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Turkish Journal of Surgery (Turk J Surg) is the official, peer reviewed, open access publication of the Turkish Surgical Society and Turkish surgical community. The journal is published quarterly on March, June, September and December and its publication language is English.

The aim of the Turkish Journal of Surgery is to publish high quality research articles, review articles on current topics and rare case reports in the field of general surgery. Additionally, expert opinions, letters to the editor, scientific letters and manuscripts on surgical techniques are accepted for publication, and various manuscripts on medicine and surgery history and ethics, surgical education and the field of forensic medicine are included in the journal.

As a surgical journal, the Turkish Journal of Surgery covers all specialties, and its target audience includes scholars, practitioners, specialists and students from all specialties of surgery.

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 (doaj.org/bestpractice).

The Turkish Journal of Surgery is currently abstracted/indexed by PubMed Central, Web of Science-Emerging Sources Citation Index, TUBITAK ULAKBIM TR Index, Scopus and EBSCO.

Processing and publication are free of charge. No fees are requested from the authors at any point throughout the evaluation and publication process. All expenses of the journal are covered by the Turkish Surgical Society.

Manuscripts must be submitted via the online submission system, which is available at [www.turkjsurg.com](http://www.turkjsurg.com). Journal guidelines, technical information, and the required forms are available on the journal's web page.

Statements or opinions expressed in the manuscripts published in the journal reflect the views of the author(s) and not the opinions of the Turkish Surgical Society, editors, editorial board, and/or publisher; thus, the editors, editorial board, and publisher disclaim any responsibility or liability for such materials.

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## INSTRUCTIONS TO AUTHORS

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Originality, high scientific quality, and citation potential are the most important criteria for a manuscript to be accepted for publication. Manuscripts submitted for evaluation should not have been previously presented or already published in an electronic or printed medium. The journal should be informed of manuscripts submitted to another journal for evaluation but rejected for publication. The submission of previous reviewer reports will expedite the evaluation process. Manuscripts presented in a meeting should be submitted with detailed information on the organization, including the name, date, and location of the organization.

Manuscripts submitted to the Turkish Journal of Surgery will go through a doubleblind peer-review process. Each submission will be reviewed by at least two external, independent peer reviewers who are experts in their fields in order to ensure an unbiased evaluation process. The editorial board will invite an external and independent editor to manage the evaluation processes of the manuscripts submitted by the editors or the editorial board members of the journal. The Editor-in-Chief is the final authority in the decision-making process for all submissions.

An approval of research protocols by the Ethics Committee in accordance with international agreements (World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects," amended in October 2013, [www.wma.net](http://www.wma.net)) is required for experimental, clinical, and drug studies and for some case reports. If required, ethics committee reports or an equivalent official document will be requested from the authors. For manuscripts concerning experimental research on humans, a statement verifying that written informed consent of the patients and volunteers was obtained following a detailed explanation of the procedures should be included. For studies carried out on animals, the measures taken to prevent pain and suffering of the animals should be stated clearly. Information on patient consent, name of the ethics committee, and the ethics committee approval number should also be stated in the Material and Methods section of the manuscript. It is the authors' responsibility to carefully protect patients' anonymity. For photographs that may reveal the identity of the patient, releases signed by the patient or his/her legal representative should be enclosed.

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3. Final approval of the version to be published; AND
4. Agreement to be accountable for all aspects of the work, and ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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other specific parts of the work. In addition, authors should have confidence in the integrity of the contributions of their co-authors.

All those designated as authors should meet all four criteria for authorship, and all who meet the four criteria should be identified as authors. Those who do not meet all four criteria should be acknowledged in the title page of the manuscript.

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Manuscripts should be prepared in accordance with ICMJE Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (updated in December 2017 - <http://www.icmje.org/icmje-recommendations.pdf>). Authors are required to prepare manuscripts in accordance with CONSORT guidelines for randomized research studies, STROBE guidelines for observational original research studies, STARD guidelines for studies on diagnostic accuracy, PRISMA guidelines for systematic reviews and meta-analysis, ARRIVE guidelines for experimental animal studies, and TREND guidelines for non-randomized public behavior.

Manuscripts can only be submitted through the journal's online manuscript submission and evaluation system, available at [www.turkjsurg.com](http://www.turkjsurg.com). Manuscripts submitted via any other medium will not be evaluated.

Manuscripts submitted to the journal will first go through a technical evaluation process by the editorial office staff to ensure that the manuscript has been prepared and submitted in accordance with the journal's guidelines. Submissions that do not conform to the journal's guidelines will be returned to the submitting author with technical correction requests.

Authors are required to submit the following:

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## INSTRUCTIONS TO AUTHORS

during the initial submission. These forms are available for download at [www.turksurg.com](http://www.turksurg.com).

### Preparation of the Manuscript

**Title page:** A separate title page should be submitted with all submissions, which should include:

- The full title of the manuscript as well as a short title (running head) of no more than 50 characters,
- Name(s), affiliations, and highest academic degree(s) of the author(s),
- Grant information and detailed information on the other sources of support,
- Name, address, telephone (including the mobile phone number) and fax numbers, and email address of the corresponding author,
- Acknowledgment of the individuals who contributed to the preparation of the manuscript but who do not fulfill the authorship criteria.

**Abstract:** English abstract should be submitted with all submissions except for Letters to the Editor. The abstract of Original Articles should be structured with subheadings (Objective, Material and Methods, Results, and Conclusion). Please check Table 1 below for word count specifications.

**Keywords:** Each submission must be accompanied by a minimum of three to a maximum of six keywords for subject indexing at the end of the abstract. The keywords should be listed in full without abbreviations. The keywords should be selected from the National Library of Medicine, Medical Subject Headings database (<https://www.nlm.nih.gov/mesh/MBrowser.html>).

### Manuscript Types

**Original Articles:** This is the most important type of article since it provides new information based on original research. The main text of original articles should be structured with Introduction, Material and Methods (with subheadings), Results, Discussion, Conclusion subheadings. Please check Table 1 for the limitations for Original Articles.

Statistical analysis to support conclusions is usually necessary. Statistical analyses must be conducted in accordance with international statistical reporting standards (Altman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. *Br Med J* 1983; 7: 1489-93). Information on statistical analyses should be provided with a separate subheading under the Material and Methods section and the statistical software that was used during the process must be specified.

Units should be prepared in accordance with the International System of Units (SI).

**Expert Opinions:** Editorial comments aim to provide a brief critical commentary by reviewers with expertise or with high reputation in the topic of the research article published in the journal. Authors are selected and invited by the journal to provide such comments. Abstract, Keywords, Tables, Figures, Images, and other media are not included.

**Review Articles:** Reviews with high citation potential prepared by authors with extensive knowledge on a particular field and whose scientific background has already been proven by a high number of publications in the related field are welcomed. These authors may even be invited by the journal. Reviews should describe, discuss, and evaluate the current level of knowledge of a topic in clinical practice and should guide future studies. The main text

should contain Introduction, Clinical and Research Consequences, and Conclusion sections. Please check Table 1 for the limitations for Review Articles.

**Case Reports:** There is limited space for case reports in the journal, and reports on rare cases or conditions constituting challenges in diagnosis and treatment, those offering new therapies or revealing insight not included in the literature, and interesting and educative case reports are accepted for publication. The text should include Introduction, Case Presentation, Discussion, and Conclusion subheadings. Please check Table 1 for the limitations for Case Reports.

**Video Articles:** We do encourage the submission of the video articles which report interesting cases and technical methods.

The details of the review process are below.

- All videos will be peer reviewed.
- All videos will be published on the journals official Web site.
- Article length: It should not exceed 500 words.
- Reference Number: Not to exceed 5 references

Diagnosis, surgical technique and outcome should be summarized. All important steps and aspects of the surgery should be mentioned in the video. If it is a new surgical technique, appropriately labeled and cited video materials may be used. Authors can use a rare case they have encountered, a surgical technique, or videos using modern technological devices.

The following items must be provided:

- The file of the video written in Word format.
- A completed copy of the online broadcast consent form (form will be prepared and linked), together with completed copies of patient consent forms, if appropriate.
- All videos must contain an English narration.
- All videos should also be in the highest resolution possible, more details on accepted file types and resolution are available at this link (authors' video article submission guidelines; <https://turksurg.com/video-article-guidelines>).
- The duration of the videos should not exceed five minutes and the maximum file size should be 300Mb.

**Letters to the Editor:** This type of manuscript discusses important parts, overlooked aspects, or lacking parts of a previously published article. Articles on subjects within the scope of the journal that might attract the readers' attention, particularly educative cases, may also be submitted in the form of a "Letter to the Editor." Readers can also present their comments on the published manuscripts in the form of a "Letter to the Editor." Abstract, Keywords, Tables, Figures, Images, and other media should not be included. The text should be unstructured. The article being commented on must be properly cited within this manuscript.

### Human Subjects Research

All research involving human participants must have been approved by the authors' Institutional Review Board (IRB) or by equivalent ethics committee(s) and must have been conducted according to the principles expressed in the Declaration of Helsinki. Authors should be able to submit, upon request, a statement from the IRB or ethics committee indicating approval of the research. The Journal reserves the right to reject work believed to have not been conducted in a high ethical standard, even when formal approval has been obtained.

**Table 1.** Limitations for each manuscript type

Type of manuscript	Word limit	Abstract word limit	Reference limit	Table limit	Figure limit
Original Article	5000	250 (Structured)	50	6	7 or total of 15 images
Review Article	5000	250	50	6	10 or total of 20 images
Case Report	1500	250	15	No tables	10 or total of 20 images
Surgical Methods	500	No abstract	5	No tables	10 or total of 20 images
Letter to the Editor	500	No abstract	5	No tables	No media



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Subjects must have been properly instructed and have indicated that they consent to participate by signing the appropriate informed consent paperwork. Authors may be asked to submit a blank, sample copy of a subject consent form. If consent was verbal instead of written, or if consent could not be obtained, the authors must explain the reason in the manuscript, and the use of verbal consent or the lack of consent must have been approved by the IRB or ethics committee.

