negative	ypT2Nx	3	Lung, CP	None	Alive

NOM: Non-operative management, CRM: Circumferential resection margin, APR: Abdominoperineal resection, ISR: Intersphincteric resection, LAR: Low anterior resection

these promising findings, there is still growing concern and uncertainty regarding perioperative complications or quality of the completeness of the TME specimen related to pelvic fibrosis and the oncological outcomes.

As discussed with the patients from the initiation of the NOM protocol, every local regrowth is an indication for "salvage surgery" such as LAR, APR or ISR. In this study, nine (82%) patients underwent sphincter preserving surgery (LAR or ISR), and only two patients (18%) had rectal amputation (APR). These results show a very high sphincter-preservation and organ-preservation rate among the whole cohort with 96% and 82%, respectively. Our rate of organ preservation (82%) is similar or even higher than other reported case series from previous studies.[7,8,9,10,11,12,13] One of the troublesome dilemmas surgeons often face is that patients with local recurrence in the distal part of the rectum commonly seek alternative treatment options, such as brachytherapy or LE, to avoid a permanent colostomy. Although some studies have reported promising clinical outcomes with LE as an alternative treatment option for salvage surgery, we did not perform LE. The reasons for this were patients undergoing LE have an increased risk of both, the need for completion TME because of underprivileged pathology greater than ypT1 and local recurrence. LE, in the form of transanal endoscopic microsurgery (TEM), is associated with partial removal of the perirectal fat, which in turn causes technical difficulties during the completion of the TEM or treatment of potential local recurrence during follow-up.[7] The final reason for avoiding LE was that postoperative scarring of the locally excised area leads to confusion and difficulty in distinguishing local recurrence from scar tissue during surveillance.

Another important, sensitive issue is whether pelvic fibrosis associated with delayed "salvage surgery" after deferral of initial surgery leads to increased perioperative complications and decreased quality of the completeness of the TME specimen. The completeness of the mesorectum and tumor-free circumferential resection margin (CRM) is associated with favorable oncological outcomes, such as decreased local recurrence and increased overall survival and are important prognostic factors.[16,17] Prolonged waiting interval after neoadjuvant treatment causes pelvic fibrosis, which is measured by subjective intraoperative scales, but it has no effect on technical difficulties or intraoperative complications.[18] Only the French GRECCAR 6 study showed a higher morbidity rate in patients with delayed surgery (11 weeks vs 7 weeks), mostly due to an increased risk of medical complications.[19] Discussion of pelvic fibrosis is beyond the scope of this study, but we had a complete TME specimen of (82%) and tumor-free CRM in all (100%) patients, mean operating time of 180 minutes and intraoperative blood loss of 90 milliliters, which is similar to other case series.[15] One patient's pathology report revealed ypT2Nx with an incomplete mesorectum and negative CRM and developed carcinomatosis peritonei and distant metastasis after "salvage surgery". In this study consisting of LARDC patients initially managed with NOM, two patients developed carcinomatosis peritonei and distant metastasis after "salvage surgery", which accounts for 3.2% of the whole NOM cohort. When enrolling patients in a NOM protocol,

we do expect some degree of increased risk in terms of distant metastasis but we should always keep in mind that even initial surgery revealing a pCR bears the risk of local recurrence of up to 2.8% and is not a definitive solution.[1]

To our knowledge, "salvage surgery" is the only and most effective choice of treatment for local regrowth, but its effectiveness in preventing distant metastasis is open to question. In our cohort, none of the patients who underwent "salvage surgery" experienced local recurrence during follow-up and pelvic tumor control was achieved in all patients (100%). However, three (27%) patients developed distant metastasis localized exclusively in the lung. Thus there was an increased rate of systemic dissemination to the lung in patients undergoing "salvage surgery" due to local regrowth compared to patients with sustained cCR (27% vs 0). In addition to our results, several other pioneering studies have shown that NOM patients with local regrowth have a higher predisposition to distant metastases than those patients with sustained cCR: 18% vs 5% and 36% vs 1%. Although our 30-month distant metastasis-free rate (73%) after salvage surgery was lower compared to the study conducted by van der Sande et al.[15] with a 24-month metastatic disease rate of 91.8%, our 30-month overall survival rate was 91% among patients undergoing "salvage surgery" and 98.4% in the entire NOM cohort, which is promising. All these findings show that local regrowth is a risk in terms of short- and long-term clinical outcomes, which cannot be overcome with frequent surveillance or "*salvage surgery*". Currently, it is still unclear whether the risk of disease progression is related to the deferral of surgery, local recurrence of tumor cells with a high metastatic progression potential, or inherited aggressive tumor biology associated with incomplete response to neoadjuvant therapy.

Study Limitations

The major limitation of the study was the small sample size and intermediate surveillance period. As we expect some degree of change in the long-term interval, another weakness was that associated with the nature of retrospective studies, including selection bias and recall bias. However, in contrast to large-scale international databases with heterogeneity in neoadjuvant treatment, interpretation of cCR, surveillance protocols, diagnosis of local regrowth, and salvage surgery approaches, our cohort consisted of two comprehensive cancers institutions collaborating for many years with precisely the same clinical approach in terms of LADRC patients NOM.

Conclusion

This study showed that a NOM protocol for LADR patients with cCR following neoadjuvant treatment was a safe and promising treatment option with a "salvage surgery" rate of 100% after local regrowth. Uncontrolled disease progression after salvage surgery among local regrowth patients was observed in 81%, and in 96.8% in the entire NOM cohort. Overall survival was 91% among local regrowth patients and 97.9% in the whole cohort. These findings suggest NOM in LADRC patients in comprehensive cancer centers with experienced multidisciplinary teams consisting of surgeons, medical and radiation oncologists, pathologists and radiologists can be effective. It is important to keep in mind that a reliable and frequent NOM surveillance protocol is the key to success.

Ethics

Ethics Committee Approval: Retrospective study.

Informed Consent: Every patient signed an infomred consent previous to NOM or surgery. They also allowed us to use their information for research.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: C.B.K., M.K., H.A.B., Concept: İ.Ö., E.B., C.B.K., Y.K., Design: İ.Ö., C.B.K., M.K., Data Collection or Processing: Analysis or Interpretation: B.G., B.A., M.T.B., D.B., E.B., Literature Search: M.B., Y.K., B.G., Writing: İ.Ö., C.B.K., M.K.

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References

1. Maas M, Nelemans PJ, Valentini V, Das P, Rödel C, Kuo LJ, Calvo FA, García-Aguilar J, Glynne-Jones R, Haustermans K, Mohiuddin M, Pucciarelli S, Small W Jr, Suárez J, Theodoropoulos G, Biondo S, Beets-Tan RG, Beets GL. Long-term outcome in patients with a pathological complete response after chemoradiation for rectal cancer: A pooled analysis of individual patient data. Lancet Oncol 2010;11:835-844.
2. Smith JJ, Strombom P, Chow OS, Roxburgh CS, Lynn P, Eaton A, Widmar M, Ganesh K, Yaeger R, Cercek A, Weiser MR, Nash GM, Guillem JG, Temple LKF, Chalasani SB, Fuqua JL, Petkovska I, Wu AJ, Reyngold M, Vakiani E, Shia J, Segal NH, Smith JD, Crane C, Gollub MJ, Gonen M, Saltz LB, Garcia-Aguilar J, Paty PB. Assessment of a Watch-and-Wait Strategy for Rectal Cancer in Patients With a Complete Response After Neoadjuvant Therapy. JAMA Oncol 2019;5:e185896.
3. de Neree Tot Babberich MPM, van Groningen JT, Dekker E, Wiggers T, Wouters MWJM, Bemelman WA, Tanis PJ; Dutch Surgical Colorectal Audit. Laparoscopic conversion in colorectal cancer surgery; is there any improvement over time at a population level? Surg Endosc 2018;32:3234-3246.
4. Paun BC, Cassie S, MacLean AR, Dixon E, Buie WD. Postoperative complications following surgery for rectal cancer. Ann Surg 2010;251:807-818.
5. Hendren SK, O'Connor BI, Liu M, Asano T, Cohen Z, Swallow CJ, Macrae HM, Gryfe R, McLeod RS. Prevalence of male and female sexual dysfunction is high following surgery for rectal cancer. Ann Surg 2005;242:212-223.

6. Habr-Gama A, Perez RO, Nadalin W, Sabbaga J, Ribeiro U Jr, Silva e Sousa AH Jr, Campos FG, Kiss DR, Gama-Rodrigues J. Operative versus nonoperative treatment for stage 0 distal rectal cancer following chemoradiation therapy: long-term results. Ann Surg 2004;240:711-718.
7. Habr-Gama A, Gama-Rodrigues J, São Julião GP, Proscurshim I, Sabbagh C, Lynn PB, Perez RO. Local recurrence after complete clinical response and watch and wait in rectal cancer after neoadjuvant chemoradiation: impact of salvage therapy on local disease control. Int J Radiat Oncol Biol Phys 2014;88:822-828.
8. Martens MH, Maas M, Heijnen LA, Lambregts DM, Leijtens JW, Stassen LP, Breukink SO, Hoff C, Belgers EJ, Melenhorst J, Jansen R, Buijsen J, Hoofwijk TG, Beets-Tan RG, Beets GL. Long-term outcome of an organ preservation program after neoadjuvant treatment for rectal cancer. J Natl Cancer Inst 2016;108:djw171.
9. Appelt AL, Pløen J, Harling H, Jensen FS, Jensen LH, Jørgensen JC, Lindebjerg J, Rafaelsen SR, Jakobsen A. High-dose chemoradiotherapy and watchful waiting for distal rectal cancer: a prospective observational study. Lancet Oncol 2015;16:919-927.
10. Renehan AG, Malcomson L, Emsley R, Gollins S, Maw A, Myint AS, Rooney PS, Susnerwala S, Blower A, Saunders MP, Wilson MS, Scott N, O'Dwyer ST. watch-and-wait approach versus surgical resection after chemoradiotherapy for patients with rectal cancer (the OnCoRe project): a propensity-score matched cohort analysis. Lancet Oncol 2016;17:174-183.
11. Dossa F, Chesney TR, Acuna SA, Baxter NN. A watch-and-wait approach for locally advanced rectal cancer after a clinical complete response following neoadjuvant chemoradiation: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol 2017;2:501-513.
12. van der Valk MJM, Hilling DE, Bastiaannet E, Meershoek-Klein Kranenbarg E, Beets GL, Figueiredo NL, Habr-Gama A, Perez RO, Renehan AG, van de Velde CJH; IWWD Consortium. Long-term outcomes of clinical complete responders after neoadjuvant treatment for rectal cancer in the International Watch & Wait Database (IWWD): an international multicentre registry study. Lancet 2018;391:2537-2545.
13. Smith JJ, Chow OS, Gollub MJ, Nash GM, Temple LK, Weiser MR, Guillem JG, Paty PB, Avila K, Garcia-Aguilar J; Rectal Cancer Consortium. Organ Preservation in Rectal Adenocarcinoma: a phase II randomized controlled trial evaluating 3-year disease-free survival in patients with locally advanced rectal cancer treated with chemoradiation plus induction or consolidation chemotherapy, and total mesorectal excision or nonoperative management. BMC Cancer 2015;15:767.
14. Beets-Tan RGH, Lambregts DMJ, Maas M, Bipat S, Barbaro B, Curvo-Semedo L, Fenlon HM, Gollub MJ, Gourtsoyianni S, Halligan S, Hoeffel C, Kim SH, Laghi A, Maier A, Rafaelsen SR, Stoker J, Taylor SA, Torkzad MR, Blomqvist L. Magnetic resonance imaging for clinical management of rectal cancer: updated recommendations from the 2016 European Society of Gastrointestinal and Abdominal Radiology (ESGAR) consensus meeting. Eur Radiol 2018;28:1465-1475.
15. van der Sande ME, Figueiredo N, Beets GL. Management and Outcome of Local Regrowths in a Watch-and-wait Prospective Cohort for Complete Responses in Rectal Cancer. Ann Surg 2021;274:1056-1062.
16. Quirke P, Steele R, Monson J, Grieve R, Khanna S, Couture J, O'Callaghan C, Myint AS, Bessell E, Thompson LC, Parmar M, Stephens RJ, Sebag-Montefiore D; MRC CR07/NCIC-CTG CO16 Trial Investigators; NCRI Colorectal Cancer Study Group. Effect of the plane of surgery achieved on local recurrence in patients with operable rectal cancer: a prospective study using data from the MRC CR07 and NCIC-CTG CO16 randomised clinical trial. Lancet 2009;373:821-828.
17. Keskin M, Bayraktar A, Sivirikoz E, Yegen G, Karip B, Saglam E, Bulut MT, Balik E. Sparing Sphincters and Laparoscopic Resection Improve Survival by Optimizing the Circumferential Resection Margin in Rectal Cancer Patients. Medicine (Baltimore) 2016;95:2669.
18. Garcia-Aguilar J, Chow OS, Smith DD, Marcet JE, Cataldo PA, Varma MG, Kumar AS, Oommen S, Coutsoftides T, Hunt SR, Stamos MJ, Ternent CA, Herzig DO, Fichera A, Polite BN, Dietz DW, Patil S, Avila K; Timing of Rectal Cancer Response to Chemoradiation Consortium. Effect of adding mFOLFOX6 after neoadjuvant chemoradiation in locally advanced rectal cancer: a multicentre, phase 2 trial. Lancet Oncol 2015;16:957-966.
19. Lefevre JH, Mineur L, Kotti S, Rullier E, Rouanet P, de Chaisemartin C, Meunier B, Mehrdad J, Cotte E, Desrame J, Karoui M, Benoist S, Kirzin S, Berger A, Panis Y, Piessen G, Saudemont A, Prudhomme M, Peschaud F, Dubois A, Loriau J, Tuech JJ, Meurette G, Lupinacci R, Goasgen N, Parc Y, Simon T, Tiret E. Effect of Interval (7 or 11 weeks) Between Neoadjuvant Radiochemotherapy and Surgery on Complete Pathologic Response in Rectal Cancer: A Multicenter, Randomized, Controlled Trial (GRECCAR-6). J Clin Oncol 2016;34:3773-3780.

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RESEARCH ARTICLE

Impact of Lymph Node Ratio as a Prognostic Factor for Survival in Colorectal Cancer Patients

Murat Bulut Özkan[1], Ahmet Erdoğan[2], Cem Emir Güldoğan[3], Erdinç Çetinkaya[4], Ahmet Keşşaf Aşlar[5]

[1]Hitit University Faculty of Medicine, Department of General Surgery, Çorum, Turkey
[2]Elbistan State Hospital, Clinic of General Surgery, Kahramanmaraş, Turkey
[3]Liv Hospital, Clinic of General Surgery, Ankara, Turkey
[4]Ankara City Hospital, Clinic of General Surgery, Ankara, Turkey
[5]Ankara Yıldırım Beyazıt University Faculty of Medicine, Department of General Surgery, Ankara, Turkey

ABSTRACT

Aim: The aim of this study was to investigate the impact of the ratio of metastatic lymph nodes to total harvested lymph nodes on survival rates.
Method: Data from patients with colorectal cancer undergoing surgery in Ankara Numune Training and Research Hospital, Clinic of General Surgery between June 2010 and June 2015 was retrospectively analyzed. We gathered data about patients' age, gender, operational status (elective or emergency), operation format (with laparotomy or laparoscopic), performed procedures, localization of the tumor, TNM stage, Dukes' stage, adjuvant/neoadjuvant chemoradiotherapy history, harvested lymph nodes, lymph node ratio (LNR) and overall survival. We conducted univariant and multivariant analyses to determine the relation between LNR and survival.
Results: Forty-five patients were excluded, resulting in a study cohort of 391 patients with a mean age of 62.7±13.7 years, of whom 234 (59.8%) were male. Based on the results of univariant analysis, the cut-off values for LNR 0.2 and 0.5 showed a significant association with survival (LNR: 0.2 $p<0.05$ and LNR: 0.5 $p<0.05$). These LNR values maintained a significant relationship with survival after multivariant analysis (LNR: 0.2 $p<0.05$ and LNR: 0.5 $p<0.05$).
Conclusion: In this retrospective study LNR was a significant prognostic factor for survival in patints undergoing surgery for colorectal cancer. To determine the prognosis of the patients with suboptimal lymph node yield and decide the adjuvant therapy choices, LNR can be used as a helpful indicator with the total number of harvested lymph nodes and the number of positive lymph nodes.
Keywords: Colon cancer, rectal cancer, lymph node ratio

Introduction

Colorectal cancer is one of the most common cancers, both globally and in Turkey, and is also one of the leading causes of cancer-related deaths. The prevalence is 24 per 100,000 in men and 15 per 100,000 women in Turkey.[1]

The stage of the disease varies according to the degree of invasion of the tumor (T), the number of metastatic lymph nodes (N), and the presence of distant metastases (M). At least 12 (10-14) lymph node sampling is required for an accurate N-staging.[2] Although a sample of 12 lymph nodes seems sufficient for accurate staging, studies have shown that removing more lymph nodes affects survival and causes a stage shift in some patients.[3,4] In the last few years, there have been studies suggesting that not only the number of lymph nodes removed but also the ratio of the number of metastatic lymph nodes to the total number of lymph nodes removed, called the lymph node ratio (LNR) should be used as a prognostic factor.[5]

TNM stage is the most important prognostic factor. While a 5-year survival of over 90% is expected in stage 1 patients, this rate is around 10% in stage 4 patients.[6] Tumor depth, the number of metastatic lymph nodes, and presence of metastases adversely affect survival separately. Despite the recommendation of sampling at least 12 lymph nodes for accurate TNM staging, after neoadjuvant protocols there has been a tendency for a decrease in the number of lymph nodes removed. In these patients, there have been reports

Address for Correspondence: Murat Bulut Özkan MD, Hitit University Faculty of Medicine, Department of General Surgery, Çorum, Turkey
E-mail: bulutozkan@gmail.com **ORCID ID:** orcid.org/0000-0003-4683-3772
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that the positive LNR is reliable to both decide on the proper adjuvant therapy and make a more accurate decision about the prognosis have started to appear recently.[7,8]

Materials and Methods

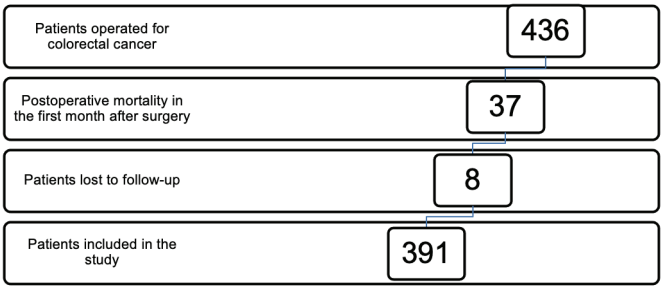
This study retrospectively analyzed the records of patients who were operated for colorectal cancer in Ankara Numune Training and Research Hospital between June 2010 and June 2015. Demographic data, date of surgery, tumor location, which operation was performed, whether the operation was emergency or elective, whether the procedure was conservative or laparoscopic, and whether the patient received adjuvant or neoadjuvant chemo/radiotherapy were examined. Disease parameters collected included the stage of the tumor, the total number of removed lymph nodes, the number of positive lymph nodes, the ratio of the number of positive lymph nodes to the total number of lymph nodes (lymph node positivity rate), the grade of the tumor, the stage according to the Dukes' (modified Astler Coller) classification, and the presence of metastases examined. Data such as survival, disease-free survival, presence of recurrence, time of recurrence, and date of death were analyzed in the postoperative follow-up.

Data from a total of 436 patients who were operated on for colorectal cancer between these dates were available. However, 45 patients were excluded from the study because: eight were lost to follow-up; 28 died in the early postoperative period (14 emergency surgery, 14 elective surgery); and nine died in the first month (three emergency, six elective surgery) (Flow Chart 1).

Approval for this study was obtained from the Ankara Numune Training and Research Hospital Clinical Research Ethics Committee (approval number: 734/2016). All patients informed consent was obtained.

Statistical Analysis

Statistical analysis was performed using the SPSS, version 23 (IBM Inc., Armonk, NY, USA). Chi-square test and univariate analysis test were used for descriptive statistical analyzes between groups. The Kaplan-Meier method was used for the analysis of survival times. The multivariate analysis test was used to analyze the factors affecting survival. A p-value of <0.05 was accepted for statistical significance.



Flow Chart 1. Flow chart of patient selection

Results

Of the study cohort of 391 patients, 157 (40.2%) were female, and 234 (59.8%) were male. The ages of the patients ranged from 32 to 95. Therefore, the mean ± standard deviation age was 62.7±13.7 years, ranging from 32 to 95 years.

Of the operations performed, 89 (22.8%) were performed as an emergency, and the remaining 302 (77.2%) were performed electively. The procedures of 63 (16.1%) patients, mostly after 2013, were completed laparoscopically, and the operations of 15 patients (3.8%) were started laparoscopically and switched to laparotomy for various reasons. The remaining 313 cases (80.1%) were performed by laparotomy. All emergency cases were performed by laparotomy.

Tumor location was as follows: rectum n=148 (38%); sigmoid colon n=96 (24.7%) and the cecum n=48 (13.3%). Tumors were staged according to the cancer staging atlas published by the American Joint Committee on Cancer in 2012. Tumor staging was: n=4 (1.0%) carcinoma *in situ* (Tis); T1-stage n=17 (4.3%); T2-stage n=25 (6.4%); T3-stage n=137 (35.0%); and T4-stage accounted for more than half of cases, n=204 (52.2%). Thus very few cases were diagnosed at an early stage. Therefore, 4 (1.0%) patient were diagnosed as stage 0, 37 (9.6%) patient as stage 1, 179 (46.5%) patient as stage 2 and 117 (30.4%) patient as stage 3, and 48 patients (12.5%) had metastatic disease at the time of diagnosis.

In terms of overall survival 297 (75.9%) of 391 patients survived, and 94 (24.1%) died. When the univariate analyzes of parametric data on survival was examined, there was no statistical relationship between gender and survival. Subtotal colectomy tended to be associated with the highest mortality rate, but there is no statistical correlation between the operations performed and survival. When the survival of the patients was assessed in terms of surgery technique, the survival of cases performed laparoscopically was higher, probably as a result of selection of patients suitable for laparoscopy and it was notable that none of the emergency cases was operated with laparoscopy. The survival of emergency cases was found to be lower than that of elective cases.

The survival rates of our population according to TNM stage, N-stage, and pathological grade of the tumor decrease as the stage and grade increase, which is consistent with the general population. While there are very low mortality rates in stage 0 and stage 1 patients according to TNM stage, we see mortality rates up to 41% in stage 4 patients.

When patients were stratified into groups according to the N-stage of the TNM classification, there were 235 patients in the N0 stage group, 107 patients in the N1-stage, and 42 patients in the N2-stage. In the survival analysis according to N-stage, the N-stage was found to be associated with survival. As seen in Table 1, when the LNR was set at 0.2, the survival rate of 58 patients above this rate was 46.6%, while the survival rate of 333 patients below this rate was 81.1.2%. When the LNR was set at 0.5, the survival rate was 42.9% in 28 patients above this value and 78.5% in 363 patients below this value. These results suggest a statistically significant relationship between LNR and survival.

The age, total lymph node counts, positive lymph node counts, LNR and follow-up times of living and deceased patients were compared by univariate analysis (Table 2).

Table 1. Survival rates by lymph node characteristics

	Total	Alive	Dead	p
LNR: 0.2				
LNR <0.2	333	270 (81.1)	63 (18.9)	<0.001*
LNR >0.2	58	27 (46.6)	31 (53.4)	
LNR: 0.5				
LNR <0.5	363	285 (78.5)	78 (21.5)	<0.001*
LNR >0.5	28	12 (42.9)	16 (57.1)	
N-stage				
N0	235	192 (81.7)	43 (18.3)	
N1	107	73 (68.2)	34 (31.8)	0.012*
N2	42	29 (69.0)	13 (31.0)	

Data are shown as n (%). LNR: Lymph node ratio, *: Statistically significant

The analysis of deaths showed that 69.1% of the deaths occurred within the first 24 months. In summary, age, the low total number of lymph nodes, a high number of positive lymph nodes, a high rate of positive lymph nodes, and a short follow-up period are statistically associated with poor survival outcomes.

Subsequently, multivariate analysis was performed to assess factors associated with survival. According to the results obtained when the parameters of gender, surgery status (emergency/elective), TNM stage, pathological grade, adjuvant/neoadjuvant chemo/radiotherapy history, N-stage, and LNR as 0.2 and 0.5 were included in the model, the TNM stage, pathological grade, adjuvant chemotherapy, N-stage, and LNR >0.2 had an effect on survival (Table 3). This model suggested that a positive LNR of 0.5 had no effect on survival because, by definition those with a LNR >0.2 also included those with a LNR >0.5. For this reason, those with a LNR >0.5 statistically reduce the effect. Therefore, we created a new model to investigate the effect of using a 0.5 LNR threshold value on survival which only included the parameter of LNR >0.5 in the model (Table 4). In this new model TNM stage, pathological grade, history of adjuvant chemotherapy, neoadjuvant radiotherapy, and LNR >0.5 were associaited with survival this time.

The relationship between N-stage, positive LNR and survival was examined by performing a projection analysis with Kaplan Meier. This showed that the average life expectancy in N0 was approximately 51 months, the average life expectancy in a patient in N2 stage was approximately 40 months. As seen in Figure 1, there was a significant difference between survivals according to lymph node stage.

In the projection analysis using a threshold value of 0.2 for the positive LNR, the average life expectancy in patients

Table 2. Univariate analysis results for non-parametric data

		Age (years)	Total LN	Positive LN	LNR	Follow-up period
	Mean	61.38	16.38	1.13	0.0672	27.3367
	Median	61.00	15.00	0.00	0.0000	25.0000
Alive	Standard deviation	13,597	11.981	2.463	0.15616	18.54180
	Minimum	32	0	0	0.00	2.00
	Maximum	89	65	17	1.00	66.00
	Mean	66.84	12.29	1.99	0.1914	19.2234
	Median	68.50	9.00	1.00	0.0400	15.5000
Dead	Standard deviation	13,093	9.487	4.007	0.28855	14.21430
	Minimum	25	0	0	0.00	2.00
	Maximum	95	41	28	1.00	56.00
p		0.001*	0.001*	0.003*	0.001*	0.001*

LN: Lymph node, LNR: Lymph node ratio, *: Statistically significant

Table 3. Multivariate analysis results - 1

Effect	Model fitting criteria	Likelihood ratio tests		
	-2 Log likelihood of reduced model	Chi-square	df	p
Intercept	182,716[a]	0.001	0	-
Gender	182,784	0.068	1	0.794
Emergency/elective	182,761	0.046	1	0.831
TNM stage	193,804	11,088	4	0.026*
Grade	196,600	13,884	3	0.003*
Adjuvant chemotherapy	190,019	7,303	1	0.007*
Neoadjuvant chemotherapy	184,006	1,290	1	0.256
Adjuvant radiotherapy	184,215	1,499	1	0.221
Neoadjuvant radiotherapy	186,327	3,611	1	0.057
LNR >0.2	191,355	8,639	1	0.003*
LNR >0.5	183,777	1,061	1	0.303
N-stage	190,951	8,235	2	0.016*

*: Statistically significant, LNR: Lymph node ratio

Table 4. Multivariate analysis results - 2

Effect	Model fitting criteria	Likelihood ratio tests		
	-2 Log likelihood of reduced model	Chi-square	df	p
Intercept	188,583[a]	0.001	0	-
Gender	188,635	0.052	1	0.819
Emergency/elective	188,754	0.172	1	0.679
TNM stage	199,355	10,773	4	0.029*
Grade	204,167	15,585	3	0.001*
Adjuvant chemotherapy	194,220	5,637	1	0.018*
Neoadjuvant chemotherapy	190,807	2,225	1	0.136
Adjuvant radiotherapy	189,901	1,318	1	0.251
Neoadjuvant radiotherapy	193,389	4,806	1	0.028*
LNR >0.5	197,385	8,802	1	0,003*
N-stage	190,675	2,092	2	0,351

*: Statistically significant, LNR: Lymph node ratio,

with a LNR<0.2 was approximately 51 months, and the life expectancy in patients with a LNR >0.2 was approximately 34 months (Figure 2) Similarly,when the LNR threshold was set at 0.5, the average life expectancy in patients with

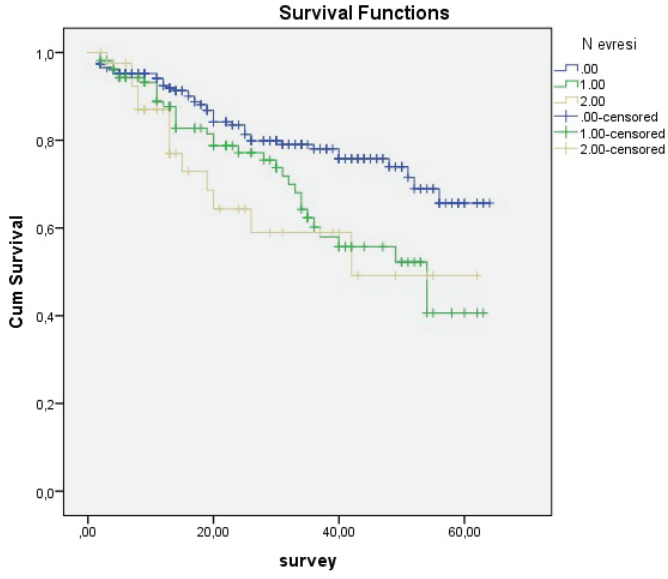


Figure 1. Projection analysis between lymph node stage (N) and survival

LNR<0.5 was approximately 49 months, while the average life expectancy in those with LNR >0.5 was approximately 33 months (Figure 3).

The estimated life expectancy of patients with insufficient lymph node number, when the LNR threshold was 0.5, was approximately 42 months for those with a LNR <0.5 and approximately 33 months for those with a LNR >0.5 (Figure 4).

