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AIMS AND SCOPE

Turkish Journal of Colorectal Disease is an open access, scientific and peer-reviewed journal in accordance with independent, unbiased, and double-blinded peer-review principles of the Turkish Society of Colon and Rectal Surgery.

The journal is published quarterly 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 that 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 managing small intestine, colon, rectum, anus, and pelvic floor diseases.

The target audience of the 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, 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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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.

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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

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

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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.

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All clinical trials must be registered in a public trials registry acceptable to the International Committee of Medical Journals Editors (ICMJE). Authors of randomized controlled trials must adhere to the CONSORT guidelines, 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 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:

1. State the importance and significance of your findings but do not repeat the details given in the Results section.

2. Limit your opinions to those strictly indicated by the facts in your report.

3. 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"

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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.

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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.

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.

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

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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 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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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.

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All individuals have individual rights that are not to be infringed. Individual participants in studies have, for example, the right to decide what happens to the (identifiable) personal data gathered, to what they have said during a study or an interview, as well as to any photograph that was taken. Hence it is essential that all participants gave their informed consent in writing before inclusion in the study. They are identifying details (names, dates of birth, identity numbers and other information) of the participants that were

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studied should not be published in written descriptions, photographs, and genetic profiles unless the information is essential for scientific purposes and the participant (or parent or guardian if the participant is incapable) gave written informed consent for publication. Complete anonymity is difficult to achieve in some cases, and informed consent should be obtained if there is any doubt. For example, masking the eye region in photographs of participants is inadequate protection of anonymity. If identifying characteristics are altered to protect anonymity, such as in genetic profiles, authors should assure that alterations do not distort scientific meaning.

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REVIEW

Systematic Review of the Effect of Non-steroidal Anti-Inflammatory Drugs on the Exacerbation of Inflammatory Bowel Disease

Monia Hayazei[1,2], Manar Abed[1,3], Semra Demirli Atıcı[1,4,5], Shahzaib Ahmad[1,6], Alaa El-Hussuna[1]

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ABSTRACT

Non-steroidal anti-inflammatory drugs (NSAIDs) are generally thought to be associated with an increased risk of inflammatory bowel disease (IBD) exacerbation. The aim of this systematic review is to investigate evidence on the role of NSAIDs in the exacerbation of IBD. Studies were identified by searching the electronic PubMed, EmBase, and Cochrane databases for articles published-up to December 2019. Data on patients, study methodology, study quality, trial setting (single or multicenter, secondary or tertiary center/department, country of origin), duration of follow-up, outcomes assessed, the definition of assessed outcome measures, intervention characteristics (type, dose, duration, mode of administration), and outcome measures were extracted. Due to the heterogeneity of the included studies, no data synthesis was performed. It remains unclear whether there is a consistent association between NSAID use and the risk of Crohn's disease and ulcerative colitis exacerbation and whether NSAIDs are important in triggering IBD relapse.

Keywords: Inflammatory bowel disease, Crohn's disease, ulcerative colitis, non-steroidal anti-inflammatory drugs, cyclooxygenase-2 inhibitor

Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are a widely used group of pharmaceutical agents. In addition to being distributed by prescription, NSAIDs are distributed as over-the-counter products and are a component of many different drug formulations. Thus, many patients may unknowingly ingest NSAIDs, which can cause a variety of colonic abnormalities including colitis, ulcers, and strictures.[1]

The mechanisms of damage caused by NSAIDs to the bowel mucosa involve the activities of prostaglandin-endoperoxide synthase 1 [PTGS1 or cyclooxygenase-1 (COX-1)] and PTGS2 (COX-2). Moreover, NSAIDs interact with phospholipids and uncouple mitochondrial oxidative phosphorylation, which initiates biochemical changes that impair the function of the gastrointestinal barrier. The resulting increase in intestinal permeability leads to low-grade inflammation. Furthermore, the NSAID's inhibition of COX enzymes, along with luminal aggressors, results in erosions and ulcers, with the potential complications of bleeding, protein loss, stricture formation, and perforation.[2]

Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), refers to chronic inflammatory disorders of the gastrointestinal tract (GIT) identified by episodes of relapse and remission.[3] The two identified subtypes of the disease involve the GIT in different patterns.[3,4] IBD is thought to result from an inappropriate inflammatory response to gut microbial flora in genetically predisposed individuals.[5]

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The NSAID mechanism of action has raised questions over whether these drugs can exacerbate IBD. These questions have been debated in many studies with divergent results.

The aim of this systematic review is to investigate evidence on the role NSAIDs play in the exacerbation of IBD.

Method

Study design: The review was conducted and reported in accordance with the recommendations in the Cochrane Handbook for Reviews of Interventions (http://www.cochrane.org) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (Figure 1).[6]

Outcome measures: The primary outcome is disease exacerbation defined as a flare of disease activity after a period of remission.

The secondary outcome measure is the worsening of disease activity in patients with active IBD. An active IBD is defined as the following: an IBD usually runs a waxing and waning course. When there is severe inflammation, the disease is considered active, and the person experiences a flare of symptoms. When there is less or no inflammation, the person usually is without symptoms and the disease is said to be in remission.[6]

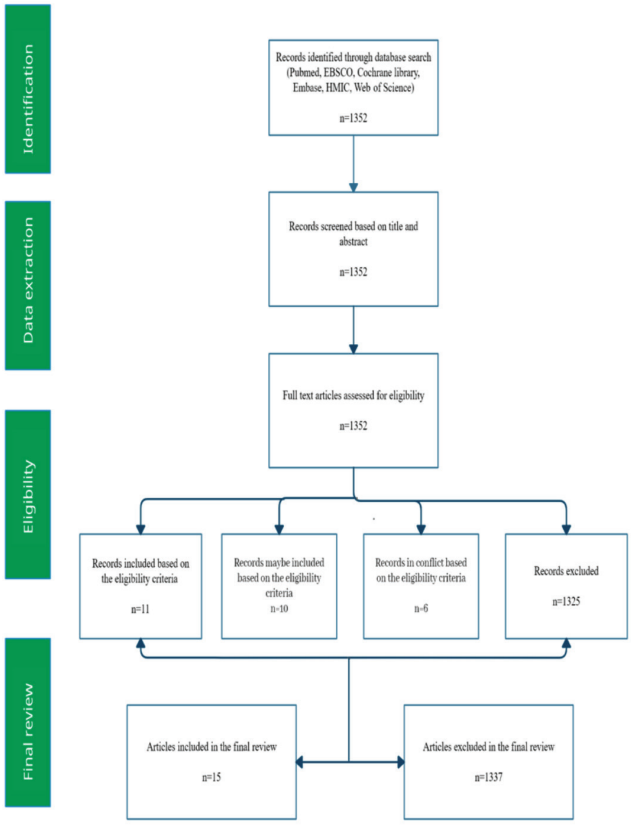

Figure 1. Preferred reporting items for systematic reviews and Preferred Reporting Items for Systematic Reviews and Meta-Analyses[6] flow diagram

Eligibility criteria:

1. Patients with IBD, including CD and UC in addition to microscopic colitis and collagen colitis.
2. No age limits.
3. All known NSAIDs, including non-specific COX inhibitors (such as aspirin, paracetamol, and ibuprofen) and COX-2 inhibitors (such as celecoxib, etoricoxib, and parecoxib). Rofecoxib and valdecoxib, which were withdrawn from the market in 2004 and 2005, respectively, because they excessively increased the risk of heart attacks and strokes with long-term use, are also included in the review, when found, as they may have caused an inflammatory effect while prescribed to patients.
4. Duration of using NSAIDs.
5. Oral, intravenous, or other methods of drug intake.
6. All observational studies (case-control and cohort studies), interventional studies [blinded or non-blinded randomized controlled trials (RCTs)], and other reviews (narrative and systematic reviews).

Studies on humans published between 2000 and 2020 were included to ensure up-to-date data. No language limit was used.

Studies were identified by searching the electronic PubMed, EmBase, and Cochrane databases. The reference lists in relevant papers were also screened for any additional studies. Additional trials were identified through the World Health Organization search portal (www.who.int/trialsearch).

The search was conducted by two authors (MH, AE). The last search date was December 6, 2019.

The search thread used was as follows:

((((((((((“anti-inflammatory agents, non-steroidal”[MeSH Terms] OR “nonsteroidal anti inflammatory”[Text Word]) OR “non steroidal anti inflammatory”[Text Word]) OR “non steroidal antiinflammatory”[Text Word]) OR “nonsteroidal antiinflammatory”[Text Word]) OR “NSAID”[Text Word]) OR “cyclooxygenase inhibitor*”[Text Word]) OR “cox inhibitor*”[Text Word]) OR “anti inflammatory analgesi*”[Text Word]) OR “anti inflammatory agent*”[Text Word]) AND (((((“Inflammatory Bowel Diseases”[MeSH Terms] OR “inflammatory bowel dis*”[Text Word]) OR “crohn*”[Text Word]) OR “colitis”[Text Word]) OR “irritable bowel dis*”[Text Word]) OR “irritable bowel syn*”[Text Word])) NOT ((((“Animals”[Mesh]) OR (mice[Text Word] OR rats[Text Word] OR rabbit*[Text Word])) NOT (((“Animals”[Mesh]) OR (mice[Text Word] OR rats[Text Word] OR rabbit*[Text Word])) AND (“Humans”[Mesh])))) AND ((((((((((“anti-inflammatory agents, non-steroidal”[MeSH Terms] OR “nonsteroidal anti inflammatory”[Text Word]) OR “non steroidal anti inflammatory”[Text Word]) OR “non steroidal antiinflammatory”[Text Word]) OR “nonsteroidal

antiinflammatory"[Text Word]) OR "NSAID"[Text Word]) OR "cyclooxygenase inhibitor*"[Text Word]) OR "cox inhibitor*"[Text Word]) OR "anti inflammatory analgesi*"[Text Word]) OR "anti inflammatory agent*"[Text Word]) AND (((((("Inflammatory Bowel Diseases"[MeSH Terms] OR "inflammatory bowel dis*"[Text Word]) OR "crohn*"[Text Word]) OR "colitis"[Text Word]) OR "irritable bowel dis*"[Text Word]) OR "irritable bowel syn*"[Text Word]))))) AND ((("Systematic Review"[Publication Type] OR "Systematic Reviews as Topic"[Mesh] OR systematic[sb] OR "Meta-Analysis as Topic"[Mesh] OR "Meta-Analysis" [Publication Type] OR metaanalys*[Title] OR meta-analys*[Title])) OR ((((((("Controlled Clinical Trial"[Publication Type] OR "Controlled Clinical Trials as Topic"[Mesh])) OR (((random*[Text Word] OR controlled[Text Word] OR crossover[Text Word] OR cross-over[Text Word] OR blind*[Text Word] OR mask*[Text Word])) AND (trial[Text Word] OR trials[Text Word] OR study[Text Word] OR studies[Text Word] OR analys*[Text Word] OR analyz*[Text Word]))) OR rct[Text Word]) OR (((singl*[Text Word] OR doubl*[Text Word] OR tripl*[Text Word])) AND (blind[Text Word] OR mask[Text Word]))) OR placebo[Text Word]))

All studies identified by the search were screened for inclusion, primarily based on title and abstract. Eligible studies were retrieved in full text. Three authors (MH, MA, SDA) performed the inclusion/exclusion phase of the study. Any disagreement was resolved by discussion among the three authors or involvement of a senior author (AE).

A Rayyan intelligent systematic review was used for the inclusion/exclusion phase.[7]

This web-based application allows a blinded inclusion/exclusion of studies to be conducted and then disagreements to be resolved.

Data extraction: Three authors (M.H., M.A., and S.D.A.) independently extracted data based on the pre-defined study protocol's inclusion criteria. Differences were resolved by consulting senior author (A.E.H.).

Data on patients, study methodology, study quality [case-control and cohort studies, interventional studies (blinded or non-blinded RCTs), narrative and systematic reviews], trial setting (single or multicenter, secondary or tertiary center/department, country of origin), duration of follow-up, outcomes assessed, definition of assessed outcome measures, intervention characteristics (type, dose, duration, mode of administration), and outcome measures were extracted.

No data synthesis was performed due to the heterogeneity of the included studies and inherent qualitative differences among studies.

Risk of bias in individual studies: The quality of bias control in the included studies was assessed by three authors independently of each other. The Cochrane risk-of-bias tool can be used for randomized trials and the Newcastle-Ottawa Scale to assess bias in observational studies. To assess bias (MH, MA, and SDA) in the included randomized trials, we used the Cochrane risk-of-bias tool for RCTs (RoB 2.0),[8] which focuses on random sequence generation (selection bias), allocation concealment (selection bias), the blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), and selective reporting (reporting bias). The Newcastle-Ottawa Scale is used to assess the quality of non-randomized studies included in a systematic review.[9] Each study was assigned a number of stars based on the selection of patients (maximum 4 stars), the comparability of cohorts (maximum 2 stars), and the ascertainment of the outcome (maximum 3 stars). The lower the number of stars is, the greater the risk of bias.

Results

In total, 1,352 articles were selected, with 11 included based on the inclusion criteria, 1,325 excluded based on the exclusion criteria, 6 disputed, and 10 that might be included. The final review included 15 articles after reading the full research text. These 15 studies were undertaken between 2000 and 2020: 1 double-blind placebo-controlled study, 1 prospective randomized placebo-controlled pilot study, 1 prospective open-label trial, 1 prospective open-label monocentric trial, 1 retrospective case-control trial, 1 prospective case-control trial, 7 systematic reviews, and 2 meta-analyses published before December 2019.[10-24] The number of participants per study ranged from 11 to 217 for the prospective and retrospective case-control, randomized, and placebo-controlled studies. The number of studies included in the meta-analyses varied between 2 and 21. The study characteristics are summarized in Table 1, 2.

Quality assessment results

Studies involving the relationship between NSAID use and IBD disease exacerbation, disease exacerbation after the IBD remission period, and the worsening of disease activity in patients with active IBD are described in Table 1, 2. The number of studies included in the meta-analyses varied between 2 and 21. The number of participants per study ranged from 11 to 217 for the prospective and retrospective case-control, randomized, and placebo-controlled studies. Using RoB 2.0, we assessed the risk of bias in the randomized trials (Table 3), and quality was assessed using the Newcastle-Ottawa Scale due to inherent qualitative differences between studies (Table 4).

Table 1. Observational studies (prospective and retrospective cohorts) and randomized controlled trials included in this systematic review

Author	Study type	Published year	Disease	Drugs used	Duration of medication	Aim	No. of participating patients	Conclusion
El Miedany et al.[10]	(Prospective) double-blind placebo-controlled study	2006	IBD	Etoricoxib tablets of 60-120 mg once a day	1 and 3 months	Gastrointestinal safety and effect on disease activity of etoricoxib, a selective COX-2 inhibitor in IBD	76 patients: UC (38) and (CD) (38). The control group included 70 patients known to have UC (35) and CD (35)	Etoricoxib therapy is safe and beneficial in most patients with IBD. Treatment with etoricoxib was not associated with the exacerbation of the underlying IBD-related and gastrointestinal-related complications.
Sandborn et al.[11]	(Prospective) randomized placebo-controlled pilot study	2006	UC	200 mg of oral celecoxib or placebo twice daily for 14 days	14 days	Safety of celecoxib in patients with UC in remission: A randomized placebo-controlled pilot study	217 patients (110 celecoxib, 107 placebo)	Therapy with celecoxib for up to 14 days did not have a greater relapse rate than placebo in patients with UC in remission who had a present or past history of non-specific arthritis, arthralgia, or other condition amenable to NSAIDs.
Biancone et al.[12]	(Prospective) open-label trial	2004	IBD	Rofecoxib (12.5 mg/day)	3 days to 3 months	Rofecoxib and early relapse of IBD	IBD group included 45 inactive patients (CD activity index <150 or UC [Mayo score <4]; 25 patients with CD and 20 with UC) with associated arthralgia. The control group included 30 patients with dyspepsia	Rofecoxib appears to control arthralgia in almost two-thirds of patients with IBD. Side effects requiring drug discontinuation are observed but only in one-quarter of patients (during the first few days of treatment).
Reinisch et al.[13]	(Prospective) open-label monocentric trial	2003	IBD (UC, CD, indeterminate colitis)	Rofecoxib (12.5 mg/day) Rofecoxib (25 mg/day)	20 days	To evaluate the safety and efficacy of rofecoxib in patients with IBD with associated peripheral arthropathy and/or arthritis	Rofecoxib (12.5 mg/day) (n=6) Rofecoxib (25 mg/day) (n=26) Total patients=32	No IBD flares occurred during the treatment phase. The CD activity index decreased; in patients with UC, the changes in the clinical disease activity index were non-significant throughout the study. The risk of aggravating intestinal symptoms by the administration of COX inhibitors may be low and mainly restricted to patients with signs of active disease.
Mahadevan et al.[14]	(Retrospective study) retrospective review chart	2002	IBD, UC, CD, pouchitis	Celecoxib or rofecoxib	9 months (range 1 week to 22 months)	Safety of selective COX-2 inhibitors in IBD	11 patients were treated with celecoxib (median dose 200 mg/day) and 16 with rofecoxib (median dose 25 mg/day)	The preliminary results suggest that COX-2 inhibitors may be safe and beneficial in most patients with IBD, but the safety of COX-2 inhibitors in patients with IBD needs to be prospectively assessed in a placebo-controlled trial.