### Animal Research

All animal research must have approval from the authors' Institutional Animal Care and Use Committee (IACUC) or equivalent ethics committee(s), and the research must have been conducted according to applicable national and international guidelines. Approval must be received prior to beginning the research.

Manuscripts reporting animal research must state in the Methods section: The full name of the relevant ethics committee that approved the work, and the associated permit number(s). Where ethical approval is not required, the manuscript should include a clear statement of this and the reason why. The author should provide any relevant regulations under which the study is exempt from the requirement of approval.

### Tables

Tables should be included in the main document, presented after the reference list, and numbered consecutively in the order they are referred to within the main text. A descriptive title must be placed above the tables. Abbreviations used in the tables should be defined below the tables by footnotes (even if they are defined within the main text). Tables should be created using the "insert table" command of the word processing software and they should be arranged clearly to provide easy reading. Data presented in the tables should not be a repetition of the data presented within the main text but should be supporting the main text.

### Figures and Figure Legends

Figures, graphics, and photographs should be submitted as separate files (in TIFF or JPEG format) through the submission system. The files should not be embedded in a Word document or the main document. When there are figure subunits, the subunits should not be merged to form a single image. Each subunit should be submitted separately through the submission system. Images should not be labeled (a, b, c, etc.) to indicate figure subunits. Thick and thin arrows, arrowheads, stars, asterisks, and similar marks can be used on the images to support figure legends. Like the rest of the submission, the figures too should be blind. Any information within the images that may indicate an individual or institution should be blinded. The minimum resolution of each submitted figure should be 300 DPI. To prevent delays in the evaluation process, all submitted figures should be clear in resolution and large in size (minimum dimensions: 100 x 100 mm). Figure legends should be listed at the end of the main document.

All acronyms and abbreviations used in the manuscript should be defined at first use, both in the abstract and in the main text. The abbreviation should be provided in parentheses following the definition.

When a drug, product, hardware, or software program is mentioned within the main text, product information, including the name of the product, the producer of the product, and city and the country of the company (including the state if in the USA) should be provided in parentheses in the following format: "Discovery St PET/CT scanner (General Electric, Milwaukee, WI, USA)"

All references, tables, and figures should be referred to within the main text and numbered consecutively in the order they are referred to within the main text.

Limitations, drawbacks, and the shortcomings of original articles should be mentioned in the Discussion section before the conclusion paragraph.

### References

While citing publications, preference should be given to the latest, most up-to-date publications. If an ahead-of-print publication is cited, the DOI number should be provided. Authors are responsible for the accuracy of references. Only references cited in the text should be included in the reference list. The reference list must be numbered according to the order of mention of the references in the text. In the main text of the manuscript, references should be cited using Arabic numbers in parentheses. Journal titles should be abbreviated in accordance with the journal abbreviations in Index Medicus/MEDLINE/PubMed. When there are six or fewer authors, all authors should be listed. If there are seven or more authors, the first six authors should be listed followed by "et al." The reference styles for different types of publications are presented in the following examples.

**Journal Article:** Rankovic A, Rancic N, Jovanovic M, Ivanović M, Gajović O, Lazić Z, et al. Impact of imaging diagnostics on the budget - Are we spending too much? *Vojnosanit Pregl* 2013; 70: 709-11.

**Book Section:** Suh KN, Keystone JS. Malaria and babesiosis. Gorbach SL, Barlett JG, Blacklow NR, editors. *Infectious Diseases*. Philadelphia: Lippincott Williams; 2004. pp. 2290-308.

**Books with a Single Author:** Sweetman SC. *Martindale the Complete Drug Reference*. 34th ed. London: Pharmaceutical Press; 2005.

**Editor(s) as Author:** Huizing EH, de Groot JAM, editors. *Functional reconstructive nasal surgery*. Stuttgart-New York: Thieme; 2003.

**Conference Proceedings:** Bengisön S, Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. *MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics*; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. pp. 1561-5.

**Scientific or Technical Report:** Cusick M, Chew EY, Hoogwerf B, Agrón E, Wu L, Lindley A, et al. Early Treatment Diabetic Retinopathy Study Research Group. Risk factors for renal replacement therapy in the Early Treatment Diabetic Retinopathy Study (ETDRS), Early Treatment Diabetic Retinopathy Study Kidney Int: 2004. Report No: 26.

**Thesis:** Yılmaz B. Ankara Üniversitesindeki Öğrencilerin Beslenme Durumları, Fiziksel Aktiviteleri ve Beden Kitle İndeksleri Kan Lipidleri Arasındaki İlişkiler. H.Ü. Sağlık Bilimleri Enstitüsü, Doktora Tezi. 2007.

**Manuscripts Accepted for Publication, Not Published Yet:** Slots J. The microflora of black stain on human primary teeth. *Scand J Dent Res* 1974.

**Epub Ahead of Print Articles:** Cai L, Yeh BM, Westphalen AC, Roberts JP, Wang ZJ. Adult living donor liver imaging. *Diagn Interv Radiol* 2016 Feb 24. doi: 10.5152/dir.2016.15323. [Epub ahead of print].

**Manuscripts Published in Electronic Format:** Morse SS. Factors in the emergence of infectious diseases. *Emerg Infect Dis* (serial online) 1995 Jan-Mar (cited 1996 June 5): 1(1): (24 screens). Available from: URL: <http://www.cdc.gov/ncidod/EID/cid.htm>.

### REVISIONS

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

Accepted manuscripts are copy-edited for grammar, punctuation, and format. Once the publication process of a manuscript is completed, it is published online on the journal's webpage as an ahead-of-print publication before it is included in its scheduled issue. A PDF proof of the accepted manuscript is sent to the corresponding author and their publication approval is requested within 2 days of their receipt of the proof.

### Turkish Journal of Surgery

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## FROM THE EDITOR'S DESK

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### The Evolving Landscape of Surgical Education

Dear Readers of the Turkish Journal of Surgery,

Surgery is dynamic and constantly evolving with innovative techniques and technologies. One area where surgical education and knowledge dissemination has changed is the rise of video articles. In an era where visualization and interactivity play an important role in learning, video articles are an invaluable tool for both aspiring and experienced surgeons.

Traditional written articles have long been a staple of the medical literature. While they provide valuable information, they often lack the dynamic visual element that is critical to understanding complex surgical procedures. Video articles fill this gap by providing an audiovisual experience that can be more engaging and informative. Surgeons can witness the nuances of a procedure, observe techniques in real time and grasp the intricacies of surgical skills that are difficult to convey through text alone. In this issue, we have a new section. We are pleased to publish the first video article in the Turkish Journal of Surgery (TJS) by Luvira et al, which focuses on a liver transection technique (1). You can find a brief written summary along with a link to the video on our official website. I would like to take this opportunity to invite you to submit your interesting videos to TJS.

Colorectal surgery is another important topic in this issue of our journal. While Tirnova et al. discuss oncologic risk factors in rectal cancer in their clinical study (2), Ahmed et al. share their experience on the use of indocyanine green for lymphadenectomy in colon surgery (3). On the other hand, Benli et al. present the results of their important clinical study on preoperative mechanical bowel preparation, a long-debated topic in colorectal surgery (4). I strongly recommend you to read these three clinical studies that can contribute to your clinical practice.

I wish you an enjoyable reading.

**Kaya SARİBEYOĞLU**

**Editor-in-Chief**

**Turkish Journal of Surgery**

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# Clinical profile and treatment outcomes of Boerhaave's syndrome: A 13-year experience from an upper gastrointestinal surgical unit

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## ABSTRACT

**Objective:** Boerhaave's syndrome (BS) is a rare, but potentially fatal condition, characterized by barogenic esophageal rupture and carries a high mortality. We aimed to study our institutional experience of managing patients with BS.

**Material and Methods:** A retrospective review of patients with BS presenting to a tertiary care centre from 2005 to 2018 was carried out in this study. Clinical presentation, diagnostic evaluations, treatments received, and treatment outcomes were studied. Perforations were classified as early (<24 hours) and delayed (>24 hours), based on the time elapsed. Surgical complications were graded using Clavien-Dindo grade. The Pittsburgh perforation severity score was correlated with short-term treatment outcomes.

**Results:** Of the 12 patients [male, 75%; mean (range) age, 53 (28-80) years] included, 10 patients had a delayed (>24 hours) presentation. Chest pain was the dominant symptom (58.3%); six patients presented either in shock (n= 1) or with organ failure (n= 3) or both (n= 2). All the perforations were sited in the lower thoracic esophagus, of which three were contained and nine were uncontained. The seal of the perforation was achieved by surgical repair in four patients (primary repair, 2; repair over a T-tube, 2) and endoscopic techniques in four patients (clipping, 1; stenting, 3). Sepsis drainage [surgical, 7 (open-5, minimally-invasive-2); non-surgical, 5] and feeding jejunostomy were performed in all patients. Five (41.7%) patients received a re-intervention. Median (range) hospital stay was 25.5 (12-101) days, 30-day operative morbidity was 50%, and there was one in-hospital death. The Pittsburgh perforation severity score was as follows: 2-5 in two patients and >5 in 10 patients; there were more delayed presentations, increased surgical interventions, post-procedure morbidity, and in-hospital mortality in the latter group, but the differences were statistically not significant. In 11 patients followed-up [median (range):1507 (17-5929) days], there was no disease recurrence, symptomatic reflux or dysphagia.

**Conclusion:** Favourable treatment outcomes, including reduced mortality and organ preservation can be achieved for Boerhaave's perforations, through a multimodality approach. Minimally invasive, endoluminal or open surgical techniques may be safely utilized in its management. The Pittsburgh severity score can be a useful clinical tool that can be used to select the initial intervention and to predict treatment outcomes.