The patient population was limited to only lymph node-positive patients and this resulted in a sub-group of 117 patients. Univariate analysis of this sub-group showed

that patient gender, the operation performed, emergency/elective status, and the type of operation had no effect on survival but the pathological grade of the tumor and LNR were found to have an impact on survival. When the LNR threshold value was set at 0.2, the survival rates were 79.0% in patients with LNR <0.2, while it was 58.3% in patients with LNT >0.2 (p<0.05). Similarly using a LNR threshold of 0.5, the survival rate was 74.8% in patients with LNR <0.5 and 57.1% in patients with LNR >0.5 (p>0.05).

In this sub-group using projection analysis and a LNR threshold of 0.2, the estimated life expectancy was approximately 40 months for LNR >0.2 and significantly longer at 49 months for LNR <0.2 (Figure 5). Repeating this analysis with an LNR threshold of 0.5 showed the estimated life expectancies to be 35 and 47 months for patients with LNR >0.5 and <0.5, respectively (Figure 6) which was significantly different.

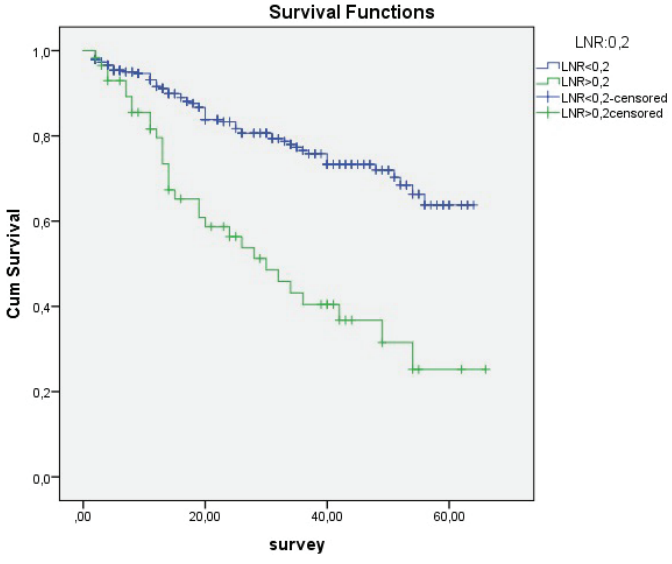


Figure 2. Projection analysis between lymph node ratio (LNR) and survival (LNR is accepted as 0.2)

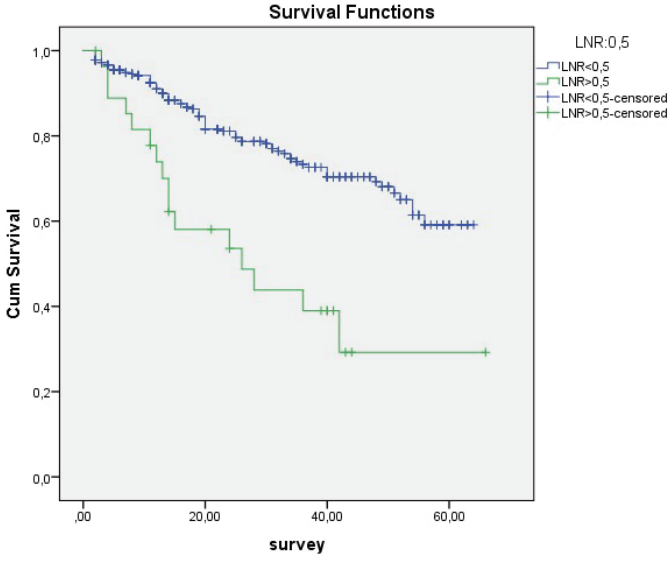


Figure 3. Projection analysis between lymph node ratio (LNR) and survival (LNR is accepted as 0.5)

Discussion

Colorectal cancer is one of the most common cancers in the world and one of the most common causes of death. Most (90%) cases occur in people aged 50 and over.[9] However, in recent years, there has been an increase in the incidence of colorectal cancer among the young population in Western

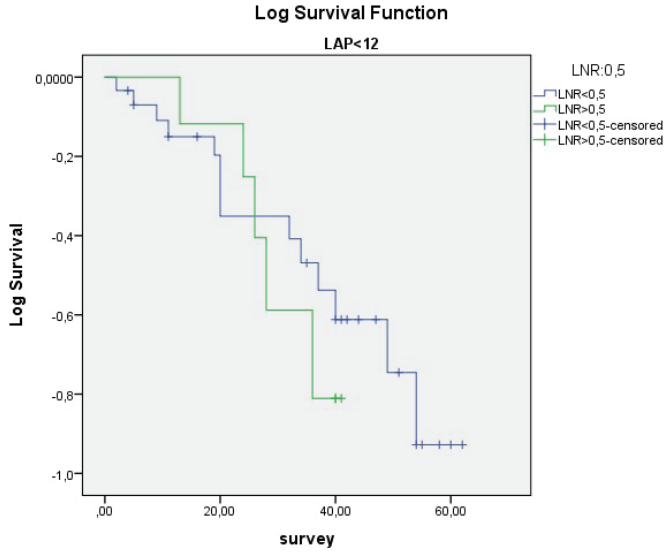


Figure 4. Projection analysis between lymph node ratio (LNR) and survival in patients with less than 12 lymph nodes removed (when LNR is accepted as 0.5)

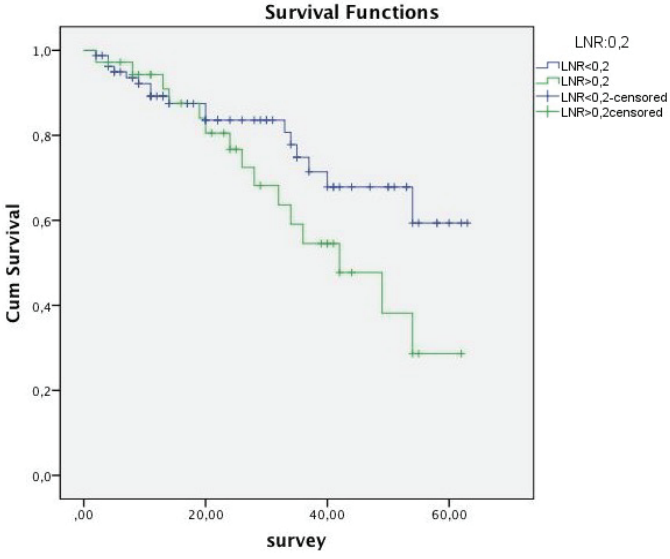


Figure 5. Projection analysis between lymph node ratio (LNR) and survival in lymph node-positive patients (LNR accepted as 0.2)

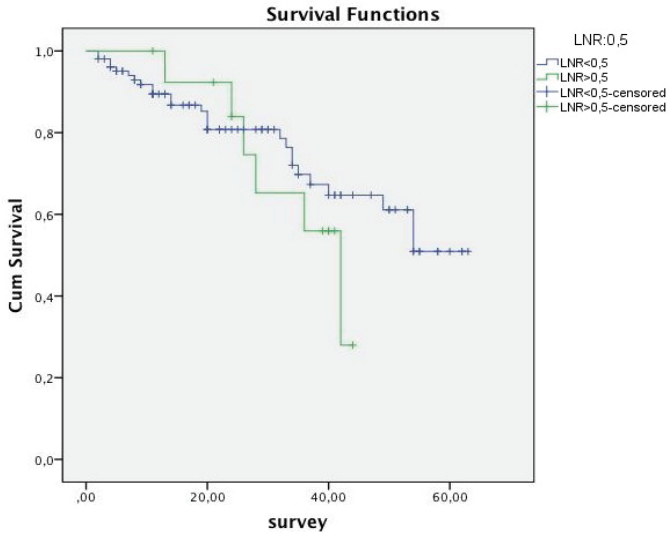


Figure 6. Projection analysis between lymph node ratio (LNR) and survival in lymph node-positive patients (LNR accepted as 0.5)

countries.[10] A decrease in colorectal cancer mortality has been reported as a result of colorectal cancer screening programs.[11] Therefore, prognostic factors are once more gaining importance, as the incidence in younger patients and survival times increase and as mortality decreases. With the widespread use of neoadjuvant chemoradiotherapy, the total number of lymph nodes removed had tended to decrease, and the LNR has gained importance in terms of both staging and prognosis.

In a study conducted by Bando et al.[12], in 650 patients who underwent curative gastrectomy and D2 lymph node dissection, a significant relationship between the rate found when the number of metastatic lymph nodes was divided by the total number of lymph nodes and 5-year survival was reported. Similarly, in a study conducted by van der Wal et al.[13] on LNR in axillary lymph nodes and survival in patients with breast cancer, it was concluded that LNR was a good predictor of survival. Berger et al.[14] also reported that LNR was a prognostic factor for both overall survival and disease-free survival in patients with pancreatic adenocarcinoma who underwent pancreaticoduodenectomy.

Rullier et al.[15] conducted a study on 495 patients, of whom 332 received preoperative chemoradiotherapy, and who were operated on for rectal cancer. When the groups that did and did not receive chemoradiotherapy were compared, it was found that there was a significant difference in the total number of lymph nodes removed and the number of positive lymph nodes.[15] In other similar studies and meta-analyses, it has been reported that preoperative chemoradiotherapy can reduce the total number of lymph nodes removed by up to 50% and that approximately 30% of patients may have insufficient lymph node numbers for staging.[16,17,18]

In our study population male patients were more common than females. While the global female/male ratio in the world is 1:1.2, this ratio was 1:1.5 in our population. This was closer to the rate in developing countries.[19] The mean and median ages were 62.6 and 63 years, respectively, which is consistent with the literature. In terms of tumor location, our study population was consistent with the literature in that rectum was the most common location followed by sigmoid colon and then cecum. TNM stage is the most important prognostic factor in colorectal cancers. In our study, most of the patients were diagnosed at stage 2 and later, and very few at stage 0 and stage 1. The survival rates, in accordance with the literature, decreased as the stage increased. While survival was 100% at stage 0, it was 58.3% in patients with TNM stage 4 disease.

Lymph node involvement is a decisive consideration for both prognosis and adjuvant therapy. The relationship between LNR and survival in colorectal cancers was first suggested by Berger et al.[6] Wang et al.[20], in an analysis of 24,477 patients, suggested that LNR was a more accurate prognostic factor than the N-stage in stage 3 patients. When our patients were classified according to the N-stage there was an assocaition between N-stage and survival. When the LNR threshold value was 0.2, the survival rate was found to be 81.1% in patients below this value and 46.6% in patients above this value. Similarly, when the LNR threshold value was 0.5, these rates changed to 78.5% and 42.9%, respectively. The multivariate analysis showed that both LNR threshold values were factors affecting survival. It was concluded that in patients with insufficient lymph nodes removed for staging, survival was shorter in patients with LNR >0.5 than in patients with LNR <0.5.

Klos et al.[21] performed a study in patients who had undergone rectal cancer surgery after neoadjuvant chemoradiotherapy and found that the probability of having less than 12 lymph nodes removed in patients was increased and that LNR was a better staging method than the number of positive lymph nodes in these patients. Similarly, in a study conducted by Sjo et al.[22], it was shown that LNR was a stronger prognostic factor than the total number of lymph nodes in stage 3 patients. A study conducted in Ireland suggested that LNR remained unchanged despite a decrease in the total lymph node number in patients receiving neoadjuvant therapy, and it was a more reliable prognostic tool for patients in this group.[23] There are also studies comparing positive lymph node rates with TNM staging. In these studies, LNR is complementary to the TNM stage, especially in stage 3 patients, since it gives more accurate results in estimating survival than the N-stage.[24,25]

The factors affecting the number of lymph nodes removed are not limited to neoadjuvant therapy. These may be related

to the patient (age, body mass index, time of diagnosis), tumor (location, T-stage, size), surgeon, and pathologist examining the specimen[26,27,28]. As there are so many factors affecting the number of sampled lymph nodes, it seems plausible that not only the number of lymph nodes but also the LNR should be a determining factor in the prognosis of colorectal cancer.

In our study, only patients who were operated on within the last five years were retrospectively investigated. Therefore, the relatively short follow-up period, the retrospective nature of the study, and the small number of patients are limiting factors of the study.

Conclusion

Colorectal cancer remains a serious health problem, despite the prevalence of screening programs and emerging treatment options. The increase in its incidence in younger patients and the prolongation of life expectancy once again emphasize the value of useful prognostic factors for the treatment of future patients.

In this study, which examined LNR as a prognostic factor, it was shown to be an important factor affecting survival. It can be used as a useful marker in addition to the number of lymph nodes removed or the number of positive lymph nodes in determining the prognosis and adjuvant treatment options in patients with insufficient lymph nodes removed for staging.

Ethics

Ethics Committee Approval: Approval for this study was obtained from the Ankara Numune Training and Research Hospital Clinical Research Ethics Committee (approval number: 734/2016).

Informed Consent: All patients informed consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.B.Ö., A.E., C.E.G., E.Ç., A.K.A., Concept: A.K.A., M.B.Ö., Design: A.K.A., E.Ç., C.E.G., M.B.Ö., Data Collection or Processing: A.E., M.B.Ö., Analysis or Interpretation: A.K.A., E.Ç., M.B.Ö., Literature Search: M.B.Ö., A.E., C.E.G., E.Ç., A.K.A., Writing: A.K.A., M.B.Ö.

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References

1. Turkish Cancer Statistics 2012. 2015; Available from: http://kanser.gov.tr/daire-faaliyetleri/kanser-istatistikleri/1710-2012-t%C3%BCrkiye-kanser-istatistikleri.html.
2. Kotake K, Honjo S, Sugihara K, Hashiguchi Y, Kato T, Kodaira S, Muto T, Koyama Y. Number of Lymph Nodes Retrieved is an Important Determinant of Survival of Patients with Stage II and Stage III Colorectal Cancer. Jpn J Clin Oncol 2011;42:29-35.
3. Bernhoff R, Holm T, Sjövall A, Granath F, Ekbom A, Martling A. Increased lymph node harvest in patients operated on for right-sided colon cancer: a population-based study. Colorectal Dis 2012;14:691-696.
4. Chen SL, Steele SR, Eberhardt J, Zhu K, Bilchik A, Stojadinovic A. Lymph Node Ratio as a Quality and Prognostic Indicator in Stage III Colon Cancer. Ann Surg 2011;253:82-87.
5. AJCC Cancer Stagin Manual 7th ed. 2010.
6. Berger AC, Sigurdson ER, LeVoyer T, Hanlon A, Mayer RJ, Macdonald JS, Catalano PJ, Haller DG. Colon Cancer Survival is Associated With Decreasing Ratio of Metastatic to Examined Lymph Nodes. J Clin Oncol 2005;23:8706-8712.
7. Park IJ, Yu CS, Lim SB, Yoon YS, Kim CW, Kim TW, Kim JH, Kim JC. Ratio of metastatic lymph nodes is more important for rectal cancer patients treated with preoperative chemoradiotherapy. World J Gastroenterol 2015;21:3274-3281.
8. Garborg K. Colorectal Cancer Screening. Surg Clin North Am 2015;95:979-989.
9. Labianca R, Nordlinger B, Beretta GD, Mosconi S, Mandalà M, Cervantes A, Arnold D; ESMO Guidelines Working Group. Early colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013;24(Suppl 6):64-72.
10. Scholefield JH, Moss SM, Mangham CM, Whynes DK, Hardcastle JD. Nottingham trial of faecal occult blood testing for colorectal cancer: a 20-year follow-up. Gut 2011;61:1036-1040.
11. Shaukat A, Mongin SJ, Geisser MS, Lederle FA, Bond JH, Mandel JS, Church TR. Long-Term Mortality after Screening for Colorectal Cancer. N Engl J Med 2013;369:1106-1114.
12. Bando E, Yonemura Y, Taniguchi K, Fushida S, Fujimura T, Miwa K. Outcome of ratio of lymph node metastasis in gastric carcinoma. Ann Surg Oncol 2002;9:775-784.
13. van der Wal BC, Butzelaar RM, van der Meij S, Boermeester MA. Axillary lymph node ratio and total number of removed lymph nodes: predictors of survival in stage I and II breast cancer. Eur J Surg Oncol 2002;28:481-489.
14. Berger AC, Watson JC, Ross EA, Hoffman JP. The metastatic/examined lymph node ratio is an important prognostic factor after pancreaticoduodenectomy for pancreatic adenocarcinoma. Am Surg 2004;70:235-240.
15. Rullier A, Laurent C, Capdepont M, Vendrely V, Belleannée G, Bioulac-Sage P, Rullier E. Lymph nodes after preoperative chemoradiotherapy for rectal carcinoma: number, status, and impact on survival. Am J Surg Pathol 2008;32:45-50.
16. Miller ED, Robb BW, Cummings OW, Johnstone PA. The Effects of Preoperative Chemoradiotherapy on Lymph Node Sampling in Rectal Cancer. Dis Colon Rectum 2012;55:1002-1007.
17. Damin DC, Rosito MA, Contu PC, Tarta C, Ferreira PR, Kliemann LM, Schwartsmann G. Lymph node retrieval after preoperative chemoradiotherapy for rectal cancer. J Gastrointest Surg 2012;16:1573-1580.
18. Ha YH, Jeong SY, Lim SB, Choi HS, Hong YS, Chang HJ, Kim DY, Jung KH, Park JG. Influence of preoperative chemoradiotherapy on the number of lymph nodes retrieved in rectal cancer. Ann Surg 2010;252:336-340.
19. GLOBOCAN 2012. Available from: http://globocan.iarc.fr/.
20. Wang J, Hassett JM, Dayton MT, Kulaylat MN. Lymph Node Ratio: Role in the Staging of Node-Positive Colon Cancer. Ann Surg Oncol 2008;15:1600-1608.
21. Klos CL, Bordeianou LG, Sylla P, Chang Y, Berger DL. The Prognostic Value of Lymph Node Ratio After Neoadjuvant Chemoradiation and Rectal Cancer Surgery. Dis Colon Rectum 2011;54:171-175.

22. Sjo OH, Merok MA, Svindland A, Nesbakken A. Prognostic Impact of Lymph Node Harvest and Lymph Node Ratio in Patients With Colon Cancer. Dis Colon Rectum 2012;55:307-315.
23. Chang KH, Kelly NP, Duff GP, Condon ET, Waldron D, Coffey JC. Neoadjuvant therapy does not affect lymph node ratio in rectal cancer. Surgeon 2016;14:270-273.
24. Zhang J, Lv L, Ye Y, Jiang K, Shen Z, Wang S. Comparison of metastatic lymph node ratio staging system with the 7th AJCC system for colorectal cancer. J Cancer Res Clin Oncol 2013;139:1947-1953.
25. Moug SJ, Oliphant R, Balsitis M, Molloy RG, Morrison DS; West of Scotland Colorectal Cancer Managed Clinical Network. The lymph node ratio optimises staging in patients with node positive colon cancer with implications for adjuvant chemotherapy. Int J Colorectal Dis 2014;29:599-604.
26. Gonsalves WI, Kanuri S, Tashi T, Aldoss I, Sama A, Al-Howaidi I, Ganta A, Kalaiah M, Thota R, Krishnamurthy J, Fang X, Townley P, Ganti AK, Subbiah S, Silberstein PT. Clinicopathologic factors associated with lymph node retrieval in resectable colon cancer: A veterans' affairs central cancer registry (VACCR) database analysis. J Surg Oncol 2011;104:667-671.
27. Morikawa T, Tanaka N, Kuchiba A, Nosho K, Yamauchi M, Hornick JL, Swanson RS, Chan AT, Meyerhardt JA, Huttenhower C, Schrag D, Fuchs CS, Ogino S. Predictors of lymph node count in colorectal cancer resections: data from US nationwide prospective cohort studies. Arch Surg 2012;147:715-723.
28. Budde CN, Tsikitis VL, Deveney KE, Diggs BS, Lu KC, Herzig DO. Increasing the Number of Lymph Nodes Examined after Colectomy Does Not Improve Colon Cancer Staging. J Am Coll Surg 2014;218:1004-1011.

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RESEARCH ARTICLE

A Rare Cause of Right Lower Quadrant Abdominal Pain: Isolated Cecal Necrosis

Semra Demirli Atıcı, Mehmet Üstün, Emran Kuzey Avcı, Tayfun Kaya, Bülent Çalık

University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital, Clinic of General Surgery, İzmir, Turkey

ABSTRACT

Aim: Isolated cecal necrosis (ICN), a variant of ischemic colitis, is a rarely seen clinical condition. This aim of this case series was to evaluate the diagnosis and management of ICN.

Method: Patients operated between December 2013-January 2020 with the presumptive diagnosis of acute abdomen and intra-operatively diagnosed as ICN were evaluated retrospectively.

Results: There were 17 patients of whom nine (52.9%) were male. The mean age of the patients was 55.8 (range: 22-85) years. All the patients had at least one co-morbid disease, the most frequent of which were coronary artery disease, hypertension, and chronic renal failure. Fourteen (82.35%) underwent right hemicolectomy, and ileotransversostomy, while two (11.8%) had right hemicolectomy and Mikulicz ileocolostomy, and one (5.9%) underwent partial colonic resection with Mikulicz ileocolostomy due to limited cecal necrosis, which was diagnosed earlier. Six (35.3%) patients died.

Conclusion: ICN must be kept in mind in the differential diagnosis of acute abdomen with right lower quadrant localization, especially in patients with co-morbid diseases. Due to delayed diagnosis and complications, such as perforation, ICN had a high rate of morbidity and mortality.

Keywords: Acute abdomen, acute appendicitis, cecal necrosis, msenteriic ischemia, tocilizumab

Introduction

Isolated cecal necrosis (ICN), a rarely seen clinical condition, is a form of non-occlusive mesenteric ischemia. ICN mostly occurs due to decreased blood flow in the right colon, which may occur as a result of hypovolemic shock, hypotension, hemodialysis, chronic heart disease, cardiac arrhythmia, atherosclerosis, and drug use.[1] Most patients diagnosed with ICN attend the emergency service with right lower quadrant abdominal pain, and the primary diagnosis is usually acute appendicitis.[2,3] Although ICN and acute appendicitis have similar clinical symptoms and physical examination findings, the surgical procedure, incision type, and postoperative course are very different.[2] Thus, being aware of ICN and making the differentiative diagnosis from acute appendicitis is fundamental. This study aimed to evaluate the diagnosis and management of ICN with a case series of 17 cases.

Materials and Methods

This study was designed as a retrospective observational study. Seventeen patients diagnosed with ICN between December 2013-January 2020, were retrospectively analyzed. All patients were operated due to acute abdomen. Definitive diagnosis was made during the operation and with subsequent histopathological examination. Demographics features, clinical symptoms, laboratory and imaging data, co-morbidities, surgical procedure, and postoperative follow up data were extracted from the hospital records.

Approval from the University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital Institutional Research Ethics Board was obtained (approval number: 2021/04-17). Written informed consent was obtained from each patient who participated in this study.

Statistical Analysis

IBM SPSS Statistics 22 program was used in the statistical analyses when evaluating the findings of the study. Descriptive statistical methods (mean, standard deviation, and frequency) were used in the comparison of qualitative data.

Address for Correspondence: Semra Demirli Atıcı, MD, University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital, Clinic of General Surgery, İzmir, Turkey
E-mail: smrdemirli@hotmail.com **ORCID ID:** orcid.org/0000-0002-8287-067X
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Results

In total there were 17 patients diagnosed with ICN during the study period, with a mean age of 55.8 (22-85) years. Nine (52.9%) of the patients were male with a mean age of 63.5 years, and eight were female with a mean age of 62.3 years. All the patients had presented to the emergency service with right lower quadrant abdominal pain, that persisted for at least one day, and nausea. During the physical examinations, all of the patients had tenderness and rebound tenderness at the right lower abdominal quadrant. Abdominal computed tomography (CT) imaging was performed on all patients. Ten out of seventeen (58.8%) had an Alvarado score between 7-8, and abdominal CT was performed to exclude the diagnosis of acute appendicitis. Seven (41.2%) of the abdominal CTs were performed due to a medical history of appendectomy. In the evaluation of the abdominal CT images, all of the patients had peri-cecal inflammation, cecal wall thickening and, in all patients who had not undergone previous appendectomy, appendix vermiformis was seen normally (Figure 1). Comorbidities present were as follows: four (23.5%) were on hemodialysis due to chronic renal failure; five (29.4%) had coronary artery disease; eight (47.1%) had hypertension; three (17.7%) had congestive heart failure; five (29.4%) had cardiac arrhythmia; four (23.5%) had diabetes mellitus; three (17.7%) had chronic obstructive pulmonary disorder; one (5.9%) patient was followed due to pancreatitis; one (5.9%) patient had lung cancer; one (5.9%) patient who had an iliac artery stent due to peripheral vascular disease; and one (5.9%), who was also the youngest patient, had aplastic anemia.

Fourteen (82.25%) patients underwent right hemicolectomy and ileotransversostomy, two (11.8%) had right hemicolectomy with and Mikulicz ileocolostomy, and one (5.9%) underwent partial colon resection with and Mikulicz ileocolostomy due to limited cecal necrosis, which was diagnosed earlier. Histoathological evaluation confirmed all patients had ICN without malignancy (Figure 2). Pathology also reported transmural necrosis and serositis isolated in the cecum with no evidence of embolism, malignancy, or vasculitis (Figure 3). The mean operation time was 117 minutes (55-170 minutes). Six (35.3%) patients died during the postoperative follow-up period. The mean hospitalization duration was 11.3 days (1-28 days). The most common postoperative complication associated with the surgery was superficial surgical site infection, which occurred in three (17.7%), and evisceration was seen in two (11.8%) cases. The patients with surgical site infection were given antibiotic treatment, and the wound dressings were changed daily. Two patients with evisceration were re-operated. Two patients who underwent right hemicolectomy with an ileostomy had fecal peritonitis with clinical suspicion of sepsis, so inotropic drugs were initiated during the surgery and continued postoperatively in the intensive care unit. However, both died on the first postoperative day due to septic shock. Two patients, both with congestive heart

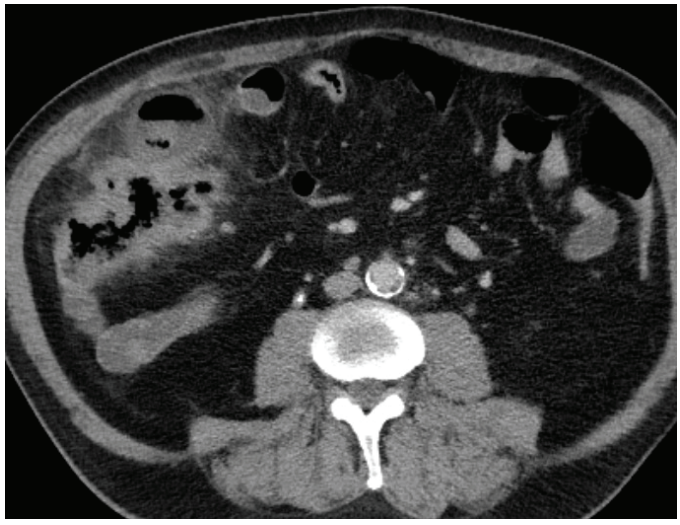

Figure 1. Computerized tomography shows circumferential bowel thickening, peri-cecal inflammation and heterogeneity

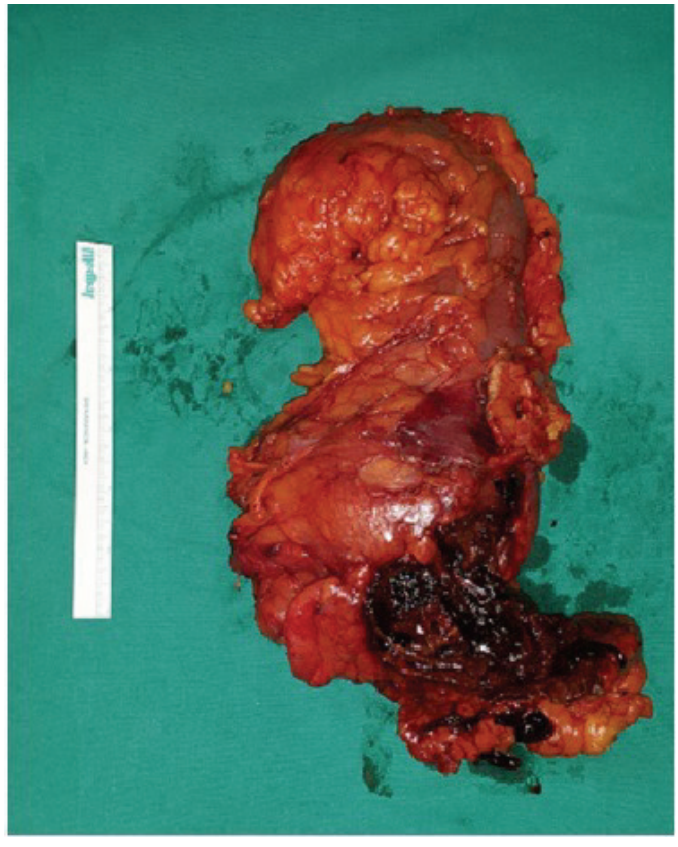

Figure 2. Macroscopic appearance of resected right hemicolectomy specimen which supported the diagnosis of isolated cecal necrosis

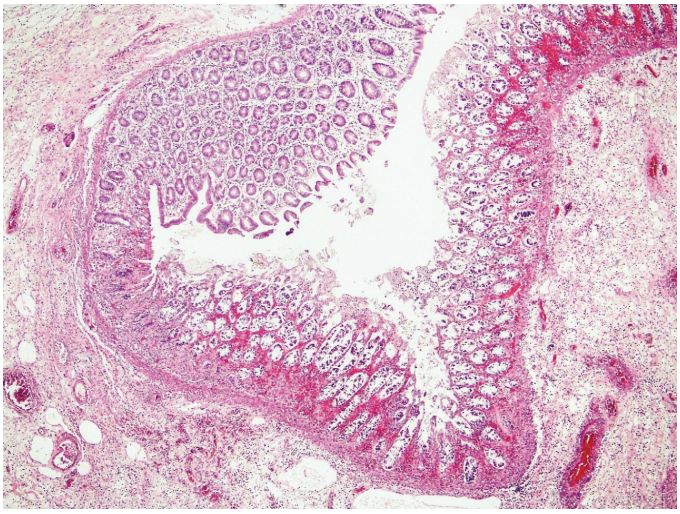

Figure 3. Sharp passage of normal colon mucosa and ischemic large intestine segment; active chronic inflammatory granulation tissue extending to the serosa, which microscopically showed a sharp transition with normal mucosa (hematoxylin and eosin, x40)

failure, died due to cardiopulmonary insufficiency on the postoperative fifth and seventh days. The patient who had a prior diagnosis of lung cancer and the patient who had obstructive sleep apnea syndrome and chronic obstructive pulmonary disorder died due to ventilator-associated pneumonia on the postoperative 16th and 23rd day. The duration of the hospital stays varied, since all patients had different and multiple comorbidities. Two patients had pneumonia, and the duration of hospitalization was 12-28 days.