Table 1. Continued

Author	Study type	Published year	Disease	Drugs used	Duration of medication	Aim	No. of participating patients	Conclusion
Beaugerie et al.[15]	(Prospective) case-control study	2001	Patient with rheumatoid arthritis without diarrhea (patient underwent a surveillance colonoscopy)	NSAIDs (type unspecified)	3 months	Identify alterations in the colonic mucosa of patients without diarrhea receiving NSAIDs, with the focus on intraepithelial lymphocyte count, epithelial apoptosis, and immunobiological features of immune cell activation	Group 1: Patient with rheumatoid arthritis without diarrhea and taking NSAIDs. Group 2: Patient with rheumatoid arthritis without diarrhea and NOT taking NSAIDs. Group 3: Surveillance colonoscopy due to benign polyps or colectomy colorectal cancer	The chronic use of NSAIDs does not result in constant inflammatory changes in colonic mucosa in humans. No changes in the colon mucosa were observed in patients with non-diarrhea rheumatoid arthritis on long-term NSAID therapy.

IBD: Inflammatory bowel disease, UC: Ulcerative colitis, CD: Crohn's disease, COX-2: Cyclooxygenase-2, NSAID: Non-steroidal anti-inflammatory drug

The publication year of the studies, subtype of inflammatory disease, type and dose of NSAIDs used in treatment, duration of NSAID drug use, and results were reviewed.

Summary of the study findings: The results of the included studies are summarized in Table 1, 2.[10-24] Three of the observational studies included in this review investigated the impact of rofecoxib in flares of IBD, reporting no flares.[12-14] Similarly, a study reported that etoricoxib was safe in cases of IBD.[10] Two studies determined that celecoxib was unrelated to IBD flares and could be used for the management of inflammatory symptoms where indicated,[11,14] as detailed in Table 1.[10-15]

Five out of 9 review studies (systematic reviews and meta-analyses) documented that NSAIDs induce relapse in IBD as a result of unknown mechanisms and induce colitis in previously asymptomatic patients. However, some studies reinforced the safety of selective COX-2 inhibitors.[20,21] The evidence synthesis in these reviews was weak, and studies with a greater sample size were recommended.[22-24]

Discussion

Active infection such as amoeba, parasite, bacterial, and viral infections in blood smear and/or stool cultures, presence of cytomegalo-virus pp65 and clostridium difficult toxin a and b antigens, use of NSAIDs, drug compliance, and type of current treatment (corticosteroid, salicylates, immunosuppressive drugs, and anti-tumor necrosis factor) were considered causes of exacerbation.[12,25,26]

Regarding the administration of NSAIDs, according to consensus guidelines from the British Society of Gastroenterology, individuals with UC (including those with extensive disease) should be given a mix of oral and enema 5-ASA, and those who do not respond well to oral 5-ASA should also receive topical medication.[27] Even in patients with pancolitis, oral and topical 5-ASA therapy is preferable to monotherapy. Despite the clear advantages of enema therapy, patients continue to find the administration and maintenance of enemas difficult, and support and education in this area are urgently required.[26]

The most common indications of the use of NSAIDs in IBD are extraintestinal manifestations, such as IBD-associated arthralgia, ankylosing spondylitis, sacroiliitis, and arthritis. However, the use of these drugs in the management of extraintestinal symptoms may lead to the exacerbation of the disease itself.[28] Hence, it is important to consider the side effects of such medications for extraintestinal manifestations because of their potential role in disease exacerbation. According to the American College of Gastroenterology, the use of NSAIDs is a possible trigger for disease exacerbation in patients with diagnosed IBD.[29] Similarly, Evans et al.[30] noted that NSAIDs play a role in relapse in patients with IBD. Therefore, patients with IBD are encouraged to avoid using NSAIDs because of concerns relating to their potential

Table 2. Published reviews on the effects of NSAIDs on IBD exacerbation

Author	Study type	Published year	Disease	Drugs used	Duration of medication	Aim	No. of studies involved	Conclusion
Forrest et al.[16]	Systematic review	2004	IBD	NSAIDs + paracetamol	Ranged from 2 hours to 6 weeks	To assess whether ingestion of paracetamol or NSAIDs is associated with IBD exacerbation	17 related to NSAIDs	NSAIDs may precipitate a relapse in some patients with IBD. This may be an idiosyncratic reaction. The published evidence does not support the view that NSAIDs are key to inducing IBD relapse. There is weak evidence that paracetamol may be more crucial
Ballinger[17]	Systematic review	2008	IBD (all types)	NSAIDs (all types)	Not mentioned	Adverse effects of NSAIDs on the colon	17	NSAIDs can induce colitis in a previously normal bowel, and symptoms can be indistinguishable from idiopathic IBD. Limited evidence suggests that NSAIDs may exacerbate preexisting IBD and should be prescribed cautiously to patients with IBD. NSAID ingestion is also associated with the development of collagenous colitis
Kefalakes et al. [18]	Systematic review	2009	IBD (all types)	NSAIDs (conventional and selective COX-2)	Not mentioned	Exacerbation of IBD associated with the use of NSAIDs	21	The available data remain contradictory and confusing, and it remains uncertain whether COX-2 inhibitors are safer than conventional NSAIDs. Further randomized double-blind trials should be performed
Singh et al.[19]	Systematic review	2009	IBD	NSAIDs (type unspecified)	Not mentioned	Whether NSAIDs, infection, antibiotics, or stress trigger flares in IBD	7 related to NSAIDs	The evidence to date does not support NSAID use as an initiator. Methodological difficulties and ambiguities were identified in the study results, limiting the ability to draw firm conclusions. To date, there is insufficient evidence to warrant NSAID avoidance in IBD among patients who require them for joint-related symptoms
Paiotti et al.[20]	Systematic review	2012	IBD (all types)	NSAIDs and COX-2 inhibitors	Not mentioned	The role of NSAIDs and COX-2 inhibitors in experimental colitis	13 studies (controlled trials, original articles, case reports, and reviews)	More studies should be conducted using a broader spectrum of cases of colitis to verify that patients with a history of IBD should avoid using NSAIDs. The relative role of COX-2 selective inhibitors in human and experimental colitis remains to be explored
Lanas et al.[21]	Systematic review	2014	IBD (UC, CD)	NSAIDs (all types), low-dose aspirin, paracetamol	Not mentioned	Safe prescription recommendations for NSAIDs: Consensus document elaborated by nominated experts of three scientific associations	7	In patients suffering from IBD, the use of NSAIDs should be avoided. NSAIDs should be used in quiescent phases of the disease, the use of COX inhibitors is recommended at low doses for a short time

Table 2. Continued

Author	Study type	Published year	Disease	Drugs used	Duration of medication	Aim	No. of studies involved	Conclusion
Miao et al.[22]	Systematic review	2014	IBD with rheumatological manifestations	COX-2 inhibitors, etoricoxib (60 to 120 mg/day) OR celecoxib (200 mg twice daily), and placebo	2-12 weeks	Evaluate the tolerability and safety of COX-2 inhibitors used for the treatment of rheumatological manifestations of IBD	Two randomized controlled trials comparing COX-2 inhibitors with placebo	Celecoxib and etoricoxib do not exacerbate IBD symptoms. However, both studies had relatively small sample sizes and short follow-up durations
Ribaldone et al.[23]	Meta-analysis	2015	IBD (UC, CD)	COX-2 inhibitors and placebo	3 days to 3 months	To show whether COX-2 inhibitors are associated with an increased risk of IBD exacerbation compared with placebo	7 studies (including patients with IBD that had to stop COX inhibitor therapy because IBD activity deteriorated)	COX inhibitors are safe in most patients with IBD (no difference in gastrointestinal adverse events in the COX inhibitor and placebo groups)
Moninuola et al.[24]	Meta-analysis	2018	IBD	NSAIDs and acetaminophen	15 days to 48 weeks	To examine the association between acetaminophen and NSAIDs, including COX-2 inhibitor use, and risk of CD and UC exacerbation	18 studies	No consistent association between NSAID use and the risk of CD and UC exacerbation. No consistent evidence for an association with acetaminophen

IBD: Inflammatory bowel disease, NSAID: Non-steroidal anti-inflammatory drug, COX-2: Cyclooxygenase-2, UC: Ulcerative colitis, CD: Crohn's disease

Table 3. Risk-of-bias assessment using Revised Cochrane risk-of-bias for randomized trials software

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
El Miedany et al.[10]	?	?	+	?	+	+	+
Sandborn et al.[11]	+	+	+	+	+	+	+

Risk-of-bias assessment: +: Low, ?: Unclear

Table 4. Risk-of-bias assessment (Newcastle-Ottawa Quality Assessment Scale Criteria) for case-control and cohort studies

Study	Selection				Comparability	Outcome			Quality score
	Representativeness of exposed cohort	Selection of the non-exposed cohort from the same source as the exposed cohort	Ascertainment of exposure	Outcome of interest was not present at the start of the study	Comparability of cohorts	Assessment of outcomes	Follow-up long enough for outcomes to occur (median duration of follow-up ≥6 months)	Adequacy of follow-up	
Biancone et al.[12]	Prospective open-label trial★	Yes★	Yes★	Yes★	The IBD group included 45 inactive patients (25 CD; 20 UC) with associated arthralgia. The control group included 30 patients with dyspepsia★	Rofecoxib and early relapse of IBD★	No	3 days to 3 months	Good
Reinisch et al.[13]	Prospective open-label monocentric trial★	Yes★	IBD (UC, CD, indeterminate colitis)	Yes★	To evaluate the safety and efficacy of rofecoxib in patients with IBD with associated peripheral arthropathy and/or arthritis★	No IBD flares occurred during the treatment phase. The CD activity index decreased; in patients with UC, changes in the clinical disease activity index were non-significant throughout the study. The risk of aggravating intestinal symptoms by the administration of COX inhibitors may be low and mainly restricted to patients with signs of active disease★	No	20 days	Fair
Mahadevan et al.[14]	Retrospective study, retrospective review chart★	No	IBD, UC, CD, pouchitis	Yes★	Retrospective review	Safety of selective COX-2 Inhibitors in IBD★	No	9 months (range 1-22 weeks) months)★	Fair

Table 4. Continued

Study	Selection			Comparability	Outcome			Quality score
Beaugerie et al.[15]	Patient with rheumatoid arthritis without diarrhea (patient underwent surveillance colonoscopy)★	Yes★	Patient with rheumatoid arthritis without diarrhea and taking NSAIDs. Group 2: Patient with rheumatoid arthritis without diarrhea and NOT taking NSAIDs. Group 3: Surveillance colonoscopy due to benign polyps or colectomy for colorectal cancer★	Yes★	Group 1: Patient with rheumatoid arthritis without diarrhea and taking NSAIDs. Group 2: Patient with rheumatoid arthritis without diarrhea and NOT taking NSAIDs. Group 3: Surveillance colonoscopy due to benign polyps or colectomy for colorectal cancer★	Chronic use of NSAIDs does not result in constant inflammatory changes in colonic mucosa in humans. No changes in the colon mucosa were observed in patients with non-diarrhea rheumatoid arthritis on long-term NSAID therapy★	Yes★	3 months	Good

Good quality: 3 or 4 stars (★) in the selection domain AND 1 or 2 stars in the comparability domain AND 2 or 3 stars in the outcome domain, Fair quality: 2 stars in the selection domain AND 1 or 2 stars in the comparability domain AND 2 or 3 stars in the outcome/exposure domain, Poor quality: 0 or 1 star in the selection domain OR 0 stars in the comparability domain OR 0 or 1 stars in the outcome/exposure domain. CD: Crohn's disease, UC: Ulcerative colitis, IBD: Inflammatory bowel disease, NSAID: Non-steroidal anti-inflammatory drug, COX-2: Cyclooxygenase-2

adverse effects on disease activity. In addition, Takeuchi et al.[31] reported that non-selective NSAID intake is associated with the frequent and early clinical recurrence of IBD, as measured using the Harvey-Bradshaw Clinical Disease Activity Index.

Regarding the possible mechanism involved in the pathophysiology of gastrointestinal damage, several mechanisms have been proposed.[2] COX-1 and COX-2, when used concomitantly, cause damage to gastric mucosa by reducing blood flow and increasing the tendency of leukocytes to adhere to the blood vessels of the GIT, thus decreasing GIT defense.[32] Although this is not the only manner in which NSAIDs can harm the gastrointestinal mucosa, the inhibition of prostaglandin synthesis is crucial in the development of mucosal injury.[33,34]

Moreover, NSAIDs cause gastrointestinal damage by interacting with cellular phospholipids and oxidative phosphorylation.[35] These drugs frequently uncouple mitochondrial oxidative phosphorylation processes, leading to changes associated with a weakened gastrointestinal barrier. These biochemical changes are important in the pathophysiology of the disease, causing intestinal permeability to rise, which then causes low-grade inflammation. Erosion and ulceration are the outcomes of the NSAID suppression of COX enzymes in conjunction with luminal aggressors, with the possibility of perforation, hemorrhage, stricture development, and protein loss as sequelae.[2,34,36]

The aforementioned processes might be used to account for the biological plausibility of IBD exacerbation with NSAID use. Because the major therapeutic objective of medicinal interventions for IBD is intestinal mucosal repair, non-selective COX inhibitors may cause GIT mucosal injury, which could delay healing. Similarly, NSAID use may lead to frequent relapses, as revealed by Forrest et al.[16]. However, the possible safety of selective COX-2 inhibitors may be explained by their lower interaction with the gastrointestinal barrier.

Study Limitations

This study has several limitations, such as the heterogeneity of the included studies. Even well-designed studies on NSAID use and IBD exacerbation risk have significant limitations in defining outcomes. Although some studies have defined the exacerbation of the disease as a subjective criterion, such as emergency admission to the hospital, there are also more objective studies using the "disease activity index."

Conclusion

The published data remain contradictory and confusing. No consistent association between NSAID use and the risk of CD

and UC exacerbation has been established, and it remains uncertain whether NSAIDs are key to inducing IBD relapse.

Peer-review: Externally peer-reviewed.

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Authorship Contributions

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

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RESEARCH ARTICLE

Fournier's Gangrene in the Turkish Population: A Two-Decade Analysis

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ABSTRACT

Aim: The nature and rarity of Fournier's gangrene (FG) limit the conducting of clinical studies with large patient populations. The present study aims to determine FG risk factors and predictors of mortality among the Turkish population using published data.

Method: A literature review was conducted via PubMed Central® using the keywords "FG" and "Turkey," revealing 95 articles published between January 2000 and December 2020. Studies including <20 patients and consecutive studies by the same author were excluded from the review. Finally, a total of 41 studies were included, and the respective correlations between mortality and the other variables were analyzed.

Results: A total of 1,919 patients were reported in the 41 studies; the majority of the patients were men (83.11%), with a median age of 55 years, and the median mortality rate was 17.39%. A total of 16 studies were published between 2000 and 2010 (the first decade). The mortality rate was lower in the studies published between 2010 and 2020 (second decade) than in the first-decade studies (14.72%±7.1 vs. 22.46%±11.62; p=0.011). The cutaneous origin and mortality (r=-0.615; p=0.033) were negatively correlated, and chronic renal failure (r=0.705; p=0.005) and fecal diversion (r=0.371; p=0.037) were positively correlated. The rate of women was higher in the high-mortality group than in the low-mortality group (27.25% vs. 4.35%; p=0.034).

Conclusion: The features of patients with FG in the Turkish population are comparable with the literature data. Proper comorbidity assessment, the female gender, origin of the disease, and avoidance of unnecessary fecal diversion may have an impact on mortality.

Keywords: Fecal diversion, Fournier's gangrene, mortality, renal failure, Turkey

Introduction

Fournier's gangrene (FG) is a rare, life-threatening, rapidly progressive, polymicrobial, and synergistic form of infective necrotizing fasciitis of the perineal, genital, or perianal regions. It leads to thrombosis of the small subcutaneous vessels and necrosis of the overlying skin. It was initially described by Baurienne in 1764; however, it was named by Jean Alfred Fournier, a Parisian dermatologist and venerologist, who reported it in 1883.[1] The treatment of FG basically consists of hemodynamic resuscitation, aggressive surgical debridement, and administration of broad-spectrum antibiotics.[2,3]

Reported overall mortality rates for FG vary between 0% and 88%.[4,5] However, studies published during the last three decades report a mortality rate ranging from 20% to 40%. In 2000, Eke[6] reviewed 1,726 cases of FG from literature written in English and reported a mortality rate of 16%. The study by Furr et al.[7], which included the largest patient population in the literature, reported a 4.7% inpatient mortality.

Since FG is a rare disease, designing a prospective clinical study may not be feasible. To overcome this limitation, which is associated with the nature of FG, the authors aimed to conduct a retrospective study with a large patient population. Thus, the authors retrospectively reviewed published literature reporting FG mortality and risk factors in the Turkish population during the last two decades.

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***This study was podium presented in 18th Turkish National Colorectal Surgery meeting.**

Materials and Methods

A database search was conducted via PubMed Central® using the keywords "FG" and "Turkey" between January 2000 and December 2020. The search revealed 95 articles. Articles that included <20 patients and those published in a country other than Turkey were excluded. In the case of consecutive publications from the same first author and institution, only the article with the largest patient number was included. A total of 41 studies were finally included. A flow chart showing the included papers is presented in Figure 1, and a full list of manuscripts is presented in Appendix 1. Approval from the institutional review board was obtained for this study.

Data regarding the etiological origin of FG, patient demographics, comorbidities, treatment methods, and mortality rates were collected from the reviewed articles. The overall data and the subgroups including two decades (2000-2010 and 2010-2020) were analyzed for factors affecting mortality. The authors aimed to evaluate whether there were differences between the patient characteristics and, in particular, the outcomes (mortality) between the two decades, as the authors believed that the outcomes may have improved with a better understanding of the disease and the advances in treatment modalities.