**Keywords:** Boerhaave's syndrome, spontaneous esophageal perforation, surgery, therapeutic endoscopy, Pittsburgh perforation severity score

## INTRODUCTION

Boerhaave's syndrome (BS) is a rare, but potentially fatal condition, characterized by transmural esophageal rupture, secondary to the sudden rise in intraluminal pressure, as in forceful emesis (1). The perforation leads to contamination of the surrounding space with esophago-gastric contents, leading to local sepsis, organ failure, and a mortality rate of 24-50% in delayed presentations (2-4). BS diagnosis is often delayed because of its rarity, non-specific symptoms, and frequent initial diagnostic errors (5). Prompt diagnosis and timely intervention correlate with favorable treatment outcomes (3).

Due to its rarity, there is lack of standard guidelines for the optimal treatment of BS. Treatment options vary from conservative treatment to surgery as radical as esophagectomy. Surgical options include primary repair, tube esophagostomy, esophageal exclusion/diversion, and esophagectomy, combined with drainage and debridement of pleuro-mediastinal cavities (5-7). In a series of 88 patients with BS by Yan et al., the best operative outcomes including reduced postoperative esophageal leak, and shorter hospital and intensive care stays have been obtained in patients presenting early and receiving a primary repair, compared to buttressed repairs in the delayed group (8). In another series by Sutcliffe et al., immediate surgery was feasible in all eight patients presenting early but it was possible only

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in 6/10 patients presenting late (9). The rates of postoperative leak (78% vs 12.5%;  $p < 0.05$ ) and mortality (40% vs. 0%;  $p < 0.05$ ) were higher in the late referral group, and within the delayed referral subgroup, the worst mortality was seen in those managed conservatively. The authors have reiterated that the operative principles for BS are pleuro-mediastinal decontamination, debridement or resection of devitalized tissues, primary perforation repair (when feasible), gastric decompression, and enteral feeding access. Aggressive surgery including resection is suggested in delayed cases with extensive esophageal tissue loss (1).

With recent advances in minimally invasive surgery and therapeutic endoscopy, there is a paradigm shift towards a more conservative treatment approach for this condition. The safety and effectiveness of minimally invasive surgical approaches have been demonstrated by Haveman et al., Aref et al., Lee et al., Cho et al., and in a recent review by Aiolfi et al (10-14). Minimally invasive surgery can potentially reduce surgical trauma, but the choice of operative access depends on the site of the perforation, the extent of pleuro-mediastinal contamination/necessity for pleural drainage. Similarly, several authors have reported the role of endoscopic therapy for the management of BS, particularly that of esophageal stents which are utilized both as a primary intervention and also as a salvage procedure for persistent leak following surgical repair (6,15,16).

Although a multitude of treatment options are available for BS and controversy exists concerning the best treatment modality, particularly for delayed presentations, optimal treatment outcomes are often achieved through a multimodality approach. Hence, patients should be managed at a centre, with appropriate facilities and the expertise to deal with this challenging condition.

In this study, it was aimed to review our institutional experience of managing patients with BS over a 13-year period, focusing on their clinical presentation, diagnostic evaluations, treatment approaches and their outcomes. We also attempted to retrospectively grade the severity of the perforation using the Pittsburgh perforation severity score (PPSS) which is a valid tool to grade the severity of esophageal perforations (17,18). PPSS has been shown to correlate with the time interval to presentation, choice of initial therapy and treatment outcomes, particularly in patient subgroups with BS (18-20).

## MATERIAL and METHODS

A retrospective review of all adult patients treated for BS in the esophagogastric surgery unit of our centre from January 2005 to January 2018 was performed. The relevant data were retrieved from the hospital's electronic medical records and included demographic details, clinical and laboratory characteristics, details of diagnostic evaluations and treatment,

intensive care unit (ICU) stay details, LoHS, 90-day morbidity (including 30-day operative morbidity), 90-day and in-hospital mortality. The study was approved by the institutional review board [Min.No.13062 (retro) dated 24.06.2020].

The severity of the comorbidities was classified using Charlson's comorbidity index (CCI) (21). Based on the time elapsed from the symptom onset to diagnosis, perforations were classified as early (<24 hours) and delayed (>24 hours). Shock was defined as systolic blood pressure <90 mmHg. Diagnosis was confirmed using contrast-esophagography and/or thoracic computed tomography (CT) and an occasional endoscopy. Perforation was classified as uncontained if there was a large amount of contrast extravasation into the pleural space or a large area of mediastinal air-fluid collections regardless of the pleural involvement; contained if there was no contrast extravasation or minimal contrast extravasation with the limited mediastinal air-fluid collection, not breaching the pleural space. Primary intervention was defined as the index procedure(s) aimed at sealing the perforation and/or drainage of sepsis and a re-intervention was defined as any subsequent procedure(s) performed to achieve similar goals. Post-procedure morbidity was recorded at the 90-day mark. Thirty-day postoperative complications were classified using Clavien-Dindo grade (CDG) and a major complication was defined as  $CDG \geq 3$  (22).

The severity of the perforation at admission was retrospectively calculated using PPSS. PPSS was calculated by assigning points to each clinical variable to a total score of 18 and three patient risk categories were identified (PPSS: <2, low risk; 2-5 intermediate risk; >5, high risk) (17,18). PPSS category was correlated with time to diagnosis, choice of primary intervention (operative vs. non-operative), the requirement for ICU stay, LoHS, and in-hospital mortality. Follow-up data were obtained from medical records and were strengthened by telephonic conversation.

Categorical variables were expressed as frequencies with percentages, and continuous variables were expressed as mean with standard deviation or median with range. To find associations between two categorical variables, Fisher's exact test or proportion test was used. The differences were considered significant if  $p < 0.05$ .

## RESULTS

Baseline demography, clinical profile and details of radiological evaluations are summarized in Table 1.

### Demography and Clinical Presentation

Twelve patients [male:female, 10:2; mean (range) age,  $53.75 \pm 14.96$  (28-80) years] were included. Ten (83.3%) patients had delayed diagnosis. Five patients were referred to our centre following an initial intervention elsewhere (Table 2). Five patients were erroneously diagnosed with pulmonary

**Table 1.** Demography, clinical profile and details of initial diagnostic evaluations

Variable	n= 12
Year of presentation	
2005-2010	3 (25.0%)
2011-2015	7 (58.3%)
2015-2018	2 (16.7%)
Age; years	53.75 ± 14.96 (28-80)
Sex	
Male	10 (83.3%)
Female	2 (16.7%)
CCI	
CCI < 2	7 (58.3%)
CCI ≥ 2	5 (31.7%)
Time interval <sup>a</sup>	
Early (<24 hours)	2 (16.7%)
Delayed (>24 hours)	10 (83.3%)
Dominant symptom	
Chest pain	7 (58.4%)
Abdomen pain	4 (33.3%)
Dyspnoea	1 (8.3%)
Precipitating factor	
Alcohol + retching/vomiting	6 (50.0%)
No alcohol but retching/vomiting	2 (16.7%)
No precipitating factor reported	4 (33.3%)
Initial admitting department	
Surgical unit	7 (58.3%)
Medical specialties <sup>b</sup>	5 (41.7%)
Presence of shock/organ failure at admission	
Shock alone	1 (8.3%)
Organ failure <sup>c</sup> alone	3 (25.0%)
Shock and organ failure <sup>c</sup>	2 (16.7%)
Laboratory evaluations	
Hemoglobin (g/dL)	13.01 ± 3.17
Albumin (g/dL)	3.1 ± 0.95
Creatinine (mg/dL)	1.08 ± 0.47
Total leukocyte count (cells/cu mm).	12,400 (4,400-19,600)
Diagnostic modality	
Chest radiograph	12
Normal	1
Pleural effusion	11
(Left, right, bilateral)	(7, 3, 1)
Diagnostic endoscopy	3
Contrast-esophagography	2
Thoracic CT scan	12
Location of perforation	
Lower thoracic esophagus	12
Perforation contained? <sup>d</sup>	
Yes	3 (25.0%)
No	9 (75.0%)

CCI: Charlson comorbidity index, CT: Computed tomography.

Values expressed in n, n (%), mean ± SD or median (range) as appropriate.

<sup>a</sup>: Time interval, from the onset of symptoms to diagnosis/initiation of treatment.<sup>b</sup>: Admitted initially under medical specialties with an alternate diagnosis.<sup>c</sup>: Acute respiratory failure with hypoxia in four patients; acute renal failure in one patient.<sup>d</sup>: As determined by the radiological evaluations.

conditions and were initially admitted under medical specialities. The dominant presenting symptom was chest pain (58.4%), and Mackler's triad (chest pain, vomiting, subcutaneous emphysema) was present in two (16.7%) patients. A total of six patients presented either in shock (n= 1) or with organ failure (n= 3) or both (n= 2).

### Laboratory and Radiological Evaluations

Median total leukocyte count was 12,400 cells/cu mm. The commonest finding in chest radiography was pleural effusion (11 patients; left, 7; right, 3; bilateral 1). Contrast-esophagography was performed in two patients, and contrast extravasation was seen in both. Thoracic CT was performed in all patients; all the perforations were localized to the lower thoracic esophagus and nine (75.0%) perforations were uncontained.

### Treatment Details and Outcomes

Individual patient profile and treatments received are detailed in Table 2.

### Sealing of the Perforation

Ten patients belonged to the delayed diagnosis group (perforation type: contained, 2; uncontained, 8) and two patients belonged to the early diagnosis group (perforation type: contained, 1; uncontained, 1). Two patients (SL No. 2 and 11) in the delayed but uncontained group, received surgical drainage, debridement and a feeding jejunostomy (FJ) alone. The initial sealing of the perforation was performed in the remaining six patients of the delayed but uncontained group, either using covered stents (n= 3) or surgery (n= 3). Two patients in the delayed but contained group received no esophageal intervention and were managed with a tube thoracostomy and FJ. In the early diagnosis group (n= 2), endo-clipping (n= 1) and surgery (n= 1) were utilized to seal the perforation.