Discussion

Ischemic colitis is a rarely seen clinical entity, which mostly affects elderly patients after the sixth decade, and is more common in female patients.[1] The disease is classified, according to its etiopathogenesis, into two groups depending on whether it occurs due to a vascular obstruction as the occlusive form, or due to poor blood flow caused by other underlying reasons as the non-occlusive form.[2,3] However, some studies classified colonic ischemia into three groups. These include the occlusive and non-occlusive forms plus phlebosclerotic colitis, which occurs due to mesenteric vein thrombosis as a result of venous obstruction caused by fibrotic sclerosis and calcification of the walls of the mesenteric veins.[4]

Vascular circulation serving the cecum is provided from the anterior and posterior cecal arteries and arterial anastomosis between them.[5,6] Ischemia of the cecum is rarely seen because of the rich collateral circulation that comes from the ileal branch and colic branch of the ileocolic artery.

ICN is a rarely seen, clinical form of ischemic colitis. Poor mesenteric perfusion, systemic hypotension, dialysis, trauma, shock, chronic heart disease, cardiac surgery, drugs, hypercoagulability, portal hypertension, smoking history, diabetes mellitus, hypertension especially among young patients, dyslipidemia, systemic chemotherapy, oral contraceptives and cocaine abuse, and pancreatitis (as in one of our patients) have all been reported to be associated with the development of ICN.[3,6,7,8] Frossard et al.[9] reported two young female patients with ICN, which occurred as a cause of a high level of circulating estrogens due to pregnancy and oral contraceptive medication. In our study, two patients had a history of new-onset monoclonal antibody drug use, which might conceivably have been involved in the development of ICN. One patient had rheumatoid arthritis and was on Tocilizumab treatment, a recombinant humanized anti-interleukin-6 receptor monoclonal antibody.[10] The other patient had aplastic anemia for which they were receiving Eculizumab, a fully-humanized immunoglobulin G monoclonal antibody to complement component C5.[11] Although Tocilizumab is used for rheumatoid arthritis, more recently it is being used in the treatment of Coronavirus disease-2019 (COVID-19) infected patients.[12,13] ICN should be kept in mind in the etiology of right lower quadrant abdominal pain, which develops suddenly in COVID-19 patients under tocilizumab treatment.

ICN is a diagnostic challenge, as it is rare and thus not well-known, and is an atypical presentation of acute colonic ischemia. The presumptive diagnosis is usually based on the combination of clinical suspicion, physical examination, and radiological imaging methods. There is no specific serum marker for ICN.[6] ICN generally presents with right lower quadrant abdominal pain and tenderness, fever, diarrhea or hematochezia, and leucocytosis. These manifestations may mimic acute appendicitis, cecal diverticulitis, stercoral perforation, or cecal carcinoma and therefore, early diagnosis is challenging.[14,15,16] Guitart Giménez et al.[6] reported that the most commonly seen findings in CT images were thickening of the cecal wall and ischemic cecal mural thickening and the ascending colon or pneumatosis of the cecal wall. In our study, cecal wall thickening and ascending colon were the most commonly seen findings. According to previous studies and case reports, most ICN cases were preoperatively diagnosed as acute appendicitis.[3,16,17,18,19] As suggested by Kohga et al.[7] this misleading preoperative diagnosis could be prevented with preoperative abdominal CT scan, a hypothesis with which we are in agreement. The use of colonoscopy in the diagnosis of ischemic colitis is still controversial. Although some authors recommend colonoscopy in the diagnosis of ischemic colitis, others suggest that colonoscopy may increase the risk of perforation

due to the increased colonic intraluminal pressure.[3,14,20] Diagnostic laparoscopy is considered a useful option to make a definitive diagnosis and eliminate acute appendicitis from the differential. Also, laparoscopy can be helpful to implement an operational strategy which includes the incision type. Based on the results of diagnostic laparoscopy, the appropriate incision type can be planned. In our study, a superior and inferior midline incision was preferred in all patients. We performed diagnostic laparoscopy in two patients with a history of appendectomy, although their physical examinations were compatible with acute appendicitis. Perko et al.[18] reported that a-73-year old patient with lower quadrant pain was diagnosed with acute appendicitis, but during the operation, ICN was detected, and partial resection was performed laparoscopically. Although these patients had multiple comorbid diseases, appropriate patients could be managed by laparoscopic partial resection if the surgeon had sufficient laparoscopic surgical experience.[7,18] We recommend that the duration of the operation be kept as short as possible in this type of emergency operation because the patients tend to have many comorbidities. Studies have shown that the primary surgical treatment was resection of the necrotic bowel segment and anastomosis or ostomy, depending on the abdomen condition, via open technique or laparoscopically.[3,7,8,18] In treatment, partial cecal resection or right hemicolectomy is the most commonly preferred method, according to the size of cecal necrosis and presence of peritonitis.[3,7,8] In our study, right hemicolectomy with ileotransversostomy was the most commonly used method, followed by right hemicolectomy with an ileocolostomy. In our study, the surgical methods were chosen according to the patient's general condition and the preference of the staff surgeon. Fourteen patients were operated with right hemicolectomy and ileotransversostomy. In two patients, right hemicolectomy and Mikulicz ileocolostomy was preferred due to fecal peritonitis and edematous intestinal wall, which increases the risk of anastomotic leak. One patient was operated with partial colonic resection with Mikulicz ileocolostomy, since the cecal necrosis was limited and early diagnosis was achieved. Previous reports have suggested that some cases of ICN showed poor prognosis.[3] In contrast, many patients with ICN showed an uneventful postoperative course. It has been reported that early diagnosis and urgent resection of the damaged intestine are essential to improve the postoperative outcomes of ICN.[3,7] Although Çakar et al.[3] reported that the prognosis was poor and the mortality rate was 83%, Gundes et al.[17] reported a lower mortality rate of 38% which was similar to our study with a rate of 35.3%. We believe that the increased mortality rate reported by Çakar et al.[3] was due to delayed diagnosis in the emergency service. Patients with co-morbid disease attending the emergency department with right quadrant pain should be evaluated carefully with a detailed physical examination. Diagnostic laparoscopy, which allows the exploration of all of the intra-abdominal organs, should be performed without delay when there is a suspicion of cecal necrosis.

Study Limitations

The limitations of our study were its retrospective nature and inclusion of uncommon cases due to the small number of cases.

Conclusion

ICN should be kept in mind during the evaluation of right lower quadrant abdominal pain, especially in patients with co-morbid diseases. For diagnosis of ICN, clinical suspicion, and findings generally confirmed by imaging methods, especially CT, and diagnostic laparoscopic surgery may be helpful and also aid in planning surgery. When diagnosis is delayed, ICN may be life-threatening.

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Ethics

Ethics Committee Approval: Approval from the University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital Institutional Research Ethics Board was obtained (approval number: 2021/04-17).

Informed Consent: Written informed consent was obtained from each patient who participated in this study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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References

1. Uchida T, Matsushima M, Orihashi Y, Dekiden-Monma M, Mizukami H, Nakahara F, Nakamura J, Fujisawa M, Koike J, Suzuki T, Mine T. A Case-control Study on the risk factors for ischemic colitis. Tokai J Exp Clin Med 2018;43:111-116.

2. Theodoropoulou A, Koutroubakis IE. Ischemic colitis: Clinical practice in diagnosis and treatment. World J Gastroenterol 2008;14:7302-7308.
3. Çakar E, Ersöz F, Bag M, Bayrak S, Çolak Ş, Bektaş H, Güneş ME, Çakar E. Isolated cecal necrosis: our surgical experience and a review of the literature. Turk J Surg 2014;30:214-218.
4. Jan YT, Yang FS. Phlebosclerotic colitis. J Am Coll Surg 2008;207:785.
5. Simon AM, Birnbaum BA, Jacobs JE. Isolated infarction of the cecum: CT findings in two patients. Radiology 2000;214:513-516.
6. Guitart Giménez J, Pagès Llinàs M, Domingo Ayllón M, Rimola Gibert J, Rodríguez Gómez S, Ayuso Colella C. Computed tomography characteristics of isolated caecal ischaemia. Radiología 2013;55:340-345.
7. Kohga A, Yajima K, Okumura T, Yamashita K, Isogaki J, Suzuki K, Komiyama A, Kawabe A. A Case of Isolated cecal necrosis preoperatively diagnosed with perforation of cecum. Medicina (Kaunas) 2019;55:9.
8. Coşkun F, Aksu NM, Akpinar E, Bozkurt S, Akkaş M, Balas S, Karakiliç E. Non-occlusive mesenteric ischemia in a chronic dialysis patient: a case report. Ulus Travma Acil Cerrahi Derg 2008;14:256-259.
9. Frossard JL, Spahr L, Queneau PE, Armenian B, Bründler MA, Hadengue A. Ischemic colitis during pregnancy and contraceptive medication. Digestion 2001;64:125-127.
10. Sheppard M, Laskou F, Stapleton PP, Hadavi S, Dasgupta B. Tocilizumab (Actemra). Human Vaccines Immunotherapeutics 2017;13:1972-1988.
11. Griffin M, Kulasekararaj A, Gandhi S, Munir T, Richards S, Arnold L, Benson-Quarm N, Copeland N, Duggins I, Riley K, Hillmen P, Marsh J, Hill A. Concurrent treatment of aplastic anemia/paroxysmal nocturnal hemoglobinuria syndrome with immunosuppressive therapy and eculizumab: a UK experience. Haematologica 2018;103:345-347.
12. Luo P, Liu Y, Qiu L, Liu X, Liu D, Li J. Tocilizumab treatment in COVID-19: A single center experience. J Med Virol 2020;92:814-814.
13. Toniati P, Piva S, Cattalini M, Garrafa E, Regola F, Castelli F, Franceschini F, Airò P, Bazzani C, Beindorf EA, Berlendis M, Bezzi M, Bossini N, Castellano M, Cattaneo S, Cavazzana I, Contessi GB, Crippa M, Delbarba A, De Peri E, Faletti A, Filippini M, Filippini M, Frassi M, Gaggiotti M, Gorla R, Lanspa M, Lorenzotti S, Marino R, Maroldi R, Metra M, Matteelli A, Modina D, Moioli G, Montani G, Muiesan ML, Odolini S, Peli E, Pesenti S, Pezzoli MC, Pirola I, Pozzi A, Proto A, Rasulo FA, Renisi G, Ricci C, Rizzoni D, Romanelli G, Rossi M, Salvetti M, Scolari F, Signorini L, Taglietti M, Tomasoni G, Tomasoni LR, Turla F, Valsecchi A, Zani D, Zuccalà F, Zunica F, Focà E, Andreoli L, Latronico N. Tocilizumab for the treatment of severe COVID-19 pneumonia with hyperinflammatory syndrome and acute respiratory failure: A single center study of 100 patients in Brescia, Italy. Autoimmun Rev 2020;19:102568.
14. Eyvaz K, Sıkar HE, Gökçeimam M, Küçük HF, Kurt N. A rare cause of acute abdomen: Isolated necrosis of the cecum. Turk J Surg 2018;36:1-3.
15. Dirican A, Unal B, Bassulu N, Tatlı F, Aydin C, Kayaalp C. Isolated cecal necrosis mimicking acute appendicitis: a case series. J Med Case Rep 2009;3:7443.
16. Ruiz-Tovar J, Gamallo C. Ischaemic caecal necrosis. Acta Chir Belg 2008;108:341-342.
17. Gundes E, Kucukkartallar T, Çolak MH, Cakir M, Aksoy F. Ischemic necrosis of the cecum: a single center experience. Korean J Gastroenterol 2013;61:265-269.
18. Perko Z, Bilan K, Vilović K, Druzijanić N, Kraljević D, Juriicić J, Krnić D, Srsen D, Pogorelić Z, Tomić S. Partial cecal necrosis treated by laparoscopic partial cecal resection. Coll Antropol 2006;30:937-939.
19. Hunter JP, Saratzis A, Zayyan K. Spontaneous, isolated caecal necrosis: report of a case, review of the literature, and updated classification. Acta Chir Belg2013;113:60-63.
20. Bradbury AW, Brittenden J, McBride K, Ruckley CV. Mesenteric ischemia: a multidisciplinary approach. Br J Surg 1995;82:1446-1459.

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RESEARCH ARTICLE

The Effect of the COVID-19 Pandemic on the Clinical and Pathological Stages of Colorectal Cancer Patients

Sefa Ergün[1], Emre Tunç[1], Taşkın Avcı[1], Şebnem Batur[2], Nuray Kepil[2], Server Sezgin Uludağ[1], Mehmet Faik Özçelik[1]

[1]İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of General Surgery, İstanbul, Turkey
[2]İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Pathology, İstanbul, Turkey

ABSTRACT

Aim: Coronavirus disease-2019 (COVID-19) appeared in Wuhan, China in December 2019 and the World Health Organization declared it a pandemic the following March. Colorectal cancer (CRC) is the third most common cause of cancer-related deaths worldwide, but the impact of the global pandemic on health services has severely affected the delivery of health care, including the diagnosis and treatment of CRC. The aim of this study was to investigate the effect of the COVID-19 pandemic on the clinical and pathological stages of CRC patients at the time of operation.

Method: Our study evaluated CRC patients who underwent surgery in a 6-month (May-October 2020) period during the COVID-19 pandemic and patients operated due to CRC in the same period of 2019, before the pandemic. Data collected included time of admission, complaints at admission, cancer stage and clinical characteristics, length of hospital stay, and complication and mortality rates.

Results: The study included 47 patients operated during the pandemic and 83 patients operated in the corresponding period, one year earlier. The number of cancerous lymph nodes, rates of lymphovascular and perineural invasion, and complication and mortality rates were significantly higher in patients operated during the pandemic, while the pathological stage and the rate of receiving adjuvant treatment were higher.

Conclusion: During the COVID-19 pandemic CRC patients presented with delayed diagnosis or more advanced cancer, leading to a significant increase in morbidity and mortality. Adjustment of health care provision during crises, such as the COVID-19 pandemic, should be planned to minimize the impact on emergency, cancer and infectious disease services.

Keywords: COVID-19, colorectal cancer, delay, increased mortality, pathological stage

Introduction

Coronavirus disease-2019 (COVID-19) emerged in Wuhan-China in December 2019 and the World Health Organization (WHO) declared it a pandemic on 11th of March the following year. COVID-19, which is caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), can cause asymptomatic infection, severe pneumonia, multiple organ failure and death. The pandemic had a major impact on the provision of health services, worldwide, leading to re-assignment of health services to COVID-19 treatment, shortages of healthcare staff and delay in patient presentations as populations sought to avoid infectious contact. Colorectal cancer (CRC) is the third most common cause of cancer-related deaths worldwide. The impact of the pandemic also affected cancer services, and has been shown to result in delays in hospital admission and diagnosis of CRC patients, resulting in increased morbidity and mortality. Complications such as obstruction, perforation, bleeding and peritonitis in CRC patients require emergency intervention, while a 6-week delay in treatment may lead to complications in early-stage CRC patients.[1,2] CRC patients are also at risk of COVID-19 but delay in seeking treatment and consequent progression of the cancer stage may occur due to later diagnosis and treatment.[2]

After the first COVID-19 case was detected in Turkey on 11.03.2020, the Turkish Ministry of Health recommended

Address for Correspondence: Sefa Ergün, MD, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of General Surgery, İstanbul, Turkey
E-mail: sefaergn@yahoo.com **ORCID ID:** orcid.org/0000-0002-0315-8044
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postponing all elective surgery on 17.03.2020 to ease the workload in hospitals and to prevent the interruption of healthcare services that would be required to deal with the pandemic. Due to the global decrease in hospitals and healthcare professionals working in a non-COVID setting, access to healthcare services became more limited for cancer patients.[3]

The aim of this study was to assess the clinical and pathological parameters of CRC patients admitted to our clinic during the COVID-19 pandemic and to examine the effect of the pandemic on these parameters by comparison with the same period of the previous year.

Materials and Methods

This study included CRC patients who underwent surgery in the General Surgery Department of İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine between May 2020 and October 2020 (a 6-month period) during the COVID-19 pandemic (group B) and patients operated due for CRC (group A) in the same period of 2019 (May-October 2019). Information about the time of admission, complaints at admission, cancer stage, length of hospital stay, complication rate and peri-operative mortality were retrieved from patient files and follow-ups, and evaluated. Perioperative mortality estimation included deaths occurring within 30 days of surgery or before discharge.

Patients aged <18 years, with benign pathologies, tumors other than adenocarcinoma, and patients with recurrence were excluded from the study.

Tumor location in the patients was determined according to preoperative colonoscopy, abdominal computed tomography (CT), and perioperative findings. Patients who were operated within 24 hours due to massive bleeding, perforation and obstructive tumor were evaluated under emergency admission. Postoperative complications were scored according to the Clavien-Dindo classification.[4]

All patients who were operated during the COVID-19 pandemic were tested for the SARS-CoV-2 virus using a polymerase chain reaction method within the 48 hours before operation and all had negative results.

The study was approved by the Ethics Committee of İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine (approval number: 12846, date: 21.01.2021). Written informed consent was obtained from all participants.

Statistical Analysis

Statistical analyses were conducted using SPSS version 17.0 (IBM Inc., Armonk, NY, USA). The normality of the variables was analyzed using histograms and the Kolmogorov-Smirnov test. Descriptive analyses were presented using mean, standard deviation and median values. Categorical variables were compared using the Pearson's chi-square test. The Mann-Whitney U test was used to compare non-normally distributed (non-parametric) data sets between groups. A $p<0.05$ was considered to indicate statistical significance.

Results

The study included a total of 130 patients, 83 in group A and 47 in group B with a mean age of 64.6±11.6 years. There were 78 (60%) male and 52 (40%) female patients.

Gender, complaints, and urgency (emergency vs elective) status of the patients were compared between group A and group B. There was no difference in age and gender distribution between the two groups of patients. Despite the lack of a statistically significant difference in complaints at admission, the rates of abdominal pain, rectal bleeding, and emergency admission were higher in group B than in group A (Table 1).

Tumor location, previous oncological treatment, requirement for intensive care, colostomy, presence of complications, and perioperative mortality were compared between group A and group B (Table 2). The rate of rectal tumor location tended to be higher in group B but there

Table 1. Patient complaints at admission and comparison between the groups

		A		B		p
		n	%	n	%	
Sex	Male	49	59.0	29	61.7	0.766
	Female	34	41.0	18	38.3	
Abdominal pain	No	47	56.6	23	48.9	0.398
	Yes	36	43.4	24	51.1	
Constipation	No	59	71.1	35	74.5	0.679
	Yes	24	28.9	12	25.5	
Change in bowel habits	No	73	87.95	43	91.5	0.532
	Yes	10	12.05	4	8.5	
Rectal bleeding	No	67	80.7	34	72.3	0.270
	Yes	16	19.3	13	27.7	
Fatigue	No	76	91.6	44	93.6	0.673
	Yes	7	8.4	3	6.4	
Incidental	No	79	95.2	46	97.9	0.443
	Yes	4	4.8	1	2.1	
Other	No	78	93.4	46	97.9	0.309
	Yes	5	6.0	1	2.1	
Emergency admission	No	63	75.9	33	70.2	0.478
	Yes	20	24.1	14	29.8	

was no significant difference in tumor location or the rate of colostomy between the groups. Although the rate of receiving neoadjuvant chemotherapy was higher in group B, again the difference was not significant. The presence of complications and perioperative mortality were significantly different between the groups, with a higher rate in group B than in group A. Using the Clavien-Dindo classification, grade 2 and higher complications in group A were: wound site infection n=3 (3.6%); and intra-abdominal collection n=2 (2.4%). In comparison, in group B, complications were: wound site infection n=4 (8.5%): intra-abdominal collection n=3 (6.4%); anastomotic leak n=2 (4.25%); intra-abdominal bleeding n=1 (2.1%); and pulmonary embolism n=1 (2.1%). Of four (8.5%) patients who died in group B, three had a history of obstructive tumors and sepsis, and one had postoperative pulmonary embolism.

The TNM (tumor, lymph node, metastasis) stage, lymphatic invasion, vascular invasion, perineural invasion, histological grade, surgical margin positivity, distant metastasis, and need for adjuvant chemotherapy were compared between group A and group B (Table 3). Although there was a high rate of advanced stage (stage 3-4) patients in group B, the difference was not significant. The comparison of rates of lymphatic invasion, vascular invasion, perineural invasion, and the number of positive lymph nodes and the need for adjuvant chemotherapy found that these were significantly higher in group B.

Age, duration of complaints (months), length of hospital stay (days) and levels of tumor markers including carcinoembryonic antigen and carbohydrate antigen 19-9 were compared between group A and group B. Although the duration of complaints and length of stay was longer in group B patients, the differences were statistically insignificant. The comparison of tumor marker levels between the groups revealed no significant difference (Table 4).

Table 2. Comparison of tumor location and complication rates between groups

		A		B		p
		n	%	n	%	
Ascending colon	No	63	75.9	39	83.0	0.346
	Yes	20	24.1	8	17.0	
Descending colon	No	74	89.2	43	91.5	0.670
	Yes	9	10.8	4	8.5	
Transverse colon	No	77	92.8	43	91.5	0.792
	Yes	6	7.2	4	8.5	
Sigmoid colon	No	47	56.6	30	63.8	0.422
	Yes	36	43.4	17	36.2	
Rectum	No	69	83.1	33	70.2	0.085
	Yes	14	16.9	14	29.8	
Previous oncological treatment	No	68	83.95	35	74.5	0.192
	Yes	13	16.05	12	25.5	
Need for ICU	No	60	73.2	36	76.6	0.668
	Yes	22	26.8	11	23.4	
Colostomy	No	54	65.1	30	63.8	0.888
	Yes	29	34.9	17	36.2	
Complications*	No	78	93.9	36	76.6	**0.015**
	Yes	5	6.1	11	23.4	
Perioperative mortality	No	83	100	43	91.5	**0.043**
	Yes	0	0	4	8.5	

*Grade 2 and higher complications according to the Clavien-Dindo classification, ICU: Intensive care unit

Discussion

With the COVID-19 pandemic, healthcare systems around the whole world encountered unexpected pressures. After

Table 3. Comparison of histopathological and clinical tumor characteristics between groups

		A		B		p
		n	%	n	%	
TNM stage	Stage 1-2	40	49.4	18	38.3	0.225
	Stage 3-4	41	50.6	29	61.7	
Lymphatic invasion	No	22	27.2	1	2.1	**<0.001**
	Yes	59	72.8	46	97.9	
Vascular invasion	No	41	50.6	4	8.5	**<0.001**
	Yes	40	49.4	43	91.5	
Perineural invasion	No	24	29.6	4	8.5	**0.005**
	Yes	57	70.4	43	91.5	
Histological grade	Low grade	59	86.8	38	90.5	0.606
	High grade	9	13.2	4	9.5	
Surgical margin positivity	Negative	78	94.0	42	89.4	0.343
	Positive	5	6.0	5	10.6	
Number of positive lymph nodes		2.19±5.70		4.21±7.17		**0.012**
Distant metastasis	No	73	87.95	42	89.4	0.809
	Yes	10	12.05	5	10.6	
Need for chemotherapy	No	23	27.8	7	12.8	**0.045**
	Yes	60	72.2	41	87.2	

TNM: Tumor, lymph node, metastasis

Table 4. Comparison of age, duration of complaints, length of stay, and tumor markers between groups

	A		B		p
	Mean ± SD	Median	Mean ± SD	Median	
Age	65.31±11.47	66.00	63.28±11.83	63.00	0.297
Duration of complaints (months)	2.20±2.44	1.00	3.36±5.06	1.00	0.699
CEA	23.23±81.95	3.00	25.46±71.76	3.52	0.741
CA19-9	28.62±71.63	11.00	15.77±17.16	8.76	0.956
Length of hospital stay (days)	13.45±7.04	12.00	11.68±7.33	10.00	0.093

CEA: Carcinoembryonic antigen

the WHO declared a pandemic, COVID-19 was prioritized by healthcare services across the world. By April 2021, a total of 150 million cases and 3.2 million deaths due to COVID-19 were reported worldwide.[5]

The bed capacity, healthcare workers and intensive care units of hospitals were redirected to deal with the pandemic. Non-emergency treatment was not provided by some centers, or postponed in a planned manner. In addition, patients also delayed consulting healthcare professionals due to the fear of the pandemic and consequently presented to hospitals when the complaints were worse than would have been likely in pre-pandemic conditions. The Turkish Ministry of Health declared most of the hospitals in the country as referral hospitals for COVID-19 on March 11, 2020, which then resulted in postponement of elective surgery in many centers.[2,3]

The delay in providing routine services because of the health service pressure caused by COVID-19 also included the treatment of cancer patients. Cancer patients have to leave their homes to be checked and treated or they have to violate quarantine requirements by receiving treatment at home or in palliative care units. Cancer patients are at high risk for COVID-19 because they are often elderly and mostly immunosuppressed due to their treatment.[6] The studies from China reported significantly higher rates of coronavirus infection (39% vs 8%) and severe infection (75% and 43%) in cancer patients presenting to hospitals for surgical therapy or chemotherapy than in the non-cancer population.[7]

It has been reported that an increase in the incidence and stage of CRC may occur as a result of delayed diagnosis and treatment due to the pandemic, and the associated decrease in availability of cancer screening programs and endoscopic diagnostic tests. In Spain, Suárez et al.[8] compared the March-June period between 2019 and 2020, and reported restrictions in colorectal screening tests, a 48% decrease in numbers diagnosed with CRC, and a significant increase in the emergency diagnosis and treatment of CRC.[9]

Primary surgery should be performed within six weeks in early-stage CRC. Complications such as intestinal obstruction, bleeding, and perforation may occur when there is a potential delay in treatment or diagnosis. Such cases are a high priority for surgical intervention. Colorectal surgical procedures for reconstruction or syndrome, in turn, can be postponed in a planned manner. During the pandemic, patients were referred for neoadjuvant chemotherapy or short-term radiotherapy to reduce the risk of COVID-19 during CRC surgery. However, delayed surgical treatment may bring additional psychological problems, for which psychological support would be beneficial.[2] Our results showed a longer duration of complaints before seeking medical help and a higher rate of neoadjuvant chemotherapy during the COVID-19 pandemic.

An Italian study by De Vincentiis et al.[10] compared the quarantine periods in 2020 due to pandemic with 2019 and 2018. These authors reported that CRC (62%) was the third most common cancer, after prostate (75%) and breast (66%) among cancer diagnoses, but diagnostic/therapeutic delay would potentially have a greater effect on survival in CRC, considering the early diagnosis of prostate and bladder. To avoid delay, general provision of fecal occult blood tests, triage by family physicians, increased use of tumor marker or mutation analyses (KRAS, NRAS, BRAF), and use of diagnostic methods other than colonoscopy, such as CT colonography or double-contrast barium enema, were recommended.

It has been demonstrated with a moderate level of evidence that delayed surgical resection in CRC leads to poor outcomes. Delay in colon cancer surgery would result in delayed staging and chemotherapy administration in advance-stage patients. It was stated that neoadjuvant chemotherapy could be considered in all colon cancers in case of a delay for any reason. Maringe et al.[11] reported that the mortality rate due to CRC increased by 15.3-16.6% in UK due to delayed diagnosis as a result of the COVID-19 pandemic in.[8,12] Our results also indicate a significantly higher rate of peri-operative mortality during the pandemic increasing from 0% in group A to 8.5% in group B.

In CRC lymphovascular and perineural invasion are considered poor prognostic factors and also risk factors for aggressive biological behavior. Tumor behavior is adversely affected due to the delay in diagnosis and treatment of patients during the COVID-19 pandemic.[13,14] Unfortunately, the results of this study found significantly higher rates of lymphovascular and perineural invasion, higher numbers of involved lymph nodes, and a greater need for adjuvant chemotherapy in CRC patients operated during the COVID-19 pandemic. These findings are in line with earlier reports.

A paper published by the COVIDSurg Collaborative, with the participation of 190 countries, reported a 12-week delay in CRC surgery in 35.9% of responders.[15] The report stated that, based on this data, cancer surgery should be continued, despite the pandemic, to avoid delayed and increasing numbers of operations for CRC, an increase in emergency cases and, given the prevalence of CRC, an increased impact on public health.

Study Limitations

The limitations of our study were the single-center design and the absence of long-term follow-up and longer-term survival comparison between the patient groups.