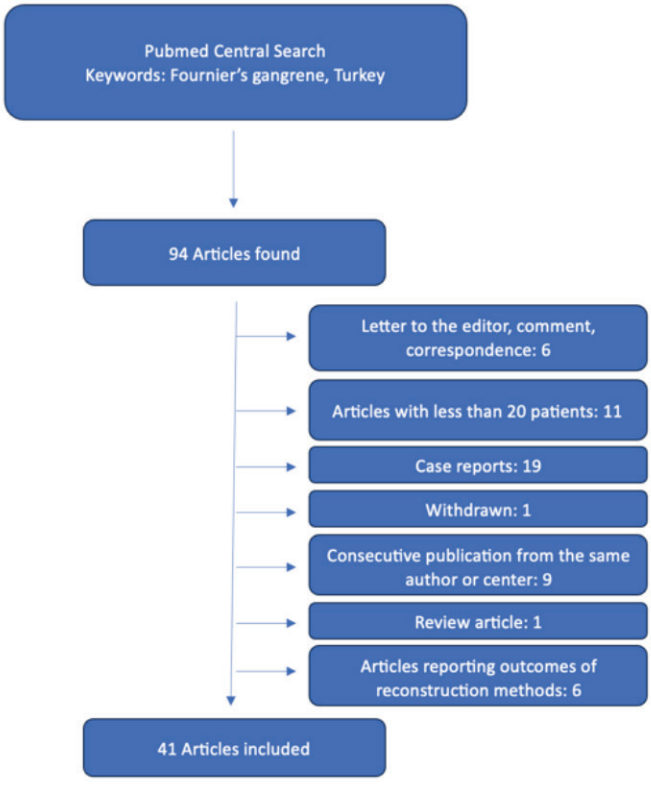

Figure 1. Flow chart of included manuscripts

Statistical Analysis

Statistical analyses were performed using SPSS for Windows version 23.0 (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp). A normality check for the data was performed using the Shapiro-Wilk test. Normally distributed variables were reported as mean ± standard deviation, and two independent groups were compared using the t-test. Non-normally distributed variables were reported as the median (minimum-maximum), and two independent groups were compared using the Mann-Whitney U test. The correlations between the variables were analyzed using the Spearman correlation coefficient. An α-value of <0.05 was accepted as statistically significant.

Results

The median patient number was 38 (20-120). The distribution of the patient numbers based on the publication date are presented in Figure 2. The reported median mortality was 6 (1-129) patients; mortality rates were calculated for every single study, and the median mortality rate was 17.39% (2.89-40.54). The distributions of mortality rates by year are shown in Figure 3. The number of patients with diabetes mellitus (DM) were reported in all studies except two; the rate of patients with DM was 50.02%±16.59% among the overall population.

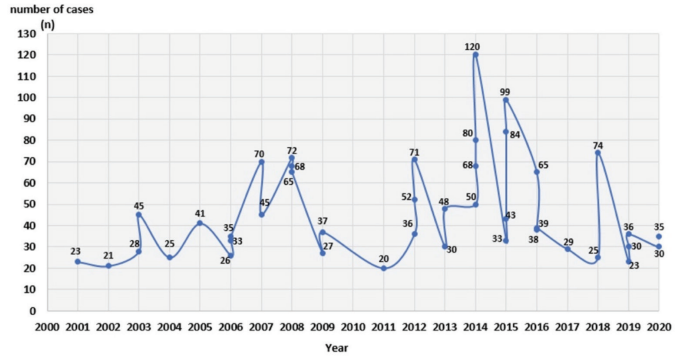

Figure 2. Distribution of the patient volume of the included studies based on the publication date

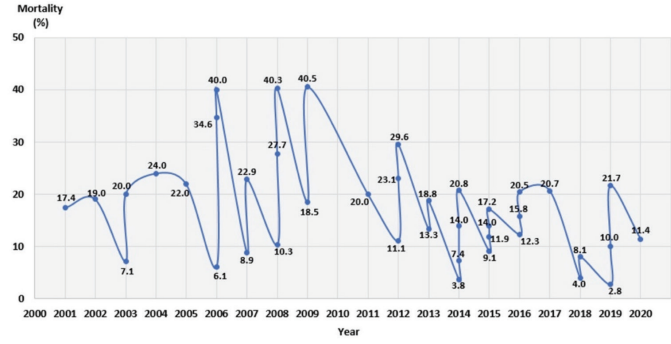

Figure 3. Distribution of the mortality rates by year

A total of 16 (39%) studies were published in the first decade (2000-2010), and 25 (61%) were published in the second decade (2010-2020). The mortality rate was 22.46%±11.62% for the studies published in the first decade and 14.72%±7.10% for studies published in the second decade. The mortality rate was significantly high for the first decade (p=0.011). Furthermore, the rate of patients with DM was higher in the second decade than in the first decade (p=0.022). The comparison of mortality rates and patients with DM between the two decades is presented in Figure 4. A summary of the comparison of the data obtained from reviewed articles, as well as the differences between the two decades are shown in Table 1.

The respective associations between the mortality rate and other variables were analyzed. The mortality rate was negatively correlated with the cutaneous origin and positively correlated with chronic renal failure (CRF) and fecal diversion (Table 2).

The studies were classified into two groups based on the median mortality rate (<17.39 "low mortality" vs. >17.39 "high mortality"). Female patients, CRF and anorectal origin rates were common in the high-mortality group, and the cutaneous origin rate was common in the low-mortality group (Table 3).

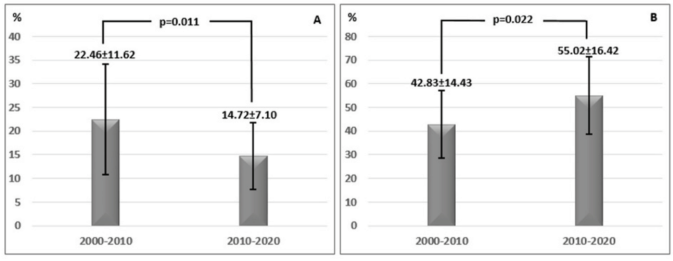

Figure 4. Comparison of (A) mortality and (B) diabetes mellitus rates between the two decades (2000-2010 and 2010-2020)

Discussion

FG is a devastating disease that can rapidly progress to sepsis, septic shock with multi-organ failure, and death.[8] In the present study, data collected from previously published articles from Turkish institutions between 2000 and 2020 were analyzed to determine the related risk factors and mortality in the Turkish population. It was shown that FG is still associated with a significant mortality rate (17.39%) and that the female gender, anorectal origin, CRF, and fecal diversion may be associated with a poor outcome.

Studies published in the last three decades report mortality rates of between 0% and 43%.[5,9] However, studies with high patient numbers published during the last two decades reported mortality rates as low as 4.7%-16%.[6,7,10] The median mortality rate was 17.39% in the present study; this rate is

Table 1. Comparison of the data reported in the articles between two decades

Variables	2000-2010		2010-2020		p-value
	n	Descriptive statistics	n	Descriptive statistics	
Patient number*	16	36 (21-72)	25	39 (20-120)	0.259
Age#	16	54.58±3.91	25	57.04±4.29	0.072
Debridement count*	5	3 (2.00-7.33)	9	2.36 (1.55-6.21)	0.298
Symptom time*	5	6.40 (3.50-8.09)	11	5.48 (3.74-7.50)	0.510
Male (%)*	16	91.55 (59.46-100)	25	82.61 (44.00-100)	0.500
Anorectal/colorectal (%)*	14	47.30 (9.09-63.08)	14	46.25 (6.06-78.26)	0.982
Urogenital (%)*	13	15.38 (4.44-69.70)	15	35.00 (4.35-68.00)	0.294
Cutaneous (%)*	7	21.21 (4.88-33.33)	5	15.38 (7.50-24.32)	0.343
Idiopathic (%)*	10	22.25 (4.44-71.43)	9	33.33 (19.23-73.53)	0.095
Hypertension (%)*	4	13.25 (5.56-28.00)	7	20.00 (10.26-51.92)	0.164
Cardiac comorbidity (%)*	4	13.18 (7.32-31.43)	8	10.39 (4.35-22.00)	0.368
Chronic renal failure (%)*	7	3.57 (2.22-20.00)	7	4.65 (1.25-17.31)	0.710
Malignancy (%)*	6	7.29 (2.22-24.62)	13	6.67 (1.47-19.72)	0.966
Alcoholism (%)*	7	8.33 (4.41-30.30)	4	6.97 (3.33-26.67)	0.648
Fecal diversion (%)*	12	33.57 (4.76-75.61)	20	18.37 (4.00-66.67)	0.076
Urinary diversion (%)*	8	11.77 (1.54-100.00)	8	6.55 (1.01-73.33)	0.279

Variables reported in * median (minimum-maximum) or #mean ± standard deviation. n: number of studies reporting the variable

comparable with that reported in Eke's[6] study (16%) but higher than those in the studies published in North America. However, the authors determined a higher mortality rate in the first decade (2000-2010) than in the second decade (2010-2020). The emerging technologies and advances in medical knowledge appear to have improved the outcome of FG by providing better surgical and medical care.

Two previously published studies with the largest patient populations reported different gender rates in FG. Eke[6] reported a 10:1 rate dominancy of men, while Sorensen et al.[10] reported that 2.32% of the included 1,680 patients were women. In the present study, the majority of the 1,919 included patients were men, with the women-patient rate 16.88%. The impact of gender on the prognosis of FG is controversial; several studies report female gender either as a risk factor or as inconsequential to the prognosis.[11-13] In the present study, the rate of women patients was higher in the high-mortality group than in the low-mortality group. The association between gender and mortality in FG might be explained by the anatomical features of the female pelvis, which allow for widespread necrotizing fasciitis.[12] However, there is a need for further studies to establish a precise explanation.

Major sources of infection are the local skin, colon, anus and rectum, and the lower urinary tract.[6] The infection has a polymicrobial and synergistic pattern and includes both Gram-positive and Gram-negative aerobe and anaerobic bacteria.[14] Colonic, anal, and rectal sources are associated

Table 2. The correlations between the mortality rate and other variables

	r	p-value
Male (%)	-0.257	0.104
Anorectal/colorectal (%)	0.253	0.194
Urogenital (%)	-0.099	0.617
Cutaneous (%)	-0.615	**0.033**
Idiopathic (%)	-0.330	0.168
Diabetes mellitus (%)	0.148	0.368
Hypertension (%)	-0.342	0.304
Cardiac comorbidity (%)	0.161	0.618
Chronic renal failure (%)	0.705	**0.005**
Malignancy (%)	0.360	0.130
Alcoholism (%)	-0.118	0.729
Fecal diversion (%)	0.371	**0.037**
Urinary diversion (%)	-0.129	0.633

Table 3. Comparison of the low- and high-mortality groups

Variables	Low-mortality group		High-mortality group		p-value
	n	Descriptive statistics	n	Descriptive statistics	
Patient number*	21	38 (23-99)	20	38 (20-120)	0.411
Age*	21	55.20 (51.98-66.30)	20	54.60 (46.22-65.91)	0.489
Debridement count*	6	2.20 (1.55-3.00)	9	2.68 (1.79-7.33)	0.282
Symptom time*	10	5.34 (3.74-6.40)	6	7.00 (3.50-8.09)	0.263
Females (%)*	21	4.35 (0.00-56.00)	20	27.25 (0.00-46.67)	**0.034**
Anorectal origin (%)*	13	31.25 (6.06-60.29)	15	49.17 (14.29-78.26)	**0.041**
Urogenital origin (%)*	14	37.25 (4.41-69.70)	14	16.35 (4.35-56.67)	0.306
Cutaneous origin (%)*	5	24.32 (15.38-33.33)	7	11.27 (4.88-24.44)	**0.048**
Idiopathic (%)*	11	32.00 (13.33-73.53)	8	21.16 (4.44-71.43)	0.206
Diabetes mellitus (%)#	20	46.71±15.25	19	53.50±17.61	0.206
Hypertension (%)*	5	20.00 (16.25-33.33)	6	13.25 (5.56-51.92)	0.247
Cardiac comorbidity (%)*	6	10.65 (8.75-22.00)	6	10.90 (4.35-31.43)	0.937
Chronic renal failure (%)*	8	3.26 (1.25-9.09)	6	7.99 (3.08-2.00)	**0.043**
Malignancy (%)*	10	4.85 (1.47-17.57)	9	12.20 (2.22-24.62)	0.182
Alcoholism (%)*	7	7.14 (3.33-30.30)	4	8.93 (5.71-12.20)	0.648
Fecal diversion (%)#	15	22.32±13.63	17	33.80±19.90	0.070
Urinary diversion (%)*	10	7.20 (1.01-73.33)	6	9.56 (1.54-100.00)	0.562

Variables reported in * median (minimum-maximum) or # mean ± standard deviation. n: Number of studies reporting the variable

with a bad prognosis.[2,6] Perianal infection is the most common of these (19%-50%), either as a primary infection or infection secondary to perianal surgical interventions.[2] In the present study, the cutaneous origin was negatively correlated with mortality, while the anorectal origin rate was higher in the high-mortality group than in the low-mortality group; these results were in line with previously published data.

Comorbidities such as DM, obesity, alcoholism, smoking, CRF, liver failure, malignancy, and HIV infection play an important role in the prognosis of FG. All these conditions may impair microcirculation and/or immunity.[15] Specifically, DM is a well-defined risk factor that may influence the frequency and the prognosis of the disease.[16] In the present study, the rate of patients with DM was significantly higher in the last decade (2010-2020) than in the first (2000-2010). The study failed to show a correlation between DM and the mortality rate, much like the previously published studies from our department;[13,17] however, the study did reveal a positive correlation between CRF and the mortality rate.

The gold standard treatment of FG includes aggressive and repeated debridement of necrotic tissue in conjunction with the administration of broad-spectrum antibiotics and hemodynamic supportive measures in the intensive care unit.[13] Recurrent surgical debridement may cause wide perianal tissue defects and impair anal sphincter functions due to direct trauma. As a result of these factors, fecal contamination of the wound may be unavoidable. Fecal diversion is an option for such patients for facilitating wound care. However, fecal diversion does not improve the treatment outcome and increases morbidity and the cost of treatment.[18] In addition, the mortality rate was reported to be relatively high in patients with a diverting stoma.[19] Similarly, the present study found a positive correlation between fecal diversion and the mortality rate. However, the need for a stoma is common in patients with extensive diseases, and it should be borne in mind that extensive disease may be another factor impairing the treatment outcome.

Study Limitations

The major limitation of this study is its retrospective nature. Since every article has its original study design, reviewing variables from previously published articles may be associated with missing data, which may affect the results of the study. Another important issue is that the manuscripts were published by different specialties from different centers, and there may be differences in disease management among the centers and specialties, which again may have affected the study outcomes. However, the high patient number provides this study with clinical value. Furthermore, this is the first study reflecting data on patients with FG in the Turkish population.

Conclusion

In conclusion, FG remains a fatal disease. The mortality rate and correlated risk factors of FG in the Turkish population appear to be comparable with the literature data. The cutaneous origin may be associated with better outcomes, and female gender, CRF, and the need for fecal diversion may be associated with a poor prognosis.