All surgical repairs were performed through an open trans-hiatal approach. A reinforced primary repair was performed in a patient who presented early but with a contained perforation. Among the three patients in the delayed presentation group receiving esophageal surgery, a buttressed primary repair was performed in one patient and a T-tube repair was performed in two patients.

### Drainage of Sepsis

In the uncontained perforation group (n= 9), thoracic drainage was achieved using either thoracoscopy/thoracotomy (n= 7) or a tube thoracostomy (n= 2). In the delayed but contained perforation group (n= 2), a tube thoracostomy alone was used to drain the reactive effusion. In a patient belonging to the early but contained perforation group receiving surgical repair of the perforation, there was no concomitant pleural drainage indicated initially. However, the patient developed a left-sided, serous effusion later, which was drained using a tube thoracostomy.

**Table 2.** Individual patient profile and treatment details

Year	Case No.	Age/ Sex	Type of intervention before referral	Time of presentation (Early vs. Delayed)	Location of perforation <sup>a</sup>	Perforation size	Contained perforation (Yes/No)	Site of pleural collection	PPSS	Details of primary intervention(s)	Re-intervention
2005	1	67/M	Non-referral	Early	Lower thoracic, 2 cm above GEJ	3 cm	Yes	None <sup>b</sup>	4	Laparotomy, trans-hiatal primary repair, omento- plasty and FJ	Tube thoracostomy for left-sided pleural effu- sion <sup>b</sup>
2008	2	80/F	Right-sided, tube thoracos- tomy	Delayed	Lower thoracic	N/I	No	Right	10	Right thoracotomy, drainage, decortication and FJ	None
	3	62/M	Left-sided, tube thoracostomy	Delayed	Lower thoracic	N/A	Yes	Left	3	Left-sided, tube tho- racostomy, gastrostomy and FJ	None
2010	4	28/M	Non-referral	Delayed	Lower thoracic	N/A	Yes	Left	9	Left-sided, tube tho- racostomy, FJ	None
2011	5	47/M	Right thoracotomy, pleural drainage alone	Delayed	Lower thoracic	N/M	No	Right	9	Right thoracotomy, drainage, decortication, esophageal stenting (FCSEMS) and FJ	Stent migration → endoscopic repositioning
	6	41/M	Left-sided, tube thoracostomy	Delayed	Lower thoracic, 2 cm above GEJ	3 cm	No	Left	10	Laparotomy, trans-hiatal repair over a T-tube, left thoracotomy, drainage, decortication, gastrosto- my and FJ	None
2012	7	61/M	Non-referral	Delayed	Lower thoracic, 37-39 cm	2 cm	No	Left	6	Left-sided, tube tho- racostomy, esophageal stenting (FCSEMS), FJ	None
2013	8	50/M	Non-referral	Delayed	Lower thoracic	3 cm	No	Left	11	Laparotomy, trans-hiatal repair over a T-tube, left thoracotomy, drainage, decortication, gastrosto- my and FJ	None
	9	47/M	Non-referral	Delayed	Lower thoracic, 2 cm above the GEJ	3 cm	No	Bilateral	12	Laparotomy, trans-hiatal primary repair, omento- plasty, bilateral thoraco- scopic drainage, gastro- stomy and FJ	None

**Table 2. (continue)** Individual patient profile and treatment details

Year	Case No.	Age/ Sex	Type of intervention before referral	Time of presentation (Early vs. Delayed)	Location of perforation <sup>a</sup>	Perforation size	Contained perforation (Yes/No)	Site of pleural collection	PPSS	Details of primary intervention(s)	Re-intervention
2014	10	55/M	Right thoracotomy, pleural drainage	Delayed	Lower thoracic, 34-36 cm	2 cm	No	Left	6	Left-side, tube thoracotomy, esophageal stenting (FCSEMS) and FJ	Left-sided residual pleural collection → image-guided drainage
2016	11	70/M	Non-referral	Delayed	Lower thoracic, just above the GEJ	1 cm	No	Left	12	On-table endoscopy, left-thoracoscopic drainage, decortication and FJ <sup>c</sup>	Post-op contrast study showed a leak → stented (FCSEMS) → stent migration → endoscopic repositioning
2018	12	37/F	Non-referral	Early	Lower thoracic, 31-33 cm	2 cm	No	Right	8	On-table endoscopy, clipping of the perforation, right-thoracoscopic drainage and FJ	Persistent leak → stented (FCSEMS) → stent migration → endoscopic repositioning

PPSS: Pittsburgh perforation severity score, M: Male, F: Female, GEJ: Gastro-esophageal junction, FJ: Feeding jejunostomy, FCSEMS: Fully covered self-expanding metal stent, N/A: Not identified (The perforation is not identified intra-op), N/A: Not applicable (No endoscopy or esophageal surgery attempted; hence size of the perforation cannot be commented on), N/M: Not mentioned (Although perforation identified either in endoscopy or intra-op, its size was not mentioned).

<sup>a</sup>: The location of the perforation was identified using either radiological or endoscopic or intra-op assessment or their combination

<sup>b</sup>: Pleural effusion developed following the primary intervention, but there was no evidence of a postoperative esophageal leak in the re-imaging

<sup>c</sup>: On-table endoscopy showed an erosion in the lower thoracic esophagus, but the CT showed no obvious contrast leak and the perforation was not identified intra-op; hence stenting was not considered during the index operation.



### Feeding Procedure and Gastrostomy

An FJ was performed in all patients, and a surgical venting gastrostomy was created in four patients.

### Re-Interventions

A total of five patients required re-intervention; one patient developed migration of the covered esophageal stent, managed by endoscopic stent repositioning, and two patients required stenting following the primary esophageal intervention (failure of clipping, 1; postoperatively evident leak, 1). The patient who received stenting following the failed clipping developed distal migration of the stent and required endoscopic repositioning. In the patient who was stented for an esophageal leak (revealed postoperatively), there were three instances of stent migration, necessitating endoscopic repositioning. Two patients developed residual pleural collection following the primary intervention and required additional drainage procedures (tube thoracostomy, 1; image-guided drainage, 1).

### Post-Treatment Outcomes and Follow-Up

Post-treatment outcome and follow-up are elaborated in Table 3. There was one re-operation for intraperitoneal bleeding, three ventilator-associated pneumonia requiring tracheostomy, one

central-line associated infection, and paroxysmal supraventricular tachycardia. Thirty-day postoperative complication was 50.0%, and all were CDG $\geq$  3 complications. All patients but two required ICU stay, and median (range) LoHS was 25.5 (12-101) days. Among patients who completed 90-day follow-up (n= 9), there was no 90-day mortality. One patient, who required multiple stent re-positioning, succumbed to multi-organ failure on the 101<sup>st</sup> postoperative day.

All esophageal stents were retrieved in the outpatient clinic, and no patient had a residual leak in the follow-up contrast-esophagography. Among the survivors (n= 11), the median (range) follow-up was 1507 (17-5929) days; one patient died of community-acquired pneumonia at nine months following discharge, and the remaining patients were alive with no recurrence, dysphagia or symptomatic reflux.

### The Clinical Significance of PPSS

PPSS was 2-5 in two patients and >5 in 10 patients. When PPSS >5 and 2-5 patient groups were compared, there were more delayed presentation (90.0% vs. 50.0%; p= 0.165), more surgical interventions (70.0% vs. 0.0%), increased rate of overall post-procedure morbidity (70.0% vs. 50.0%; p= 0.583) and in-hospital mortality (10.0% vs. 0.0%) in the former group (Table 4). Eight

**Table 3.** Post-treatment outcomes and follow-up

Patient SL. No. <sup>a</sup>	Post-procedure additional morbidity <sup>b</sup>	CDG	PPSS	PPSS risk category (Intermediate; 2-5 vs. high; >5)	ICU (Yes/No)	LoHS (Days) (Days)	Mortality (90-day, in-hospital)	Follow-up (Days)	Recurrence (Yes/No)
1	Tracheostomy	3a	4	Intermediate	Yes	31	No, No	5929	No
2	CLABSI, VAP, multi-organ failure	4b	10	High	Yes	68	No, No	1507	No
3	None	N/A	3	Intermediate	Yes	18	No, No	272	No
4	None	N/A	9	High	No	17	No, No	49	No
5	None	N/A	9	High	Yes	20	No, No	3467	No
6	VAP, tracheostomy	3b	10	High	Yes	38	No, No	17	No
7	None	N/A	6	High	Yes	19	No, No	65	No
8	Bleeding from a hiatal vessel needing laparoscopic ligation	3b	11	High	Yes	40	No, No	3007	No
9	PSVT treated medically	3a	12	High	Yes	12	No, No	2956	No
10	None	N/A	6	High	No	32	No, No	2630	No
11	VAP, tracheostomy	5	12	High	Yes	101	No, Yes	N/A	N/A
12	None	N/A	8	High	Yes	17	No, No	1142	No

CDG: Clavien-Dindo grading, ICU: Intensive care unit, LoHS: Length of hospital stay, CLABSI: Central-line associated bloodstream infection, VAP: Ventilator-associated pneumonia, PSVT: Paroxysmal supraventricular tachycardia, N/A: Not applicable.

<sup>a</sup>: Patient serial number in the same order as in Table 2.

<sup>b</sup>: Additional post-procedure morbidity (excluding any form of esophago-pleural re-interventions).