Conclusion

Adjustments of health policies during the COVID-19 pandemic should consider not only the patients with COVID-19 patients, but also those with other urgent medical conditions. Patients without COVID-19 present with delayed diagnosis or more advanced cancer, leading to a significant increase in morbidity and mortality. Thus, healthcare systems should be planned in a way to ensure appropriate treatment for both infectious diseases and normal emergency or cancer patients during future crises affecting healthcare services.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine (approval number: 12846, date: 21.01.2021).

Informed Consent: Written informed consent was obtained from all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.E., E.T., Design: S.E., T.A., Ş.B., M.F.Ö., Supervision: S.E., N.K., S.S.U., Materials: S.E., E.T., T.A., Ş.B., Data Collection or Processing: E.T., T.A., Ş.B., S.S.U., Analysis or Interpretation: S.E., M.F.Ö., N.K., Literature Search: S.E., E.T., Writing: S.E., E.T., Ş.B., Critical Review: S.E., E.T., Ş.B., M.F.Ö.

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References

1. Di Saverio S, Pata F, Gallo G, Carrano F, Scorza A, Sileri P, Smart N, Spinelli A, Pellino G. Coronavirus pandemic and Colorectal surgery: practical advice based on the Italian experience. Colorectal Disease 2020;22:625-634.
2. Vecchione L, Stintzing S, Pentheroudakis G, Douillard JY, Lordick F. ESMO management and treatment adapted recommendations in the COVID-19 era: colorectal cancer. ESMO Open 2020;5(Suppl 3):e000826.
3. Akyol C, Koç MA, Utkan G, Yıldız F, Kuzu MA. The COVID 19 Pandemic and Colorectal Cancer: 5W1H-What Should We Do to Whom, When, Why, Where and How. Turk J Colorectal Dis 2020;30:67-75.
4. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-213.
5. Worldometer. COVID-19 coronavirus pandemic. (Accesed on 23 April 2021). Avaliable online https://www. worldometers.info/coronavirus/
6. Tuech JJ, Gangloff A, Di Fiore F, Michel P, Brigand C, Slim K, Pocard M, Schwarz L. Strategy for the practice of digestive and oncological surgery during the Covid-19 epidemic. J Visc Surg 2020;157(3 Suppl 1):7-12.
7. Liang W, Guan W, Chen R, Wang W, Li J, Xu K, Li C, Ai Q, Lu W, Liang H, Li S, He J. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol 2020;21:335-337.
8. Suárez J, Mata E, Guerra A, Jiménez G, Montes M, Arias F, Ciga MA, Ursúa E, Ederra M, Arín B, Laiglesia M, Sanz A, Vera R. Impact of the COVID-19 pandemic during Spain's state of emergency on the diagnosis of colorectal cancer. J Surg Oncol 2021;123:32-36.
9. Del Vecchio Blanco G, Calabrese E, Biancone L, Monteleone G, Paoluzi OA. The impact of COVID-19 pandemic in the colorectal cancer prevention. Int J Colorectal Dis 2020;35:1951-1954
10. De Vincentiis L, Carr RA, Mariani MP, Ferrara G. Cancer diagnostic rates during the 2020 'lockdown', due to COVID-19 pandemic, compared with the 2018-2019: an audit study from cellular pathology. J Clin Pathol 2021;74:187-189.
11. Maringe C, Spicer J, Morris M, Purushotham A, Nolte E, Sullivan R, Rachet B, Aggarwal A. The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study. Lancet Oncol 2020;21:1023-1034.
12. Tørring ML, Murchie P, Hamilton W, Vedsted P, Esteva M, Lautrup M, Winget M, Rubin G. Evidence of advanced stage colorectal cancer with longer diagnostic intervals: a pooled analysis of seven primary care cohorts comprising 11 720 patients in five countries. Br J Cancer 2017;117:888-897.
13. Hu G, Li L, Hu K. Clinical implications of perineural invasion in patients with colorectal cancer. Medicine (Baltimore) 2020;99:19860.
14. Zhong JW, Yang SX, Chen RP, Zhou YH, Ye MS, Miao L, Xue ZX, Lu GR. Prognostic Value of Lymphovascular Invasion in Patients with Stage III Colorectal Cancer: A Retrospective Study. Med Sci Monit 2019;25:6043-6050.
15. COVIDSurg Collaborative. Elective surgery cancellations due to the COVID-19 pandemic: global predictive modelling to inform surgical recovery plans. Br J Surg 2020;107:1440-1449.

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RESEARCH ARTICLE

Factors Affecting Morbidity in Appendectomy: A Single Center Experience

Tolga Kalaycı[1], Sevcan Balcı[2]

[1]Erzurum Regional Training and Research Hospital, Clinic of General Surgery, Erzurum, Turkey
[2]Iğdır State Hospital, Clinic of Pathology, Iğdır, Turkey

ABSTRACT

Aim: To determine the factors affecting morbidity in acute appendicitis (AA) and to compare the results with previously published findings.
Method: After ethics committee approval, patients who underwent appendectomy in Iğdır State Hospital between January 2019 and July 2020 were retrospectively reviewed. Preoperative, intraoperative and postoperative data were collected and differences in morbidity were statistically evaluated. Factors associated with morbidity were investigated using logistic regression methodology.
Results: One hundred and fifty-eight patients were operated for AA, of whom 98 (62%) were male. The mean ± standard deviation age was 32.5±13.4 years, with a range of 18-93 years. The overall morbidity rate was 20.2% with no mortality. Preoperative fever [odds ratio (OR): 3,000 95% confidence interval (CI): 1,344-6,697; p=0.007)], late hospital admission (OR: 1,108, 95% CI: 1,026-1,196; p=0.009), preoperative diagnosis (OR: 4,130, 95% CI: 1,372-12,376; p=0.012), postoperative antibiotic type (OR: 4,387, 95% CI: 1,836-10,483; p<0.001), and length of stay (OR: 1,546, 95% CI: 1,280-1,866; p<0.001) affected morbidity. The rate of morbidity was significantly higher in the single antibiotic group compared to the combined antibiotic group (43.3% vs 14.8%; p<0.001). Patients suffering morbidity had significantly longer hospital stay (5.78 vs 3.3 days; p<0.001).
Conclusion: Preoperative fever, late hospital admission, complicated appendicitis, single antibiotic use and prolonged hospital stay increased morbidity. We recommend the use of combined antibiotics in the treatment of AA patients and discharge of patients as early as possible.
Keywords: Appendicitis, combine antibiotic, fever, morbidity, single antibiotic

Introduction

Acute appendicitis (AA) is the most common cause of acute abdomen in patients admitted to the emergency department in all age groups.[1,2] The clinical signs of AA begin with increased sensitivity of the visceral peritoneum. The clinical picture expands to include parietal peritoneum sensitivity with increased inflammation. Pain usually progresses to the right lower quadrant with increased parietal peritoneal inflammation, although initially there is no precise localization of the pain.

The symptoms and physical findings of the patients are diagnostic. Laboratory findings, such as white blood cell (WBC) count, leukocyte count, C-reactive protein (CRP) level, and screening methods such as ultrasonography (USG), computed tomography (CT) and magnetic resonance imaging aim to support the diagnosis of AA. In addition, scoring systems such as the Alvarado score and Ohmann score,[1] are helpful for diagnosis. If the diagnosis has not been made despite these additional tests but AA is still suspected, diagnostic operations should be performed as a last resort.[3]

In the case of delay in either the diagnosis or surgery for AA, both morbidity and mortality increase. Morbidity rates of up to 10% and mortality rates of up to 5% for AA have been reported.[4] To reduce both morbidity and mortality, diagnosis should be made as soon as possible, and appropriate treatment should be initiated quickly.

The aim of this study was to determine the factors affecting morbidity in AA and to compare the results with previously published findings, thus expanding the evidence base.

Materials and Methods

A retrospective evaluation of patients who were operated on due to AA between January 2019 and July 2020 in Iğdır State Hospital was performed. Ethics committee approval

Address for Correspondence: Tolga Kalaycı, MD, Erzurum Regional Training and Research Hospital, Clinic of General Surgery, Erzurum, Turkey
E-mail: dr.tolgakalayci@gmail.com **ORCID ID:** orcid.org/0000-0002-6977-1757
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was received from Non-invasive Clinical Research Ethics Committee of Erzurum Regional Training and Research Hospital (approval number: 2021/04-72). Subsequently, pre-, intra- and post-operative data were extracted from hospital records, consultation and operation notes, pathology reports and clinical charts of the patients. Exclusion criteria included: patients in the pediatric age group (0-18 years); pregnant patients; and patients treated at other centers and then admitted to our center. Patients were divided into two groups: morbidity positive (+) group and morbidity negative (-) group.

Preoperative Factors

Age and gender, admission symptoms and findings, and time from onset of symptoms to hospital admission were collected. Pre-operative hematological parameters, biochemical parameters, international normalized ratio value and CRP levels were collected from laboratory results. The Alvarado score was calculated for each patient. Imaging studies and reports thereof, including USG and CT scans, were used to record appendix diameter, presence or absence of fecalith and intra-abdominal fluid volumes.

Intraoperative Factors

Intra-operative data collected included operation time divided into day (08:00 a.m.-11:59 p.m.) or night (12:00-07:59 a.m.), type of surgery (laparoscopic or open), and type of incision (laparoscopic incision, McBurney incision or midline incision).

Postoperative Factors

The number and types of antibiotics used in the hospital after surgery, postoperative complications and treatment of these complications were evaluated. Pathological diagnosis of the resected specimen, appendix diameter, appendix length, omental tissue volume resected with the appendix, and the presence of perforation in the appendix sample were obtained from histopathology reports. Hospital stay was compared between the morbidity (+) and (-) groups.

Statistical Analysis

Statistical analyses were performed using SPSS, version 22.0 (IBM Inc., Armonk, NY, USA). Shapiro-Wilk test was used to assess the normality distribution of quantitative variables. Data are presented as mean and standard deviation (SD) or median and range, depending on normality of distribution. Independent samples t-test or Mann-Whitney U test was used to compare groups, as appropriate for the data set normality distributions. Chi-square tests (Fisher's exact test, Pearson chi-square and likelihood ratio test) were used to compare qualitative variables. Binary logistic regression was used to find factors affecting morbidity. A p-value below 0.05 was considered statistically significant.

The Process for Treatment of AA in Our Clinic from Presentation to Final Treatment

The presenting complaints and the duration of these complaints were questioned in all patients. A detailed physical examination was performed for each patient. Basic laboratory tests and screening imaging tools were used to confirm the diagnosis. Surgery was planned for patients definitely diagnosed with AA following clinical evaluation, laboratory and screening tests. Diagnostic operation was also performed in patients with suspected AA.

Laparoscopic surgery was the first choice for AA surgery. However, open surgery with McBurney incision was performed in septic patients, patients with intra-abdominal abscess or perforation. Laparoscopic surgery was performed with three trocars; a 10 or 12 mm trocar inserted supraumbilically, a 5 mm trocar inserted suprapubically, and a 10 or 12 mm trocar inserted from the left para-rectal area.

While open surgery was performed with McBurney incision in eight patients, midline incisions were used in converted surgery cases. The appendix was found and suspended after entering the abdominal cavity. The meso-appendix is sealed with energy devices and the appendix was released, two or, rarely, three Hem-o-lok clips were used to close the appendicial stump routinely. The appendix specimen was taken out of the abdomen with the help of a glove bag from the left para-rectal trocar opening. Depending on the amount of fluid present in the abdomen, an aspiration catheter was inserted into the pouch of Douglas.

Patients were followed up in the clinic postoperatively. Intravenous antibiotherapy was started for each patient. The antibiotics used were selected according to the findings determined during surgery and according to the antibiotic stock available in the hospital. Three different antibiotic groups were used: cephalosporin, 5-nitroimidazole, and carbapenem. While in the cephalosporin group, first generation cephalosporin (intravenous cefazolin sodium 1 g/every 12 hours) or third generation cephalosporin (intravenous ceftriaxone 1 g/every 12 hours) was used, in the 5-nitroimidazole group metronidazole (500 mg/100 mL) every 8 hours was used, and ertapenem 1 g/every 24 hours was used in carbapenem group. Simple analgesics, such as intravenous acetaminophen (500 mg/mL/every 12 hours) or intramuscular diclofenac sodium (2 x 25 mg/mL) were used for postoperative pain control.

Intravenous antibiotics were used during hospital stay. In general, combination therapy (cefazolin sodium plus metronidazole or ceftriaxone plus metronidazole) was preferred as the first choice antibiotherapy in most patients. The duration of both combined therapy and single therapy was adjusted according to the clinical improvement of the

patients. Postoperative carbapenem treatment was routinely started in patients with appendix perforation and intra-abdominal diffuse abscess. Carbapenem treatment was generally used for five days in patients, but treatment was extended to 7-10 days, if infection parameters suggested continuing infection.

Results

Between January 2019 and July 2020, 158 patients were operated for AA. Patients were divided into two groups: morbidity positive (+) group (n=32, 20.25%) and morbidity negative (-) group (n=126, 79.75%). Of the study cohort, 98 (62%) were male and the mean ± standard deviation age was 32.5±13.4 years, ranging from 18-93 years. Preoperative, intraoperative and postoperative data of the patients were compared between the groups. Neither gender distribution nor mean age differed between the morbidity groups (p=0.969 and p=0.638, respectively).

While 138 (87.3%) patients had abdominal pain on admission, 121 (76.6%) patients had migrative pain, 82 (51.9%) patients had vomiting and nausea, and 104 (65.8%) had lack of appetite. In addition, 154 (97.5%) patients had right iliac fossa tenderness, 152 (96.2%) had rebound on physical examination and 65 (41.1%) had fever. When the pre-operative signs and symptoms were compared between the groups, patients with morbidity were significantly more likely to present with fever (p=0.006) and to have a longer duration of symptoms before attending hospital (p=0.03). The demographic characteristics, and patients' symptoms and signs are shown in Table 1.

While 134 (84.8%) patients had leukocytosis, 96 (60.8%) had neutrophilia. Neither leukocytosis nor neutrophilia had an association with morbidity, (p=0.582 and p=0.821, respectively). There was no difference in the parameters evaluated in comparison.

USG was used as first-line radiological tool for the diagnosis of AA in 108 (68.3%) patients. While 78 (49.4%) patients had clear findings of AA (mean appendix diameter: 9.01±1.74 mm), the appendix could not be detected on ultrasound in 20 (12.7%) patients. AA continued to be considered in 10 (6.3%) patients with secondary findings, such as edema, heterogeneity, perforated appendicitis or plastron appendicitis, and CT investigation was recommended by the radiologist. In 13 (8.2%) cases, there was fluid located in the right lower quadrant and pelvic simultaneously. In addition, a fecalith was identified in six patients on USG.

CT scan was used in 89 (56.3%) in total, either as a second step radiological technique or in cases where appendicitis could not be diagnosed on ultrasound. While 74 (46.8%) patients had clear evidence of AA (mean appendix diameter: 10.8±2.8 mm), in 10 (6.3%) patients the appendix could not be detected on CT. In five (3.2%) cases, a diagnosis of AA was suspicious on CT scan. In 16 (10.1%) cases, there was fluid located in the right lower quadrant and pelvic simultaneously. In addition, a fecalith was identified in 19 (12%) patients on CT.

Table 1. Comparison of demographic data, and symptoms and signs at admission between patients with and without morbidity

Parameters	Morbidity (+) (n=32)	Morbidity (-) (n=126)	p-value
Gender, n (%)			0.638*
- Male	11 (18.3)	49 (81.7)	-
- Female	21 (21.4)	77 (78.6)	-
Age (mean rank)	79.78	79.43	0.969**
Symptoms and signs on admission			
Migrative abdominal pain, n (%)			0.817*
- Yes	25 (20.7)	96 (79.3)	-
- No	7 (18.9)	30 (81.1)	-
Vomiting and nausea, n (%)			0.082*
- Yes	21 (25.6)	61 (74.4)	-
- No	11 (14.4)	65 (85.6)	-
Lack of appetite, n (%)			0.696*
- Yes	22 (21.1)	82 (78.9)	-
- No	10 (18.5)	44 (81.5)	-
Right iliac fossa tenderness, n (%)			0.583*
- Yes	32 (20.8)	122 (79.2)	-
- No	0 (0)	4 (100)	-
Rebound, n (%)			0.349*
- Yes	32 (21)	120 (79)	-
- No	0 (0)	6 (100)	-
Fever, n (%)			**0.006***
- Yes	20 (30.8)	45 (69.2)	-
- No	12 (12.9)	81 (87.1)	-
Alvarado score, n (%)			0.072***
- 5-6	4 (12.9)	27 (87.1)	-
- 7-8	16 (17.6)	75 (82.4)	-
- >8	12 (33.3)	24 (66.7)	-
Time home to hospital (mean rank)	100.84	74.08	**0.003****

*Chi-square test, **Mann-Whitney U test, ***Likelihood ratio test

There was no difference between the morbidity groups in terms of appendix diameter, presence of AA findings, presence of intra-abdominal fluid and presence of fecaliths, both by USG and CT (p>0.05). Preoperative laboratory parameters and results of imaging tools are shown in Table 2.

Complicated appendicitis was considered preoperatively in 15 (9.5%) patients, including perforated or plastron appendicitis and diffuse intra-abdominal or right lower quadrant abscess. While the morbidity rate in complicated group was 46.7%, the morbidity rate in non-complicated group was 17.5% (p=0.014).

In terms of surgical technique, 145 (91.8%) patients were operated with laparoscopic surgery, and only five (3.2%) patients were operated with open surgery. In the remaining 7 of 8 patients, because of difficulty at dissection, laparoscopic surgery was switched to open surgery. In one patient, the operation was completed via open surgery because of mesenteric vascular bleeding due to iatrogenic trocar injury. We found that open surgery did not increase the morbidity rate, which was 30.8% in the open surgery arm and 19.3% in the laparoscopic surgery arm (p=0.301). Similarly, the incision type did not affect the morbidity rate (p=0.510). There was no correlation between timing of the operation (day vs night) and morbidity (p=0.664). Table 3 shows operative and postoperative factors of the patients.

Postoperative antibiotherapy use was classified as single antibiotherapy use or combined antibiotherapy use. Single antibiotics were cephalosporins (cefazolin sodium or ceftriaxone), 5-nitroimidazole group (metronidazole) and carbapenem group (ertapenem). In the combined antibiotic group there were two combinations: cefazolin with metronidazole or ceftriaxone with metronidazole.

In the single antibiotic group there was a significant difference (p=0.010) in morbidity rates: 0% in the cefazolin arm, 11.1% in ceftriaxone arm, 78.6% in ertapenem arm, and 100% in metronidazole arm. Total morbidity rate in the single antibiotic group was 43.3%. In the combined antibiotic group, there was no difference in morbidity rate between the two arms (p=0.22) However, the morbidity associated with single antibiotic usage was significantly higher at 43.3% compared to the same rate for combined antibiotic use which was 14.8% (p<0.001).

There were five histopathological diagnoses reported: AA (11.4%); AA with peri-appendicitis (16.5%); AA with serositis (4.4%); AA with localized peritonitis (66.4%); and perforated appendicitis (1.3%). No correlation was found between appendix length, diameter, simultaneously resected omental volume, presence of perforation at appendix specimen and morbidity (p>0.05).

Table 2. Comparison of groups according to laboratory and screening tools parameters

Parameters	Morbidity (+) (n=32)	Morbidity (-) (n=126)	p-value
Laboratory values on admission (mean)			
- WBC (10^3/mm^3)	14.8	14.5	0.770*
- Hb (g/dL)	14.5	14.6	0.839**
- Platelet (10^3/mm^3)	268.0	257.3	0.523*
- Neutrophil (%)	76.4	76.7	0.746*
- Lymphocyte (%)	16.4	16.5	0.552*
- ALT (U/L)	31.9	22.2	0.082*
- AST (U/L)	24.7	21.8	0.119*
- Creatine (mg/dL)	0.82	0.78	0.243*
- CRP (mg/L)	11.31	7.73	0.879*
- INR	1.35	1	0.495*
USG criterias (n=108)			
Appendix diameter (n=78) (mean, mm)	9.2	8.95	0.619*
Acute appendicitis, n (%)			0.068***
- Positive or suspicious	21 (24.1)	66 (75.9)	-
- Negative	1 (4.8)	20 (95.2)	-
Fecalith, n (%)			0.600***
- Yes	2 (33.3)	4 (66.7)	-
- No	20 (19.6)	82 (80.4)	-
Abdominal fluid, n (%)			0.461***
- Yes	4 (30.8)	9 (69.2)	-
- No	18 (19)	77 (81)	-
CT criteria (n=89)			
Mean appendix diameter (n=74), (mm)	11.54	10.63	0.252*
Acute appendicitis, n (%)			>0.999***
- Positive or suspicious	14 (18)	64 (82)	-
- Negative	2 (18.1)	9 (81.9)	-
Fecalith, n (%)			>0.999***
- Yes	3 (5)	57 (95)	-
- No	13 (44.9)	16 (55.1)	-
Abdominal fluid, n (%)			>0.999***
- Yes	3 (18.75)	13 (81.25)	-
- No	13 (17.8)	60 (82.2)	-
Diagnosis before surgery, n (%)			**0.014*****
- Non-complicated AA	25 (17.5)	118 (82.5)	-
- Complicated AA	7 (46.7)	8 (53.3)	-

WBC: White blood cell count, Hb: Hemoglobin, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CRP: C-reactive protein, INR: International normalized ratio, USG: Ultrasonography, CT: Computed tomography, AA: Acute appendicitis, *: Mann-Whitney U test result, **: Independent t-test result, ***chi-square test

Table 3. Comparison of the groups with (+) and without (-) morbidity in terms of intraoperative and postoperative factors

Parameters	Morbidity (+) (n=32)	Morbidity (-) (n=126)	p-value
Operation time, n (%)			0.664*
- 08:00 a.m. - 11:59 p.m.	30 (20)	120 (80)	-
- 12:00 a.m. - 07:59 a.m.	2 (25)	6 (75)	-
Operation type, n (%)			0.301*
- Laparoscopic	28 (19.3)	117 (80.7)	-
- Open	4 (30.8)	9 (69.2)	-
Type of incision, n (%)			0.510**
- 3 trocar	28 (19.3)	117 (80.7)	-
- McBurney	3 (37.5)	5 (625)	-
- UMI + LMI	1 (20)	4 (80)	-
Type of antibiotics after surgery (single vs combine)			**<0.001***
Single antibiotherapy, n (%)			**0.010****
- Cefazolin IV	0 (0)	6 (100)	-
- Ceftriaxone IV	1 (11.1)	8 (88.9)	-
- Metronidazole IV	1 (100)	0 (0)	-
- Ertapenem IV	11 (78.6)	3 (21.4)	-
Combine antibiotherapy, n (%)			0.218**
- Ceftriaxone IV with metronidazole IV	13 (12.7)	89 (87.3)	-
- Cefazolin IV with metronidazole IV	6 (23)	20 (77)	-
Pathological specimen evaluation			
Mean appendix length (cm)	4.48	4.94	0.612***
Mean appendix diameter (cm)	0.99	1.05	0.615***
Mean resected omental volume (cm^3)	13.8	12.41	0.096***
Presence of appendix perforation, n (%)			0.204*
- Yes	3 (37.5)	5 (625)	-
- No	29 (19.3)	121 (80.7)	-
Pathological diagnosis			0.580**
- AA with peri appendicitis	2 (7.7)	24 (92.3)	-
- AA with localized peritonitis	25 (23.8)	80 (76.2)	-
- AA with serositis	1 (14.3)	6 (85.7)	-
- AA	4 (22.2)	14 (77.8)	-
- Congested appendix	0 (0)	2 (100)	-
Mean hospital stay (days)	5.8	3.3	**<0.001*****

UMI: Upper midline incision, LMI: Lower midline incision, IV: Intravenous, AA: Acute appendicitis, *chi-square test, **Likelihood ratio test, ***Mann-Whitney U test result

Postoperative complications after appendectomy are shown in Table 4. In this study, the most common complications were trocar site infection (10.1%) and intra-abdominal infection (3.8%). In the morbidity (+) group, there was a longer hospital stay (5.78 days) compared to 3.3 days in the morbidity (-) group (p<0.001). Notably, the mortality rate during the study period for AA was 0%.

Regression analysis showed that preoperative fever (OR: 3,000, 95% CI: 1,344-6,697; p=0.007), time between onset of symptoms and presentation at hospital (OR: 1,108, 95% CI: 1,026-1,196; p=0.009), preoperative diagnosis (OR: 4,130, 95% CI: 1,372-12,376; p=0.012), postoperative antibiotic type (OR: 4,387, 95% CI: 1,836-10,483; p<0.001) and length of hospital stay (OR: 1,546, 95% CI: 1,280-1,866; p<0.001) were associated with morbidity.

Table 4. Postoperative complications and treatments methods

Complication	Treatment	n (%)
SSI (trocar)	Drainage and daily cleaning	16 (10.1)
Intra-abdominal abscess		6 (3.8)
- Localized at RLQ	Spontaneous regression (antibiotherapy)	5 (3.2)
- Localized right flank	Surgical drainage	1 (0.6)
Ileus	Medical	4 (2.5)
Seroma (trocar)	Drainage and daily cleaning	3 (1.9)
Port hernia (umbilical)	Hernia repair	1 (0.6)
Hematoma (intra-abdominal)	Spontaneous regression	1 (0.6)
Hematoma (trocar)	Re-suturation	1 (0.6)
Total	-	32 (20.2)

SSI: Surgical site infection, RLQ: Right lower quadrant

Discussion

AA is an emergency surgical problem affecting all age groups of patients. Most of the patients present to emergency clinics with a typical history and physical examination findings. While laboratory tests and imaging investigations help the diagnosis in most patients, AA cannot be diagnosed in a small number of patients, despite all examinations.

Morbidity due to AA has been evaluated by many studies. While most authors showed that complications were higher in elderly patients,[5,6,7,8] Bos et al.[9] showed that younger patients were susceptible to morbidity. In addition, complications are more common in males.[7,10,11] However, in this study, the gender and age of the patients did not affect morbidity.

Preoperative symptoms and signs are the main predictors at diagnosis of AA. Abdominal migratory pain, lack of appetite, and vomiting and nausea are the main complaints, and these complaints should be investigated carefully. Right lower quadrant tenderness, rebound, and fever are present in most patients. While tenderness and rebound can be seen in each period of the AA, preoperative fever has been reported to indicate complicated AA. Thus, fever has previously been reported as a predictive factor for morbidity, and our results are consistent with this.[7,12]

Early diagnosis of AA is important because the possibility of appendix perforation increases as diagnosis delay increases. Delay in appendectomy affects both the possibility of intra-abdominal abscess and postoperative complications.[13] However, there are studies indicating that delayed appendectomy does not affect morbidity.[14,15] Other studies have shown that early appendectomy reduces the risk of perforation and surgical site infections.[16,17] Our findings support the reports of delayed hospital admission increasing morbidity.

Complicated appendicitis is defined as perforated appendicitis, peri-appendicular abscess or peritonitis, which is defined as acute inflammation of the peritoneum secondary to appendiceal infection. These diagnoses are investigated, but may not be identified, by imaging tools such as USG and CT.[18] In the present study, the morbidity rate of the complicated group was 46.7% but only 17.5% in the non-complicated group which is in keeping with earlier reports of complicated appendicitis being related to morbidity.[5,9,19]

Laboratory parameters are useful to confirm diagnosis. The main laboratory findings are increased WBC count, presence of leukocytosis, WBC shift to the left, and increased CRP levels. Leukocytosis and shift of WBC to the left are also Alvarado score parameters. Increased WBC count was a predictor of morbidity in the study of Andert et al.[5] and shift of WBC to the left was a predictor in the study of Sheu et al.[7], while increased CRP levels was associated with morbidity in several studies.[5,8] In contrast, in the present study, no relationship was found between laboratory parameters and morbidity.

There is no definite consensus that operative factors affect morbidity. However, many studies have shown that operative factors play a role in morbidity. Open surgery,[20,21,22,23,24] conversion to open surgery,[5] operation at night,[5] and adverse events[19] were reported to have a negative effect on morbidity. However, in contrast to this, no operative factor was associated with increased morbidity in this study.

Postoperative factors also play a major role on the occurrence of morbidity. Longer hospital stay,[6,8] unsuitable or longer antibiotics usage,[6] and severity of pathological findings had a negative effect on morbidity. In our study longer hospital stay was associated with higher morbidity while single antibiotic use had a significant effect on the likelihood of morbidity.

Conclusion

The aim of this study was to analyze risk factors associated with postoperative complications after appendectomy. The overall morbidity rate was 20.2% with no mortality. Preoperative fever, delayed hospital admission, complicated appendicitis, and single antibiotic use all increased morbidity while prolonged hospital stay was associated with morbidity. Although there is no factor increasing the likelihood of morbidity that is amenable to alteration, we recommend the use of combined antibiotics in the treatment of AA patients to reduce morbidity and to discharge the patients as early as possible.

Ethics

Ethics Committee Approval: Ethics committee approval was received from Non-invasive Clinical Research Ethics Committee of Erzurum Regional Training and Research Hospital (approval number: 2021/04-72).

Informed Consent: As the study was designed retrospectively, anonymized data was collected from clinical archives and no individual patient consent was required.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.K., S.B., Concept: T.K., S.B., Design: T.K., Data Collection or Processing: T.K., S.B., Analysis or Interpretation: T.K., S.B., Literature Search: T.K., S.B., Writing: T.K.