Ethics

Ethics Committee Approval: The study was approved by the Bursa Uludağ University Local Ethics Committee (approval number: 2023-17/43, date: 19.09.2023).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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Appendix 1. A full list of manuscripts

No	Author	Article title	Journal	Publication year
1	Kılıç	Fourniers's gangrene: etiology, treatment and complications	Ann Plast Surg	2001
2	Atakan	A life - threatening infection: Fourniers's gangrene	Int Urol Nephrol	2002
3	Gürdal	Predisposing factors and treatment outcome in Fournier's gangrene	Urol Int	2003
4	Korkut	Outcome analysis in patients with Fournier's gangrene: report of 45 cases	Dis Colon Rectum	2003
5	Yeniyol	Fournier's gangrene: experience with 25 patients and use of Fournier's gangrene severity index score	Urology	2004
6	Ayan	Fournier's gangrene: a retrspective clinical study on forty - one patients	ANZ J Surg	2005
7	Ünal	Fournier's gangrene: approaches to diagnosis and treatment	Saudi Med J	2006
8	Tahmaz	Fournier's gangrene: report of thirty - three cases and a review of the literature	Int J Urol	2006
9	Yanar	Fournier's gangrene: risk factors and strategies for management	World J Surg	2006
10	Ersay	Factors affecting mortality of Fournier's gangrene: review of 70 patients	ANZ J Surg	2007
11	Başoğlu	Management of Fournier's gangrene: review of 45 cases	Surg Today	2007
12	Ünalp	Fournier's gangrene: evalation of 68 patients and analysis of prognostic variables	J Postgrad Med	2008
13	Kabay	The clinical features of Fournier's gangrene and the predictivity of the Fournier's gangrene severity index on the outcomes	Int Urol Nephrol	2008
14	Çakmak	Fournier's gangrene: is it scrotal gangrene?	Adv Ther	2008
15	Uluğ	The evaluation of microbiology and Fournier's gangrene severity index in 27 patients	Int J Infect Dis	2009
16	Akcan	Necessity of preventive colostomy for Fournier's gangrene of the anorectal region	Ulus Travma Acil Cerrahi Derg	2009
17	Çelik	Fournier's gangrene: series of twenty patients	Eur Surg Res	2011
18	Göktaş	Factors affecting the number of debridements in Fournier's gangrene: our results in 36 cases	Ulus Travma Acil Cerrahi Derg	2012
19	Ersöz	Factors affecting mortality in Fournier's gangrene: experience with fifty - two patients	Singapore Med	2012
20	Arıdoğan	Epidemiological characteristics of Fournier's gangrene: a report of 71 patients	Urol Int	2012
21	Tuncel	Comparison of different scoring systems for outcome prediction in patients with Fournier's gangrene: experience with 50 patients	Scand J Urol	2014
22	Kahramanca	Are neutrophil - lymphocyte ratio ant platelet - lymphocyte ratio as affective as Fournier's gangrene severity index for predicting the number of debriedements in Fournier's gangrene?	Ulus Travma Acil Cerrahi Derg	2014

Appendix 1. Continued

No	Author	Article title	Journal	Publication year
23	Eskitaşçıoğlu	Experience of 80 cases with Fournier's gangrene and "trauma" as trigger factor in etiopathogenesis	Ulus Travma Acil Cerrahi Derg	2014
24	Yılmazlar	Fournier's gangrene; review of 120 patients and predicts of mortality	Ulus Travma Acil Cerrahi Derg	2014
25	Bozkurt	Evaluation of the utility of different scoring systems (FSGI, LRINEC and NLR) in the management of Fournier's gangrene	Int Urol Nephrol	2015
26	Oğuz	Fournier's gangrene: a summary of 10 years clinical experience	Int Surg	2015
27	Erol	Low magnesium levels an important new prognostic parameter can be overlooked in patients with Fournier's gangrene: a multicentric study	Int Urol Nephrol	2015
28	Eray	Comparison of diverting colostomy and bowel management catheter applications in Fournier's gangrene cases requiring fecal diversion	Indian J Surg	2015
29	Erdoğan	Simple scoring system for prediction of mortality in Fournier's gangrene	Eur J Trauma Emerg Surg	2016
30	Taken	Fournier's gangrene: causes, presentation and survivial of sixty - five patients	Pak J Med Sci	2016
31	Şen	Is hemoglobin A1c level effective in predicting the prognosis of Fournier's gangrene?	Urol Ann	2016
32	Doluoğlu	Overview of different scoring systems in Fournier's gangrene and assessment of prognostic factors	Turk J Urol	2016
33	Yanaral	Comparition of conventional dressings and vacuum - assisted closure in the wound theraphy of Fournier's gangrene	Arch Ital Urol Androl	2017
34	Üreyen	Usefulness of FSGI and UFGI scoring systems for predicting mortality in partinents with Fournier's gangrene	Ulus Travma Acil Cerrahi Derg	2017
35	Yücel	Fournier's gangrene: a retrospecite analysis of 25 patients	Ulus Travma Acil Cerrahi Derg	2017
36	Demir	Fournier's gangrene; association of mortality with the complate blood count parameters	Plast Reconstr Surg	2018
37	Pehlivanlı	Factors affecting mortality in Fournier's single center experience	Surg Infect	2019
38	Selvi	A different perspective for morbidity related to Fournier's gangrene: which scoring system is mode more reliable to predict requirement of skin graft and flaps in surviviors of Fournier's gangrene?	Int Urol Nephrol	2019
39	Çalışkan	Fournier's gangrene: review of 36 cases	Ulus Travma Acil Cerrahi Derg	2019
40	Hatipoğlu	Fournier's gangrene; Five years' experience from a single center in Turkey	Ulus Travma Acil Cerrahi Derg	2020
41	Egin	Comparison of mortality in Fournier's gangrene with two scoring systems	J Coll Pyhsicians Surg Pak	2020

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RESEARCH ARTICLE

The Effect of a Warm Menthol Oil Sitz Bath on Pain After Hemorrhoidectomy

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ABSTRACT

Aim: This study will examine the use of warm sitz baths with menthol oil as a non-pharmacological method of pain control after hemorrhoidectomy. To determine the effect of warm sitz baths with menthol oil on pain after hemorrhoidectomy.

Method: This interventional study was conducted with inpatients of a general surgery ward between June 2018 and September 2019. The study sample of 64 patients was divided into two groups: an intervention group (n=32) and a control group (n=32). Patients were given a warm (30-40 °C) sitz bath at three time points: four hours after surgery, after the first defecation, and after 18 hours. Menthol oil was added to the intervention group's bathwater. Data were collected using a patient information form and a numerical rating scale to assess pain level. Pain intensity before and after first defecation was evaluated in both groups prior to and following the sitz bath.

Results: It was found that the pain intensity of both groups decreased significantly after the sitz bath compared with before the bath ($p<0.05$). Although there was no significant difference when the two groups were compared, the pain level of the intervention group was lower than in the control group ($p>0.05$).

Conclusion: The results show that warm sitz baths with or without menthol oil decrease patients' pain levels when used after hemorrhoidectomy.

Keywords: Aromatherapy, hemorrhoidectomy, menthol oil, nursing care, pain, sitting bath

Introduction

Pain is the most common problem following hemorrhoidectomy[1,2] and can manifest as either resting pain or pain upon defecation. Resting pain affects most patients and can occur spontaneously without strain or attempts to defecate. Thus, pain relief is of great importance in the postoperative period. Pain is generally quite severe in the first 24 h after surgery and gradually decreases in intensity from the second postoperative day onwards. Painful defecation occurs when irritation in the anorectal region from the passage of stool around the surgical wound causes internal anal sphincter spasms during or after defecation.[2] In pain management, local anesthetics, calcium channel inhibitors, and vasodilators are used both orally and topically as medicinal therapies.[2-5] In addition, non-pharmacologic nursing approaches, such as sitz baths, thermal applications, hirudotherapy, and water spraying, are used to relieve pain and increase patient comfort in the periods before and after surgery.[6] Sitz baths are used before surgery and in the postoperative period in the conservative treatment of anorectal disorders (e.g., anal fissures, fistulas, and hemorrhoids) to accelerate wound healing, prevent infection, and significantly relieve pain by relaxing the internal anal sphincter and increasing blood flow.[2,5-8] In the literature, sitz baths are recommended to be performed three times daily for 1-2 weeks starting from the first postoperative day and after defecation.[6]

The use of aromatic oils in sitz baths plays an important role in recovery and the relief of postoperative pain.[9] Myrtle, clove, and menthol aromatic oils are used topically and in sitz baths to treat hemorrhoids.[9-11] Due to its anti-spasmolytic and anesthetic effects on anorectal sphincters, menthol oil is used in both the medical and surgical treatment of hemorrhoids in a sitz bath.[10-14] Owing to these

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effects, the application is expected to reduce the pain in the anal area after hemorrhoidectomy and during the first defecation. Clinical studies have shown that topical menthol is safe and effective in treating various painful conditions, including musculoskeletal pain, sports injuries, neuropathic pain, and migraines.[12] Relieving pain has the positive effects of enabling patients to resume feeding earlier, eliminating any gap in self-care, and reducing urinary retention and the use of analgesics, all of which allow the patient to be discharged early and return to normal life in a short time.[14,15]

After hemorrhoidectomy, the evaluation of the patient's pain by the nurse and the planning and implementation of appropriate nursing interventions are important for pain management. This study will contribute to the literature by providing information on the effect of warm sitz baths with menthol oil given after hemorrhoidectomy on pain intensity, and its use as a non-pharmacologic method in pain control. In addition, it is thought to be important in increasing the comfort of the patient, planning, and implementing holistic nursing interventions, improving the quality of life of individuals, increasing the quality of nursing care, and creating a guide for nurses who provide care after hemorrhoidectomy.

Materials and Methods

Trial Design

This was an interventional study.

Place and Time

This study was conducted in the general surgery clinic of a private hospital in İstanbul between June 2018 and September 2019 and involved patients who had undergone traditional hemorrhoidectomy surgery.

Population and Sample

The study population consisted of patients scheduled for elective hemorrhoidectomy procedures between June 2018 and September 2019 who met the inclusion criteria, agreed to participate, and underwent conventional hemorrhoidectomy surgery (i.e., via electrocautery) and general anesthesia. The use of enemas and diclofenac type 2x1 (dicloron) intramuscularly as an analgesic are routine in clinical practice at the 9th and tenth hours for postoperative pain control. A power analysis of the sample size was performed using G*Power 3.1 software. To exceed the study power of 80% (df=40; t=1,684), it was necessary to include at least 42 people in the study sample (21 in each group), with a significance level of 5% and an effect size of 0.8. To take possible losses into account and perform better subgroup analysis, 32 people were ultimately recruited for each group.

The inclusion criteria were as follows: 18 y of age or older; absence of any problems that would interfere with communication; continued treatment with a single type of analgesic drug after surgery; non-use of any complementary treatment methods; a 4th-degree hemorrhoid diagnosis; undergoing of elective, traditional hemorrhoidectomy; and willingness to participate in the study. The exclusion criteria were as follows: presence of any known allergies and undergoing of hemorrhoidectomy via the Longo method.

Ethical Statement

Ethical approval and written permission for this study were obtained from the İstanbul Medipol University Non-Interventional Research Ethics Committee (decision no: 10840098-604.01.01.-F21938, approval number: 392; date: 27.06.2018). The identities of study participants were kept confidential. After informing study participants of the purposes and importance of the study, their consent was obtained verbally and in writing.

Data Collection Tools

Data were collected using a patient information form and a numeric rating scale (NRS) to evaluate pain levels.

Patient Information Form: The patient information form was prepared by the study researchers and consisted of 22 questions in line with the literature. The first part of the form collected demographic information, such as age, sex, and nutritional level, as well as frequency of constipation and presence of hemorrhoid-related symptoms.[7-9,16] The form was completed face-to-face with the study participants 30 min before surgery.

The second part of the form was used to record the hour of the first postoperative defecation, the timepoints when pain was evaluated, and notes about pain levels.

Numeric Rating Scale: Patients' pain levels were determined using numbers on a linear line, with 0 indicating no pain, 1-3 indicating mild pain, 4-6 indicating moderate pain, and 7-10 indicating severe pain.[17]

Data Collection

Before data were collected, participants were informed about the purposes of the study, and their consent was obtained. Participant data was collected using the patient information form at least one hour before surgery and at the fourth and eighteenth hours after surgery (before and after the sitz bath), and pain intensity was evaluated before and after the first postoperative defecation using the NRS.

Research Application

Control group: A sitz bath was performed for about 15 minutes in a container filled with water heated to 30-40 °C at the 4th hour after the surgery, after the first defecation, and at the 18th hour. Pain levels were evaluated and recorded

using the NRS just before the sitz bath and 15 minutes after the bath.

Intervention group: At the 4th hour after the surgery, after defecation, and at the 18th hour, 5 drops of menthol oil (measured with a dropper) were added into the container and a sitz bath was performed for approximately 15 minutes. Pain levels were evaluated and recorded with NRS just before the sitz bath and 15 minutes after the bath.

Pain levels were evaluated using the NRS before the enema and after defecation at the 9-10th hour.

Statistical Analysis

Study findings were evaluated using SPSS v. 22.0 statistical software. Descriptive statistical methods, such as mean, standard deviation, frequency, and percentage, were used to evaluate data. The Student's t-test was used to compare continuous quantitative data between the two groups. Changes between repeated measurements were analyzed using a repeated measures analysis of variance. A chi-squared (χ^2) test was used to analyze the distribution of descriptive features by group. Results were evaluated with a significance level of $p<0.05$ and a confidence interval of 95%.

Results

Participants' introductory characteristics are shown in Table 1. The mean age of patients was 45.56±13.72 y in the intervention group and 44.59±12.40 y in the control group. No significant differences existed between the two groups in terms of age, sex, marital status, educational level, profession, social security, income status, presence of chronic disease, or constipation ($p>0.05$) (Table 1).

Table 1. Comparison of participants' descriptive characteristics (n=64)

Descriptive characteristics		Intervention group, (n=32)		Control group, (n=32)		p
		Mean	SD	Mean	SD	
Age (y)		45.56	13.72	44.59	12.40	0.768
Body mass index (kg/m²)		28.61	5.74	28.27	6.02	0.818
		n	%	n	%	χ^{2*}/p
Sex	Female	11	34.4	14	43.8	χ^{2*}=0.591; p=0.304
	Male	21	65.6	18	56.2	
Marital status	Married	8	25.0	6	18.8	χ^{2*}=0.366; p=0.382
	Single	24	75.0	26	81.2	
Educational level	Primary school	1	3.1	2	6.2	χ^{2*}=4.772; p=0.311
	Elementary school	0	0.0	3	9.4	
	High school	19	59.4	16	50.0	
	Graduate	12	37.5	11	34.3	
Profession	Housewife	10	31.2	9	28.1	χ^{2*}=2.872; p=0.897
	Worker/Civil servant	4	12.4	3	9.3	
	Retired	5	15.6	7	21.9	
	Self-employment	8	25.0	6	18.8	
	Student	2	6.2	3	9.4	
	Other	3	9.3	4	12.5	
Chronic disease status	Yes	8	25.0	10	31.2	χ^{2**}=0.309; p=0.391
	No	24	75.0	22	68.8	
Constipation	Yes	22	68.8	27	84.4	χ^{2**}=2.177; p=0.119
	No	10	31.2	5	15.6	
Previous anorectal surgery status	Yes	3	9.4	12	37.5	χ^{2**}=7.053; p=0.008
	No	29	90.6	20	62.5	

*More than one option was selected, **Data were analyzed using a χ^2 test, SD: Standard deviation

The mean NRS scores of patients in the intervention and control groups before the first defecation were 3.75±1.95 and 3.94±2.01, respectively. When the patients in the intervention and control groups were examined according to their NRS scores after the first defecation, the mean scores of the intervention group and control group were 4.56±1.83 and 5.16±2.14, respectively (p>0.05). The increase in pain intensity after defecation was found to be statistically significant in patients in both groups compared with before the first defecation (p=0.001) (Table 2).

Pain intensity decreased significantly in both groups after the sitz baths given at the fourth and eighteenth hours after surgery (p<0.05). There was no statistically significant difference in pain intensity between the two groups before and after the baths (p>0.05) (Table 3). First postoperative defecation occurred at a mean time of 9.880±2.803 h in the intervention group and 9.280±2.275 h in the control group, and the difference was not statistically significant (p>0.05). The decrease in NRS scores after the first defecation compared with before the sitz bath after the first defecation (mean: 3.160) was found to be significant in both the intervention and control groups (p=0.001 and p<0.05, respectively) (Table 4).

Discussion

Pain is observed in the anorectal region in the early period after hemorrhoidectomy.[1,2,16] Various medicines and herbal drugs can be added to warm sitz baths to alleviate the symptoms of hemorrhoids before and after surgery, reduce pain, support healing, and increase patient comfort and satisfaction.[6,7,9-11,17] Some studies recommend the use of conservative and medical pain management strategies, as they are non-invasive and reduce the risk of anal sphincter injury.[18,19] This study found that pain intensity decreased significantly after sitz baths given 4 and 18 h after surgery. In a study by Hsu et al. on the effect of warm water spray and sitz baths after hemorrhoidectomy, the authors stated that both methods had similar effects after hemorrhoidectomy and that a sitz bath should be performed four times daily after defecation in the first week after hemorrhoidectomy, and twice daily in the following weeks.[6] Abd-Elmaged et al.[20] assert that sitz baths given once before defecation and three times daily for four weeks help relax anal sphincters and reduce pain, burning, and itching in the anorectal region. A study by Lang et al.[7] evaluating the effectiveness of sitz baths in patients with anorectal diseases emphasized

Table 2. NRS mean scores of the groups before and after the first defecation

	Intervention group, (n=32)		Control group, (n=32)		t*	p
	Mean	SD	Mean	SD		
NRS before the first defecation	3.75	1.951	3.94	2.015	0.378	0.707
NRS after the first defecation	4.56	1.831	5.16	2.142	1.192	0.238
F	21.839		4.929			
p	0.001		**0.034**			

*Data were analyzed using a Student's t-test. NRS: Numeric rating scale, SD: Standard deviation, F: Repeated measures analysis of variance test

Table 3. Comparison of NRS scores before and after sitz bath

Intervention time		Intervention group, (n=32)		Control group, (n=32)		t*	p
		Mean	SD	Mean	SD		
4th hour	Pre-application NRS score	5.56	1.76	5.25	2.34	-0.604	0.548
	Post-application NRS score	4.12	1.62	4.25	2.05	0.271	0.788
	F	54.12		35.43			
	p	<0.001		<0.001			
18th hour	Pre-application NRS score	3.69	2.07	3.88	2.28	0.344	0.732
	Post-application NRS score	2.66	1.77	3.16	1.99	1.063	0.292
	F	28.54		19.36			
	p	0.001		0.001			

*Data were analyzed using a Student's t-test, NRS: Numeric rating scale, SD: Standard deviation, F: Repeated measures analysis of variance test

Table 4. Comprasion of NRS mean scores of groups before and after the first defecation and sitz bath

	Intervention group, (n=32)		Control group, (n=32)		t*	p
	Mean	SD	Mean	SD		
NRS score before first defecation and sitz bath	4.56	1.83	5.16	2.14	1.192	0.238
NRS after first defecation and sitz bath	2.66	1.77	3.16	1.99	1.063	0.292
t	8.735		5.173			
p	0.001		0.001			

*Data were analyzed using a Student's t-test. NRS: Numeric rating scale, SD: Standard deviation

that sitz baths should be performed four times per day as well as after defecation to relieve the anorectal region and reduce edema. In a 2015 randomized controlled study investigating the effect of hot water bag use on pain in the early period after hemorrhoidectomy, Balta et al.[21] found that postoperative pain scores in the hot water bag group were significantly lower than in the control group on the first and third postoperative days.