**Table 4.** PPSS and its correlation with treatment selection and post-treatment outcomes

Variable	PPSS (n= 12)		p
	Intermediate risk (2-5) (2, 16.7%)	High risk (>5) (10, 83.3%)	
Time of presentation			
<24 hours	1 (50%)	1 (10%)	0.165
>24 hours	1 (50%)	9 (90%)	
Primary intervention(s)			
Surgery ± other interventions	0 (0%)	7 (70%)	-
Endoscopic alone	0 (0%)	0 (0%)	
Radiological alone	2 (100%)	0 (0%)	
Endoscopic & Radiological	0 (0%)	3 (30%)	
Re-intervention requirement <sup>a</sup>			
Yes	1 (50%)	4 (40%)	-
No	1 (50%)	6 (60%)	
Post-procedure morbidity <sup>b</sup>			
Yes	1 (50%)	7 (70%)	0.583
No	1 (50%)	3 (30%)	
Need for ICU stay			
Yes	2 (100%)	8 (80%)	0.488
No	0 (0%)	2 (20%)	
Median LoHS, days	24.5	26	-
Mortality			
90-day	0% (0%)	0 (0%)	-
In-hospital	0% (0%)	1 (10%)	

PPSS: Pittsburgh severity score, ICU: Intensive care unit, LoHS: Length of hospital stay.

<sup>a</sup>: Includes the patient in whom a re-intervention was warranted (stenting for persistent esophago-pleural fistula) but refused.

<sup>b</sup>: Post-procedure morbidity includes re-interventions also.

PPSS was calculated by assigning points to each clinical variable to a total score of 18 and three patient risk categories were identified (low risk <2, intermediate risk 2-5, high risk >5): 1= age >75 years, heart rate >100 beats per minute, white cell count >10 × 10<sup>9</sup>/mL, pleural effusion; 2= fever (>38.5 °C), uncontained leak (radiological studies), respiratory compromise (respiratory rate >30 per minute, need for increasing oxygen or mechanical ventilation), time of diagnosis >24 h; 3= oesophageal cancer, hypotension (17,18).

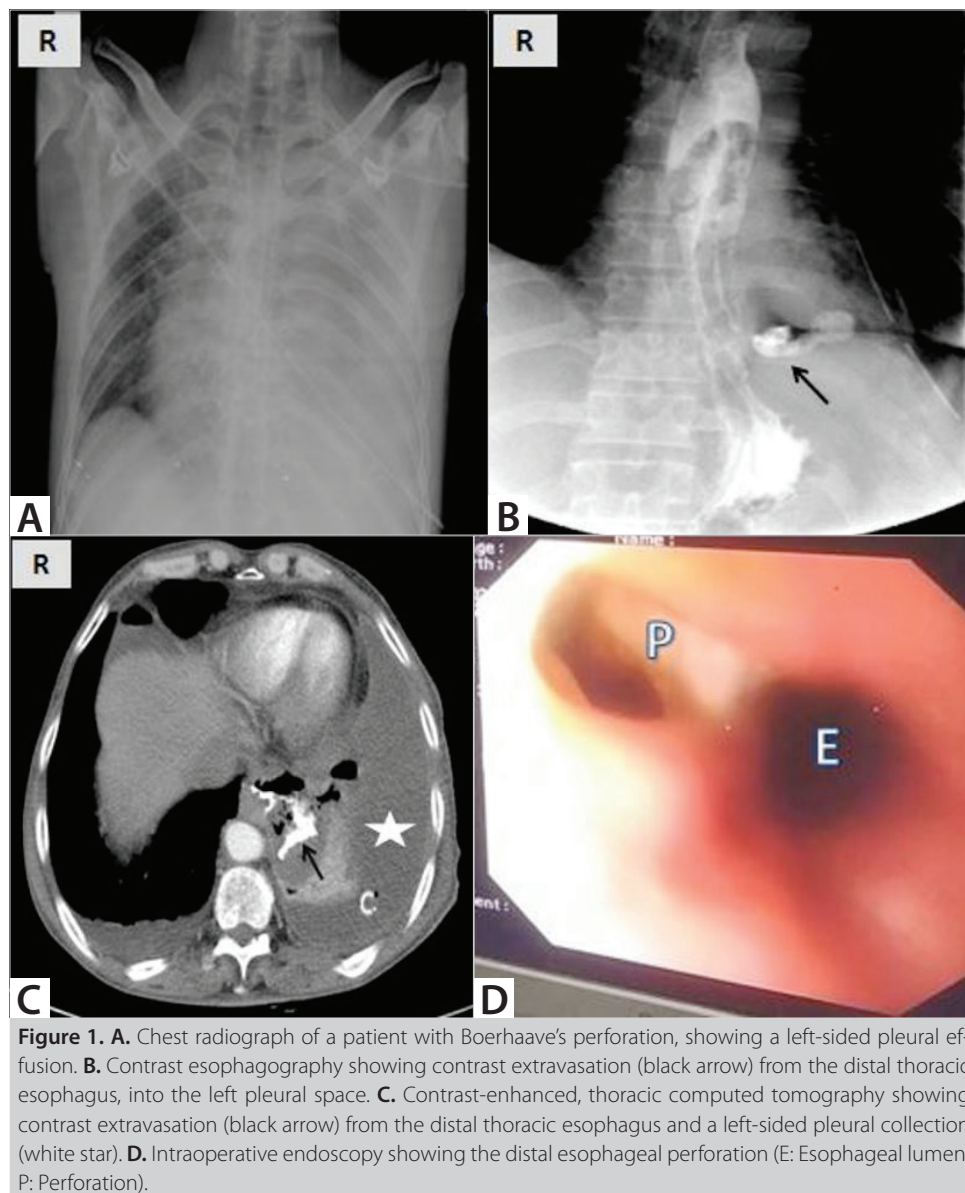
(80%) patients with PPSS > 5 and all patients with PPSS 2-5 required ICU stay (p= 0.488). There was no clinically relevant difference in re-intervention rate (50.0% vs. 50%) or LoHS (24.5 days vs. 26 days) between PPSS patient groups.

## DISCUSSION

Early detection and timely management of BS can reduce its morbidity and mortality, but the optimal therapeutic approach remains controversial (18). Traditionally, aggressive surgical approaches including resection were favoured. However, with recent developments in endoluminal therapy and minimally invasive surgery, there is a paradigm shift in the management approach to this condition. This case series reports the treatment outcomes of BS, from an upper gastrointestinal surgical unit, over a period of 13 years. All available treatment options have also evolved over the period of the study.

In our series, majority of the patients were middle-aged males, the diagnosis was often delayed, chest pain was the dominant symptom, and all perforations were sited in the distal thoracic esophagus; a trend concurrent with the reported literature (1,5,20,23). Abnormal chest radiography findings in BS include

pleural effusion (Figure 1A), pneumomediastinum, subcutaneous emphysema, hydropneumothorax, and rarely pneumoperitoneum. In this series, chest radiography showed pleural effusion in all patients. Although contrast-esophagography (Figure 1B) is a useful investigation to confirm diagnosis, false-negative rates can reach 15-25% and its application is often limited by the patient's ability to swallow the contrast; it was possible in two of our patients, confirming the diagnosis in both (5,24). Thoracic CT (Figure 1C) gives valuable information regarding the site of perforation, its contained vs. uncontained nature, and the presence of additional esophageal pathologies and can guide effective sepsis drainage (1,24). In our experience, thoracic CT had excellent sensitivity in detecting perforation, and majority of the perforations (75.0%) were uncontained type. Endoscopy has a sensitivity of 100% and specificity of 80-93% in diagnosis, but can potentially worsen the esophageal tear (1,3,5). Routine diagnostic endoscopy is not performed in our centre but was utilized for intra-operative localization of the perforation in three patients (Figure 1D), where an immediate endoluminal intervention was followed.



**Figure 1.** **A.** Chest radiograph of a patient with Boerhaave's perforation, showing a left-sided pleural effusion. **B.** Contrast esophagography showing contrast extravasation (black arrow) from the distal thoracic esophagus, into the left pleural space. **C.** Contrast-enhanced, thoracic computed tomography showing contrast extravasation (black arrow) from the distal thoracic esophagus and a left-sided pleural collection (white star). **D.** Intraoperative endoscopy showing the distal esophageal perforation (E: Esophageal lumen, P: Perforation).

Initial management of BS consists of fluid resuscitation, antibiotics and antifungals, acid suppression, analgesia, and cardio-respiratory support. The specific treatment approach depends on the patient's general condition and comorbidities, the location and extent of the perforation, esophageal viability, the extent of pleuro-mediastinal soiling, and the availability of expertise (24). The treatment of BS is primarily aimed at three important steps: 1. sealing the perforation and maintaining the luminal continuity, 2. drainage of sepsis, and 3. nutritional support.

In our series, either surgery or endoscopic interventions were performed to achieve the sealing of the perforation. Although transthoracic approach is considered to be the standard operative approach for BS, trans-hiatal approach was found to