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References

1. Yılmaz EM, Kapçı M, Çelik S, Manoğlu B, Avcil M, Karacan E. Should Alvarado and Ohmann scores be real indicators for diagnosis of appendicitis and severity of inflammation? Ulus Travma Acil Cerrahi Derg 2017;23:29-33.
2. Kotan Ç, Köseoğlu B, Barut İ, Aras A, Bilici S, Sönmez R. The Comparison of Clinical Features of Acute Appendicitis in Childs, Adults and Elderly Population. Van Med J 2000;7:133-137.
3. Ahmed HO, Muhedin R, Boujan A, Aziz AHS, Abdulla AM, Hardi RA, Abdulla AA, Sidiq TA. A five-year longitudinal observational study in morbidity and mortality of negative appendectomy in Sulaimani teaching Hospital/Kurdistan Region/Iraq. Sci Rep 2020;10:2028.
4. Gomes CA, Sartelli M, Di Saverio S, Ansaloni L, Catena F, Coccolini F, Inaba K, Demetriades D, Gomes FC, Gomes CC. Acute appendicitis: proposal

of a new comprehensive grading system based on clinical, imaging and laparoscopic findings. World J Emerg Surg 2015;10:60.

5. Andert A, Alizai HP, Klink CD, Neitzke N, Fitzner C, Heidenhain C, Kroh A, Neumann UP, Binnebösel M. Risk factors for morbidity after appendectomy. Langenbecks Arch Surg 2017;402:987-993.
6. Calis H. Morbidity and Mortality in Appendicitis in the Elderly. J Coll Physicians Surg Pak 2018;28:875-878.
7. Sheu BF, Chiu TF, Chen JC, Tung MS, Chang MW, Young YR. Risk factors associated with perforated appendicitis in elderly patients presenting with signs and symptoms of acute appendicitis. ANZ J Surg 2007;77:662-666.
8. Chen CC, Ting CT, Tsai MJ, Hsu WC, Chen PC, Lee MD, Liu MH, Shih HC. Appendectomy timing: Will delayed surgery increase the complications? J Chin Med Assoc 2015;78:395-399.
9. Bos C, Doumouras AG, Akhtar-Danesh GG, Flageole H, Hong D. A population-based cohort examining factors affecting all-cause morbidity and cost after pediatric appendectomy: Does annual adult procedure volume matter? Am J Surg 2019;218:619-623.
10. Augustin T, Cagir B, VanderMeer TJ. Characteristics of perforated appendicitis: effect of delay is confounded by age and gender. J Gastrointest Surg 2011;15:1223-1231.
11. Hale DA, Molloy M, Pearl RH, Schutt DC, Jaques DP. Appendectomy: a contemporary appraisal. Ann Surg 1997;225:252-261.
12. Iamarino APM, Juliano Y, Rosa OM, Novo NF, Favaro ML, Ribeiro MAF Júnior. Risk factors associated with complications of acute appendicitis. Rev Col Bras Cir 2017;44:560-566.
13. Papandria D, Goldstein SD, Rhee D, Salazar JH, Arlikar J, Gorgy A, Ortega G, Zhang Y, Abdullah F. Risk of perforation increases with delay in recognition and surgery for acute appendicitis. J Surg Res 2013;184:723-729.
14. Almström M, Svensson JF, Patkova B, Svenningsson A, Wester T. In-hospital Surgical Delay Does Not Increase the Risk for Perforated Appendicitis in Children: A Single-center Retrospective Cohort Study. Ann Surg 2017;265:616-621.
15. Yardeni D, Hirschl RB, Drongowski RA, Teitelbaum DH, Geiger JD, Coran AG. Delayed versus immediate surgery in acute appendicitis: do we need to operate during the night? J Pediatr Surg 2004;39:464-469.
16. Ditillo MF, Dziura JD, Rabinovici R. Is it safe to delay appendectomy in adults with acute appendicitis? Ann Surg 2006;244:656-660.
17. Busch M, Gutzwiller FS, Aellig S, Kuettel R, Metzger U, Zingg U. In-hospital delay increases the risk of perforation in adults with appendicitis. World J Surg 2011;35:1626-1633.
18. Mariage M, Sabbagh C, Grelpois G, Prevot F, Darmon I, Regimbeau JM. Surgeon's Definition of Complicated Appendicitis: A Prospective Video Survey Study. Euroasian J Hepato-gastroenterol 2019;9:1-4.
19. Walędziak M, Lasek A, Wysocki M, Su M, Bobowicz M, Myśliwiec P, Astapczyk K, Burdzel M, Chruściel K, Cygan R, Czubek W, Dowgiałło-Wnukiewicz N, Droś J, Franczak P, Hołówko W, Kacprzyk A, Karcz WK, Kenig J, Konrad P, Kopiejć A, Kot A, Krakowska K, Kukla M, Leszko A, Łozowski L, Major P, Makarewicz W, Malinowska-Torbicz P, Matyja M, Michalik M, Niekurzak A, Nowiński D, Ostaszewski R, Pabis M, Polańska-Płachta M, Rubinkiewicz M, Stefura T, Stępień A, Szabat P, Śmiechowski R, Tomaszewski S, von Ehrlich-Treuenstätt V, Wasilczuk M, Wierdak M, Wojdyła A, Wroński JW, Zwolakiewicz L, Pędziwiatr M. Risk factors for serious morbidity, prolonged length of stay and hospital readmission after laparoscopic appendectomy-results from Pol-LA (Polish Laparoscopic Appendectomy) multicenter large cohort study. Sci Rep 2019;9:14793.
20. Ortega AE, Hunter JG, Peters JH, Swanstrom LL, Schirmer B. A prospective, randomized comparison of laparoscopic appendectomy with open appendectomy. Am J Surg 1995;169:208-213.
21. Ohtani H, Tamamori Y, Arimoto Y, Nishiguchi Y, Maeda K, Hirakawa K. Meta-analysis of the results of randomized controlled trials that compared laparoscopic and open surgery for acute appendicitis. J Gastrointest Surg 2012;16:1929-1939.
22. Wei B, Qi CL, Chen TF, Zheng ZH, Huang JL, Hu BG, Wei HB. Laparoscopic versus open appendectomy for acute appendicitis: a metaanalysis. Surg Endosc 2011;25:1199-1208.
23. Gupta R, Sample C, Bamehriz F, Birch DW. Infectious complications following laparoscopic appendectomy. Can J Surg 2006;49:397-400.
24. Pedersen AG, Petersen OB, Wara P, Rønning H, Qvist N, Laurberg S. Randomized clinical trial of laparoscopic versus open appendicectomy. Br J Surg 2001;88:200-205.

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RESEARCH ARTICLE

Assessing Thirst Symptom of Patients Undergoing Abdominal Surgery: A Scale Development Study

Bediye Öztaş[1], Muharrem Öztaş[2], Sibel Yılmaz Şahin[1], Emine İyigün[1], Ümit Alkuş[2]

[1]University of Health Sciences Turkey, Gülhane Faculty of Nursing, Ankara, Turkey
[2]University of Health Sciences Turkey, Gülhane Training and Research Hospital, Ankara, Turkey

ABSTRACT

Aim: The aim of this study was to develop a postoperative thirst rating scale for patients undergoing major abdominal surgery.
Method: The study was carried out methodologically. Fifty four patients who underwent major abdominal surgery in the general surgery clinic were included in the study. The data of the study were collected between June 2019 and December 2020. In this study in sequence, scale items were created, assessed through expert opinion, tested in a sample of patients and data collected, validity and reliability of the scale were evaluated, and the results were analyzed.
Results: The Cronbach's alpha value of the scale was 0.957. Test and retest results to test the reliability of the scale were $p<0.001$ and $r=0.976$. Content and construct validity results, which were conducted to test the validity of the scale, showed that the scale was valid. The final scale consisted of six items with excellent reliability and validity. The final version of the scale had a potential minimum score of 0 and maximum score of 18, with higher scores indicating worse thirst. The mean thirst score was 13.03±2.92.
Conclusion: The scale developed to evaluate the thirst status of patients undergoing abdominal surgery is a valid and reliable scale, and its use is recommended.
Keywords: Abdominal surgery, postoperative, thirst, scale

Introduction

Thirst is a symptom defined as the desire to drink water.[1,2] Thirst is a subjective symptom. It is a problem that affects the patient physiologically, psychologically, socially and spiritually during the perioperative period.[1,3] Postoperative thirst is reported to affect from 43.8% to 75% of patients following surgery.[4,5] Robleda et al.[6] investigated the problems patients undergoing abdominal surgery experienced and reported that dry mouth was the most common, affecting 88% of their subjects.

Surgical patients are at high risk of thirst for many reasons. These include the preoperative fasting period when being prepared for surgery, preoperative nutritional status, preoperative examinations and bowel preparation for the surgical procedure, drugs used, intubation, blood loss, fluid-electrolyte imbalance, and neuroendocrine response to the stress caused by surgery.[1,4,7] Patients undergoing surgery are likely to develop both osmotic and hypovolemic thirst.[1] When anxiety, irritability, stress and fear regarding the postoperative process are also present, patients may experience the feeling of thirst much more intensely due to the activation of the sympathetic nervous system.[1,4,8]

Based on the literature and our clinical experience, it seems evident that patients experience very high rates of thirst and symptoms of dry mouth during the postoperative period. However, these symptom are still not evaluated by health professionals in a desirable way and are not included in nursing diagnosis systems, and very few methods are used to alleviate this situation.[9,10,11,12,13,14] There is no measurement tool in our country that health professionals can use to objectively measure the experiences of patients after surgery. The aim of this study, therefore was to develop a valid and reliable measurement scale to evaluate the sensation of thirst experienced by patients undergoing abdominal surgery in the postoperative period.

Address for Correspondence: Bediye Öztaş, RN, PhD, University of Health Sciences Turkey, Gülhane Faculty of Nursing, Ankara, Turkey
E-mail: oztasbediye2@gmail.com **ORCID ID:** orcid.org/0000-0001-6775-1405
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Materials and Methods

The study was carried out methodologically. In scale studies, there should be a sample number between 5 and 30 for each item according to the number of scale items.[15] This study was completed with 54 patients. The data of the study were collected between June 2019 and December 2020. Patients undergoing major abdominal surgery in a general surgery service were invited to the study. Patients who agreed to participate in the study, who spoke Turkish, who had American Society of Anesthesiologists (ASA) Physical Status Score 1 and 2, and who underwent major abdominal surgery were included in the study. Exclusion criteria were patients with general condition disorders that might cause difficulty in communicating and patients with diagnoses, such as Sjögren's syndrome and xerostomia, that might affect their thirst status.

Developing the Scale

Formation of items: Face-to-face interviews were conducted with 11 patients who underwent abdominal surgery. Using a semi-structured form, the patients were asked, "What was your most disturbing complaint in the post-operative period? How would you describe your thirst complaint? In which parts of your body (tongue, throat, mouth, lips...) did you feel thirsty? How did thirst make you feel? What did you do when you felt thirsty? How did you express it?". Audio recordings of the interviews with the patients were collected. These recordings were independently listened and transcribed by two researchers. It was concluded that the patients felt dryness in their lips, tongue, palate and throat, they experienced saliva deficiency, they wanted to drink water, and their body temperature increased. Afterwards, studies on thirst were scanned[1,2,3,4,5,6,7,8,9,10,11,12,13,14,16] and nine scale items were created.

Pilot application: A pilot application was conducted with five patients.

Analysis: Reliability analysis and validity analysis of the scale were performed.

Validity analysis: Content, construct and criterion validities were performed for the validity analysis of the scale. In order to test the content validity of the scale items, expert opinions were obtained from eight faculty nurses and six general surgeons. DAVIS method was used for this evaluation. Experts evaluated each scale item according to the options "1: the item is appropriate, 2: the item should be slightly revised, 3: the item should be reviewed seriously, 4: the item is not appropriate". For the item analysis in the construct validity of the scale, firstly, mean and standard deviation values were calculated for each item. Then, whether there was a difference between the item averages was evaluated with the Friedman test. In addition, item-total correlation analyzes were performed. Items with a negative corrected item total correlation coefficient and items with coefficient below 0.30 were excluded from the scale.[17] Explanatory factor analysis and confirmatory factor analysis were used for the construct validity of the scale. Before the factor analysis, whether the sample size was sufficient or not was evaluated with the Kaiser Meyer-Olkin (KMO) test. A KMO value above 0.60 has been shown to indicate that the sample size is sufficient for factor analysis.[18] For criterion validity, a numerical scale numbered between 0 and 10 (0; I do not feel thirsty at all, 10; I feel very thirsty) was used to measure the degree of thirst.

Reliability analysis: Test-retest analysis was used for the reliability analysis of the scale. The scale was reapplied to the entire sample group with an interval of one hour. The purpose of applying it with only a one hour interval was to enable patients to respond independently of their previous answers and without any change in their thirst status. An evaluation was made by calculating the correlation coefficient between the two measurements.

Data Collection

Data collection was carried out in two stages. In the first stage, the patients were interviewed about their thirst experience using a semi-structured form. In the second stage, data were collected with the data collection form (date of birth, gender, height, weight, marital status, education level, ASA score, diagnosis, operation time) and thirst assessment scale created by the researchers.

Responses to scale items were scored as: none: 0; few: 1; moderate: 2; and much: 3. There was no reverse coded item in the scale. As the score obtained from the scale increased, the degree of thirst increased. The aim of the study was explained by face-to-face interviews with the patients before the surgery. Consent was obtained from the patients who agreed to participate in the study.

Ethical Approval

Ethics committee approval of the study was obtained (approval number: 19/10, date: 17.01.2019). The study was carried out on a voluntary basis. Verbal and written consent was obtained from the participants. Data were collected through face-to-face interviews with patients.

Statistical Analysis

SPSS for Windows, Version 21.00 (SPSS Inc. Chicago, IL, USA) statistical package program and IBM SPSS AMOS 24 statistical program were used for data analysis. Number, percentage, mean and standard deviation values were used for descriptive statistics. Exploratory factor analysis and confirmatory factor analysis were used for the validity analysis of the scale. For reliability analysis, Cronbach's

alpha coefficient and intraclass correlation coefficient were calculated.

Results

Sociodemographic Data

Sociodemographic data of the patients participating in the study are given in Table 1. For the whole cohort of 54 patients, 64.8% were male, all were married. In the educational status groupings, the largest group was "completed primary education" (42.6%). All but one of the patients (98.1%) had an ASA score of 2 and 64.8% of the patients underwent surgery for colorectal cancer. The mean age of the patients was 61.52±9.57 years, mean body mass index was 26.42±4.35, and the mean operation time was 188.80±74.50 minutes.

Table 1. Sociodemographic and clinical characteristics of the patients

Sociodemographic feature	n	%
Gender		
Women	19	35.20
Men	35	64.80
Marital status		
Married	54	100
Educational status		
Literate	7	13
Primary education	23	42.60
High school	20	37
University	4	7.40
ASA		
ASA1	1	1.90
ASA2	53	98.10
Diagnosis		
Colorectal Ca	35	64.81
Stomach Ca	9	16.66
Esophageal Ca	1	1.85
Pancreatic Ca	4	7.40
Diverticulitis perforation	1	1.85
Liver giant hydatid cyst	1	1.85
Intra-abdominal mass	2	3.70
Small intestine perforation	1	1.85
	Min.-Max.	**Mean ± SD**
Age	42-88	61.52±9.57
BMI	15.79-36.75	26.42±4.35
Operation time	85-465	188.80±74.50

ASA: American Society of Anesthesiologists, Ca: Cancer, SD: Standard deviation, Min.: Minimum, Max.: Maximum, BMI: Body mass index

Data of the Scale

Formation of the items: As a result of the pilot interviews and the literature review, nine items related to thirst were developed.

Validity analysis: For the content validity of the scale, the scale items submitted to expert opinions were evaluated with the DAVIS method. As a result, the scores obtained for each item were summed and divided by the number of experts[14] and eight items with a content validity ratio above 0.80 (content validity ratios were 1, 1, 1, 0.5, 1, 1, 0.85, 0.85, and 0.92, respectively) were identified. In order to determine the degree to which the items could measure the desired target factors related to thirst, mean and standard deviation values of each item and item total correlation analyzes were performed. The difference between the item averages was evaluated with the Friedman test and two items (with means of 0.67 and 0.65) were removed from the scale. In the corrected item-total correlation analysis performed subsequently, there was no item with a negative coefficient or coefficient below 0.30. The corrected item-total score correlation coefficients of the items were found to be between 0.668 and 0.973 (Table 2). The Kaiser-Meyer-Olkin test result, in which the sample size was evaluated for exploratory factor analysis, was 0.902 indicating a sufficient sample size (Bartlett's test of sphericity X^2=429.427, p<0.001). According to the results of the exploratory factor analysis, the scale items were grouped under a single factor. Factor loads of items were: item 1: 0.748; item 2: 0.983; item 3: 0.925; item 4: 0.962; item 5: 0.947; and item 6: 0.866.

The confirmatory factor analysis results showed that the scale was within the perfect fit criteria (Figure 1 and Table 3). Goodness of fit indices of the scale were as follows; goodness of fit index (GFI): 0.992; adjusted (A)GFI: 0.981; comparative fit index: 1,000; normed fit index: 0.997; root mean square error of approximation: 0.001; and RMR: 0.002.

The mean score of the numerical scale used for criterion validity was 6.70±1.17 (range: 5-9). A statistically significant and positive strong correlation was found between the thirst total scale score and the numerical scale total scale score (r=0.828, p<0.001).

Reliability analysis: The total mean score of the thirst scale was 13.03±2.92 (range: 7-18), and the mean retest score was 13.13±2.68 (range: 8-18). The intra-class correlation coefficient between the total mean score of the scale and the mean score of the retest was 0.976 (p<0.001). The internal consistency coefficient of the scale was 0.957.

Table 2. Item analysis results.

Item	Mean	Standard deviation	Scale mean after the item was deleted	Scale variance when the item was deleted	Corrected item-total score correlation	Cronbach alpha value when the item was deleted
1. I feel dry on my lips because of my thirst	2.35	0.482	10.69	6.635	0.668	0.969
2. I feel dry on my tongue because of my thirst	2.13	0.551	10.91	5.671	0.973	0.937
3. I feel dry on my palate because of my thirst	2.07	0.544	10.96	5.885	0.888	0.947
4. I feel dry in my throat because of my thirst	2.15	0.563	10.89	5.686	0.940	0.941
5. I feel that my saliva is insufficient	2.09	0.559	10.94	5.752	0.919	0.943
6. I want to drink a lot of water to quench my thirst	2.24	0.512	10.80	6.203	0.809	0.955

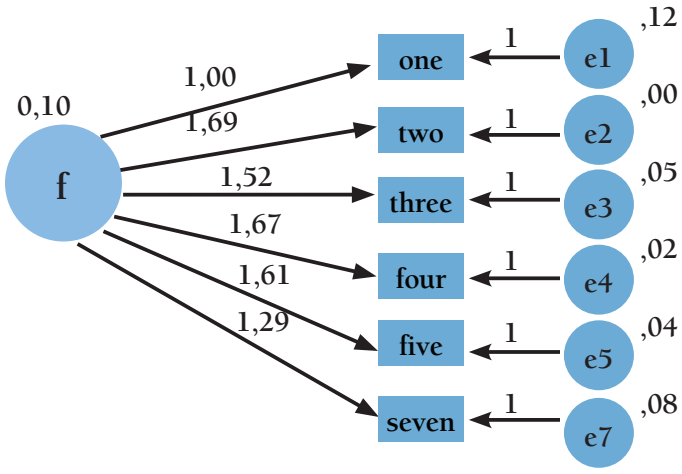

Figure 1. Result of confirmatory factor analysis

Table 3. Goodness of fit indices of the scale

Fit indices	Thirst scale	Perfect fit criteria	Acceptable fit criteria
Chi-square	1.359	-	-
Degree of freedom	9	-	-
RMSEA	0.001 (p<0.05)	0≤ RMSEA ≤0.05	0.05≤ RMSA ≤0.08
CFI	1.000	0.90≤ CFI ≤1.00	0.80≤ CFI ≤0.90
NFI	0.997	≥0.90	≥0.80
GFI	0.992	≥0.90	≥0.80
AGFI	0.981	0.95≤ AGFI ≤1.00	0.80≤ AGFI ≤0.95

RMSEA: Root Mean Square Error of Approximation, CFI: Comparative fit index, NFI: Normed fit index, GFI: Goodness of fit index, AGFI: Adjusted goodnes of fit index

The final version of the scale developed to evaluate the thirst levels of patients who underwent abdominal surgery was a single factor scale consisting of six items. Each item was scored from 0 (none) to 3 (much). Therefore the minimum and maximum possible scores from the scale were 0 and 18, respectively. As the score obtained from the scale increased, the severity of thirst increased.

Discussion

Thirst is a symptom that patients often experience. Restricting oral intake for reasons such as bowel preparation and anastomosis safety, especially in patients undergoing abdominal surgery, increases the likelihood of patient post-operative thirst. Scales related to thirst have been developed for hemodialysis patients, patients with heart failure and surgical patients.[1,2,16] No scale was found in our country to evaluate the thirst symptoms experienced by patients who underwent abdominal surgery. It is important to evaluate these symptoms that occur in a high proportion of patients, and especially in those who have undergone major abdominal surgery, to make the post-operative experience as easy as possible and also to evaluate the effectiveness of any intervention. The study conducted for this purpose was a methodological study in which a tool was developed to evaluate the symptoms of thirst experienced by the patients and the validity-reliability of the scale was evaluated. The thirst scale developed according to the results obtained was shown to be a valid and reliable scale.

Scale validity is a criterion that shows how accurately the item to be measured with the scale is measured. For this purpose, content validity was first performed and the DAVIS technique was used. The number of experts should be between 3-40 in order to evaluate the content validity.[17,19,20,21] In the present study, 14 experts were consulted. Similarly,

the content validity index (CVI) result for each item should be 0.80 or above.[17,19,20,21] In this study, it was observed that the CVI of the items ranged from 0.5 to 1. One item with an CVI <0.8 was removed from the scale, leaving eight of the original nine items for evaluation. Whether there is a difference between the averages of the items needs to be evaluated statistically.[17] Two items with a lower average than the other items were excluded from the scale. In addition, mean and standard deviation values of each item were calculated and item-total correlation analyzes was performed. It is accepted items with a negative corrected item-total correlation coefficient and items with coefficient below 0.30 can be excluded.[22] In this study, no items were removed from the scale at this stage, since there was no item below this value.

The fact that the scale items are compatible with each other and in a similarly homogeneous structure is a feature that shows the construct validity of the scale. The analyzes made for this purpose are factor analysis including exploratory and confirmatory factor analyzes.[17] The adequacy of the sample size should be evaluated before the exploratory factor analysis.[17,23] A KMO value above 0.6 is the accepted value for sample adequacy.[18,19,20,21,22,23,24] In this study this value was above the accepted limit, it showed that the sample size was sufficient. Exploratory factor analysis is an analysis method in which the factor structure in the data is determined with the help of observed variables.[17] According to the results of the exploratory factor analysis conducted in this study, the scale items were grouped under one factor. Furthermore, items with factor loads above 0.30 can remain in the scale.[22] All the factor loads of the remaining six items were above 0.30. Confirmatory factor analysis is a method to assess the theoretical structure determined by the researcher using the data obtsained.[17] In the present study the confirmatory factor analysis fitted the criteria for a perfect fit (Figure 1, Table 3). It was confirmed that the scale items were collected in a single factor.

The test-retest method is a method used for the reliability analysis of the developed scale and evaluating variability over time.[17] It is recommended to apply the test-retest method 2 to 6 weeks after the initial evaluation.[18,25] However, thirst symptoms can rapidly change in the postoperative period. Therefore, test was repeated only one hour after the first evaluation, as subjective thirst may have changed. This was an attempt to ensure that the patients responded independently of their previous evaluations and that they responded without any change in thirst symptoms. The test-retest correlation coefficient was 0.976 ($p<0.001$). A correlation number close to 1 indicates high reliability.[17,25] This result over a normal test-retest time-scale would indicate excellent test-retest reliability but as the delay between test and retest was only one hour, this result may be somewhat unreliable.

The closer the Cronbach's alpha coefficient is to 1, the more reliable the scale is.[17,25] In this study, the internal consistency coefficient of the thirst scale was found to be 0.957. This result showed that the thirst scale was a reliable scale.

Study Limitations

Conducting the study in a single center was a limitation of the study. Another limitation was the use of a non-valid and unreliable numerical scale in the assessment of thirst for criterion validity.

Conclusion

According to the results of this study, the thirst scale, which was developed to evaluate thirst symptoms experienced in the postoperative period in patients who underwent major abdominal surgery, was a valid and reliable measurement tool. It is recommended to use the thirst scale in the evaluation of thirst symptoms experienced by patients who have undergone abdominal surgery in the early postoperative period.

Ethic

Ethics Committee Approval: Ethics committee approval of the study was obtained (approval number: 19/10, date: 17.01.2019).

Informed Consent: Verbal and written consent was obtained from the participants.

Peer-review: Externally peer-reviewed.

Author Contributions

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

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References

1. Martins PR, Fonseca LF, Rossetto EG. Developing and validating the Perioperative Thirst Discomfort Scale. Rev Esc Enferm USP 2017;51:e03240.
2. Kara B. Validity and reliability of the Turkish Version of The Thirst Distress Scale in patients on hemodialysis. Asian Nursing Res (Korean Soc Nurs Sci) 2013;212-218.
3. Hüppe M, Kemter A, Schmidtke C, Klotz KF. Postoperative complaints. Gender differences in expectations, prevalence and appraisal. Anaesthesist 2013;62:528-536.

4. Sebaee HAA, Elhadary SM. Effectiveness of a care bundle on postoperative thirst relief and oral condition among patients undergoing abdominal surgeries. Journal of Nursing and Health Science 2017;6:82-90.
5. Puntillo KA, Arai S, Cohen NH, Gropper MA, Neuhaus J, Paul SM, Miaskowski C. Symptoms experienced by intensive care unit patients at high risk of dying. Crit Care Med 2010;38:2155-2160.
6. Robleda G, Roche-Campo F, Sánchez V, Gich I, Baños JE. Postoperative discomfort after abdominal surgery: An obsevational study. J Perianesth Nurs 2015;30:272-279.
7. Aroni P, Nascimento LA, Fonseca LF. Assessment strategies for the management of thirst in the post-anesthetic recovery room. Acta Paul Enferm 2012;25:530-536.
8. McKinley MJ, Johnson AK. The physiological regulation of thirst and fluid intake. News Physiol Sci 2004;19:1-6.
9. Garcia AKA, Fonseca LF, Aroni P, Galvão CM. Strategies for thirst relief: Integrative literature review. Rev Bras Enferm 2016;69:1148-1155.
10. Puntillo K, Arai SR, Cooper BA, Stotts NA, Nelson JE. A randomized clinical trial of an intervention to relieve thirst and dry mouth in intensive care unit patients. Intensive Care Med 2014;40:1295-1302.
11. Moon YH, Lee YH, Jeong IS. A comparison of effect between wet gauze with cold normal saline and wet gauze with cold water on postoperative thirst, oral cavity condition, and saliva pH. J Korean Acad Fundam Nurs 2015;22:398-405.
12. Sebaee HAA, Elhadary SM. Effectiveness of a care bundle on postoperative thirst relief and oral condition among patients undergoing abdominal surgeries. IOSR Journal of Nursing and Health Science (IOSR-JNHS) 2017;6:82-90.
13. Conchon MF, Fonseca LF. Efficacy of an ice popsicle on thirst management in the immediate postoperative period: A randomized clinical trial. J Perianesth Nurs 2018;33:153-161.
14. Pavani MM, Fonseca LF, Conchon MF. Thirst in surgical patients: Perceptions of the nursing team in inpatient units. J Nurs UFPE 2016;10:3352-3360.
15. O'Rourke N, Hatcher L. Path analysis, A step-by-step approach to using SAS for factor analysis and structural equation modeling, 2th ed. USA; 2013:107-114.
16. Waldréus N, Jaarsma T, van der Wal MH, Kato NP. Development and psychometric evaluation of the Thirst Distress Scale for patients with heart failure. Eur J Cardiovasc Nurs 2018;17:226-234.
17. Alpar R. Geçerlik ve Güvenirlik, Spor, Sağlık ve Eğitim Bilimlerinden Örneklerle Uygulamalı İstatistik ve Geçerlik-Güvenirlik-SPSS'de Çözümleme Adımları ile Birlikte, 5.Baskı, Ankara; Şubat, 2018:493-604.
18. Çam OM, Arabacı BL. Tutum ölçeği hazırlamada nitel ve nicel adımlar. Hemşirelikte Araştırma Geliştirme Dergisi 2010;2:59-71.
19. Aksayan S,Gözüm S. Kültürler arası ölçek uyarlaması için rehber I: Ölçek uyarlama aşamaları ve dil uyarlaması. Hemşirelik Araştırma Dergisi 2002;4:9-14.
20. Özgüven İ. Psikolojik Testler. 1. Baskı, Ankara, 2004.
21. Erdoğan S, Nahçıvan N, Esin MN. Hemşirelikte Araştırma, Süreç, Uygulama ve Kritik, 1.Baskı, İstanbul, 2014.
22. Büyüköztürk Ş. Temel Kavramlar ve Ölçek Geliştirmede Kullanımı. Kuram ve Uygulamada Eğitim Yönetimi 2002;32:470-483.
23. Akgül A. İstatistiksel Analiz Teknikleri. 3.Baskı, Ankara, 2003.
24. Şencan H. Sosyal ve davranışsal ölçümlerde güvenirlik ve geçerlilik. Ankara, 2005
25. Tavşancıl E. Tutumların Ölçülmesi ve SPSS ile Veri Analizi. 4.Baskı, Ankara, 2010.

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RESEARCH ARTICLE

Comparison of Anismus and Perineal Descent on Static Images of Magnetic Resonance Defecography: Can We Rule Out Anismus in Patients Who Can not Defecate?

Nuray Haliloğlu, Mustafa Fatih Arslan, Ayşe Erden

Ankara University Faculty of Medicine, Department of Radiology, Ankara, Turkey

ABSTRACT

Aim: Both anismus and perineal descent may cause symptoms of obstructed defecation, and impaired rectal evacuation may be a major finding of anismus, or due to insufficient patient co-operation. The aim was to compare static magnetic resonance defecography (MRD) measurements in patients with anismus and perineal descent, and to identify findings which may rule out anismus in patients who can not defecate.