In the present study, the average pain scores after the first defecation decreased significantly in both groups after the sitz baths. Comparing the effect of water spraying and sitz baths on pain after hemorrhoidectomy, Hsu et al.[6] reported that there was no statistically significant difference in pain reduction between the two methods after defecation. A study by Lang et al.[7] investigating the effectiveness of sitz baths in managing symptoms of anorectal diseases reported that pain gradually decreased between the intervention and control groups. Shen et al.[22] used warm sitz baths as a control and applied Xiaozhi (an ointment made from a Chinese plant) as an intervention and found that the intervention group experienced not only lower pain levels but also less analgesic consumption than the control group. Joksimovic et al.[23] evaluated the effectiveness of topical hyaluronic acid and tea tree oil gel forms in reducing the symptoms of hemorrhoids and found a statistically significant reduction in pain during defecation in the preoperative period in both intervention groups. These findings suggest that sitz baths stimulate the sensory receptors in the anorectal region, causing relaxation in the inner sphincter and reducing pain during and after defecation.

Menthol has been used as a topical pain reliever since ancient times.[12] This study demonstrates that warm sitz baths, with or without menthol oil, reduce pain intensity after hemorrhoidectomy. A study by Amato et al.[24] investigating the effect of menthol on the muscles of the large intestine states menthol oil can be applied topically or as an enema. Menthol oil, an ingredient in some hemorrhoid drugs, has been used for hemorrhoids and in enemas in the preoperative period.[25] Kolassa[26] report that menthol oil differs from other essential oils in its mechanism of action, and that the ointment contained menthol oil to alleviate the symptoms of hemorrhoids. Yoshida et al.[27] determined that menthol injected into the colon could prevent spasms during colonoscopy. The literature states that, when used topically, menthol oil gives a cooling and then a warming sensation and slows the transmission of calcium in the tissues. These anesthetic and vasodilating properties of menthol oil promote relaxation of the muscles and sphincters in the areas to which it is applied.[12,13,23,25]

Study Limitations

This study has several limitations. The follow-up period was limited to 24 h because patients were discharged on the first day after hemorrhoidectomy; thus, patients' post-discharge pain intensity was not monitored at home, and the effect of menthol on edema in the surgical field was not evaluated. The short follow-up time may have prevented the study from fully assessing the effects of menthol on pain. The use of sitz baths with menthol oil should be followed up for a minimum of 72 h in future studies to demonstrate their effect on pain. Another limitation of this study is that it cannot be generalized to all patients undergoing hemorrhoidectomy because the study sample was limited to patients undergoing traditional hemorrhoidectomy in the general surgery department of a private hospital.

Conclusion

The findings of this study show that warm sitz baths with menthol oil decrease pain intensity in patients who have undergone hemorrhoidectomy. Further research evaluating the effectiveness of various postoperative pain control methods is necessary to achieve the important goal of relieving pain in patients. The use of at-home remedies alongside pharmacologic methods of pain control is recommended, and more studies on their effects should be conducted in order to reap the full benefits of aromatic oil use in nursing care practice.

Ethics

Ethics Committee Approval: Ethical approval and written permission for this study were obtained from the İstanbul Medipol University Non-Interventional Research Ethics Committee (decision no: 10840098-604.01.01.-F21938, approval number: 392; date: 27.06.2018).

Informed Consent: Their consent was obtained verbally and in writing.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.G., Design: S.M.T., S.G., Data Collection or Processing: S.M.T., Analysis or Interpretation: S.G., Literature Search: S.M.T., S.G., Writing: S.M.T., S.G.

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RESEARCH ARTICLE

Pit-Picking with Laser Treatment Versus Pit-Picking Alone in Pilonidal Disease: Retrospective Mid-Term Results

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ABSTRACT

Aim: This study aimed to compare the 36-month recurrence rates between pit-picking alone and pit-picking with laser treatment (LT) in the management of pilonidal disease (PD).

Method: Patients with Tezel type 3, 4, and V PD who underwent pit-picking were included in the study. All the patients underwent pit-picking; LT was added for those willing to receive the treatment. Follow-up evaluations were conducted through outpatient visits on postoperative days 3 and 10 and at 1, 6, and 12 months. Recurrence was monitored through telephone calls at 24 and 36 months. The primary outcome measure was recurrence at 36 months.

Results: A total of 121 patients were included between March 2018 and October 2022; 80 underwent pit-picking only (the "pit-picking group"), and 41 were in the group that received pit-picking followed by LT (the "LT group"). The mean age was 24.5±5.9 years, and 63 (52%) patients were female. Postoperative complications were seen in 14 (11.6%) patients. Patients in the LT group had no complications, whereas the overall complication rate in the pit-picking group was 17.5% (p=0.002). The LT group had a significantly shorter return-to-work time (3.2±2.2 vs. 6.7±2.3 days, p<0.001) and "sit-pain-free time" (i.e., the time until sitting becomes painless) (5.1±2.1 vs. 7.8±3.1 days, p=0.003). The mean complete healing time was shorter in the LT group (10.1±2.3 vs. 14.1±3.8 days, p<0.001). The median follow-up was 46 (43-65) months. Thirteen (10.7%) patients had recurrence; 9 (11.3%) in the pit-picking group and 4 (9.8%) in the LT group (p=0.534). The mean time-to-recurrence was 14.7±5.6 days.

Conclusion: LT when added to pit-picking does not affect mid-term recurrence rate but significantly reduces postoperative complications, pain, and workday loss.

Keywords: Pilonidal disease, laser treatment, pit-picking, minimally invasive surgery

Introduction

Pilonidal disease (PD) is a common condition that affects the sacrococcygeal region and is characterized by the development of a cyst or sinus tract containing hair and debris. The management of PD has been a topic of debate for many years, with several surgical and non-surgical treatment options available. Although surgical excision is currently the standard treatment for chronic PD,[1] it is accompanied by a high incidence of morbidity and recurrence rates, as well as a long time away from work.[2]

Even though off-midline flap procedures demonstrated the lowest recurrence rates (10% at 5 years) and good postoperative wound healing (complication rate 8%-16%) in two meta-analyses,[3,4] there is intensive demand for outpatient treatments from both surgeons and mostly working patients.[5] Since Bascom[6] described the cleft lift technique, all minimally invasive methods have evolved based on this "focused" management with slightly modified procedures such as microsinusectomy, pit-picking, and Gips.[7,8] Several methods that share strong similarities, and sometimes even the same techniques, have been identified, although referred to by different names. Regardless of nomenclature, most minimally invasive treatments provide shorter hospital stays, decreased postoperative morbidity, and a faster return to normal daily activities.[9] The fundamental principle in all these methods is the excision or curettage of the diseased tissue and debris

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through very small incisions. Over time, new technologies, such as laser and endoscopy, and additional applications, such as phenol and fibrin glue, have been integrated into this technique to further enhance the outcomes.[10-15]

Pit-picking is a minimally invasive surgical technique that has gained popularity due to its low morbidity and short recovery time. However, it still has not yielded the expected outcomes in terms of relapse and loss of workdays. A few studies for simple pit-picking in the literature revealed a recurrence rate of 10%-51% with follow-up times of 12-83 months.[3,8,16] Laser treatment (LT) has been proposed as an adjunct to pit-picking, with potential advantages such as reduced bleeding, decreased pain, and improved healing.[17,18] In a recent review, primary healing after LT has been reported at 94.4%, and a recurrence rate with a median of 12 (7-25) months was found to be 3.8%.[19] However, the follow-up periods of published studies are too short, and it is unclear whether the observed effectiveness of this technique is due to the use of LT or the pit-picking alone.

The objective of this study was to ascertain whether the mid-term effectiveness of pit-picking with LT can be attributed to the addition of LT or solely to the pit-picking technique itself.

Materials and Methods

This study protocol was registered with clinicaltrials.gov (ID: NCT05569135) and approved by the İstanbul Medipol University Institutional Ethics Committee (approval number: 447, date: 11.05.2022). The patients were informed about the protocol and provided written consent. Prospectively collected data of patients treated for PD by a single surgeon (CA) was reviewed retrospectively. The study period started in March 2018, when LT was introduced at our institution. Patients aged >18 years who underwent pit-picking and completed at least 36 months of follow-up were included in the study. The exclusion criteria were as follows: immunosuppression, antibiotherapy and/or abscess drainage within 2 weeks before surgery, procedures other than pit-picking, and loss of follow-up for 36 months.

Study Groups

The institution uses Tezel's[20] navicular area classification to assist in decision-making (Table 1). Recommended procedures at the institution include local hair removal and careful hygiene in type 1 (asymptomatic) disease, abscess drainage in type 2 (acute abscess) disease, and pit-picking in type 3 (pits within the navicular area) and type 4 (pits outside the navicular area) disease. For patients with type 5 (recurrent) disease, pit-picking is usually preferred; however, in some patients with wide lateral extensions and chronic fistulas or in cases of accompanying hidradenitis suppurativa, off-midline flap procedures are performed. Patients with type 2 disease are recommended pit-picking following abscess drainage and antibiotics after achieving complete healing of infection. This period is ≥2 weeks.

All patients included in the study underwent pit-picking and were offered supplementary LT since its availability at the institution in 2018. Those who provided consent received additional LT, whereas those who declined were

Table 1. Demographic and clinical characteristics of the patients

	Total, (n=121)	Pit picking only, (n=80)	Pit picking + laser treatment, (n=41)	p
Age (years, mean ± SD)	24.5±5.9	24.9±5.6	23.7±6.3	0.284
Sex				
Male	58 (48)	41 (51.3)	17 (41.5)	0.204
Female	63 (52)	39 (48.8)	24 (58.5)	
BMI (kg/m^2, mean ± SD)	26.2±3.4	26.1±3.2	26.6±3.6	0.640
Duration of the symptoms (months, mean ± SD)	11 (1-18)	16.19±19.7	18.6±17.8	0.503
History of abscess drainage	41 (33.9%)	26 (32.5%)	12 (29.3%)	0.837
Family history (+)	14 (11.6)	11	3	0.232
Smoking (+)	47 (38.8)	35	12	0.088
Tezel Classification[20]				
III	71 (58.7)	44 (55)	27 (66)	0.503
IV	42 (34.7)	30 (37.5)	12 (30)	
V	8 (6.6)	6 (7.5)	2 (4)	

SD: Standard deviation, BMI: Body mass index

managed with standard pit-picking. The results of the two groups were compared. The primary outcome measure was recurrence at 36 months. The secondary outcome measures were morbidity, return-to-work time, time to complete healing, and comparison of the characteristics of patients with and without recurrence.

Surgical Technique

All the procedures were day-case surgery without any general anesthesia or sedation, except for five patients who demanded general anesthesia due to anxiety. No antibiotic prophylaxis was performed. The patients were operated upon in a prone position with local anesthesia (20 mL prilocaine 1%). Sinus openings were identified, and 1-3 sinuses-depending on the extension of the tracts and the number of sinuses-were enlarged with a no: 11 scalpel or a clamp (Figure 1). Hair and/or necrotic tissues were removed through the pits using a clamp, curette, and/or brush (Figure 2). The cavity was rinsed with saline.

For the LT group, a radial laser probe with a wavelength of 1,470 nm and operating in continuous mode was inserted through the pits, and a total of 100-110 joules of energy per 1 cm-long region was administered at 10 W by retracting the probe along with the entire tract (Figure 3). The probe was introduced to all lateral sinus extensions and tracts if present (Figure 4). In both groups, a pressure dressing was applied and advised to be kept for 3 hours after the procedure.

Follow-Up

The patients were discharged and permitted to sit and shower the area immediately after surgery. Hair removal for 1 year with depilation gel was recommended to all patients. Follow-up evaluations were conducted through outpatient visits on postoperative days 3 and 10 and at 1, 6, and 12 months. Recurrence was monitored through phone calls at 24 and 36 months after the first year. At discharge, patients were given a visual analog scale (VAS) chart and instructed to complete it on days 1, 7, and 30 post-surgery. The chart was used to assess the maximum pain level (0-10) experienced by patients at each time point. The same chart included a section for patients to record the sit-pain-free time.

Patients who reported any reappearance of the symptoms on a telephone call were invited to visit the clinic to confirm recurrence. Since treatment is not recommended for asymptomatic disease, recurrence was determined based on patient-reported symptoms. Seroma was defined as the accumulation of fluid in subcutaneous tissue without any evidence of infection. Hematoma was defined as blood or clot accumulation in subcutaneous tissue. Surgical site infection was defined as the presence of purulent drainage or incision opened by the surgeon with at least one of the following symptoms: pain, tenderness, swelling, redness, and

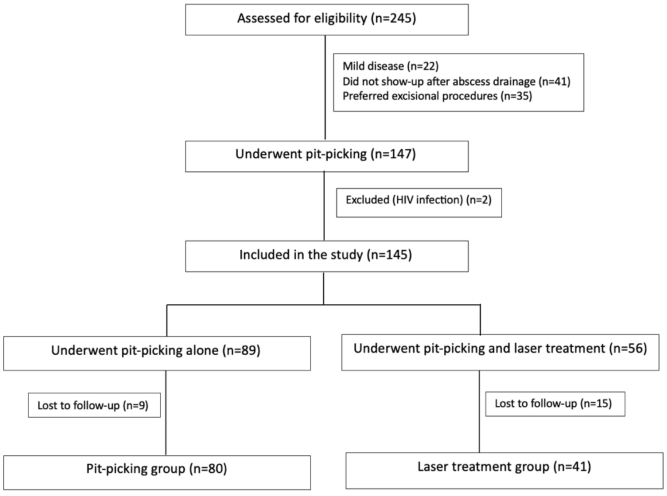

Figure 1. Flow diagram of the study

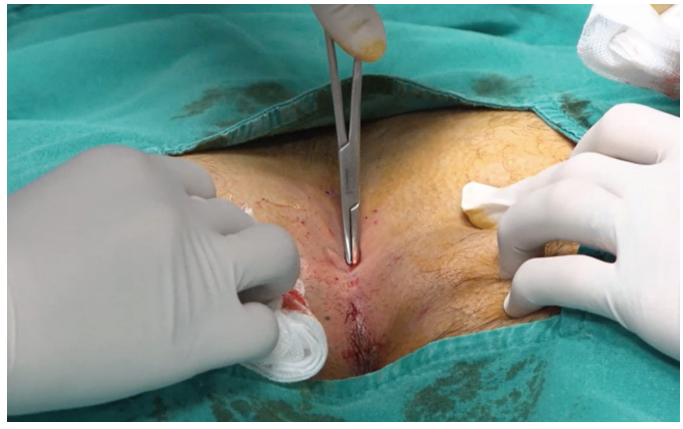

Figure 2. Enlargement of the pits with a clamp

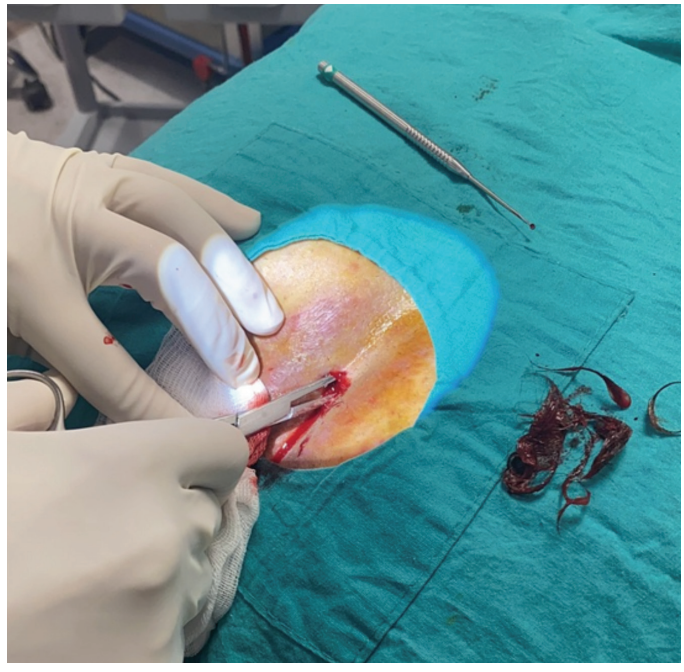

Figure 3. Removal of the hair and necrotic tissue through pits

heat, with or without culture confirmation.[21] The number of days until returning to a daily routine was recorded as the return-to-work time. The sit-pain-free time was also recorded. Complete healing was defined as complete closure of the pits without any spontaneous or provoked discharge (Figure 5). In cases where the symptoms persisted for 4 weeks after surgery, they were recorded as non-healing. If the symptoms reappeared after complete healing, this was defined as recurrence.

Statistical Analysis

Statistics were analyzed using the IBM SPSS for Windows v.26 software package. The distribution of the data was evaluated using histograms. Variables that were normally distributed were reported as mean and standard deviation, and means were compared by the independent sample t-test; skewed variables were reported as median, and range and means were compared by the Mann-Whitney U test. A p-value <0.05 was defined as statistically significant.