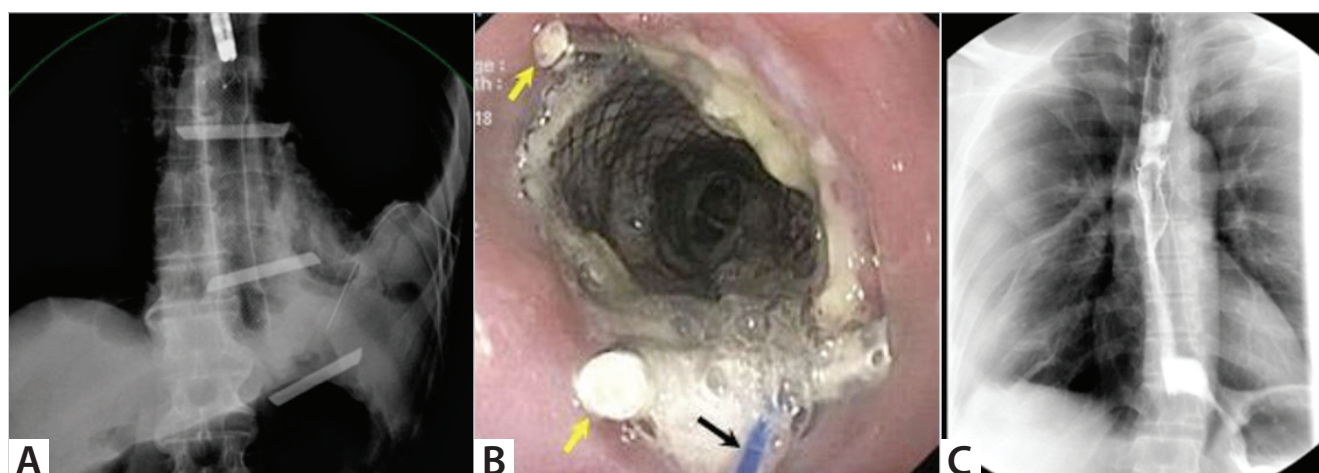
be feasible and safe in our experience, as also reported by others (2,4,9,25). In addition to providing direct access to the perforation, this operative approach allows for the drainage of the mediastinum, placement of an omental patch, performance of a concomitant FJ, and an occasional gastrostomy. During the early part of the series, surgery was often utilized to achieve sealing of the perforation and the technique of repair was either a primary buttressed repair or a T-tube esophagostomy. Primary repair in patients presenting early is reported to have low postoperative leakage, shorter LoHS and ICU stay, and the reinforcement of the repair using vascularized tissues can reduce the postoperative leakage (4,8). A reinforced primary repair was possible in two patients, one each in the early and delayed diagnosis groups, and adequate sealing was achieved

in both. Key steps of primary repair include debridement of non-viable tissues, esophageal myotomy on either end of the perforation to expose healthy mucosal edges and a meticulous closure, preferably in double layers (1,24). Trans-thoracic repair can be reinforced with a pleural, pericardial or intercostal muscle flap or a gastric fundal wrap, whereas an omental or a gastric fundal wrap may be utilized to buttress a trans-hiatal repair (1,12). Although delayed diagnosis does not preclude a primary repair, a high risk of a postoperative leak, re-interventions and mortality is reported, particularly when the delay is >48 hours (1,5,8,9,25). In such a scenario, repair over a T-tube is preferred, which creates a controlled esophago-cutaneous fistula; a technique that had successful outcomes in two of our patients presenting late (2,4,7,9). In our opinion, this technique is an attractive alternative in patients with delayed diagnosis, where the feasibility of a primary repair is limited, due to edematous and friable tissues, thereby avoiding or delaying other morbid operative procedures (diversion, exclusion or resection).

During the later phase of the study, endoscopic stenting with covered self-expanding metal stents (Figure 2) was more commonly used. Stenting is an effective, minimally invasive, primary modality for sealing the perforation in BS. Initial successful stenting can avoid radical surgeries, facilitates early oral alimentation, and can shorten the LoHS, ICU stay, and ventilator days (15,16,26). It can also be a salvage option in patients with persistent postoperative leak (6,7). In three of our patients with delayed diagnosis, the initial sealing of the perforation could be achieved by stenting. Additionally, one patient received stenting for a perforation that was not localized during the index operation but revealed later (Patient SL No. 11). Endoscopic clips, particularly over the scope clips are recommended for early perforations, measuring up to 30 mm

(1,3,24). Although we utilized this technique in one patient who presented early, a persistent leak warranted stent implantation later. This patient had an uncontained perforation which perhaps increased the likelihood of a re-leak, despite initial thoracic drainage.

The selection of primary esophageal intervention should be individualized based on patient and perforation characteristics. In a recent meta-analysis, surgery has been found to be the most favoured therapeutic approach, being utilized in 76% of the patients with BS, particularly when the diagnosis is made early; endoluminal techniques and non-operative management (NOM) are utilized predominantly in case of a delayed diagnosis (27). We prefer surgical repair over stenting for patients presenting early. However, in the early phase of this study, surgery was also performed in patients with a delayed diagnosis if the perforations were localized near the gastro-esophageal junction (GEJ) and patients could tolerate esophageal surgery, a practice similarly reported by others (8,9,25). Stenting, as the primary treatment modality for BS, has been demonstrated to have favourable clinical success, irrespective of the time to diagnosis (6,15,16,26). However, when the diagnosis is delayed, stenting may be associated with increased re-interventions, morbidity and mortality (16,26). In our recent experience, stenting was often utilized in delayed presentations, particularly if the perforations were localized away from the GEJ or the local esophageal condition and if the patient's poor general condition did not permit an immediate esophageal surgery. However, we ensured adequate pleuro-mediastinal drainage  $\pm$  debridement in all patients receiving stenting, which perhaps contributed to the absence of persistent leakage in this subgroup. Distal migration can frequently be seen in patients with BS receiving stenting (20-33%) and a high risk of persistent dysphagia is expected following a failed endoluminal



**Figure 2.** A. Endoluminal stenting for a Boerhaave's perforation, as seen in an image-intensifier. B. Endoscopic view of a fully deployed esophageal stent, anchored utilizing endoclips (yellow arrows) and a prolene thread (black arrow). C. Contrast esophagogram, showing an esophageal stent, providing adequate sealing of the distal thoracic esophageal perforation.



stenting (3,6,15,16,26). Although stent migration developed in three of our patients, these were successfully re-positioned endoscopically, and immediate additional interventions were not indicated in any patient, except one. There were no instances of esophageal stenosis and symptomatic reflux in the stented group. In our opinion, appropriate patient and stent type selection, the availability of expertise, and adequate sepsis drainage are paramount to minimise stent failure and its complications.

Adequate pleuro-mediastinal sepsis control is the key component in the treatment of BS and is a mandatory step to improve the success of any esophageal interventions. Tube thoracostomy or image-guided drainage is an accepted initial modality for drainage of localized contaminations, as utilized in five of our patients. However, since perforation in BS is barogenic, thoracic cavity is frequently contaminated with alimentary contents, warranting surgical debridement and drainage at some time point. In our series, majority of the patients with an uncontained perforation received surgical drainage and debridement, particularly when the diagnosis was delayed or when the pleural collections were loculated.

Nutritional access is a key treatment component for BS. We performed tube jejunostomy in all patients to facilitate early enteral nutrition. A nasojejunal tube is also an accepted alternative for feeding. Venting gastrostomy can reduce the incidence of postoperative reflux, particularly in perforations near the GEJ, and was performed in four of our patients. We generally avoid routine feeding or venting gastrostomy for perforations related to B, since it allows gastric preservation, for esophageal reconstruction, if an esophagectomy is indicated.

Surgical repair of esophageal perforation and sepsis drainage could also be achieved with minimally invasive surgery (10,12,13,19,23). Haveman et al. have demonstrated comparable effectiveness and safety of pleural sepsis drainage utilizing video-assisted thoracoscopic surgery (VATS) and open thoracotomy techniques (10). In a recent review, minimally invasive surgery has been found to be feasible and safe for esophageal repair and thoracic debridement/drainage, especially in patients presenting early with stable vitals (14). Recently, VATS is our preferred operative approach for addressing thoracic sepsis, as in three of our patients. Although we preferred laparotomy for the repair of the perforations, the feasibility and safety of laparoscopic, trans-hiatal, and video-assisted trans-thoracic repairs have been shown by other authors, including in patients with delayed diagnosis (12,13,19,23).

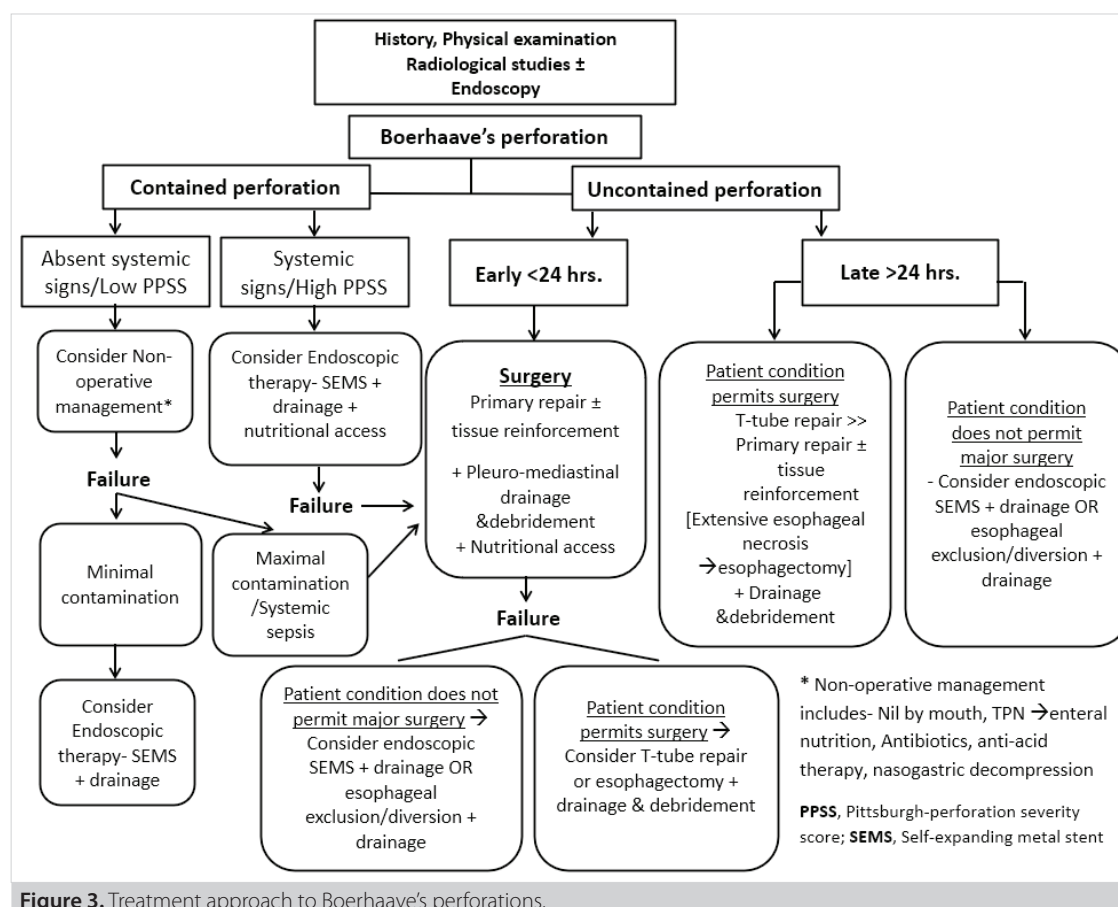
In carefully selected patients with BS, successful treatment outcomes are achievable by NOM, provided the following criteria are satisfied: a contained perforation within the mediastinum and drainage flowing back to the esophageal

lumen, minimal symptoms, no overt signs of systemic sepsis, and availability of appropriate radiological studies and thoracic surgery expertise (28). A true NOM consist of nil by mouth, intravenous fluids, anti-acid therapy, broad-spectrum antibiotics and enteral tube feeding, but is rarely possible in BS, due to its frequent delayed presentation. No patient received a true NOM in our series, but two patients with delayed but contained type perforation with no overt signs of sepsis, received conservative treatment approach including tube thoracostomy and nutritional access, without esophageal interventions, and their recovery was uneventful. An initial esophageal intervention is preferably avoided in this sub-group of patients and favourable treatment outcomes could result from drainage and nutritional support alone (1,2).