Method: Patients with symptoms of obstructed defecation who underwent MRD between July 2016 and March 2018 were retrospectively evaluated. Thickness of anal sphincter was measured on T2W axial images. Anorectal angle (ARA) and M-line were measured on static MRD images with distended rectum.

After all measurements were completed, patients were divided into two groups depending on the diagnosis indicated by MRD. Group 1 consisted of patients with findings suggesting anismus and group 2 consisted of patients with perineal descent.

The measurements of ARA, M line and thicknesses of anal sphincter were compared.

Results: In total 90 patients (68 female; 75.6%) were included. Group 1 consisted of 37 (20 female) patients with a mean age of 46 years. Group 2 consisted of 53 (48 female) patients with a mean age of 52 years. Both the age (p=0.039) and the gender distribution (p<0.01) differed significantly between the groups, while the thickness of the internal and external anal sphincter was not significantly different. Both the ARA measurements (p=0.025) and difference in the length of M-line (p=0.047) were significantly different between the groups on images with distended rectum.

Conclusion: Patients with anismus were younger but there was no gender predilection. When the rectum was filled with contrast media, the ARA was wider and M-line was longer in patients with perineal descent.

Keywords: Anismus, defecography, dyssynergic defecation, perineal descent

Introduction

In patients with perineal descensus syndrome there is an excessive pelvic floor descent, and in anismus there is an inappropriate contraction of the pelvic floor during defecation.[1] In both abnormalities, patients may present with symptoms of obstructed defecation, such as incomplete evacuation, need to apply digital support and excessive straining during defecation with repeated and prolonged attempts for evacuation.[2] Magnetic resonance defecography (MRD) is the method of choice in the assessment of pelvic floor disorders, especially defecatory dysfunctions. An appropriate MRD should include T2-weighted (T2W) axial, coronal, and sagittal images, and also dynamic sequences at rest, and during squeezing, straining, and evacuation. It is strongly recommended that the patient must be informed about the examination before the procedure and the importance of patient co-operation must be emphasized.[3,4] Asking the patient to evacuate in a supine position within the MR unit is not comfortable, physiological or dignified during defecation. Therefore the entire study is clearly explained to

Address for Correspondence: Nuray Haliloğlu, MD, Ankara University Faculty of Medicine, Department of Radiology, Ankara, Turkey
E-mail: nurayunsal2@hotmail.com **ORCID ID:** orcid.org/0000-0002-1125-4896
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our patients at their first visit. We attempt to comfort them before the examination and repeat the evacuation phase at least three times to ensure the best possible dynamic images are obtained. Nevertheless, some patients still cannot defecate during the examination, which may or may not be associated with anismus.

It has been suggested that MRD may overdiagnose anismus, and should not be used solely for the diagnosis.[5] As impaired rectal evacuation may be a major finding of anismus, or due to insufficient patient co-operation, and both anismus and perineal descent may cause symptoms of obstructed defecation, a careful examination of MR images is of the utmost importance before reaching a final diagnosis that depends on radiological findings. We aimed to assess and compare static MRD measurements in patients with anismus and perineal descent, and to investigate if there were any findings that could aid in diagnosis of anismus in patients who cannot defecate.

Materials and Methods

The Institutional Ethics Committee approved this retrospective study protocol (approval number: 08-624-19) and waived informed consent.

Patient Population

We retrospectively evaluated 114 consecutive patients with symptoms of obstructed defecation (prolonged evacuation, the need to interdigitate the rectum, excessive straining, incomplete evacuation of stool) or chronic constipation who underwent MRD in a single center between July 2016 and March 2018. Patients who had a history of anorectal surgery, those with poor quality MR images due to artefacts or did not have adequate static images due to fecal incontinence or suboptimal patient cooperation were excluded. As a part of our standard procedure all patients were fully informed about the examination and the importance of patient cooperation.

MR Imaging Protocol

MRD was performed using a 1.5 Tesla system (General Electric, Optima MR 450 W). Patients were in the supine position using a phased array body coil. After obtaining T2W fast-spin echo static images in axial, coronal, and sagittal planes, the patient was placed in the left lateral decubitus position and approximately 150 mL of ultrasound gel was inserted via a rectal tube. When the rectum was filled with ultrasound gel, the patient was asked to lie in supine position, and a pillow was placed under the knee with slight flexion in order to be close to the physiological defecation position. Dynamic imaging was performed at rest and during evacuation in the sagittal plane using two-dimensional (2D) balanced, steady-state, free precession cine sequences. Consecutive images were obtained from the middle (including symphysis pubis, bladder, vagina, rectum and coccyx) and from a 1.5 cm distance on both sides of the midline, with a cross-sectional thickness of 5 mm. CINE images in the defecation phase were repeated three or four times or until the rectum was completely emptied.

Image Interpretation

Static MR images were retrospectively evaluated by a radiologist with 10 years experience in pelvic floor imaging, who was blind to the clinical data and dynamic MR imaging findings. Thickness of the internal and external anal sphincter was measured on T2W axial images. The pubococcygeal line (PCL) was drawn from the inferior tip of the pubic symphysis to the last coccygeal joint. The anorectal angle (ARA), defined as the angle between the anal canal and the posterior wall of the inferior rectum and M-line (the distance between the PCL and anorectal junction) were measured on static images with a distended rectum. Measurements below the PCL were considered as positive (+) values.

After recording all measurements on static images, dynamic images were reviewed and patients were divided into two groups, depending on the diagnosis reached through MRD. Group 1 consisted of patients with MRD findings suggesting anismus, including prolonged and incomplete evacuation, paradoxical contraction of the puborectalis muscle during defecation, inadequate opening of the anal canal and insufficient increase or decrease in ARA. Group 2 consisted of patients with any degree of perineal descent but with no sign of anismus. According to the "rule of three" pelvic floor descent was graded as "mild" if a pelvic organ prolapse was 3 cm or less below the PCL, "moderate" if it was between 3 cm to 6 cm below the PCL, and "severe" if descent was 6 cm or more below the PCL. Patients with coexisting anismus and perineal descent were excluded.

Thickness of anal sphincters, length of M-line, and degree of ARA were compared between the two groups.

Statistical Analysis

Data are presented as count and percentage (%), mean ± standard deviation or median and range, as appropriate. The t-test was used for the analysis of ages, and Pearson chi-square test was used to assess gender distribution in the groups. As data were nonparametric, Mann-Whitney U test was employed to compare the measurements of ARA, M-line and thicknesses of anal sphincters between the two groups. A $p<0.05$ was considered to be statistically significant.

Results

After excluding ineligible patients, a total of 90 patients (68 female, 75.6%) with a mean age of 49 years were evaluated. There were 17 male (45.9%), and 20 female (54.1%) patients in group 1 and 5 male (9.4%), and 48 female (90.6%) patients in group 2. Gender difference between the groups was significant (p<0.01). The mean age of the patients were 46±13.02 years in group 1 and 52±12.3 years in group 2. The mean ages of the patients were significantly different between the two groups (p=0.039).

Mean value of internal and external anal sphincter thickness was 4.7 and 4.9 mm, respectively in group 1 and 4.8 and 4.9 mm, respectively in group 2. Thickness of internal and external anal sphincters was not different.

The mean size of the ARA on static defecography images was 94±9.28° in group 1 and 97±10.53° in group 2. The median (range) values were 96° (80°-122°) in group 1 and 100° (85°-140°) in group 2 (Figure 1A, B). There was a significant difference in ARA measurements on static defecography images with a distended rectum (p=0.025).

Median values of M-line was +10 mm in group 1 and +16 mm in group 2 on static defecography images with a distended rectum (Figure 2A, B). There was a significant difference in the length of M-line (p=0.047). Results are summarized in Table 1.

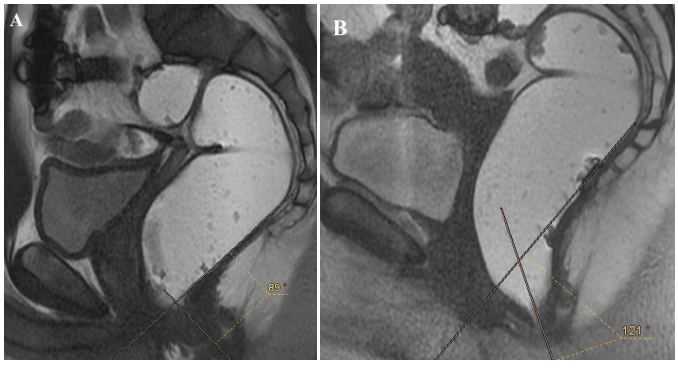

Figure 1. (A, B) Anorectal angle (the angle between the anal canal and the posterior wall of the inferior rectum). The angle is measured as 89° in a 40-year-old male patient with anismus (A), and 121° in a 56-year-old female patient with anterior and middle compartment descent (B)

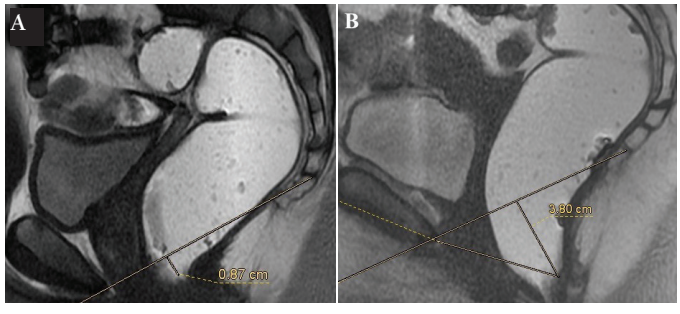

Figure 2. M-line (distance between pubococcygeal line and anorectal junction) measurements of the patients in Figure 1. The M line is much longer in the patient with descent (B)

Table 1. Comparison of patients with anismus and perineal descent

	Anismus (group 1)	Perineal descent (group 2)	p
Gender, n (%)	Male, (n=17) (45.9) Female, (n=20) (54.1)	Male, (n=5) (9.4) Female, (n=48) (90.6)	<0.01
Mean age, years	46	52	0.039
IAS thickness, mm	4.7	4.8	>0.05
EAS thickness, mm	4.9	4.9	>0.05
Mean anorectal angle	96°	100°	0.025
M line length, mm	+10	+16	0.047

n: Number of patients, IAS: Internal anal sphincter, EAS: External anal sphincter

Discussion

With the increased use of MRD, it has become obligatory to have a good understanding of anorectal morphology and function. Although dynamic sequences remain very important, static sequences should not be underestimated.

It has been reported that the success of defecation phase in MRD is variable and some patients may demonstrate no evacuation.[6,7] Besides being an indication of anismus, the non-physiological defecation position, poor instruction by the MR staff, limited numbers of attempts to defecate, lack of privacy and performance anxiety may all be causes of incomplete evacuation.[5,6] In order to avoid over-diagnosing anismus, the radiologist must pay careful attention to all sequences, including the images at rest. There is no reference diagnostic method for anismus, and a limited number of studies have been conducted in this field. Therefore diagnosis of anismus is usually a challenge for both clinicians and radiologists.

Both anismus and descending perineum syndrome may cause symptoms of obstructed defecation, but typical MR findings during evacuation are completely different.[3,4] Nevertheless little to no correlation was reported between patient symptoms and MRD findings.[6] It has also been suggested that there are no morphological abnormalities on defecography that are significantly associated with anismus.[5] Tirumanisetty et al.[8] assessed anal sphincter morphology and anorectal motion in healthy women and found that the perineum was lower at rest and during defecation in older women, as a result of increased perineal laxity. The distance between the anorectal junction and the PCL should not be greater than 2 cm.[9]

It has been suggested that aging is a risk factor for pelvic floor dysfunction, although this excludes cases of anismus. Descending perineum syndrome is more frequent among women over 50 years of age.[10] Our study also demonstrated that patients with anismus are significantly younger than patients with perineal descent, and approximately half of the patients with anismus were male. Interestingly, Piloni et al.[11], investigated MRD findings in male patients with obstructed defecation syndrome, and found that men with anismus tended to be older than those with rectal prolapse.

We found that the M-line was slightly longer in patients with perineal descent than in patients with anismus. We suggest that perineal laxity becomes obvious when rectum is distended, and an experienced radiologist can identify this, even on static images from MRD.

The mean thickness of the internal and external anal sphincters is about 3.5 mm and 4 mm, respectively. The external sphincter merges with the sling-like puborectalis muscle.[12] It has been reported that there is an increase in both internal and external anal sphincter thickness with age.[13] Although there is an abnormal muscular contraction in anismus, we could not find a significant difference in the thickness of anal sphincters in our patient population. This may be due to the relatively young age of the patients.

The ARA is normally measured to be in the range 90°-100° at rest and increases by about 15°-20° during defecation.[9,14] Age, body mass index and parity all influence ARA to varying degrees.[8] We found that ARA was slightly but significantly wider in patients with perineal descent than those with anismus, even at rest.

As MRD is an uncomfortable examination, it is not easy to conduct studies including asymptomatic volunteers. Most of our patients admitted to the MR unit for defecography have suffered from chronic symptoms and complain about seeking help for a long period of time. Therefore, almost every patient undergoing MRD has some type and degree of pelvic floor dysfunction, and it is not usually possible to generate a control group in MRD studies.

Study Limitations

Our study has some limitations. First, we do not have a control group of asymptomatic volunteers. Second, we have grouped the patients depending on the diagnosis reached by MRD and we did not have a gold standard technique to confirm the diagnosis. Third, our patients with perineal descent are a heterogenous group with variable severity of an abnormality that included different compartments of the pelvic floor in different patients. The retrospective nature of the study is also a notable limitation.

Conclusion

There is no significant gender predilection in anismus. Patients with anismus tended to be relatively younger than patients with perineal descent. The thickness of the anal sphincters did not differ between patients diagnosed with anismus and perineal descent on T2W images. However, when rectum was filled with contrast medium, the ARA was wider and the M-line was longer in patients with perineal descent, even at rest. These findings may help to rule out anismus in patients who cannot defecate during the examination.

Ethics

Ethics Committee Approval: The Institutional Ethics Committee approved this retrospective study protocol (approval number: 08-624-19).

Informed Consent: It wasn't obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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

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

References

1. Ganeshan A, Anderson EM, Upponi S, Planner AC, Slater A, Moore N, D'Costa H, Bungay H. Imaging of obstructed defecation. Clin Radiol 2008;63:18-26.
2. Piloni V, Tosi P, Vernelli M. MR-defecography in obstructed defecation syndrome (ODS): technique, diagnostic criteria and grading. Tech Coloproctol 2013;17:501-510.
3. Salvador JC, Coutinho MP, Venâncio JM, Viamonte B. Dynamic magnetic resonance imaging of the female pelvic floor-a pictorial review. Insights Imaging 2019;10:4.
4. Khatri G, Leon AD, Lockhart ME. MR Imaging of the pelvic floor. Magn Reson Imaging Clin N Am 2017;25:457-480.
5. Pisano U, Irvine L, Szczachor J, Jawad A, MacLeod A, Lim M. Anismus, physiology, radiology: is it time for some pragmatism? A comparative study of radiological and anorectal physiology findings in patients with anismus. Ann Coloproctol 2016;32:170-174.
6. Ramage L, Georgiou P, Qiu S, McLean P, Khan N, Kontnvounisios C, Tekkis P, Tan E. Can we correlate pelvic floor dysfunction severity on MR defecography with patient-reported symptom severity? Updates Surg 2018;70:467-476.
7. Pilkington SA, Nugent KP, Brenner J, Harris S, Clarke A, Lamparelli M, Thomas C, Tarver D. Barium proctography vs magnetic resonance proctography for pelvic floor disorders: a comparative study. Colorectal Dis 2012;14:1224-1230.
8. Tirumanisetty P, Prichard D, Fletcher JG, Chakraborty S, Zinsmeister AR, Bharucha AE. Normal values for assessment of anal sphincter morphology,

anorectal motion, and pelvic organ prolapse with MRI in healthy women. Neurogastroenterol Motil 2018;30:e13314.

9. Brandão AC, Ianez P. MR imaging of the pelvic floor defecography. Magn Reson Imaging Clin N Am 2013;21:427-445.
10. Murad-Regadas SM, Rodrigues LV, Furtado DC, Regadas FS, Olivia da S Fernandes G, Regadas Filho FS, Gondim AC, de Paula Joca da Silva R. The influence of age on posterior pelvic floor dysfunction in women with obstructed defecation syndrome. Tech Coloproctol 2012;16:227-232.
11. Piloni V, Bergamasco M, Melara G, Garavello P. The clinical value of magnetic resonance defecography in males with obstructed defecation syndrome. Tech Coloproctol 2018;22:179-190.
12. Erden A. MRI of anal canal: normal anatomy, imaging protocol, and perianal fistulas: Part 1. Abdom Radiol (NY) 2018;43:1334-1352.
13. Erden A, Peker E, Gençtürk ZB. Chronic anal fissure: morphometric analysis of the anal canal at 3.0 Tesla MR imaging. Abdom Radiol (NY) 2017;42:423-434.
14. Chamié LP, Ribeiro DMFR, Caiado AHM, Warmbrand G, Serafini PC. Translabial US and dynamic MR imaging of the pelvic floor: normal anatomy and dysfunction. Radiographics 2018;38:287-308.

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RESEARCH ARTICLE

Effect of a Surgical Endoscopy Training Program on Postgraduate Daily Practice: Results from a Single-Center

Timuçin Erol[1], Aynur Safiyeva[2], Ala Elcircevi[3], Bülent Erkek[3], Cihangir Akyol[3], Mehmet Ayhan Kuzu[3]

[1]Hacettepe University Faculty of Medicine, Department of General Surgery, Ankara, Turkey
[2]Central Customs Hospital, Clinic of General Surgery, Baku, Azerbaijan
[3]Ankara University Faculty of Medicine, Department of General Surgery, Ankara, Turkey

ABSTRACT

Aim: To evaluate the impact of surgical endoscopy training on the daily practice of post-graduate surgeons.
Method: Surgeons who completed gastrointestinal endoscopy training at Ankara University Faculty of Medicine, Department of General Surgery, Surgical Endoscopy Unit were invited to complete a web-based survey designed to assess the impact of training on post-graduate training.
Results: Of the 43 graduates, 32 (74.4%) completed the survey. All respondents continued to practice gastrointestinal endoscopy. Of the respondents, 19 (59.4%) were of the opinion that earlier training had a significant impact on their practice while 12 (37.5%) felt it had some impact. Furthermore, 20 (62.5%) reported that, post-training, they had experienced an increase in operating on patients for gastrointestinal surgical procedures.
Conclusion: Respondents were of the opinion that surgical endoscopy training had a positive impact on their daily surgical practice. We suggest that evaluation by objective parameters and generalized monitoring of all centers may promote continuous improvement in surgical endoscopy training.
Keywords: Post-graduate training, skill acquisition, surgical endoscopy

Introduction

The aim of gastrointestinal endoscopy training programmes should be to provide essential knowledge and technical skills and develop highly qualified professionals who are capable of performing safe, effective, and well-documented endoscopic procedures. Currently, there is no universal training program across Europe.

In Turkey, surgical endoscopy training is a part of the core education program of surgical residents. However, not all of the training facilities have their own endoscopy units. To provide an educational environment for those who do not have these facilities at their own institutes, beginning in 2009, the Turkish Surgical Association established the Surgical Endoscopy Training program for the surgeons. Up to date forty-one centers across Turkey are certified to provide practical education in surgical endoscopy. A list of these centers can be found on the website of the Turkish Surgical Association.[1]

This program aimed to educate surgeons willing to learn surgical endoscopy or renew and improve their skills. According to the Turkish Surgical Association, this program includes a minimum of three months of full-time participation, including theoretical lectures, a minimum of 200 endoscopy and colonoscopy procedures performed under supervision, and success in the written examination at the end of the program. This surgical endoscopy training aims to develop surgeons who can identify gastrointestinal lesions, obtain proper tissue samples, and utilize some therapeutic interventions.[2]

Ankara University Faculty of Medicine, Department of General Surgery, is one of these forty-one centers and

Address for Correspondence: Timuçin Erol, MD, Hacettepe University Faculty of Medicine, Department of General Surgery, Ankara, Turkey
E-mail: timucinerol@hacettepe.edu.tr **ORCID ID:** orcid.org/0000-0002-3475-3639
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actively continues the training of its own and other centers' trainees. This study aimed to evaluate the impact of surgical endoscopy training on the daily practice of post-graduate surgeons.

Materials and Methods

In order to evaluate the effect of training on post-graduate practice all trainees who graduated from our center were invited to complete a web-based survey. At the time of writing, forty-three trainees graduated from Ankara University surgical endoscopy training program. The survey did not include any patient data. The complete survey can be seen as suplementary material.

All of the trainers were senior faculty members, routinely perform both diagnostic and therapeutic interventions, and actively participate in endoscopy training. At the beginning of the training program, theoretical lectures were given. Subsequently, all trainees start to perform endoscopic interventions under the supervision of a senior faculty member.

The Ankara University Institutional Ethics Committee approved the study (approval number: İ5-307-21).

Statistical Analysis

No statistical analysis perfomed due to the nature of the study. All data given as numbers and percentages.

Results

A total of 43 students had graduated from the course and of those 32 (74.4%) completed the survey. Participants were currently working in: university hospital (n=9, 28.1%); education and research hospital (n=7, 21.9%); government hospital (n=5, 15.6%); and private hospital (n=11, 34.4%). Seventeen (53%) continued to perform endoscopy and colonoscopy >5 years after completion of training. Of the 32, 22 (71%) did not have any experience of endoscopic procedures prior to attending the training program but after completion, all of the participants began to perform routine endoscopy/colonoscopy at their own institutes. Moreover, 24 (66.7%) were executives of their respective endoscopy units at the time of the survey.

Endoscopic procedures constituted <20% of the daily activity of 15 (46.5%), between 20-40% of the daily activity of 11 (34.4%), >40-60% of the daily activity of 4 (12.5%) and >60% of the daily activity of two (6.25%). Proportion of daily activity taken up by endoscopic procedures is shown in Figure 1.

Fourteen (43.75%) reported that they performed 1-19 gastroscopies, while eleven (34.4%) performed 20-39 and seven (21.9%) performed >40 gastroscopies in the month prior to survey completion. In terms of colonoscopies, these figures were twenty (62.5%) performed 1-19, eleven

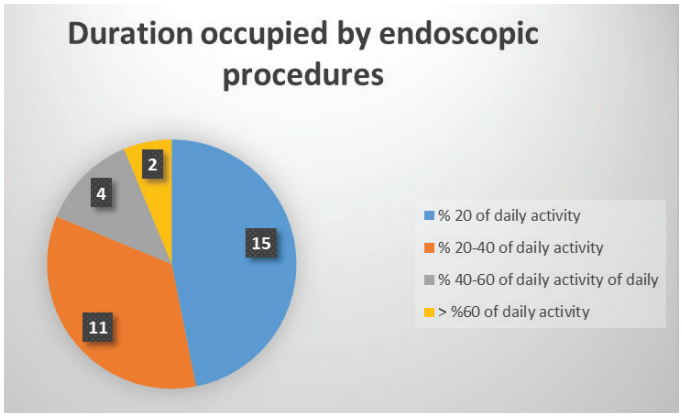

Figure 1. Proportion of daily activity taken up by endoscopic procedures of the respondents

(34.4%) performed 20-39 and on (3.1%) performed >40 colonoscopies. The number of procedures performed by participants at their institutes in the month preceding the survey is shown in Table 1.

During colonoscopy, the rate of cecal intubation was reported to be >80% by 22, (71%) graduates and 60-80% by 5 (16%) graduates. The mean process duration reported by participants is shown in Figure 2.

Respondents were also asked to report on therapeutic procedures performed. In terms of polypectomies performed in the month prior to the survey, 18 (56.25%) performed 1-9, 9 (28.1%) performed 10-29, 2 (6.25%) performed 30-50 and 3 (9.4%) performed >50 in the preceding month. Participants' average monthly therapeutic procedure numbers are given in Table 2.

Twelve (37.5%) participants had experienced a complication during practice, including perforation, bleeding, and oropharyngeal trauma. Twenty (62.5%) reported that they had an increase in gastrointestinal surgery rates and patient numbers after endoscopy/colonoscopy training while 11 (34.4%) said the training course had made no difference to the numbers of cases they dealt with (Figure 3A, B). Nineteen (59.4%) felt that surgical endoscopy training had made a significant impact on their daily practice while twelve (37.5%) felt it had made some difference to their daily practice. Encouragingly, all of the participants strongly recommended expanding surgical endoscopy training and expressed the opinion that all surgeons should learn to perform gastrointestinal endoscopy, at least for diagnostic purposes.

Discussion

Surgical endoscopy is a central element of both surgical training and practice. Unfortunately, in Turkey every surgery department does not have its own endoscopy unit so not all surgeons receive endoscopy training during residency.[3]

Table 1. Number of procedures performed by participants at their own institutes in the month preceding the survey

	Number of participants		
Number of procedures	Gastroscopy	Rectosigmoidoscopy	Colonoscopy
1-19	n=14	n=27	n=20
20-39	n=11	n=5	n=11
>40	n=7		n=1

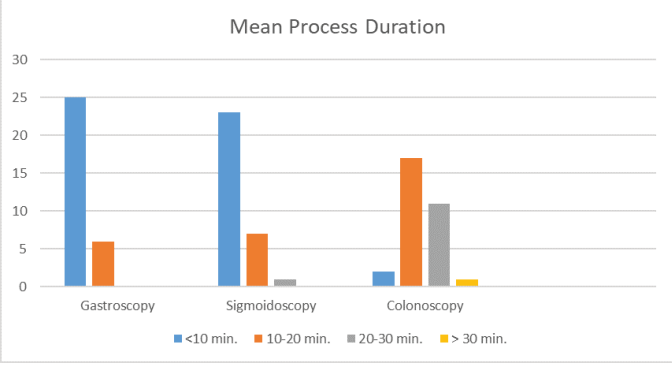

Figure 2. Mean process duration

Table 2. Average monthly therapeutic procedure numbers performed by respondents at their own institutes

	Number of participants		
Number of procedures	Polypectomy	Foreign body retreival	Hemostasis
1-10	n=18	n=31	n=28
10-30	n=9	-	n=3
30-50	n=2	-	-
>50	n=3	-	-

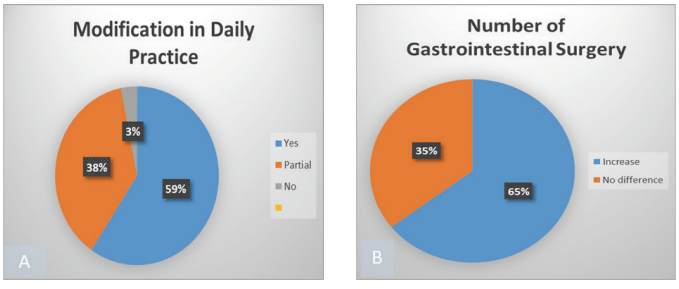

Figure 3. A) Effect of surgical endoscopy training on daily practice, B) Effect of surgical endoscopy training on gastrointestinal surgery cases

Establishing a proper environment for surgical endoscopy training has great importance, especially for surgeons who did not have the chance to learn gastrointestinal endoscopy practice during residency and also for those who are willing to renew their knowledge and improve skills. These training facilities may increase the number of surgeons who can perform high-quality endoscopic interventions.

Historically, the learning curve for gastrointestinal endoscopy only focused on procedural volume and there was great variability in terms of required minimum procedure numbers to be considered experienced in a procedure. These numbers have been been revised over time. For example, for competence in colonoscopy the American Society for Gastrointestinal Endoscopy revised the minimum required number from 100 to 275 in their guidelines published in1998 and 2017, respectively.[4,5] These numbers are lower for gastroscopy.[5] These numbers also vary by expert society guidelines and from nation to nation.[6,7] To date there is no current consensus on the minimum number of procedures. However, it is clear that only the number of procedures cannot reflect the competence of an intervention as personal skill of the practitioner and attitude of trainees attending training may also affect skill acquisition. Competence must be determined by direct observation and objective criteria.[5,8,9] One of the limitations of this study is that it lacks any objective measurement of practice, in terms of both actual as opposed to reported procedures and, most importantly, clinical outcomes. A second limitation is inherent in the design as this was a "web-based retrospective survey". It is notable that all of the respondents have the opportunity and continue to perform gastrointestinal endoscopy after proper training and most felt strongly that training had contributed positively to their daily practice. Moreover, six (18.75%) had established new endoscopy units or reactivated former units in their hospitals. Increasing the number of well-trained surgical endoscopists has a crucial role, especially in rural areas where access to a gastroenterologist is limited. Surgeons who are capable of performing emergency endoscopic procedures can play a critical role, especially in these areas.[3] Additionally, colorectal cancer is the third most common malignancy in Turkey, and a population-based colorectal cancer screening program from the Turkish Ministry of Health recommends colonoscopy, beginning from 50 years old and repeated every 10 years up to the age of 70 years for average-risk individuals.[10] As screening programs for colorectal cancer have been proven to reduce mortality, access to a gastroenterologist, especially in rural areas, can be problematic and cause reduced screening rates or longer waiting times.[11,12] After proper gastrointestinal endoscopy training, surgeons, and especially those working

in rural areas, may help to meet this demand and play a role in effective colorectal cancer screening.

However, to be a competent training center the quality of the training provided must be confirmed and regularly monitored through clear documentation of the clinical results, adherence to quality metrics, and the efficiency of these programs.[13] There is no doubt that, if the postgraduates do not perform endoscopic procedures with minimum quality requirements, then the training program is redundant. This survey showed that a the majority of trainees continued to perform surgical endoscopy, which may be an indicator of the effectiveness of the program. We believe that the most important result of this study, besides numeric data, is that most of the graduates continued to perform routine endoscopic procedures in their daily practice, which suggests that the program produced confident graduates. Of course, as this was a single-center survey, there is a need to investigate the results of the other centers and their graduate surgeons. To this end, some objective measurement is necessary in terms of case numbers, variability, duration of intervention and complication rates and final clinical outcomes.