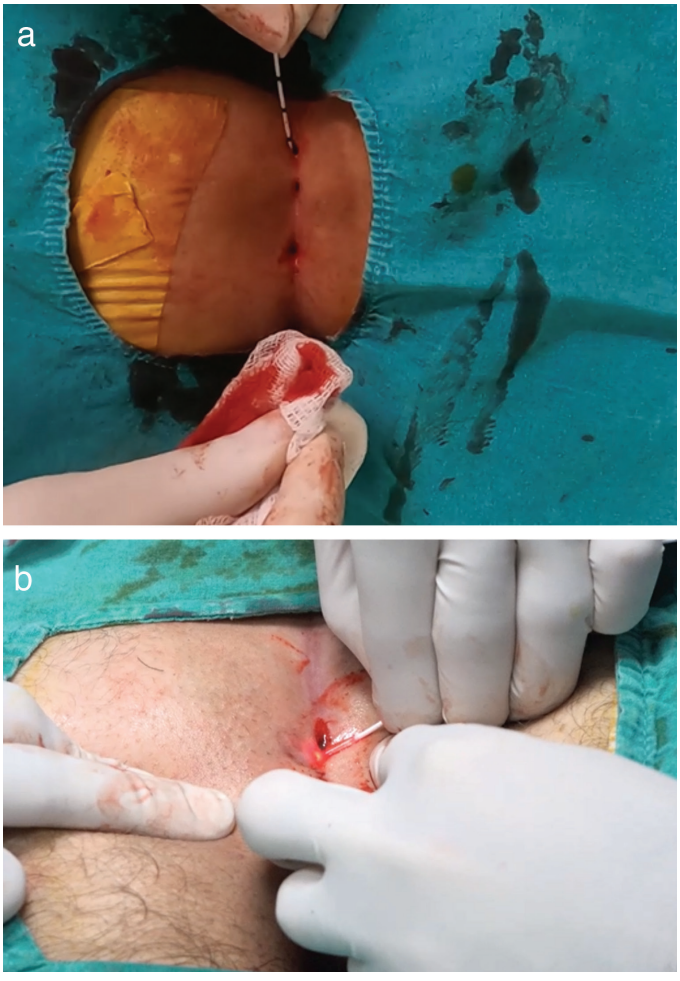

Figure 4. (a) Insertion of the laser probe through pits; (b) ablation of the lateral tracts by laser probe

Results

A total of 245 patients were treated for PD in the institution between March 2018 and October 2019. Twenty-two were advised conservative treatments for mild disease, 41 underwent abscess drainage but did not come back for definitive treatment, and 35 preferred to undergo excisional procedures. Among 147 patients who received pit-picking, 2 were excluded for HIV infection and 24 were lost to follow-up. Among 121 patients included in the final analysis, 80 were in the pit-picking group and 41 were in the LT group. A flow diagram of the study is shown in Figure 1.

The mean age was 24.5±5.9 years. Fifty-eight (48%) patients were male and 63 (52%) were female. The mean body mass index (BMI) was 26.2±3.4. The median duration of the symptoms was 11 (1-18) months, and 41 (33.9%) patients had previous abscess drainage. Seventy-one (58.7%) patients had Tezel III PD, 42 (34.7%) had Tezel IV PD, and 8 (6.6%) had recurrent (Tezel V) PD. There was no difference in demographic or clinical features between the two groups (Table 1).

The mean operative time was 25.7±5.8 minutes. Postoperative complications were seen in 14 (11.6%) patients, comprised of 10 (8.3%) seroma, 6 (5%) bleeding, and 2 (1.7%) surgical site infections; all patients were managed conservatively, and none of them required reoperation or hospitalization. Patients in the LT group had no complications, whereas

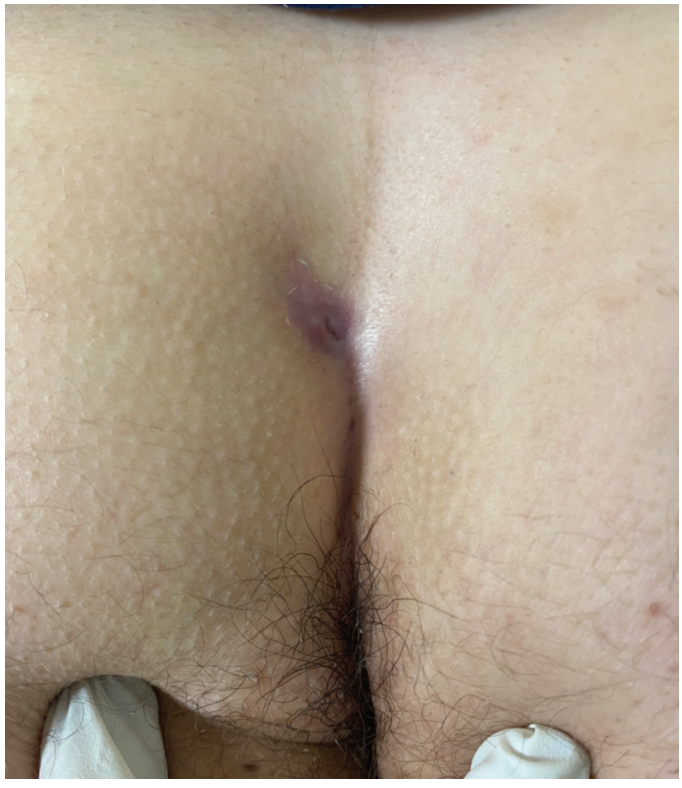

Figure 5. Healing at 1 week visit

the overall complication rate in the pit-picking group was 11.6% (n=14) (p=0.002). Seroma (12.5% vs. 0%, p=0.013), bleeding (7.5% vs. 0%, p=0.078), and surgical site infection (2.5% vs. 0%, p=0.435) rates were higher in the pit-picking group; however, the differences were not statistically significant (Table 2).

The mean return-to-work time and sit-pain-free time were 5.5±2.8 and 6.9±3.1 days, respectively. The LT group had significantly shorter durations to return to work (3.2±2.2 vs. 6.7±2.3 days, p<0.001) and sit-pain-free time (5.1±2.1 vs. 7.8±3.1 days, p=0.003). The mean complete healing was 12.7±3.8 days and significantly shorter in the LT group (10.1±2.3 vs. 14.1±3.8 days, p<0.001). The mean VAS was 2.7±1.2 at 24 hours, 1.1±0.9 on day 7, and 0.2±0.4 at 1 month. On day 7, the mean VAS score was 0.9±0.7 in the LT group and 1.3±0.9 in the pit-picking group (p=0.040) (Table 2).

The median follow-up time was 46 (43-65) months. No non-healing was recorded. Thirteen (10.7%) patients had recurrence; 9 (11.3%) in the pit-picking group and 4 (9.8%) in the LT group (p=0.534). The mean time-to-recurrence was 14.7±5.6 months (Table 2).

When recurrent and non-recurrent patients were compared, patients with recurrence had a higher mean BMI (30.1±4.2 vs. 25.8±2.9, p=0.003). Recurrence was not seen in any of the patients with Tezel III disease, whereas 8 (19%) of the patients with Tezel IV and 5 (62.5%) with Tezel V disease had recurrent disease (p<0.001). Four (28.6%) patients with postoperative complications had recurrence versus 9 (8.4%) patients without postoperative complications (p=0.044) (Table 3).

Discussion

Our results showed no significant advantage of LT on the recurrence rate, which was the primary outcome of the study. However, the return-to-work time, sit-pain-free time, and time to complete healing were shorter in the LT group. Moreover, the LT group exhibited a reduced incidence of overall complications. Risk factors for recurrence in our series were high BMI, severity of the disease, and occurrence of postoperative complications. Our mid-term results showed that the addition of LT to pit-picking provides lower complication rates, faster recovery, and lower postoperative pain scores. The early and mid-term outcomes of the overall

Table 2. Comparison of surgical characteristics and outcome

	Total, (n=121)	Pit picking only, (n=80)	Pit picking + laser ablation, (n=41)	p
Anesthesia				0.447
General	5 (4.1)	4 (5%)	1 (2.4%)	
Local	116 (95.9)	76 (95%)	40 (97.6%)	
Operative time (min, mean ± SD)	25.7±5.8	25.4±5	26.6±7	0.280
Complications	14 (11.6%)	14 (17.5%)	0	0.002
Seroma	10 (8.3%)	10 (12.5%)	0	0.013
Bleeding	6 (5%)	6 (7.5%)	0	0.078
Surgical site infection	2 (1.7%)	2 (2.5%)	0	0.435
Time to return to work (days, mean ± SD)	5.5±2.8	6.7±2.3	3.2±2.2	<0.001
Time to sit pain-free (days, mean ± SD)	6.9±3.1	7.8±3.1	5.1±2.1	0.003
Time to complete healing (days, mean ± SD)	12.7±3.8	14.1±3.8	10.1±2.3	<0.001
Pain score (VAS, mean ± SD)				
24 hours	2.7±1.2	2.7±1.25	2.7±1.1	0.974
7 days	1.1±0.9	1.3±0.9	0.9±0.7	0.040
30 days	0.2±0.4	0.1±0.3	0.2±0.4	0.309
Follow-up (months, mean ± SD)	47.6±4.5	47.3±4.1	48.1±5.1	0.367
Recurrence (n,%)	13 (10.7%)	9 (11.3%)	4 (9.8%)	0.534
Time-to-recurrence (months, mean ± SD)	14.7±5.6	16.4±5.4	10.8±4.3	0.079

SD: Standard deviation, VAS: Visual analogue scale

series were comparable with excisional methods. This result supports the utilization of minimally invasive treatments for PD.

In the past 10 years, several guidelines, results of national attitude surveys, and consensus reports have been published from America, Germany, Italy, and the Netherlands.[1,22-24] A common conclusion reached in these reports is that it is important to select treatment according to the severity of the PD. According to all guidelines, minimally invasive techniques are considered a promising treatment option for mild PD, whereas off-midline techniques are recommended for severe or recurrent disease. In alignment with this

Table 3. Comparison of the characteristics of the patients regarding recurrence

	Recurrence (-), (n=110)	Recurrence (+), (n=11)	p
Age (years, mean ± SD)	24.5±6	24.6±4.7	0.937
Sex			
Male	52 (89.7%)	7 (11.1%)	0.564
Female	56 (88.9%)	6 (10.3%)	
BMI (kg/m^2, mean ± SD)	25.8±2.9	30.1±4.2	**0.003**
Duration of the symptoms (months, median, range)	11 (1-72)	10 (3-108)	0.975
History of abscess drainage			
(-)	75 (90.4%)	8 (9.6%)	0.385
(+)	33 (86.8%)	5 (13.2%)	
Family history			
(-)	85 (88.8%)	12 (11.2%)	0.538
(+)	13 (92.9%)	1 (7.1%)	
Smoking			
(-)	66 (89.2%)	8 (10.8%)	0.613
(+)	42 (89.4%)	5 (10.6%)	
Tezel Classification[20]			
III	71 (100%)	0	
IV	34 (81%)	8 (19%)	**<0.001**
V	3 (37.5%)	5 (62.5%)	
Surgery			
Pit picking	71 (88.8%)	9 (11.3%)	0.534
Pit picking + laser ablation	37 (90.2%)	4 (9.8%)	
Overall complications			
(-)	98 (91.6%)	9 (8.4%)	**0.044**
(+)	10 (71.4%)	4 (28.6%)	
Seroma			
(-)	100 (90.1%)	11 (9.9%)	NA
(+)	8 (80%)	2 (20%)	
Bleeding			
(-)	105 (91.3%)	10 (8.7%)	NA
(+)	3 (50%)	3 (50%)	
Surgical site infection			
(-)	107 (89.9%)	12 (10.1%)	NA
(+)	1 (50%)	1 (50%)	

SD: Standard deviation, BMI: Body mass index, NA: Not available due to small numbers in groups

perspective, our series also demonstrated no recurrences in Tezel III disease. Recurrence occurred in one-fifth of patients with severe disease and two-thirds of recurrent patients.

Excisional surgery remains the standard of care, with reported 2-year recurrence rates of 1.6% and 0.6% for the Limberg and Karydakis procedures, respectively.[3] However, a meta-analysis showed that the recurrence rate increases up to approximately 11% for the Limberg and Karydakis procedures when the follow-up duration extends to 60 months. Recurrence after excision and mid-line closure is even higher-up to 21.9% at 60 months and 67.9% at 240 months.[3] The same meta-analysis reported 15.6% recurrence for pit-picking at 60 months; unfortunately, there were no data regarding LT, since no randomized trials were available at that time.[3] Another meta-analysis, which included studies with a minimum follow-up of 5 years, also reported a 10% recurrence after off-midline closure techniques.[4] For LT, there are limited data in the literature. A recent review, which included 971 patients who underwent LT, reported 3.8% recurrence with a median follow-up of 12 (7-25) months.[19] Our overall recurrence rate was 10.7%, which is comparable with excisional methods, with no difference between the pit-picking and laser groups. Considering the relatively recent dissemination of minimally invasive techniques worldwide, a 46-month median follow-up of our series may provide insights into the feasibility of minimally invasive techniques.

The results of pit-picking in the literature are very heterogeneous. A retrospective study compared simple pit-picking with cleft closure and reported that pit-picking had fewer postoperative complications (9.4% vs 36.2%, p=0.002), and had a shorter return-to-work time (14 days vs. 21 days, p<0.001) than did cleft closure; however, long-term follow-up of median 9.3 years revealed a significantly higher recurrence for pit-picking (50.9% vs. 10.3%, HR 6.65, p<0.001).[8] The authors concluded that pit-picking should be saved as an option for mild disease. A recent meta-analysis of 4,286 Gips procedures reported a 7.8% wound complication rate and 4.7 months mean wound healing period.[7] In our pit-picking group, the complication rate was 17.5% and most of the complications were seroma (10/14). The return-to-work time was 1 week, and complete healing was observed at 2 weeks.

A multicenter study of 226 laser procedures reported 8% wound infections and 41 days mean time to heal.[10] A recent study of 106 LT procedures with or without endoscopic camera use found that one-third of the patients had no pain on the first postoperative day, the mean return-to-work time was 4.5 days, and the complication rate was 10.4%. Endoscopy did not affect early postoperative outcome and recurrence.[25] Our LT group did not show any postoperative complications. The mean return-to-work time was 3.2 days and complete healing was observed after 10 days. Laser ablation added to pit-picking resulted in a significantly lower complication rate and shorter recovery time. The disparity between the results in the literature and our findings likely stems from the heterogeneity in surgical techniques. There is no standardized technique for pit-picking, and variations, particularly in the incision site and size, could contribute to the heterogeneity of healing time and complication rates.

Study Limitations

Comparatively to the literature, our series demonstrates notably superior early surgical outcomes and recurrence rates. There are several possible reasons for this. First, the higher proportion of female patient admissions may be attributed to the fact that the operating surgeon was female. Second, the surgeon's early adoption of laser technology and affiliation with a specialized healthcare institution could have led to a higher frequency of suitable patients seeking her services for minimally invasive methods. When interpreting our results, it is important to bear in mind that 52% of our patient cohort were female, and 60% had stage 3 disease. A third limitation of our study is the non-randomized design and relatively small sample sizes. Considering that all recurrences in our series occurred within the first 2 years, our follow-up period of approximately 4 years can be considered sufficient when compared with the literature.

The most important limitation of our study is the lack of cost analysis. Although we have not conducted a cost analysis, it is evident that the cost of LT would be higher. Taking into account this and the result that laser has no impact on recurrence, future studies should place greater emphasis on the financial burden associated with LT.

Conclusion

Pit-picking with or without LT for PD is safe and feasible. The addition of LT may enhance postoperative outcomes regarding complications, pain scores, and return-to-work time; however, it does not affect recurrence rates. The early and mid-term outcome of pit-picking and LT is promising in mild disease. Further randomized trials are needed for patient selection and indications.

Ethics

Ethics Committee Approval: This study protocol was registered with clinicaltrials.gov (ID: NCT05569135) and approved by the İstanbul Medipol University Institutional Ethics Committee (approval number: 447, date: 11.05.2022).

Informed Consent: The patients were informed about the protocol and provided written consent.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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RESEARCH ARTICLE

Validation of the Turkish version of the Quality of Life in Patients with Anal Fistula Questionnaire

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ABSTRACT

Aim: This study aimed to examine the psychometric properties of the Turkish version of the Quality of Life in Patients with Anal Fistula Questionnaire (QoLAF-Q), recently introduced to the literature, in line with the principle that every disease should have its own quality of life (QoL) scale. The 14-question QoLAF-Q has not been validated in Turkey and was validated in this study for use in practice with Turkish individuals by assessing whether it yields similar results to the Short Form-12 Health Survey (SF-12).

Method: This was an observational cross-sectional study to facilitate the development and validation of the QoLAF-Q and was conducted between 2020 and 2023.

Results: All questions passed the 0.35 threshold in confirmatory factor analysis (CFA). The Tucker-Lewis Index value was 0.979 (>0.90 acceptable, >0.95 perfect). The comparative fit index was 0.983 (>0.90 acceptable, >0.95 perfect), and the root mean square error of approximation was 0.075 (<0.08 acceptable, <0.05 perfect) based on the 14-question, two-factor CFA result. The Physical Component Summary (PCS) and Mental Component Summary (MCS) scores of the SF-12, as well as the PCS and MCS scores of the QoLAF-Q, had a significant relationship (p>0.05).

Conclusion: As demonstrated in a previous Spanish study, the QoLAF-Q is a valuable measurement tool that possesses sufficient psychometric properties for assessing general health status and health-related QoL in clinical practice and scientific research in Turkey.

Keywords: Questionnare, validation, QoLAF-Q

Introduction

The concept of being healthy is one that continually evolves. In 1947, the World Health Organization defined health as "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity".[1] Physicians have strived to align their treatments with this definition, with efforts to comprehend the meaning of health first initiated in the 1960s.[2] Although treatments benefit the afflicted, they can also have unintended consequences, such as antibiotic resistance in response to treating infections. This has prompted physicians to contemplate the ethical boundaries of these treatments.