PPSS is a valuable clinical tool to stratify risk among patients with esophageal perforation, particularly in the context of BS (17-20). Patients who present early with a contained leak and do not have overt signs of sepsis often have a low PPSS and are ideal candidates for initial NOM in specialized esophageal centres (1). An operation in this subset of patients may have a worse treatment outcome (17,23). In our series, none of the patients had PPSS of  $\leq 2$  and no patient received a true NOM. The severity of complications, LoHS and mortality is shown to correlate with PPSS (17). In this study, there were more delayed presentations, increased surgical interventions, increased post-procedure morbidity, and in-hospital mortality in those patients with a PPSS  $\geq 5$ , compared to those with PPSS 2-5 but these differences were not statistically significant. Further analysis to evaluate the effect of PPSS on treatment selection and outcomes was not feasible in this study, considering its small study population.

Despite advances in therapeutics for BS, treatment-related morbidity can reach 70.0%, major operative morbidity can reach 36.0%, re-intervention rate can be 40%, mortality can be 8-40%, and prolonged ICU care and LoHS is not uncommon (10,13,19,20,23,27). In this study, overall post-treatment complication was 50% (CDG  $\geq 3$ , 100%), and majority of the patients had a prolonged LoHS. However, despite these adverse outcomes, there was only one death (8.3%) and the esophagus could be salvaged in all patients. No patients required esophageal re-interventions following discharge; all stents were successfully retrieved and there were no stent-related complications, except the migrations. Further, there were no instances of dysphagia, symptomatic reflux or recurrent perforation.

Owing to the rarity and life-threatening nature of this condition, prospective studies to evaluate the effects of different treatment approaches are difficult to execute, and hence, the current evidence concerning the efficacy and safety of various treatment options are retrospective studies. A treatment



**Figure 3.** Treatment approach to Boerhaave's perforations.

algorithm based on our experience and the data available in the literature is formed (Figure 3).

This study had a few limitations. Firstly, it was a single institution, retrospective study with a relatively small number of patients, and hence, has its inherent biases. Secondly, a few patients were referred to us following some form of primary intervention at the index hospital. Hence, PPSS at the presentation in our centre is not a true reflection of their actual PPSS. Lastly, various patient and treatment-related factors which can help choose a particular treatment strategy and predict the treatment success could not be established, due to the small study population. Keeping aside the limitations, the current study focused solely on BS-related perforations, from a low-middle-income country, where timely access to a specialized esophageal centre is often limited. Also, the results from this study do support the view that favourable treatment outcomes could be achieved, by utilizing hybrid therapeutic techniques. We feel that future studies should focus on a multidimensional approach to BS, rather than comparing various therapeutic approaches.

## CONCLUSION

Boerhaave's syndrome is a rare esophageal emergency and remains a diagnostic and therapeutic challenge. Despite an inc-

reased disease and treatment-related morbidity and prolonged hospital stay, successful treatment outcomes including reduced mortality, organ preservation, and better functional outcomes could be achieved through timely, individualized, multimodality management. Recent advances in minimally invasive, endoluminal and surgical techniques can further improve treatment outcomes. Pittsburgh severity score is a useful tool to select the initial treatment strategy and can possibly predict treatment-related outcomes.

**Ethics Committee Approval:** This study was approved by Christian Medical College Ethics Committee (Decision no: 13062, Date: 24.06.2020).

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - SS, CV, MY, IS; Design - SS, CV, MY, IS; Supervision - IS; Materials - SS, CV, MY, NP, SC, AJ, EGS, IS; Data Collection and/or Processing - SS, CV, MY, NP, SC, AJ, EGS, IS; Analysis and/or Interpretation - SS, CV, MY, NP, SC, AJ, EGS, IS; Literature Search - SS, CV, MY, NP, SC, AJ, EGS, IS; Writing Manuscript - SS, CV; Critical Reviews - SS, MY, NP, SC, AJ, EGS, IS.

**Conflict of Interest:** The authors have no conflicts of interest to declare.

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## ORİJİNAL ÇALIŞMA-ÖZET

Türk J Surg 2023; 39 (3): 177-189

## Boerhaave sendromunun klinik profili ve tedavi sonuçları: Bir üst gastrointestinal cerrahi ünitesinin 13 yıllık deneyimi

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### ÖZET

**Giriş ve Amaç:** Boerhaave sendromu (BS), barojenik özofagus rüptürü ile karakterize, nadir fakat potansiyel olarak ölümcül bir durumdur ve yüksek mortalite taşır. BS'li hastaları yönetme konusundaki kurumsal deneyimimizi incelemeyi amaçladık.

**Gereç ve Yöntem:** Bu çalışmada 2005'ten 2018'e kadar üçüncü basamak bir bakım merkezine başvuran BS'li hastaların retrospektif bir incelemesi yapılmıştır. Klinik prezentasyon, tanısız değerlendirilmeler, alınan tedaviler ve tedavi sonuçları incelendi. Perforasyonlar geçen süreye göre erken (<24 saat) ve gecikmiş (>24 saat) olarak sınıflandırıldı. Cerrahi komplikasyonlar Clavien-Dindo derecesine göre derecelendirildi. Pittsburgh perforasyon şiddeti skoru, kısa vadeli tedavi sonuçları ile korele idi.

**Bulgular:** Dahil edilmiş 12 hastanın [erkek, %75; ortalama (aralık) yaş, 53 (28-80) yıl] 10'unda gecikmiş (>24 saat) başvuru vardı. Göğüs ağrısı baskın semptomdu (%58.3); altı hasta ya şokta (n= 1) ya da organ yetmezliği (n= 3) ya da her ikisi (n= 2) ile başvurdu. Tüm perforasyonlar alt torasik özofagus yerleştirilmiş olup, bunların üçü kontrollü ve dokuzu kontrolsüz idi. Perforasyonun kapatılması dört hastada cerrahi onarım (primer onarım, 2; T-tüpü üzerinden onarım, 2) ve dört hastada endoskopik teknikler (klipsleme, 1; stentleme, 3) ile sağlandı. Sepsis drenajı [cerrahi, 7 (açık-5, minimal invaziv-2); cerrahi olmayan, 5] ve beslenme jejunostomisi tüm hastalara uygulandı. Beş (%41,7) hasta yeniden girişim aldı. Ortanca (aralık) hastanede kalış süresi 25,5 (12-101) gündü, 30 günlük operatif morbidite %50 idi ve bir hastane içi ölüm meydana geldi. Pittsburgh perforasyon şiddeti skoru iki hastada 2-5 ve 10 hastada >5; ikinci grupta daha fazla gecikmiş başvurular, artmış cerrahi müdahaleler, işlem sonrası morbidite ve hastane içi mortalite vardı ancak farklılıklar istatistiksel olarak anlamlı değildi. Takip edilen 11 hastada [medyan (aralık): 1507 (17-5929) gün] hastalık nüksü, semptomatik reflü veya disfaji görülmedi.

**Sonuç:** Boerhaave perforasyonları için çok yönlü bir yaklaşımla, azaltılmış mortalite ve organ koruması da dahil olmak üzere olumlu tedavi sonuçları elde edilebilir. Tedavisinde minimal invaziv, endoluminal veya açık cerrahi teknikler güvenle kullanılabilir. Pittsburgh şiddet skoru, ilk müdahaleyi seçmek ve tedavi sonuçlarını tahmin etmek için kullanılabilecek yararlı bir klinik araç olabilir.

**Anahtar Kelimeler:** Boerhaave sendromu, spontan özofagus perforasyonu, cerrahi, terapötik endoskopi, Pittsburgh perforasyon şiddet skoru

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# Indocyanine green guided sentinel lymph node biopsy may have a high sensitivity for early (T1/T2) colon cancer: A prospective study in Indian patients

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## ABSTRACT

**Objective:** Indocyanine green (ICG) dye guided near infrared fluorescence (NIR) imaging is a promising tool for mapping lymphatics. The aim of this study was to evaluate the role of ICG guided SLN biopsy in Indian colon cancer patients.

**Material and Methods:** Forty-eight patients of clinically staged T1-T3 node negative colon cancer underwent laparoscopic/open resection. Patients received colonoscopic peritumoral submucosal ICG injections for laparoscopic (n= 32) and subserosal injections for open resections (n= 16) followed by the detection of SLN using NIR camera. SLNs underwent conventional hematoxylin and eosin (H & E) staging with additional serial sectioning and immunohistochemistry for pancytokeratin antibody (ultra-staging). Detection rate and upstaging rate were the primary end points.