Conclusion

We believe that proper surgical endoscopy training must be a part of the core education of all general surgeons. This study has shown that in this survey, education was reported to have a positive impact on daily surgical practice. To confirm these findings, objective metrics to measure course graduate performance would be required and would also aid in monitoring the graduates of all centers. Development of these metrics would also result in the ability to provide and promote continuous professional improvement for all gastrointestinal endoscopists.

Ethics

Ethics Committee Approval: The Ankara University Institutional Ethics Committee approved the study (approval number: İ5-307-21).

Informed Consent: None aplicable as no patient data used for the study.

Peer-review: Externally peer-reviewed

Authorship Contributions

Concept: M.A.K., C.A., B.E., T.E., Design: M.A.K., C.A., B.E., T.E., Data Collection or Processing: T.E., A.E., A.S., Analysis or Interpretation: T.E., A.E., A.S., Literature Search: T.E., A.S., A.E., B.E., C.A., M.A.K., Writing: T.E., C.A., M.A.K.

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

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

References

1. [Available from: https://www.turkcer.org.tr/kurs/cerrahi-endoskopi-egitimi-kursu
2. Lee SH, Chung IK, Kim SJ, Kim JO, Ko BM, Hwangbo Y, Kim WH, Park DH, Lee SK, Park CH, Baek IH, Park DI, Park SJ, Ji JS, Jang BI, Jeen YT, Shin JE, Byeon JS, Eun CS, Han DS. An adequate level of training for technical competence in screening and diagnostic colonoscopy: a prospective multicenter evaluation of the learning curve. Gastrointest Endosc 2008;67:683-689.
3. Yıldız İ, Koca YS, Bülbül MT, Musri ÖC. Emergency Endoscopy and the Importance of Endoscopy Training in General Surgery Residency: A Survey-Based Study. Med Sci Monit 2017;23:5184-5188.
4. Guidelines for credentialing and granting privileges for gastrointestinal endoscopy. Gastrointest Endosc 1998;48:679-682.
5. ASGE Standards of Practice Committee, Faulx AL, Lightdale JR, Acosta RD, Agrawal D, Bruining DH, Chandrasekhara V, Eloubeidi MA, Gurudu SR, Kelsey L, Khashab MA, Kothari S, Muthusamy VR, Qumseya BJ, Shaukat A, Wang A, Wani SB, Yang J, DeWitt JM. Guidelines for privileging, credentialing, and proctoring to perform GI endoscopy. Gastrointest Endosc 2017;85:273-281.
6. Ward ST, Mohammed MA, Walt R, Valori R, Ismail T, Dunckley P. An analysis of the learning curve to achieve competency at colonoscopy using the JETS database. Gut 2014;63:1746-1754.
7. Spier BJ, Durkin ET, Walker AJ, Foley E, Gaumnitz EA, Pfau PR. Surgical resident's training in colonoscopy: numbers, competency, and perceptions. Surg Endosc 2010;24:2556-2561.
8. Eisen GM, Baron TH, Dominitz JA, Faigel DO, Goldstein JL, Johanson JF, Mallery JS, Raddawi HM, Vargo JJ 2nd, Waring JP, Fanelli RD, Wheeler-Harbough J; American Society for Gastrointestinal Endoscopy. Methods of granting hospital privileges to perform gastrointestinal endoscopy. Gastrointest Endosc 2002;55:780-783.
9. Forbes N, Mohamed R, Raman M. Learning curve for endoscopy training: Is it all about numbers? Best Pract Res Clin Gastroenterol 2016;30:349-356.
10. T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü. Cancer Statistics. https://hsgm.saglik.gov.tr/tr/kanser-istatistikleri
11. Komaravolu SS, Kim JJ, Singh S, Merchant AM. Colonoscopy utilization in rural areas by general surgeons: An analysis of the National Ambulatory Medical Care Survey. Am J Surg 2019;218:281-287.
12. Ladabaum U, Dominitz JA, Kahi C, Schoen RE. Strategies for Colorectal Cancer Screening. Gastroenterology 2020;158:418-432.
13. Pearl J, Fellinger E, Dunkin B, Pauli E, Trus T, Marks J, Fanelli R, Meara M, Stefanidis D, Richardson W. Guidelines for privileging and credentialing physicians in gastrointestinal endoscopy. Surg Endosc 2016;30:3184-3190.

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RESEARCH ARTICLE

The Effect of Symptom/Waiting Periods and Appendectomy Timing on Clinical Outcomes in Patients with Appendectomy

Mehmet Mahir Fersahoğlu, Hüseyin Çiyiltepe, Ayşe Tuba Fersahoğlu, Nuriye Esen Bulut, Anıl Ergin, Mehmet Timuçin Aydın, Yasin Güneş, Yetkin Özcabi, İksan Taşdelen, Zuhal Yananlı, Ali Cihan Bilgili

University of Health of Sciences Turkey, Fatih Sultan Mehmet Training and Research Hospital, Clinic of General Surgery, İstanbul, Turkey

ABSTRACT

Aim: To examine the effects of pre-hospital and pre-operative hospital time and timing of surgery on clinical outcomes in patients with acute appendicitis (AA).

Method: Patients who underwent appendectomy between January 2015 and June 2020 were included. Demographic data, operation/anesthesia type, American Society of Anesthesiologists score, hospital admission times, hospital preparation time and total time (sum of duration of symptoms plus hospital preparation time), operation timing, peroperative findings and complications were evaluated.

Results: In total 1,865 cases were reviewed. The mean duration of symptoms was 20.7 hours, the mean preparation time was 14.5 hours, and the mean total time was 35.2 hours. In terms of operation timing and complication rates these were: 25.6% between 08:00-16:00 (5% complication rate); 41.9% between 16:00-24:00 (3.1% complication rate) and 32.5% between 24:00-08:00 (5.9% complication rate). When evaluated in terms of duration of symptoms and complications, this period was longer in the group with complications (20.4 versus 37.4 hours). When evaluated in terms of total time, it was found that this period was significantly longer in patients who developed complications (34.8 hours vs 42.4 hours, p=0.004). Duration of symptoms ≥11.5 hours was significantly associated with the development of complications. Furthermore, the complication rate increased when the total time was ≥30.5 hours.

Conclusion: The time from the onset of symptoms to appendectomy in AA is closely associated with the development of complications. Patients admitted to the hospital ≥11.5 hours after the onset of symptoms or operated ≥30.5 hours after symptom onset have an increased complication rate after appendectomy.

Keywords: Acute appendicitis, appendectomy, surgical outcomes, timing of the operation

Introduction

The lifetime incidence of acute appendicitis (AA) is around 8% and it is one of the most common causes of acute abdomen.[1] Pathogenesis of AA may be external (lymphoid hyperplasia) or internal (impacted stool, appendicolitis) compression, both types leading to lumen obstruction. This obstruction leads to increased mucus production, bacterial overgrowth, and stasis, which increase appendiceal wall tension.[2] Consequently, the decrease in blood and lymph flow creates a situation conducive to the development of necrosis and perforation. The incidence of complicated appendicitis progression from simple appendicitis, including gangrenous or perforated appendicitis, is 28-29%.[3,4] Postoperative morbidity rates are between 2% and 23%, which may include superficial or deep surgical site infections, adhesions, fistulas, vascular injuries, and urinary tract infections.[5,6] Appendectomy, which was first performed by Dr. Claudius Amyand in 1735, is one of the most common general surgical procedures in the treatment of AA.[7]

Recent successful trials of non-operative treatment of mild/moderate appendicitis predict that short delays may be

Address for Correspondence: Mehmet Mahir Fersahoğlu, MD, University of Health of Sciences Turkey, Fatih Sultan Mehmet Training and Research Hospital, Clinic of General Surgery, İstanbul, Türkiye
E-mail: fersahoglu@yahoo.com **ORCID ID:** orcid.org/0000-0003-2526-1832
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possible before planned emergency surgery.[8] Although delaying surgery increases the development of complicated appendicitis and post-operative complications,[9,10] controversy continues regarding the timing of appendectomy. Factors affecting the timing of the appendectomy include the patient's clinical picture, as well as the facilities available in the treating hospital, such as physical conditions or number of staff. Elective surgery lists and life-threatening emergencies are also important factors in delay.[11,12] There are a number of known potential disadvantages of emergency surgery and, sometimes, night surgery. In addition, there are reports that patient-related factors[9,13] have more effect than hospital-related factors[14,15] on the delay of treatment. Although some studies[16,17] reported higher rates of morbidity and complications associated with night surgery, no difference was found in other studies,[18,19] supporting the role of patient-related factors on AA surgery outcomes.

The aim of this study was to determine the effects of the time from the onset of symptoms to surgery and the period of the 24-hour cycle in which the appendectomy was performed on clinical outcomes and complication rates in patients with appendicitis.

Materials and Methods

The data of 1,865 patients who underwent appendectomy with a pre-diagnosis of AA between January 2015 and June 2020 in Fatih Sultan Mehmet Training and Research Hospital, Clinic of General Surgery were retrospectively analyzed. Ethics committee approval was obtained for this study from the hospital ethics committee (approval number: 30.03.2021/E-17073117-050.06). Informed consent was obtained from the patients. Parameters evaluated in the study included patient demographic data (age/gender), type of operation/anesthesia, American Society of Anesthesiologists (ASA) score, duration of symptoms, duration of preparation and total duration, defined as the sum of the former two periods, operation time divided into three periods (first period 08.00-17.00, second period 17.00-00.00, and third period 00.00-08.00), per-operative findings and data about post-operative complications in the first 30 days, based on the Clavien-Dindo classification.

The patients were examined by the emergency physician after presentation to the emergency department. Following physical examination and medical history taking, laboratory tests and ultrasound or computed tomography were planned. The time between the time when the patient first noticed symptoms such as fever, anorexia, nausea, vomiting, abdominal pain, and the time of presentation to the emergency service was defined as the "duration of symptoms". The onset time of symptoms was recorded by emergency department doctors. Later, the patient was admitted to the general surgery service with a pre-diagnosis of AA, and anesthesia preparation was completed.

Appendectomies were almost always initiated with a laparoscopic approach if there were no contraindications. Open appendectomy and/or spinal anesthesia was preferred when contraindications existed. Conversion to open surgery was at the option of individual surgeons at any stage, if the operating surgeon thought the laparoscopic procedure was unsafe.

In this study, the appendicitis was defined as simple in the surgical absence of gangrene, perforation, abscess, localized purulent fluid accumulation, and generalized peritonitis. In the presence of these findings, it was defined as complicated appendicitis.

Patients who were not diagnosed with complicated appendicitis were generally discharged within 24-48 hours, and intravenous antibiotic therapy was not used in the post-operative period, in line with the recommendations of current guidelines. In patients with complicated appendicitis, intravenous (iv) Ceftriaxone 2 g/day as two doses and iv Metronidazole 1,500 mg/day as three doses were preferred. Patients who tolerated a regular diet could be discharged when approved by the follow-up surgeon. All patients were called to the outpatient clinic after their first week of discharge. Post-operative complication was accepted as being present in patients who were admitted to the emergency department with any symptoms within the first 30 days during the follow-up period and who were subsequently hospitalized.

Histopathological evaluation of surgical excision samples was carried out by a specialist pathologist. Pathology was defined as: 1) AA, infiltration of muscularis propria with neutrophils without signs of purulent exudate; 2) Acute Suppurative Appendicitis, presence of purulent exudate in the lumen of the appendix with or without abscess formation in the appendiceal wall; 3) Acute Gangrenous Appendicitis, presence of gangrenous necrosis in the entire wall without evidence of perforation; and 4) Perforated Appendicitis, presence of roughly identifiable open perforation foci.

All patients over the age of 18 with a pre-diagnosis of AA were included in the study, while patients who underwent appendectomy for a reason other than AA diagnosis and patients with missing data were excluded from the study.

Statistical Analysis

SPSS, version 22 (IBM Inc., Armonk, NY, USA) software was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, frequency) were used to evaluate the study data, a One-Way ANOVA test was used to compare normally distributed parameters between groups in the comparison of quantitative data. Chi-square test and

Binary logistic tests were used to compare the qualitative data. Significance was assumed when p<0.05.

Results

There was a total of 1,865 patients who underwent appendectomy for AA included in the study. The mean age of all patients was 35.2 years and 1,178 (63.2%) were male and 687 (36.8%) were female. In addition, 67.1% were ASA 1 and 99.5% of the operations were performed under general anesthesia. While 1,776 patients (95.2%) were operated using a laparoscopic method, the open method was preferred in 70 (3.8%) patients at initial surgical planning. During surgery, 19 (1.0%) were converted from laparoscopic to open surgery. Analysis of the periods of the day in which operations were performed showed that, 477 (25.6%) were operated between 08.00 and 16.00, 781 (41.9%) were operated between 16.00 and 00.00, and 607 (32.5%) were operated between 00.00 and 08.00. During surgery, 1,490 (79.9%) patients had findings consistent with AA, and 375 (20.1%) patients had findings consistent with complicated appendicitis. The mean duration of the symptoms was 20.7 hours, the mean duration of preparation was 14.5 hours, resulting in a mean total duration of 35.2 hours. While no complications were detected in 1,781 (95.5%) patients, complications were observed in 84 (4.5%) patients. The most common complication grade was Clavien-Dindo 2 (59/84; 70.2%). Histopathological examination diagnosed AA in 48.5%, phlegmonous appendicitis in 25.5%, and gangrenous appendicitis in 12.9% (Table 1).

The patients were divided into two groups based on the absence (group 1) or presence (group 2) of complication (Table 2). The two groups were similar in terms of age and gender and complication rates were similar between patients with AA and complicated appendicitis. Duration of hospital preparation were also similar between the two groups However, when complications were evaluated by the method of surgery, complications rates were 15.8% in patients with conversion, 10.0% in open operations, and 4.2% in the laparoscopic group. When evaluated in terms of the operation period, the complication rate was 5.0% in 477 patients operated between 08.00 and 16.00, 3.1% in 781 patients operated between 16.00 and 00.00, and 5.9% in 607 patients operated between 00.00-08.00. When the patients were evaluated in terms of duration of symptoms and the presence of complications, this period was 20.4 hours in group 1 and 37.4 hours in group 2, and the difference was statistically significant. When evaluated in terms of total duration, it was found that this period was longer in patients who developed complications (p=0.004). Unsurprisingly, patients with complications stayed significantly longer in hospital post-operatively (p<0.001).

Table 1. Demographic data

Gender	
Male	1178 (63.2%)
Female	687 (36.8%)
Age	35.16±13.9 (15-84)
ASA	
I	1252 (67.1%)
II	478 (%5.6)
III	125 (6.7%)
IV	10 (0.5%)
Method of operation	
Open	70 (3.8%)
Laparoscopic	1776 (95.2%)
Conversion	19 (1%)
Application time	20.69±20.06 (1-168 h)
Waiting time in the hospital	14.53±10.92 (1-192 h)
Total duration	35.18±23.80 (6-240 h)
Operation period	
Period 1 (08-16)	477 (25.6%)
Period 2 (16-24)	781 (41.9%)
Period 3 (24-08)	607 (32.5%)
Operative finding	
Acute appendicitis	1490 (79.9%)
Complicated appendicitis	375 (20.1%)
Histopathology finding	
Acute appendicitis	904 (48.5%)
Phlegmonous appendicitis	476 (25.5%)
Gangrenous appendicitis	241 (12.9%)
Malignancy	12 (0.6%)
Perforated appendicitis	146 (7.8%)
Lymphoid hyperplasia/periappendicitis	86 (4.61%)
Complication	
No complication	1781 (95.5%)
Clavien-Dindo 1	3 (0.2%)
Clavien-Dindo 2	59 (3.2%)
Clavien-Dindo 3a	9 (0.5%)
Clavien-Dindo 3b	9 (0.5%)
Clavien-Dindo 4	4 (0.2%)
Length of hospital stay	2.12±1.79 (1-26 days)

ASA: American Society of Anesthesiologists

Table 2. Factors affecting the presence of complications

	Complication (n=84)	No complication (n=1781)	Univariate analysis	Multivariate analysis
Age	33.93	35.22	0.407[a]	-
Gender				
Female	29 (34.5%)	658 (36.9%)	0.372[b]	-
Male	55 (65.5%)	1123 (63.1%)	-	-
Type of operation				
Open	7 (8.3%)	63 (3.5%)	0.004[b]	0.367[c]
Laparoscopic	74 (88.1%)	1702 (95.6%)	-	-
Conversion	3 (3.6%)	16 (0.9%)	-	-
Operation period				
1	24 (28.6%)	453 (25.4%)	0.032[b]	0.590[c]
2	24 (28.6%)	757 (42.5%)	-	-
3	36 (42.9%)	571 (32.1%)	-	-
Operative finding				
A. appendicitis	64 (76.2%)	1,425 (80.0%)	0.234[b]	-
Complicated appendicitis	20 (23.8%)	356 (20.0%)		
Duration of symptoms	27.39	20.37	0.002[a]	0.311[c]
Duration of preparation	15.08	14.51	0.636[a]	-
Total duration of waiting	42.43	34.83	0.004[a]	0.805[c]
Length of hospital stay	3.05	2.08	<0.001[a]	0.002[c]

[a]One-Way ANOVA, [b]chi-square test, [c]Binary logistic

When Receiver Operator Curve (ROC) analysis was used to investigate duration of symptoms, a cut-off of ≥11.5 hours was identified for the risk of developing complications [area under the curve (AUC): 0.521 95% confidence interval (CI): 0.456-0.586; 47.6% sensitivity, 49.4% specificity, p=0.03]. When a similar ROC analysis was performed in terms of total duration of symptoms and preparation the cut-off was found to be 30.5 hours (AUC: 0.586, 95% CI: 0.523-0.650; 58.3% sensitivity, 56.1% specificity; p=0.007).

A subgroup analysis was performed in the complicated appendicitis group (Table 3). This found that the delay was higher in females compared to males in terms of both duration of symptoms and duration of preparation.

In a subgroup analysis performed in the complicated appendicitis group, the relationship between complications and age was examined (Table 4). For the duration of symptoms (11.5 hours), patients with complicated appendicitis were significantly older than patients with simple appendicitis (p<0.001). Similarly, for the total duration of waiting (30.5 hours), the complicated appendicitis group was again found to be significantly older than the simple appendicitis group (p=0.003).

Table 3. The effect of gender on the development of complications during the time until surgery

	Female	Male	p
Duration of symptoms	22.52±21.55	19.61±19.06	0.003[a]
Duration of preparation	15.87±13.44	13.75±90.5	<0.001[a]

[a]One-Way ANOVA

Table 4. The effect of age on the development of complications during the period until surgery

	Age	p
Duration of symptoms		
≥11.5 h	36.16±14.63	<0.001[a]
<11.5 h	33.61±12.55	
Total duration of waiting		
≥30.5	36.23±14.59	0.003[a]
<30.5	34.30±13.27	
[a]One-Way ANOVA		

Discussion

In this study, it was observed that the prolongation of the time from the onset of symptoms to surgery in patients who underwent appendectomy with a diagnosis of AA increased complications in the post-operative period and prolonged the length of hospital stay. This delay was related to duration of symptoms rather than duration of preparation.

Currently, although the suggestions on the timing of appendectomy are contradictory, only two guidelines[20,21] make recommendations about timing. The meta-analysis used by these guidelines reported that there was no significant difference in complicated appendicitis rates if the delay was less than 12 hours or up to 24 hours. The 2016 World Society of Emergency Surgery guidelines[20] concluded that a 12-24 hour delay in hospital for simple appendicitis did not have adverse effects on clinical outcomes. In contrast, The European Society of Endoscopic Surgery[21], which published its guide in 2016, recommended that delaying appendectomy will increase the risk of perforated appendicitis and complications, therefore appendectomy should be performed as quickly as possible.

A study by Ditillo et al.[2] showed that the severity of the pathological diagnosis and the risk of developing complications are proportional to time, and that delaying appendectomy is associated with a poor prognosis. They found that the delay in the time of the patient's transportation to the hospital was more closely related to the worsening of the pathology than delays occurring in the hospital. Similar findings were previously reported in two different series but with a much smaller number of patients (114 and 95, respectively). Since it does not seem possible to ameliorate the delay in admission to the hospital, every effort should be made in hospital in order to diagnose these patients rapidly and speed up their operations.[2]

Many studies have been conducted evaluating the effect of the time interval from hospital to surgery on results in patients with AA.[22,23] In addition to studies reporting that waiting for 12 hours or more significantly increased the risk of perforation and complications,[22] another analysis including 4529 patients showed that surgical site infections increased if the delay was ≥6 hours.[24] In contrast, in another study by Shin et al.[25], it was reported that an eight-hour threshold did not create a significant difference in results between subgroups waiting for the operation. Some other studies have found that waiting for 24 hours does not pose any risk.[26,27]

Numerous studies have shown a direct relationship between the time to surgery and complications.[22,28] Although surgeons try to avoid a possible delay for their operations, it is not always possible for the patient to be operated quickly. The diagnostic process or scheduled consultations with patients with comorbidities may take time. Limitations in operating room availablility may also delay the surgery. In addition, since the admission of patients with AA is often in the evening or after midnight, as in our study, the limited number of healthcare staff at these hours constitute other reasons for the delay. While 18 hours was the threshold in the study of Lee et al., 11.5 hours was found to be critical for the development of complications in our series.

The most important issue regarding the delay of appendectomy is the risk of perforation, as this leads to increased morbidity and mortality rates and longer hospital stays. Busch et al.[22] found that the risk of perforation increased with time and a threshold of 12 hours was critical in this process. Temple et al.[9] concluded that most perforation occurred due to a delay in admission.

In analyzes conducted to investigate the effect of gender on the occurrence of complications, the differences identified may be due to differences in perception of pain between genders. Studies have noted that females have more clinical pain.[29] Another analysis showed that longer duration of preparation affected older patients and females (19%) more than males (9%). It has been found that gynecological pathologies cause symptoms indistinguishable from appendicitis, especially in females in the premenopausal period.[30] In our study, both duration of symptoms and duration of preparation were found to be longer in females, probably due in part to some of the causes identified in earlier studies.

Anatomical and physiological changes in the appendix have been suggested as a reason for the rapid progression of the disease at older ages.[31] Although it has been reported that age did not make any difference in terms of the degree of inflammation, it was found that a significant portion (37%) of patients with complicated appendicitis were over the age of 50 years.[14,32,33] In our study, simple and complicated appendicitis groups were found to be similar in terms of age. However, the age difference between the complicated appendicitis group and the simple appendicitis group was statistically significant and in favor of the complicated group in the subgroup analysis.

Study Limitations

The limitation of this study is the retrospective analysis of data from a single hospital, and the small number of patients who developed complications despite the large overall cohort size.

Conclusion

A significant relationship was found between delayed surgery and postoperative complication rates in patients

with AA. The most important factor affecting the delay time is the prolongation from the onset of the patient's symptoms to admission to the hospital. Both duration of symptoms and duration of preparation were found to be longer in female patients. Total duration exceeding 30.5 hours increases the rate of complications after appendectomy.

Ethics

Ethics Committee Approval: Ethics committee approval was obtained for this study from the hospital ethics committee (approval number: 30.03.2021/E-17073117-050.06).

Informed Consent: Informed consent was obtained from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.M.F., N.E.B., A.E., Concept: M.T.A., A.T.F., Z.Y., Design: H.Ç., N.E.B., Data Collection or Processing: H.Ç., A.E., Analysis or Interpretation: A.T.F., Y.G., Y.Ö., Literature Search: M.T.A., İ.T., Z.Y., A.C.B., Writing: M.M.F., M.T.A.

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References

1. Bhangu A, Søreide K, Di Saverio S, Assarsson JH, Drake FT. Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. Lancet 2015;386:1278-1287.
2. Ditillo MF, Dziura JD, Rabinovici R. Is it safe to delay appendectomy in adults with acute appendicitis? Ann Surg 2006;244:656-660.
3. Cueto J, D'Allemagne B, Vázquez-Frias JA, Gomez S, Delgado F, Trullenque L, Fajardo R, Valencia S, Poggi L, Ballí J, Diaz J, González R, Mansur JH, Franklin ME. Morbidity of laparoscopic surgery for complicated appendicitis: an international study. Surg Endosc 2006;20:717-720.
4. Yaghoubian A, de Virgilio C, Lee SL. Appendicitis outcomes are better at resident teaching institutions: a multi-institutional analysis. Am J Surg 2010;200:810-813.
5. Leung TT, Dixon E, Gill M, Mador BD, Moulton KM, Kaplan GG, MacLean AR. Bowel obstruction following appendectomy: what is the true incidence? Ann Surg 2009;250:51-53.
6. Poprom N, Numthavaj P, Wilasrusmee C, Rattanasiri S, Attia J, McEvoy M, The efficacy of antibiotic treatment versus surgical treatment of uncomplicated acute appendicitis: systematic review and network meta-analysis of randomized controlled trial. Am J Surg 2018;218:192-200.
7. Drake FT, Mottey NE, Farrokhi ET, Florence MG, Johnson MG, Mock C, Steele SR, Thirlby RC, Flum DR. Time to appendectomy and risk of perforation in acute appendicitis. JAMA Surg 2014;149:837-844.
8. Varadhan KK, Neal KR, Lobo DN. Safety and efficacy of antibiotics compared with appendicectomy for treatment of uncomplicated acute appendicitis: meta-analysis of randomised controlled trials. BMJ 2012;344:e2156.
9. Temple CL, Huchcroft SA, Temple WJ. The natural history of appendicitis in adults. A prospective study. Ann Surg 1995;221:278-281.
10. Berry J Jr, Malt RA. Appendicitis near its centenary. Ann Surg 1984;200:567-575.
11. Martin IC. Who operates when? II: the National Confidential Enquiry into perioperative deaths 2003. Hosp Med 200465:196-197.
12. Leff DR, Aggarwal R, Rana M, Nakhjavani B, Purkayastha S, Khullar V, Darzi AW. Laparoscopic skills suffer on the first shift of sequential night shifts: program directors beware and residents prepare. Ann Surg 2008;247:530-539
13. Maroju NK, Robinson Smile S, Sistla SC, Narasimhan R, Sahai A. Delay in surgery for acute appendicitis. ANZ J Surg 2004;74:773-776.
14. Hale DA, Molloy M, Pearl RH, Schutt DC, Jaques DP. Appendectomy: a contemporary appraisal. Ann Surg 1997;225:252-261.
15. Von Titte SN, McCabe CJ, Ottinger LW. Delayed appendectomy for appendicitis: causes and consequences. Am J Emerg Med 1996;14:620-622.
16. Kelz RR, Freeman KM, Hosokawa PW, Asch DA, Spitz FR, Moskowitz M, Henderson WG, Mitchell ME, Itani KM. Time of day is associated with postoperative morbidity: an analysis of the national surgical quality improvement program data. Ann Surg 2008;247:544-552.
17. Lockley SW, Cronin JW, Evans EE, Cade BE, Lee CJ, Landrigan CP, Rothschild JM, Katz JT, Lilly CM, Stone PH, Aeschbach D, Czeisler CA; Harvard Work Hours, Health and Safety Group. Effect of reducing interns' weekly work hours on sleep and attentional failures. N Engl J Med 2004;351:1829-1837.
18. Jørgensen AB, Amirian I,Watt SK, Boel T, Gögenur I. No circadian variation in surgeons' ability to diagnose acute appendicitis. J Surg Educ 2016;73:275-280.
19. Hall AB, Freeman T, Banks S. Is it safe? Appendectomies at night at a low-volume center. J Surg Educ 2011;68:199-201.
20. Di Saverio S, Birindelli A, Kelly MD, Catena F, Weber DG, Sartelli M, Sugrue M, De Moya M, Gomes CA, Bhangu A, Agresta F, Moore EE, Soreide K, Griffiths E, De Castro S, Kashuk J, Kluger Y, Leppaniemi A, Ansaloni L, Andersson M, Coccolini F, Coimbra R, Gurusamy KS, Campanile FC, Biffl W, Chiara O, Moore F, Peitzman AB, Fraga GP, Costa D, Maier RV, Rizoli S, Balogh ZJ, Bendinelli C, Cirocchi R, Tonini V, Piccinini A, Tugnoli G, Jovine E, Persiani R, Biondi A, Scalea T, Stahel P, Ivatury R, Velmahos G, Andersson R. WSES Jerusalem guidelines for diagnosis and treatment of acute appendicitis.World J Emerg Surg 2016;11:34.
21. Gorter RR, Eker HH, Gorter-Stam MA, Abis GS, Acharya A, Ankersmit M, Antoniou SA, Arolfo S, Babic B, Boni L, Bruntink M, van Dam DA, Defoort B, Deijen CL, DeLacy FB, Go PM, Harmsen AM, van den Helder RS, Iordache F, Ket JC, Muysoms FE, Ozmen MM, Papoulas M, Rhodes M, Straatman J, Tenhagen M, Turrado V, Vereczkei A, Vilallonga R, Deelder JD, Bonjer J. Diagnosis and management of acute appendicitis. EAES consensus development conference 2015. Surg Endosc 2016;30:4668-4690.
22. Busch M, Gutzwiller FS, Aellig S, Kuettel R, Metzger U, Zingg U. In-hospital delay increases the risk of perforation in adults with appendicitis. World J Surg 2011;35:1626-1633.
23. Stahlfeld K, Hower J, Homitsky S, Madden J. Is acute appendicitis a surgical emergency? Am Sur 2007;73:626-629.
24. Teixeira PG, Sivrikoz E, Inaba K, Talving P, Lam L, Demetriades D. Appendectomy timing: waiting until the next morning increases the risk of surgical site infections. Ann Surg 2012;256:538-543.
25. Shin CS, Roh YN, Kim JI. Delayed appendectomy versus early appendectomy in the treatment of acute appendicitis: a retrospective study. World J Emerg Surg 2014;9:8.
26. Giraudo G, Baracchi F, Pellegrino L, Dal Corso HM, Borghi F. Prompt or delayed appendectomy? Influence of timing of surgery for acute appendicitis. Surg Today 2013;43:392-396.
27. United Kingdom National Surgical Research Collaborative, Bhangu A. Safety of short, in-hospital delays before surgery for acute appendicitis: multicentre cohort study, systematic review, and meta-analysis. Ann Surg 2014;259:894-903.