In 1966, the Annals of Internal Medicine articulated the desire of every physician for their patients, young or old, as not merely the absence of death but a life imbued with the vitality associated with youthful vigor.[3]

In this context, health-related quality of life (HRQoL) tools have been developed to assess patients' well-being. With the advent of customized treatments for specific ailments, the need for tailored HRQoL tools has grown.[4] However, customized HRQoL assessment tools for patients with anal fistula (AF) are lacking.[5,6]

AF presents with common symptoms such as suppuration, hemorrhage, and pain, often following the drainage of a perianal abscess, considerably affecting patients' quality of life (QoL).[5-8] Various surgical procedures are available to treat AF, but they come with a potential recurrence risk ranging from approximately 10% to 60%. Moreover, surgical complications, including incontinence, abscesses, and the necessity for multiple interventions, can further impact patients' QoL.[5,9,10] Therefore, colorectal surgeons typically consider patient QoL when determining the

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most appropriate treatment approach and evaluating its effectiveness.[10]

A literature review revealed that the assessment instruments employed to evaluate QoL in patients diagnosed with AF were originally developed for assessing general HRQoL. These instruments include the Short Form-12 Health Survey (SF-12) and the SF-36.[11] In particular, the SF-12v2, a 12-item self-rated scale, has been validated in numerous languages and for various medical conditions.[4]

In this study, we utilized the Quality of Life in Patients with Anal Fistula Questionnaire (QoLAF-Q), recently introduced to the literature by Ferrer-Márquez et al.[5], in line with the principle that every disease should have its own QoL scale. The purpose of this research was to examine the psychometric properties of the Turkish version of the QoLAF-Q and validate it for the Turkish population by comparing its results to those of the SF-12.

Materials and Methods

Study Design

The current investigation employed an observational cross-sectional design to facilitate the development and validation of the QoLAF-Q. This study was conducted between 2020 and 2023. The inclusion criteria for participation were age ≥18 years and a diagnosis of cryptoglandular AF. The exclusion criteria for participation were as follows: 1) patients whose native language was not Turkish; 2) patients with comprehension and speech disorders due to cognitive problems; 3) patients with anovaginal fistula; 4) a history of radiotherapy; and 5) the presence of anal cancer. The study procedures were approved by the Ankara University Human Research Ethics Committee (approval number: İ01-32-23, date: 23.01.2023). Prior to participating in this research, volunteers completed an informed consent form. Demographic data, including age, sex, and prior anal surgery, were collected using the personal information form included with the questionnaire. The questionnaires were administered on postoperative days 15 and 30. Concurrently, the SF-12 was also administered to the patients.

SF-12

Ware et al.[12] developed a more practical and concise version of the SF-36 in 1995, resulting in the SF-12, which includes the same subscales as the SF-36 but with a reduced number of questions. The advantage of the SF-12 is its ability to yield the same component summary scores as the SF-36, and it takes less time to administer due to its reduced item count. The reliability of the scale, evaluated by calculating Cronbach's alpha, was 0.73 for the Physical Component Summary (PCS) and 0.72 for the Mental Component Summary (MCS). The SF-12 has been validated in multiple languages.

QoLAF-Q

The initial version of the QoLAF-Q was developed in Spanish. The answers were based on a 5-point Likert scale. Fourteen questions were validated in the Spanish version of the QoLAF-Q. The reliability of the QoLAF-Q was assessed by calculating Cronbach's alpha, which was 0.908.

The researchers involved in the creation of the QoLAF-Q, including manuel Ferrer-Márquez, were contacted, and the necessary permissions were obtained.

During the translation process, the questionnaire was initially translated into Turkish by two native English speakers. The translated version was then reviewed by two colorectal surgeons (CA, MAK), who are native Turkish speakers and proficient in English (Supplement Table 1). This process resulted in a version of the questionnaire that was in a common language and easily understood.

Statistical Analysis

Internal Construct Validity

Two-factor confirmatory factor analysis (CFA) was conducted using categorical data in MPlus to assess the dimensionality of the "Anal Fistula Scale".[13] Factor loadings that were positive and/or above 0.35 were retained in the scale. The Tucker-Lewis Index [(TLI); >0.90, considered acceptable; >0.95, considered excellent], Comparative Fit Index [(CFI); >0.90, considered acceptable; >0.95, considered excellent], and root mean square error of approximation [(RMSEA); <0.08, considered acceptable; <0.05, considered excellent] were used as measures of goodness-of-fit.[14]

Known-Group Validity

The scale's ability to discern expected differences based on patient age, sex, and anal surgery history was examined. The disparities in subdimension scores based on sex and anal surgery history were analyzed using the Mann-Whitney U test, and the correlation with age was assessed using Spearman's correlation coefficient.

External Construct Validity

In the context of external construct validity, the relationship between the scores obtained from the Anal Fistula Scale and those of the SF-12 was evaluated using Spearman's correlation coefficient.

Reliability

Following the confirmation of internal and external construct validity, reliability was assessed for both internal consistency and test–retest reliability. Internal consistency was evaluated using Cronbach's alpha coefficient and test-retest reliability was measured using the intraclass correlation coefficient along with its associated confidence interval.[15,16]

RESULTS

Patient Demographics

A total of 100 individuals participated in our study. The sample had an average age of 43.3 years, ranging from 18 to 72 years. Twenty-four percent of the participants were female, and 76% of the participants had no history of anal surgery.

Understandability

Independent native Turkish speakers reported no difficulties when reading and completing the QoLAF-Q. Furthermore, the mean completion time was less than 5 minutes, ranging from 4 to 6 minutes.

Internal Construct Validity

Following the CFA conducted on the 14 questions with a 2-factor structure, goodness-of-fit statistics slightly below acceptable limits were observed. In response, two modifications recommended by the program were applied to improve the fit. Specifically, the error values of "How often do you experience discharge (suppuration) from the fistula?" were correlated with the error values of "How much discharge (suppuration) from the fistula do you experience?", and the error values of "How often do you experience uncontrollable flatulence (farting) since having the fistula?" were correlated with the error values of "What is the amount of unintentional stool loss that you usually experience since having the fistula?." These adjustments aimed to address errors related to the questions. Following these modifications, the TLI was 0.979, the CFI was 0.983, and the RMSEA was 0.075, according to the 14-question, two-factor CFA result. The factor loadings of the questions based on the factors are presented in Table 1.

Known-Group Validity

The scale's ability to disclose the expected differences based on the age, sex, and previous anal surgery of the patients was assessed, and the results are presented in Table 2.

Statistically significant differences in the known groups, including age, sex, and previous anal surgery, were not determined.

External Construct Validity

In terms of external construct validity, the relationship between the scores obtained from the QoLAF-Q and the SF-12 was evaluated using Spearman's correlation coefficient, and the results are presented in Table 3.

Table 1. Results of the CFA

Questions	Physical	Biopsychosocial
How often do you experience discharge (suppuration) from the fistula?	0.543	
How much discharge (suppuration) from the fistula do you experience?	0.578	
How often do you experience uncontrollable flatulence (farting) since having the fistula?	0.387	
How often do you experience unintentional loss of stool since having the fistula?	0.423	
What is the amount of unintentional stool loss that you usually experience since having the fistula?	0.504	
How often do you experience pain in the anal area because of the fistula?	0.901	
What is the intensity of the pain that you experience because of the anal fistula?	0.879	
Since suffering the symptoms of the anal fistula, how would you describe your health?		0.715
How much does the anal fistula affect your physical health? (e.g., energy and activity levels, sleeping patterns, general well-being...)		0.898
How much does the anal fistula affect your psychological health? (e.g., your body image, self-esteem, state of mind, ability to focus on a particular task...)		0.856
How much does the anal fistula affect your independence level? (e.g., mobility, ability to work, daily activities...)		0.913
How much does the anal fistula affect your social relationships and interactions with others? (e.g., your relationships with friends, family, partner...)		0.762
How much does the anal fistula affect your sexual relationships?		0.673
How much does the anal fistula affect other aspects of your life? (e.g., your freedom, your economic income, your free time...)		0.792

CFA: Confirmatory factor analysis

The MCS and PCS scores of both the SF-12 and QoLAF-Q exhibited a statistically significant correlation. The QoLAF-Q and SF-12 demonstrated moderate consistency in correlation coefficients.

Reliability

Reliability was tested for both internal consistency and test-retest reliability, and the results are presented in Table 4.

Discussion

It is of crucial importance to not only treat patients with AF but also evaluate their QoL after necessary treatment methods have been applied. This is partly to understand the negative impact of AF complications (e.g., incontinence, hemorrhage, and disease recurrence) on patients' QoL and partly to assess the effectiveness of applied treatment methods. To date, general health questionnaires such as the SF-12 have been used to evaluate the QoL of patients with AF in Turkey. However, there was no previously designed, validated, and published specific tool for assessing the QoL in Turkish patients with AF.

Table 2. Results of known-group validity

		Physical	Biopsychosocial
Sex*	Female	1.2989 (1-2,29)	1.4656 (1-3,89)
	Male	1.2272 (1-2,17)	1.3953 (1-3,60)
	p	0.369	0.393
Anal surgery history*	Yes	1.3881 (1-2,29)	1.8511 (1-3,13)
	No	1.3004 (1-2,17)	1.4806 (1-3,89)
	p	0.567	0.267
Age		0.002 (0.982)	-0.109 (0.281)

*For the variables indicated with, the cell values correspond to the median (minimum-maximum) and the correlation coefficient (p-value) for age

Table 3. Correlation coefficients of the QoLAF-Q and SF-12

	Physical	Biopsychosocial
SF-12_PCS	-0.366 (<0.001)	-0.378 (<0.001)
SF-12_MCS	-0.305 (0.002)	-0.512 (<0.001)

Cell values represent the correlation coefficient (p-value). QoLAF-Q: Quality of Life in Patients with Anal Fistula Questionnaire, SF-12: Short Form-12 Health Survey, PCS: Physical Component Summary, MCS: Mental Component Summary

Table 4. Reliability results

	Cronbach's alpha coefficient	ICC (95% confidence interval)
Physical	0.721	0.664 (0.539-0.761)
Biopsychosocial	0.893	0.681 (0.560-0.773)

ICC: Intraclass correlation coefficient

The properties of the QoLAF-Q must be understood in terms of its ability to accurately evaluate psychometric qualities, what it truly measures, and its practicality for daily use. Psychometric analysis conducted on these properties demonstrated that the internal consistency and stability of the QoLAF-Q are adequate. Such qualities can be considered evidence of the reliability and repeatability of the evaluation tool. Moreover, having an average completion time of 5 minutes can be associated with understandability and practicality. The results of external construct validity showed that, even though the correlation between these questionnaires was moderate, the QoLAF-Q is still as effective as the SF-12 in measuring HRQoL (Table 3). Therefore, both the SF-12 and QoLAF-Q can be used to evaluate HRQoL in patients with AF.

The known-group analysis involved age, sex, and prior anal surgery. It was anticipated that anal sphincter tone would be influenced by these factors, subsequently impacting the QoL of patients with AF. However, the investigation revealed that a statistically significant difference between the known groups themselves was not established in the QoLAF-Q. In a study conducted in Korea by Kim et al.[17], it was observed that age is related to worsening anorectal functions due to lower anal resting and squeezing pressure, anal sphincter denervation, increased anal compliance, and decreased anal senses. A separate study conducted in Spain by Pla-Martí et al.[18] evaluated the relationship among previous anal surgery, incontinence, and QoL. In our study, we also analyzed the known groups, including previous anal surgery, sex, and age groups. However, a statistically significant difference was not determined.

When internal consistency was analyzed, the Cronbach's alpha value for the physical component was 0.721 and the biopsychosocial component value was 0.893. This indicates that the QoLAF-Q assesses the physical and biopsychosocial components collectively, concurrently, and intentionally. According to the scale, these values are considered to represent "good" consistency.[19] Similarly, in other studies (e.g., the original QoLAF-Q study, an Iranian validation study, and a Nigerian validation study), the determined values ranged between good and excellent.[20,21] Notably, a Chinese survey revealed relatively low values (0.67 for the PCS and 0.60 for the MCS).[22]

The intraclass correlation coefficient value for the physical component was 0.663, and the biopsychosocial value was 0.681. These satisfactory values were obtained from the evaluation of the consistency coefficients and the reliability coefficient re-evaluation, which was conducted 2 weeks later. These values indicate the stability of the QoLAF-Q, signifying that similar scores were and will be obtained in measurements taken at different times. This also supports the reliability of the Turkish version of the QoLAF-Q.

Study Limitations

In our study, we included only patients with cryptoglandular AF. Patients with Crohn's disease were not included, which is considered a limitation of our research. Therefore, our study does not provide information regarding the properties of the QoLAF-Q related to Crohn's disease. This subject can be further evaluated in future studies. It is also important to note that female patients accounted for only 24% of the participants. This does not align with the sex distribution of the general population and can be considered another limitation. Therefore, a future study with a more homogeneous and larger sample size can be conducted to address these limitations.

Conclusion

As demonstrated in the previous Spanish study, the QoLAF-Q is a valuable measurement tool. It possesses sufficient psychometric properties for assessing general health status and health-related QoL in clinical practice and scientific research in Turkey. The introduction of a Turkish HRQoL measurement tool for patients with AF that is both easily understandable and allows for quick QoL assessment is expected to facilitate the expansion of applications and research in the field of AF.

Ethics

Ethics Committee Approval: The study procedures were approved by the Ankara University Human Research Ethics Committee (approval number: İ01-32-23, date: 23.01.2023).

Informed Consent: Prior to participating in this research, volunteers completed an informed consent form.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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Supplement Table 1. Turkish version of QoLAF-Q

İsim-soyisim:
Tarih:
1. Ne sıklıkla fistülden akıntı (irin) yaşamaktasınız?
1. Hiçbir zaman, 2. Nadiren (haftalarca irin sızıntısı olmaz), 3. Bazen, 4. Sık sık (neredeyse her gün), 5. Her zaman ya da sürekli (her gün).
2. Fistülünüzden ne kadar akıntı (irin) gelmektedir?
1. Hiç, 2. Biraz (iç çamaşırlarında küçük lekeler), 3. Orta derecede (iç çamaşırında biraz fazla leke ve günde bir gazlı bez ihtiyacı), 4. Biraz fazla (günde bir ped ya da birden fazla gazlı bez kullanmam gerekiyor), 5. Çok fazla (günde 4 pedden ya da bir paket gazlı bezden daha fazlasını kullanmam gerekiyor).
3. Fistülünüz oluştuktan beri ne sıklıkla istemsiz gaz çıkarma (osuruk) yaşamaktasınız?
1. Hiç, 2. Çok az (iç çamaşırında hafıf kirlenme), 3. Orta derecede (daha fazla kirlenme ve günde 1 gazlı bez ihtiyacı), 4. Biraz fazla (günde bir ped ya da birden fazla gazlı bez kullanmam gerekiyor), 5. Çok fazla (günde 4 pedden ya da bir paket gazlı bezden daha fazlasını kullanmam gerekiyor).
4. Fistülünüz oluştuktan beri ne sıklıkla istemsiz gayta kaçırma yaşamaktasınız?
1. Hiçbir zaman, 2. Nadiren (haftalarca ağrı olmaz), 3. Bazen, 4. Sık sık (neredeyse her gün), 5. Her zaman ya da sürekli (her gün).
5. Fistülünüz oluştuktan beri kaçırmakta olduğunuz gayta miktarı nedir?
1. Hiç, 2. Çok az (iç çamaşırında hafıf kirlenme), 3. Orta derecede (daha fazla kirlenme ve günde 1 gazlı bez ihtiyacı), 4. Biraz fazla (günde bir ped ya da birden fazla gazlı bez kullanmam gerekiyor), 5. Çok fazla (günde 4 pedden ya da bir paket gazlı bezden daha fazlasını kullanmam gerekiyor).
6. Ne sıklıkla anal bölgenizde fistüle bağlı ağrı yaşamaktasınız?
1. Hiçbir zaman , 2. Nadiren (haftalarca ağrı olmaz), 3. Bazen, 4. Sık sık (neredeyse her gün), 5. Her zaman ya da sürekli (her gün).
7. Anal bölgenizde fistüle bağlı yaşadığınız ağrının şiddeti nedir?
1. Hiç, 2. Hafif, 3. Orta derecede, 4. Yüksek, 5. Aşırı derecede ya da hayal edilemeyecek kadar kötü.

Supplement Table 1. Continued

8. Anal fistül semptomları yaşamaya başladığınızdan beri sağlığınızı nasıl tanımlarsınız?

1. Mükemmel,
2. İyi,
3. Makul,
4. Kötü,
5. Berbat.

9. Anal fistül fiziksel sağlığınızı ne kadar etkilemektedir? (örneğin; enerji ve aktivite seviyeniz, uyku modeliniz, genel iyilik haliniz, ...)

1. Hiç,
2. Az,
3. Biraz,
4. Oldukça fazla,
5. Çok fazla.

10. Anal fistül ruh sağlığınızı ne kadar etkilemektedir? (örneğin; vücut imajınız, özgüven, ruhsal durum, bir işe odaklanma becerisi, ...)

1. Hiç,
2. Az,
3. Biraz,
4. Oldukça fazla,
5. Çok fazla.

11. Anal fistül özgürlük seviyenizi ne kadar etkilemektedir? (eg, hareket, iş yapma kabiliyeti, günlük aktiviteler, ...)

1. Hiç,
2. Az,
3. Biraz,
4. Oldukça fazla,
5. Çok fazla.

12. Anal fistül başkalarıyla sosyal ilişki ve etkileşiminizi ne kadar etkilemektedir? (örneğin; arkadaşlarınızla ilişkiniz, aile, partner, ...)