28. N. Sicard, P. Tousignant, R. Pineault, S. Dube, Non-patient factors related to rates of ruptured appendicitis, Br J Surg 2007;94:214-221.
29. Fillingim RB, King CD, Ribeiro-Dasilva MC, Rahim-Williams B, Riley JL 3rd. Sex, gender, and pain: a review of recent clinical and experimental findings. J Pain 2009;10:447-485.
30. Hansson LE, Laurell H, Gunnarsson U. Impact of Time in the Development of Acute Appendicitis. Dig Surg 2008;25:394-399.
31. Paajanen H, Kettunen J, Kostiainen S. Emergency appendectomies in patients over 80 years. Am Surg 1994;60:950-953.
32. Körner H, Söndenaa K, Söreide JA, Andersen E, Nysted A, Lende TH, Kjellevold KH. Incidence of acute nonperforated and perforated appendicitis: age-specific and sex-specific analysis. World J Surg 1997;21:313-317.
33. Moss JG, Barrie JL, Gunn AA. Delay in surgery for acute appendicitis. J R Coll Surg Edinb 1985;30:290-293.

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CASE REPORT

Cecal Diverticulitis: A Rare Cause of Right Lower Quadrant Pain

Murat Aba, Ahmet Onur Demirel, Ahmet Rencüzoğulları

Çukurova University Faculty of Medicine, Department of General Surgery, Adana, Turkey

ABSTRACT

Cecal diverticula and diverticulitis are rare conditions, which present with pain in the lower quadrant of the abdomen. It is a rare cause of acute abdomen and is more often seen in young female adults. The diagnosis of cecal diverticulitis requires advanced radiological imaging techniques because physical examination and routine laboratory blood tests may be inconclusive. Cecal diverticulitis has been most frequently misdiagnosed as acute appendicitis. There is no consensus on the optimal clinical management.

Keywords: Cecum, diverticula, diverticulitis

Introduction

Cecum diverticula (CD) are true diverticula, often involving all layers of the colon, and are a rare cause of right lower quadrant pain that can be confused with acute appendicitis. The first case of solitary cecum diverticulum was described by Potier in 1912.[1] CD often requires emergency surgery because it is difficult to diagnose clinically and radiologically in the preoperative period. CD is often diagnosed during the operation, and varies depending on the additional conditions associated with the management and operation procedure. The aim of this case report is to describe and discuss this rare disease.

Case Report

A 26-year-old male patient was admitted to our emergency department complaining of abdominal pain, nausea and loss of appetite for two days. On physical examination, there was defense, rebound and tenderness in the right lower quadrant. It was learned that the patient had the same complaints about two years earlier, but did not attend the hospital. In the laboratory tests of the patient, white blood cell count was 11,800/mm.[3] Other parameters were within normal limits. There were intense gas shadows on direct radiography. Ultrasonography (US) was evaluated as suboptimal due to intense gas shadows. On oral and intravenous contrast-enhanced computed tomography (CT) the appendix appeared normal but there was a 1.5 cm diverticulum formation in the posterior wall of the cecum and intense inflammation around it, consistent with acute diverticulitis (Figure 1). Intravenous hydration and appropriate antibiotherapy treatment was initiated.

Diagnostic laparoscopy was performed because physical examination findings had not improved during the 3-day follow-up. On intraoperative observation, the highly hyperemic, inflamed and edematous appearance of the diverticulum, located 1 cm from the appendix and on the posterior aspect of the cecum was compatible with diverticulitis. Other parts of the cecum were normal in appearance. Due to the close proximity of the appendix, the patient underwent laparoscopic diverticulectomy and appendectomy with endoscopic linear stapler. An oral regimen was started on the second postoperative day for the patient, who had gas and stool output during the service follow-up. The patient was discharged on the third postoperative day without complication.

Histopathological examination confirmed perforated cecum diverticulitis with normal appendix vermiformis (Figure 2). Informed consent was obtained.

Address for Correspondence: Ahmet Onur Demirel, MD, Çukurova University Faculty of Medicine, Department of General Surgery, Adana, Turkey
E-mail: ahmetonur.demirel@gmail.com **ORCID ID:** orcid.org/0000-0002-0313-5467
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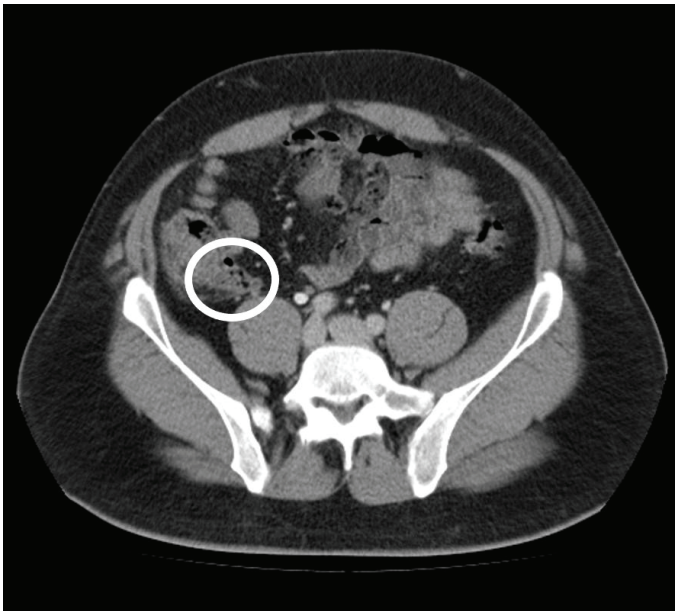

Figure 1. CT image of the cecum, diverticulitis formation showed in the white circled area
CT: Computed tomography

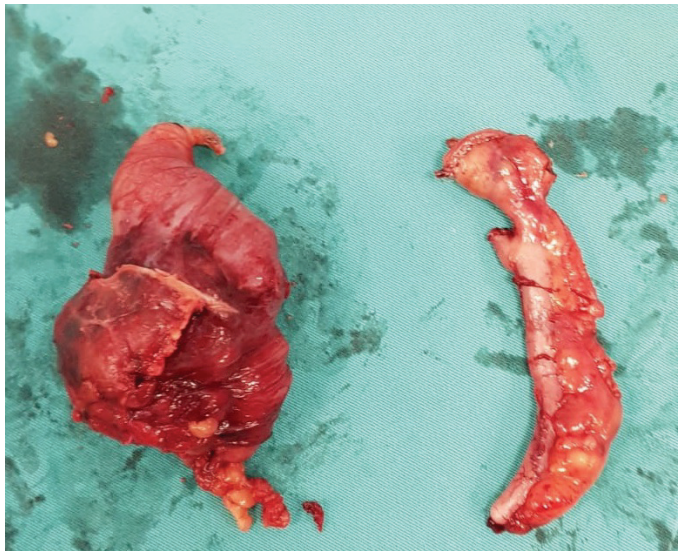

Figure 2. Specimen image of cecum diverticulitis and appendix vermiformis

Discussion

While 85% of all colon diverticula are asymptomatic, approximately 4-15% present with an acute diverticulitis attack.[2] In the differential diagnosis of right lower quadrant pain, cecum diverticulitis should be considered, together with pathologies such as acute appendicitis, cecum tumors, inflammatory bowel diseases, ovarian pathologies, pelvic inflammatory disease, ameboma, and gastrointestinal tuberculosis involvement.[3] Although the exact frequency of CD is unclear, it is seen in approximately 1:300 appendectomy cases.[4] As CDs are congenital, they differ from distal colon diverticula.[5] They are mostly located on a single and anterior face.[6] However, in our case, the CD was located on the posterior face. CD are often seen in young and female patients.[7] Clinical management of the cases described varies. Medical follow-up, including broad spectrum antibiotherapy was recommended in some cases, while right hemicolectomy or isolated diverticulectomy was recommended in other cases.[8] In our case, laparoscopic diverticulectomy and appendectomy were preferred due to the patient's age and the location of the diverticulum. In the diagnosis of CD, the utility of US and CT have been reported to be insufficient so that diagnosis was made intraoperatively. However, thanks to advances in technology including improvements in the resolution achievable with new CT devices, it is now easier to make preoperative diagnosis with radiological evaluation. In our case, it was found that the appendix was clearly normal and CD was identified on CT.

There is no consensus regarding the clinical management of CD. In our case, medical treatment was applied in the first place and surgical treatment was performed due to persistent severe abdominal pain. We believe that decisions about treatment and surgical timing should be made according to the clinical condition of the patient.

CD is a disease that mimics acute appendicitis, and deficiencies in diagnosis and treatment can cause mortality and morbidity. Laparoscopic diverticulectomy may be an appropriate option in some patients. Colonoscopy should be recommended to the patients in the first six weeks after an acute attack of diverticulitis in order to investigate possible right colonic lesions.[9]

Ethics

Informed Consent: It was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.A., A.R., Concept: M.A., A.O.D., A.R., Design: M.A., A.O.D., A.R., Data Collection or Processing: M.A., A.O.D., Analysis or Interpretation: M.A., A.O.D., A.R., Literature Search: M.A., A.O.D., Writing: M.A., A.O.D., A.R.

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References

1. Potier F. Diverticulite et appendicite. Bulletins et Memoires de la Societe Anatomique de Paris 1912;137:29-31 https://www.scirp.org/(S(351jmbntvnsjt1aadkposzje))/reference/ReferencesPapers.aspx?ReferenceID=1672133

2. Shahedi K, Fuller G, Bolus R, Cohen E, Vu M, Shah R, Agarwal N, Kaneshiro M, Atia M, Sheen V, Kurzbard N, van Oijen MG, Yen L, Hodgkins P, Erder MH, Spiegel B. Long-term risk of acute diverticulitis among patients with incidental diverticulosis found during colonoscopy. Clin Gastroenterol Hepatol 2013;11:1609-1613.
3. Ruiz-Tovar J, Reguero-Callejas ME, González Palacios F. Inflammation and perforation of a solitary diverticulum of the cecum. A report of 5 cases and literature review. Rev Esp Enferm Dig 2006;98:875-880.
4. Oudenhoven LF, Koumans RK, Puylaert JB. Right colonic diverticulitis: US and CT findings--new insights about frequency and natural history. Radiology 1998;208:611-618.
5. Cole M, Ayantunde AA, Payne J. Cecum diverticulitis presenting as acute appendicitis: a case report. World J Emerg Surg 2009;4:29.
6. Karatepe O, Gulcicek OB, Adas G, Battal M, Ozdenkaya Y, Kurtulus I, Altiok M, Karahan S. Cecal diverticulitis mimicking acute Appendicitis: a report of 4 cases. World J Emerg Surg 2008;3:16.
7. Kumar S, Fitzmaurice GJ, O'Donnell ME, Brown R. Acute right iliac fossa pain: not always appendicitis or a caecal tumour: Two case reports. Cases J 2009;2:88.
8. Yuksel A, Civil O, Colakoglu MK, Sumer F, Eruyar AT. Solitary cecal diverticulitis, a rare cause of right lower quadrant pain: Four cases. North Clin Istanb 2018;5:148-152.
9. You H, Sweeny A, Cooper ML, Von Papen M, Innes J. The management of diverticulitis: a review of the guidelines. Med J Aust 2019;211:421-427.

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CASE REPORT

A Rare Cause of Ileus: Acute Idiopathic Colonic Pseudo-Obstruction (Ogilvie Syndrome)

Recep Çağlar, İbrahim Öner

Mersin City Training and Research Hospital, Clinic of General Surgery, Mersin, Turkey

ABSTRACT

Acute idiopathic colonic pseudo-obstruction, also known as Ogilvie syndrome, is a rare disease characterized by acute dilation of the colon without a mechanical cause. Although its pathogenesis is not clearly known, it is thought that the main underlying cause is a defect in autonomic innervations. The etiology is multifactorial, but it usually occurs in critically ill, hospitalized patients, patients with trauma, patients who have undergone surgery, and in association with electrolyte disturbances. The most worrying complications of the disease are ischemia and perforation. The first step in treatment is the conservative approach. In patients resistant to medical therapy, surgical intervention is necessary if there are signs of colonic ischemia or perforation. In this article, a patient with Ogilvie syndrome causing ileus is presented.

Keywords: Ileus, Ogilvie syndrome, acute idiopathic colonic pseudo-obstruction

Introduction

Acute idiopathic colonic pseudo-obstruction (AICPO), also known as Ogilvie syndrome, is a rare disease characterized by acute dilation of the colon without a mechanical cause. It was first described by Sir William Ogilvie in 1948.[1]

Although the pathogenesis of AICPO is not clearly known, it is thought to result from a defect in the autonomic regulation of colonic motor function. Etiology includes various conditions, such as surgery, trauma, infection, cardiac, renal, neurological, metabolic causes, drugs, malignancy, and major burns.[2]

Diagnosis is made clinically and radiologically. Appropriate conservative measures, pharmacological treatment, colonoscopic decompression, and surgery are all used in the treatment of AICPO.[3]

The diagnosis of AICPO is difficult and often delayed. Early diagnosis and treatment are important to minimize morbidity and mortality. In this article, a patient with AICPO causing ileus is presented.

Case Report

A 54-year-old male patient presented to the emergency department with complaints of abdominal pain, swelling in the abdomen, and inability to pass gas and stool. In his anamnesis, it was learned that he was admitted to the hospital several times with the same complaints and was discharged after supportive treatment was given and an outpatient clinic appointment was offered. On physical examination, severe respiratory distress, generalized abdominal tenderness, rebound, excessive distension and tympanism were present. In terms of laboratory results, biochemistry findings were within normal limits. However, hematological parameters were deranged, including anemia (hemoglobin: 10.5 g/dL), leukocytosis (leukocyte count: 11,720/mm^3) and thrombocytosis (platelet count: 508,000/mm^3). Widespread dilated colon loops were observed in the entire colon on standing direct abdominal X-ray (Figure 1). On computed tomography (CT), severe dilation in the colon segments, decrease in the volume of the right lung in the inferior thoracic aperture, increased compensatory aeration in the left lung, and displacement of the heart to the right were observed (Figure 2, 3). The rectum was markedly wide and no obstructive masses were detected. The patient underwent emergency surgery with the diagnosis of ileus. During surgery, it was observed that the entire colon was excessively dilated and pressed on the thorax. Total abdominal colectomy, ileal J pouch, ileorectal anastomosis, and diverting loop ileostomy were performed. Informed consent was obtained.

Address for Correspondence: Recep Çağlar, MD, Mersin City Training and Research Hospital, Clinic of General Surgery, Mersin, Turkey
E-mail: rcaglarr@gmail.com **ORCID ID:** orcid.org/0000-0003-0987-9202
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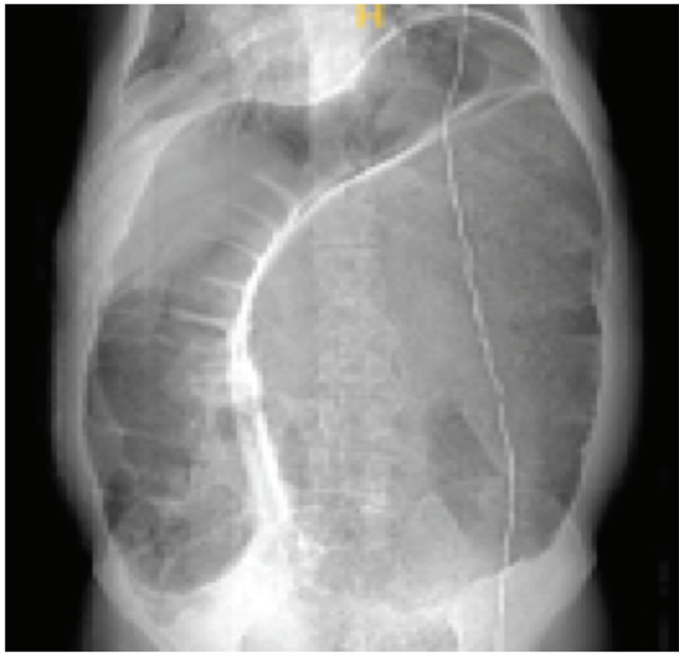

Figure 1. ADBG

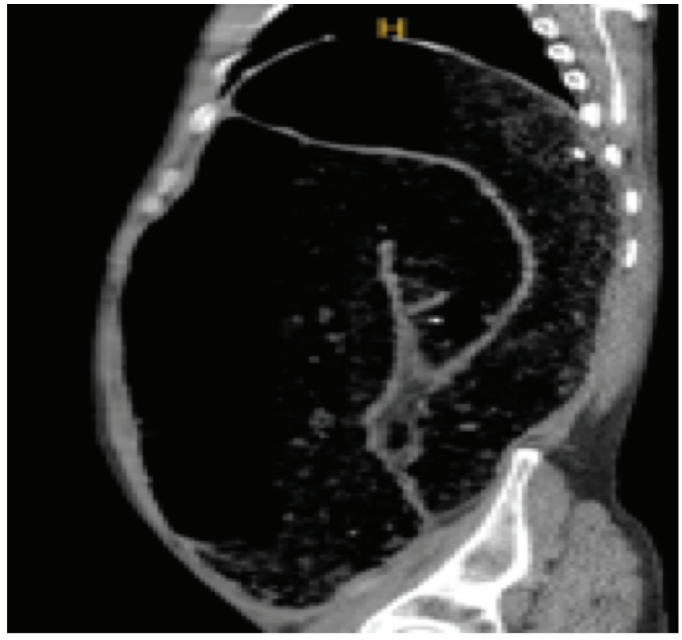

Figure 3. CT: Dilated megacolon
CT: Computed tomography

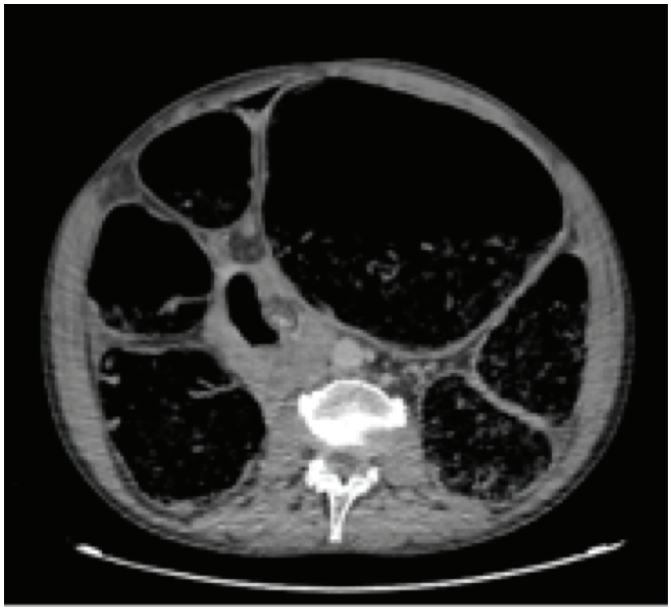

Figure 2. CT: Dilated megacolon
CT: Computed tomography

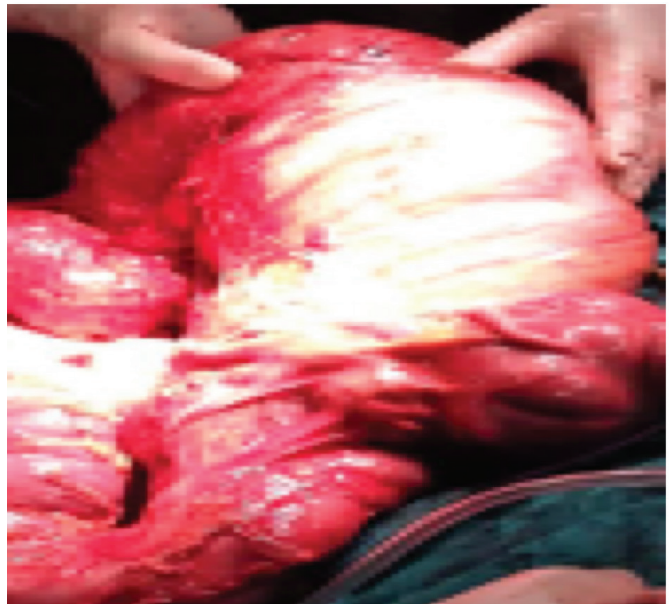

Figure 4. Intraoperative

Discussion

AICPO is a rare condition characterized by signs and symptoms of colonic obstruction without a mechanical cause. AICPO probably results from an imbalance in autonomic regulation of the distal colon. The main clinical feature in patients with AICPO is gradually increasing abdominal distension. Abdominal pain, nausea, vomiting and dyspnea are less common. It is more common in men and patients over 50 years of age. Historically, the mortality rate has been shown to be 25-31%. Although it is usually seen in the cecum and right colon, the dilation may also extend into the rectum.[4] Our patient was male and aged 54 which was consistent with the common characteristics of Ogilvie syndrome. Widespread dilations, kinks and compression of the diaphragm were observed in the entire colon, especially in the left colon, intraoperatively (Figure 4, 5). The most important mortal complications are ischemia and perforation. Spontaneous perforation has been reported in 3-15% of patients, and the mortality rate in these patients is over 40%.[5]

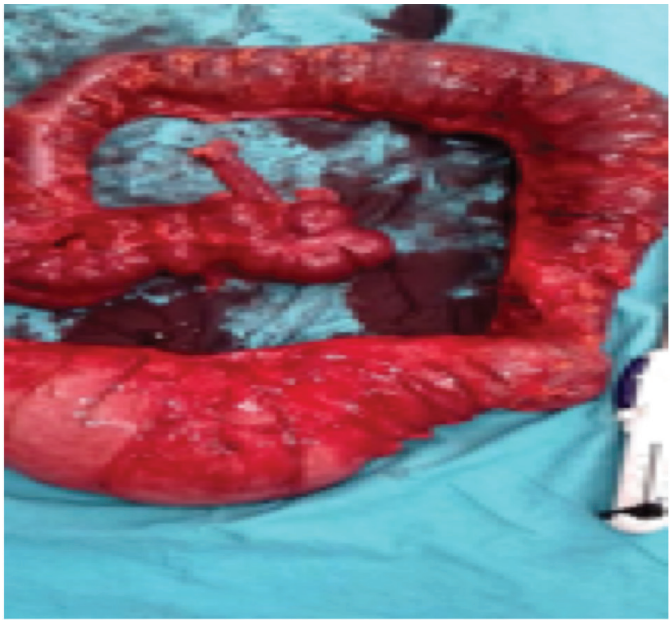

Figure 5. Postoperative

In general, it is not always possible to make a preoperative diagnosis in patients with Ogilvie syndrome. Contrast enema is the gold standard for excluding mechanical obstruction and confirming the diagnosis. CT may be useful in excluding mechanical causes and in those who cannot have a contrast enema. Colonoscopy is useful in the diagnosis and treatment of colonic lesions and decompression of the dilated colon.[6] Manometry is generally useful in determining the severity of pseudo-obstruction in children, especially in children with Hirschsprung's disease.[7]

Patients are treated conservatively if there is no sign of ischemia or perforation, and neostigmine is effective in most of the patients. For pharmacological therapy, neostigmine is given at a dose of 2 mg intravenously over 5 minutes, under continuous cardiac monitoring. The effect of neostigmine lasts between 30-120 minutes.[8] Another option is colonoscopic decompression. In patients resistant to medical therapy, if there are signs of colonic ischemia or perforation, surgical intervention is required with a high mortality rate. Worsening abdominal pain, fever, leukocytosis and lactic acidosis should raise the suspicion of mucosal ischemia. Full-thickness ischemia manifests with peritonitis.[9] Pneumatosis and/or gas in the mesenteric veins are symptoms associated with intestinal wall thickening and intestinal infarction.[10]

Surgery is indicated in medically refractory patients, if the cecum diameter is >12 cm, and if there are signs of colonic ischemia or perforation. Depending on the patient's clinical condition and intraoperative findings, surgical options include cecostomy, colectomy + primary anastomosis + diverting ileostomy, and subtotal colectomy with Hartmann pouch.[11] In our patient, emergency surgical treatment was performed because the patient had dyspnea and findings indicating peritoneal irritation, and the diameter of the colon on CT was greater than 15 cm. Differential diagnosis from adult Hirschsprung's disease was made, based on the pathology result. In our patient, no known etiological cause could be found and it was accepted as an idiopathic form. In this patient, total abdominal colectomy, ileal J pouch, ileorectal anastomosis, and diverting loop ileostomy were performed.

Early diagnosis and treatment are critical to minimize morbidity and mortality.

Ethics

Informed Consent: It was obtained.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: R.Ç., İ.Ö., Concept: R.Ç., Design: R.Ç., Data Collection or Processing: R.Ç., Analysis or Interpretation: R.Ç., Literature Search: R.Ç., Writing: R.Ç.

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

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References

1. Ogilvie H. Large-intestine Colic due to sympathetic deprivation. Br Med J 1948;2:671-673.
2. Jetmore AB, Timmcke AE, Gathright JB Jr, Hicks TC, Ray JE, Baker JW. Ogilvie's syndrome: colonoscopic decompression and analysis of predisposing factors. Dis Colon Rectum 1992;35:1135-1142.
3. Yokota T, Suda T, Tsukioka S, Takahashi T, Honma T, Seki K, Matsuzawa J, Miura M, Aoyagi Y, Asakura H. The striking effect of hyperbaric oxygenation therapy in the management of chronic idiopathic intestinal pseudo-obstruction. Am J Gastroenterol 2000;95:285-288.
4. Vanek VW, Al-Salti M. Acute pseudo-obstruction of the colon (Ogilvie's syndrome). An analysis of 400 cases. Dis Colon Rectum 1986;29:203-210.
5. Rex DK. Colonoscopy and acute colonic pseudo-obstruction. Gastrointest Endosc Clin N Am 1997;7:499-508.
6. Storch I, Barkin JS. Contraindications to capsule endoscopy: do any still exist? Gastrointest Endosc Clin N Am 2006;16:329-336.
7. Martin MJ, Steele SR, Noel JM, Weichmann D, Azarow KS. Total colonic manometry as a guide for surgical management of functional colonic obstruction: Preliminary results. J Pediatr Surg 2001;36:1757-1763.
8. Kayani B, Spalding DR, Jiao LR, Habib NA, Zacharakis E. Does neostigmine improve time to resolution of symptoms in acute colonic pseudo-obstruction? Int J Surg 2012;10:453-457.
9. Bullard Dun KM, Rothenberger DA. Colon, rectum, and anus. In: Brunicardi F, Andersen DK, Billiar TR, Dunn DL, Hunter JG, Matthews JB, Pollock RE, (eds). Schwartz's Principles of Surgery, 10e. McGraw Hill; 2015. (Accessed: March 04, 2022). https://accessmedicine.mhmedical.com/content.aspx?bookid=980&sectionid=59610871
10. Theodoropoulou A, Koutroubakis IE. Ischemic colitis: clinical practice in diagnosis and treatment. World J Gastroenterol 2008;14:7302-7308.
11. Stanghellini V, Cogliandro RF, De Giorgio R, Barbara G, Morselli-Labate AM, Cogliandro L, Corinaldesi R. Natural history of chronic idiopathic intestinal pseudo -obstruction in adults: a single center study. Clin Gastroenterol Hepatol 2005;3:449-458.

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LETTER TO THE EDITOR

Factors Associated with Poor Lymph Node Dissection for Colon Neoplasms

Erdinç Kamer

University of Health Sciences Turkey, İzmir Faculty of Medicine, Department of General Surgery, İzmir, Turkey

Keywords: Colon cancer, letter to editor, lymph node

Dear Editor,

I read with interest the study entitled "Factors Associated with Poor Lymph Node Dissection of Colon Neoplasms" by Bostancı et al.[1] In this study, the authors aimed to determine the factors affecting inadequate lymph node dissection.

It is known that the number of lymph nodes removed in colon cancers is affected by the surgeon and the pathologist, as well as other factors such as obesity, age, emergency surgery and right colon tumors.[2] It would be useful to specify whether a single surgeon or multiple surgeons performed the surgeries in this study. In addition, it is known that laparoscopic lymph node dissection is a safe and applicable method in stage 2 and 3 colon cancers, and the oncological results are similar to open surgery.[3] I believe that in this period when laparoscopic colon surgery has become widespread, it will be beneficial to inform the reader about whether colon surgery was performed openly or laparoscopically in this study.

Peer-review: Externally peer-reviewed.

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

References

1. Bostancı MT, Yılmaz İ, Saydam M, Seki A, Demir P, İnanç İmamoğlu G, Gökçe A. Factors Associated with Poor Lymph Node Dissection of Colon Neoplasm. Turk J Colorectal Dis 2021;31:322-329.
2. Chang GJ, Rodriguez-Bigas MA, Skibber JM, Moyer VA. Lymph node evaluation and survival after curative resection of colon cancer: systematic review. J Natl Cancer Inst 2007;21:433-441.
3. Yi XJ, Lu XQ, Li HM, Wang W, Xiong WJ, Wan J, Diao DC. Feasibility and efficacy of laparoscopic radical right hemicolectomy with complete mesocolic excision using an 'artery-first' approach. Gastroenterol Rep (Oxf) 2019;7:199-204.

Address for Correspondence: Erdinç Kamer, MD, University of Health Sciences Turkey, İzmir Faculty of Medicine, Department of General Surgery, İzmir, Turkey
E-mail: erdinc.kamer@gmail.com **ORCID ID:** orcid.org/0000-0002-5084-5867
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