1. Hiç,
2. Az,
3. Biraz,
4. Oldukça fazla,
5. Çok fazla.

13. Anal fistül cinsel ilişkilerinizi ne kadar etkilemektedir?

1. Hiç,
2. Az,
3. Biraz,
4. Oldukça fazla,
5. Çok fazla.

14. Anal fistül hayatınızın diğer alanlarını nasıl etkilemektedir? (örneğin; bağımsızlığınız, gelir durumunuz, boş zamanlarınız, ...)

1. Hiç,
2. Az,
3. Biraz,
4. Oldukça fazla,
5. Çok fazla.

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CASE REPORT

Challenging Perineal Hernia Management Following Extralevator Abdominoperineal Excision: A Compelling Case Report

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ABSTRACT

This case report describes a rare perineal hernia complication following laparoscopic extralevator abdominoperineal excision in a patient with low rectal adenocarcinoma. The patient presented with a reducible perineal swelling over the surgical scar, which was diagnosed as a pelvic floor defect containing a small bowel loop and mesentery. The hernia was repaired one year following the index surgery using a transperineal approach with synthetic mesh and suture fixation to anatomical landmarks. The patient remained free of hernia recurrence one year following the repair and had an improved quality of life. This report highlights the importance of careful planning and individualized surgical management in the repair of perineal hernias following complex pelvic surgery.

Keywords: Abdominoperineal excision, perineal hernia, mesh, flap, surgery

Introduction

Perineal herniation (PH) is a rare but potentially debilitating complication following abdominoperineal excision (APE) for rectal cancer. With the growing use of extralevator abdominoperineal excision (ELAPE) and pelvic radiation therapy in the surgical management of low rectal cancer, the incidence of PH is reportedly on the rise. Although its reported incidence following conventional APE is <1%, this rate rises to up to 10% following ELAPE.[1-3]

The management of PH is challenging, with a high recurrence rate reported following repair. Moreover, its diagnosis and management following laparoscopic ELAPE remains poorly defined due to its rarity. In this report, a case of PH following laparoscopic ELAPE in a patient with low rectal cancer is presented. The clinical presentation, diagnosis, and management of this rare complication is also discussed, with a focus on the challenges encountered in laparoscopic ELAPE.

Case Report

A 61-year-old man with a medical history of hypertension was diagnosed with low rectal adenocarcinoma. The patient underwent neoadjuvant chemotherapy and long-course pelvic radiotherapy, followed by laparoscopic ELAPE. At the six-month follow-up date, the patient reported perineal swelling that was more prominent when standing and reduced when supine. A physical examination revealed an 8x6 cm reducible perineal swelling over the perineal surgical scar (Figure 1). Further investigation involving a computed tomography scan of the pelvis revealed a pelvic floor defect with a neck measurement of 6.2 cm, containing a small bowel loop and mesentery (Figure 2).

After a discussion with the patient and a comprehensive evaluation, it was determined that the best course of action was to perform a PH repair one year following the index surgery. The PH repair was approached transperineally, with the patient positioned in a prone jack-knife position, and the buttocks were strapped apart to ensure optimal exposure. A vertical midline incision was made below the coccyx along

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the previous perineal scar until the hernia sac was reached. The Lone Star Retractor System™ (Cooper Surgical, CT, USA) was used, and following entry into the hernia sac, the contents were inspected and reduced. The hernia sac was dissected away from the surrounding tissues, trimmed, and closed continuously using a coated polyglactin 910 2/0 suture (Vicryl®, Ethicon, USA). To provide additional support to the repaired area, a macroporous partially absorbable mesh (ULTRAPRO®, Ethicon, USA) was anchored anteriorly to the ischiopubic ramus and posteriorly to the coccygeal periosteum. It was also placed laterally to the ischial tuberosity, sacrotuberous ligament, and surrounding pelvic floor muscles with a polypropylene 2/0 suture (PROLENE®, Ethicon, USA) (Figure 3). Two low-pressure vacuum drains were placed superficially to the mesh and subcutaneously. The patient was discharged in a stable condition on the fourth day following the surgery after the drain removal. At the one-year follow-up, the patient remained free of hernia recurrence and had an improved quality of life. Informed consent was obtained from the patient for this publication.

Discussion

ELAPE is increasingly practiced due to its superior oncological outcomes compared with conventional APE. However, ELAPE has a higher incidence rate of PH of up to 26%, with a more prevalent incidence in the laparoscopic-assisted ELAPE group.[3] Primary pelvic peritoneal closure has been shown to reduce the incidence of PH and perineal wound complications following pelvic surgery.[4,5] To minimize potential PH following ELAPE, perineal reconstruction can be performed immediately, ranging from simple layered closure to more complex myocutaneous and fasciocutaneous reconstruction.[6] Various flap reconstruction methods have been described to minimize the incidence of post-operative PH, but this requires careful planning and consideration of the defect size, body habitus, and pelvic radiation. Ideally, reconstruction following a major surgical

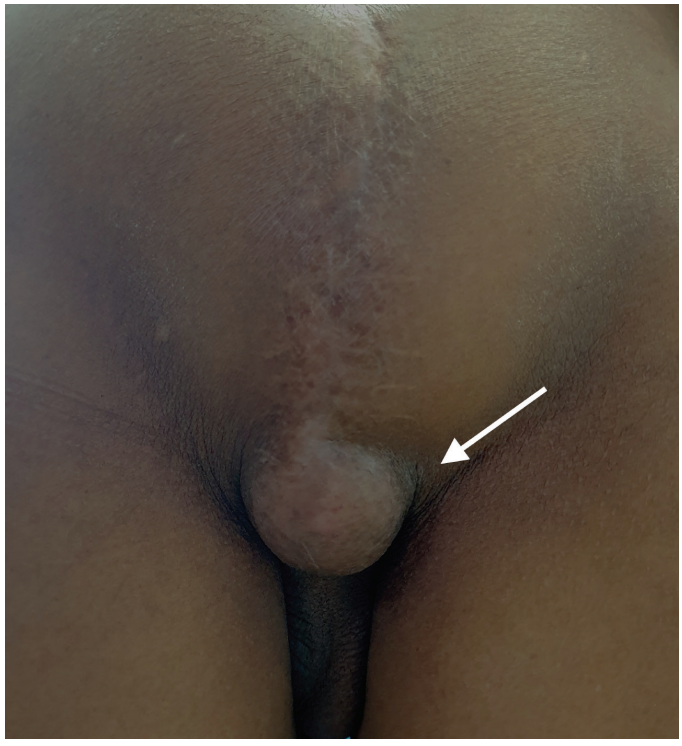

Figure 1. Perineal hernia following abdominal perineal excision prominent on the upright position

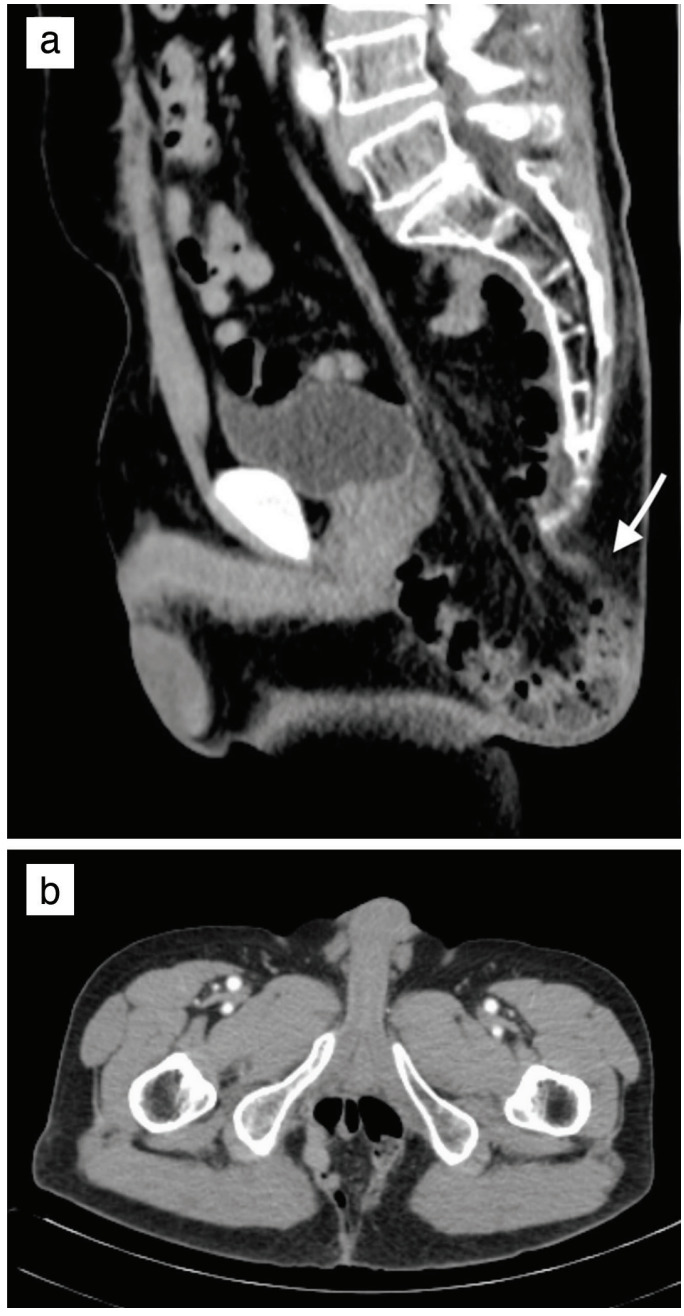

Figure 2. Contrast-enhanced computed tomography of the pelvis demonstrating herniating small bowel and mesentery through perineal floor defect: a) sagittal view and b) axial view

procedure such as ELAPE should be performed immediately if needed. However, universal application lacks consensus, as not all patients develop PH post-operatively, and flap reconstruction can be time consuming.

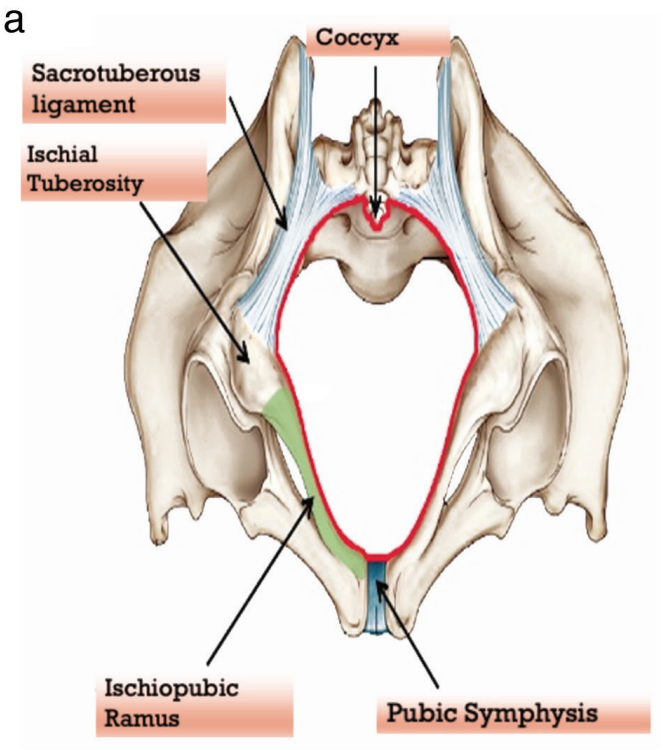

Figure 3. a) Perineum illustration in the prone jack-knife position and anatomical landmarks for mesh fixation. b) A macroporous partially absorbable mesh (ULTRAPRO®, Ethicon, USA) anchored anteriorly to the ischiopubic ramus and posteriorly to the coccyx periosteum, as well as laterally to the ischial tuberosity, sacrotuberous ligament, and surrounding pelvic floor muscles with polypropylene 2/0 suture

There is limited literature on post-operative PH repair operative strategies. Surgical repair has been described in terms of transperineal, transabdominal, or combined abdominoperineal approaches, but there is insufficient evidence to provide recommendations on optimal operative strategies.[7,8] Transabdominal repair is challenging due to the possibility of deep pelvic adhesions and mesh placement in the narrow, deep pelvic floor. Moreover, the use of laparoscopic tackers is potentially associated with post-operative chronic pain and morbidity.[9] In this case, the transperineal approach was chosen as the perineal defect was directly accessible and wider dissection for mesh placement and suture fixation to anatomical landmarks was uncomplicated.

Both synthetic and bioprosthetic mesh have been used for PH repair. Synthetic mesh is associated with a lower incidence of recurrence and mesh infection, and a recent systematic review and meta-analysis showed that mesh infection is rarely reported using this type of mesh.[2,8] Moreover, bioprosthetic mesh is equally effective, but it is costly and not widely available. In either case, it is important to augment the repair with surrounding native tissue to obliterate dead space prior to mesh placement.

Despite the lack of a consensus on the optimal management of PH, the described repair method using synthetic mesh via a transperineal approach is a promising alternative. However, individualized treatment plans must be developed for each patient while considering the size of the defect, the presence of a radiated pelvis, and the condition of local tissues.

Further research is needed to establish a standard approach to the management of PH, including the use of synthetic mesh, biological mesh, and other reconstructive techniques. Long-term studies are also needed to assess the durability and safety of these interventions, including the risk of mesh infection, chronic pain, and recurrence. In addition, cost-effectiveness analyses are needed to evaluate the economic impact of these treatments and to ensure equitable access to care.

Ethics

Informed Consent: Informed consent was obtained from the patient for this publication.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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

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LETTER TO THE EDITOR

Comment on "The Impact of Body Mass Index on Oncological Outcomes of Locally Advanced Rectal Cancer: A Comparative Study in a High Obesity Rate Country"

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Keywords: Body mass index, oncology, rectal cancer

Dear Editor,

The manuscript titled "The Impact of Body Mass Index on Oncological Outcomes of Locally Advanced Rectal Cancer: A Comparative Study in a High Obesity Rate Country" delves into a vital area of colorectal cancer (CRC) research. It focuses on a demographic that has previously been underrepresented in such studies.[1] In the context of a global obesity epidemic, it is increasingly common for patients with obesity to present with locally advanced rectal cancer (LARC). We commend the authors for undertaking this clinically critical study. However, several aspects of the study warrant correction and/or additional clarification.

While the introduction effectively addresses obesity as a risk factor for CRC, it lacks a clear rationale for conducting this specific study, particularly in terms of the prognostic significance of obesity. Establishing a well-defined context would more effectively bridge the introduction and the study's results. This study aims to assess the impact of body mass index (BMI) on the prognosis of rectal cancer by employing a cut-off value of 30. However, this binary classification of BMI into merely two broad groups-overlooking the prognostic implications of underweight and possibly malnourished statuses-could be seen as a limitation.[2] Adopting the standardized World Health Organization classification of body weight, which considers underweight, normal weight, pre-obesity, and obesity categories, would align this study with others in the literature and provide a more comprehensive understanding of BMI's impact on the study outcomes.[3]

One of the key findings of this study suggests that obese patients are more responsive to neoadjuvant therapy and exhibit improved disease-free survival. However, this finding conflicts with multiple studies in the existing literature, which report similar or worse chemotherapy responses in obese CRC patients.[4-6] Given the surgical complexities encountered in patients with high BMI, it is essential to furnish detailed information regarding the integrity of the mesorectum, analyze the outcomes of laparoscopic versus open methods, examine local recurrence statistics, and clarify the prevalence of lateral versus distal margin positivity, all of which remain ambiguously addressed.

Furthermore, rather than relying on univariate analysis to compare patients with a BMI ≥30 to those with a BMI <30, it would be more informative to match the two groups based on critical variables such as patient characteristics, comorbidities, disease stage, carcinoembryonic antigen levels, etc. Alternatively, conducting a multivariate analysis that accounts for all patient- and disease-related variables would more accurately demonstrate BMI's independent and realistic effects on study outcomes, as highlighted in

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referenced studies.[7,8] Additionally, the tables in the current study would benefit from including percentage values alongside the raw data to enhance comprehensibility and facilitate comparisons between different groups. It is also advisable to include the standard deviation for the mean number of lymph nodes retrieved.

The risk of an anastomotic leak increases as the level of anastomosis becomes more distal.[9] For this reason, creating a diverting ostomy in surgeries for distal rectal tumors, such as intersphincteric resection, is considered safer. This study characterizes ostomies as postoperative events that require further clarification. It remains unclear whether these ostomies are created for protective reasons or in response to an anastomotic leak. Furthermore, clinical interpretation of the data on surgical site infection rates and incisional hernia appears infeasible without information regarding the proportion of surgeries utilizing laparoscopic techniques.

In the current study conducted by Al-Masri et al.[1], patients with LARC at stage II T3/4, node-negative, or stage III node-positive, who underwent neoadjuvant chemoradiotherapy followed by total mesorectal excision, were analyzed. Notably, the authors report that all patients completed their adjuvant therapy. Considering the data on adherence to intended postoperative chemotherapy, which varies between 43% and 80%, readers would be interested in information about the severity of postoperative complications, toxic effects of perioperative chemotherapy, disease progression, and patient refusal, if applicable.[10,11]

In conclusion, addressing and correcting the abovementioned issues is crucial for drawing more robust conclusions from this study. Controlling for confounding variables through appropriate statistical analysis and providing additional essential information will enhance the validity and reliability of the study's findings.

Ethics

Peer-review: Internally peer-reviewed.

Authorship Contributions

Analysis or Interpretation: A.R., Literature Search: S.S., S.N.K., A.R., Writing: S.S., A.R.

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

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