**Results:** Forty-eight patients were recruited. An average of  $2.08 \pm 1.27$  SLNs were identified in 45 patients at a mean time of  $8.2 \pm 3.68$  minutes with a detection rate of 93.75%. Mean age and mean BMI were  $59.7 \pm 12.54$  years and  $24.8 \pm 4.09$  kg/m<sup>2</sup>, respectively. Eighteen patients had node positive disease, and SLN was false negative in four of these patients resulting in a sensitivity of 77.77% with a trend towards higher sensitivity for T1-T2 tumours (90% vs. 62.5%, p= 0.068). Upstaging rate was 10%. Negative predictive value (NPV) and accuracy of the procedure were 87.09% and 91.11%, respectively.

**Conclusion:** ICG guided SLN biopsy can identify metastatic lymph nodes in colon cancer patients that can be missed on H & E staging with relatively higher sensitivity for early (T1/T2) tumours.

**Keywords:** Sentinel lymph node, colorectal neoplasms, Indocyanine green

## INTRODUCTION

Colorectal cancer is the third most common cancer diagnosed in both men and women in the United States and the third leading cause of cancer death in the world (1). The strongest predictive factor for patient survival in patients with colon cancer is lymph node metastasis (2). It has been estimated that 20-30% patients with early-stage node-negative disease will develop distant metastasis despite adequate surgical resection (3). One of the reasons for recurrence in pathologically node-negative patients could be missed micrometastasis and occult tumor cells on routine histopathological examination or inadequate lymph node harvesting leading to understaging (4). Ideally, all harvested lymph nodes should undergo serial sectioning and immunohistochemistry (IHC) routinely to detect these occult metastasis but they are time consuming and expensive (5). Hence, it is not part of routine pathological evaluation.

Sentinel lymph node (SLN) biopsy technique has been described in colon cancer to detect micrometastasis (MM) (6). Near-infrared (NIR) fluorescence imaging for SLN metastasis has been recently used for SLN biopsy with encouraging results (7,8). NIR-fluorescence imaging has high penetration depth and real-time optical guidance which is useful in identifying lymph nodes that are located in unfavorable locations beneath fatty mesocolon (9).

Previous published studies have elucidated the role of SLN biopsy in Caucasian and East Asian patients (6,10). To the best of our knowledge, this is the first study in a south Asian population. This study was conducted to evaluate the role of SLN biopsy using NIR-fluorescence in colon cancer patients with respect to detection rate, upstaging rate, frequency of aberrant lymph node drainage, accuracy, and sensitivity of the SLN biopsy procedure.

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## MATERIAL and METHODS

### Study Design

A single arm prospective cohort study was conducted at a tertiary referral centre. Colon cancer patients who met the eligibility criteria were enrolled from June, 2020 to June, 2022. The study was approved by the Institute Ethics Committee (Ref. No. AIG/IEC-Post BH & R 02/12.2019/ER-01; 10 January, 2020) and was prospectively registered with the clinical trials registry (NCT04351009). The study was HIPAA compliant and adhered to the tenets of Declaration of Helsinki. A written informed consent was obtained from each patient prior to the enrolment.

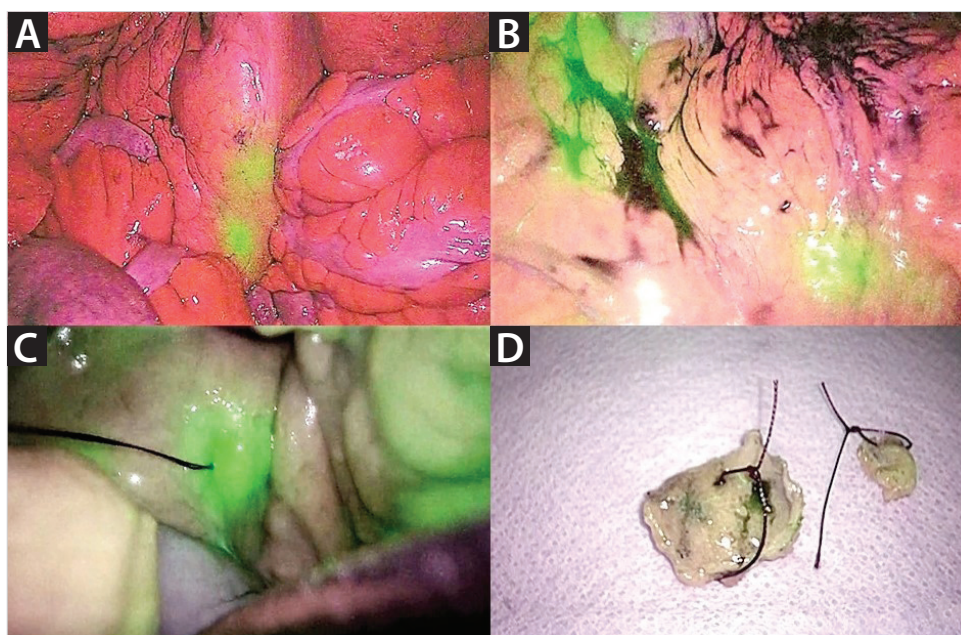
Biopsy proven colon cancer patients with age at least 18 years old who were scheduled for elective laparoscopic/open colectomy were recruited. Patients had to be willing to provide oral and written informed consent.

Exclusion criteria included patients with prior colorectal surgery, gross lymph node involvement or tumour infiltration on preoperative imaging or intraoperative staging, history of allergy to iodine containing compounds, indocyanine green or human albumin, history of hyperthyroidism or thyroid adenoma, patients undergoing purely palliative surgery and patients with advanced renal or hepatic insufficiency.

### Perioperative Intervention

Exploration of the abdominal cavity was performed to search for any metastatic spread in both open and laparoscopic approaches after induction of anesthesia. Subsequently, patients underwent on-table colonoscopy for laparoscopy cases. All laparoscopic

cases received colonoscopic submucosal injections and all open cases received subserosal injections. Twenty-five mg indocyanine green dye (Aurogreen, Aurolab, Madurai, India) diluted in 1 mL of 20% albumin solution and 9 mL of 0.9% normal saline solution was used as described by Ankersmit et al (6). Injections (0.5-1 mL) were given in the submucosa at 2-4 points around the tumor. After colonoscopic injection, excess ICG was washed and suctioned from the lumen. Similarly, subserosal injections were given, the injection sites were pressed with sterile swabs to prevent spillage. Dissection was avoided to prevent damage to the lymphatics. After the injection, a rigid NIR scope (WA53000A, Olympus Medical Systems Corp, Tokyo, Japan) coupled to a laparoscopic NIR camera system (VISERA ELITE II, Olympus Medical Systems Corp, Tokyo, Japan) was used to examine the colon and mesocolon. This system illuminated the target organ with a near-infrared light of 760-780 nm wavelength resulting in emission of ICG fluorescence at wavelengths of 800-850 nm which was detected by the camera system in normal white light mode, fluorescent mode and onlay mode. The first lymph node or group of lymph nodes to show fluorescence were considered the sentinel lymph node. The site of sentinel lymph nodes was determined according to the Japanese Society for Cancer of the Colon and Rectum classification (11). D1 lymph nodes were defined as lymph nodes along the marginal artery (paracolic/epicolic), D2 lymph nodes along named tumor bearing arteries (intermediate) and D3 lymph nodes along the origin of main artery (central). All sentinel nodes were marked with laparoscopic titanium clips or 3-0 silk sutures. All sentinel lymph nodes outside the planned resection margins were underwent excision biopsy



**Figure 1.** Intermediate sentinel lymph nodes in case of carcinoma sigmoid (A), intermediate sentinel lymph nodes along the middle colic artery in a case of carcinoma hepatic flexure of colon (B), a sentinel lymph node marked with 3-0 silk sutures (C), excised sentinel lymph nodes (D).



but the resection margins were not modified (Figure 1A-D). Standard oncological resections with medial to lateral vessel first approach with high arterial ligation was done in all patients irrespective of laparoscopic or open access.

### Pathological Analysis

After resection of the specimen, the tagged lymph node(s) were excised and sent separately as SLN (Figure 1D). Non-sentinel lymph nodes were examined by a central section with H & E staining. All labelled sentinel lymph nodes were processed separately. Lymph nodes less than 5 mm in diameter were embedded entirely in toto whereas larger lymph nodes (>5 mm) were sectioned in slices up to maximally 3 mm and processed to paraffin blocks for hematoxylin and eosin staining. If none of sentinel lymph nodes showed metastasis on initial H & E staining in the presence on negative non-sentinel lymph nodes, the paraffin blocks underwent stepwise sections at intervals of 150 micron-meter. At each level, at least three serial sections were cut at 5 µm thickness and one section underwent H & E staining. This was followed by immunohistochemistry with pan-cytokeratin antibody on the other sections if no metastasis was identified on standard H & E staining.

As per the American Joint Committee on Cancer (AJCC) eighth edition, micrometastasis were defined as clumps of tumor cells  $\geq 0.2$  mm and <2 mm in diameter or clusters of 20 or more tumor cells. Detection of single cells or clumps of tumor cells <0.2 mm were described as isolated tumor cells (12). Patients with micrometastasis were considered SLN positive. All collected data were entered into a computerized database and processed for statistical analysis. After computing the true positive (TP), true negative (TN), false positive (FP), false negative (FN) sentinel nodes, the sensitivity, accuracy, negative predictive value, upstaging rate and detection rate were calculated.

### Outcome

Primary outcome was detection rate which was defined as proportion of successful SLN procedures divided by all executed SLN procedures, upstaging rate and secondary outcomes were sensitivity, accuracy, negative predictive value, and frequency of aberrant lymph node drainage. Number of true positives in patients with positive histopathological findings (TP/TP + FN) was defined as sensitivity. Accuracy was defined as (TN + TP/TN + TP + FP + FN) to calculate the number of times the nodal state was correctly predicted by SLN biopsy. Negative predictive value (TN/TN + FN) was defined as number of times a negative SLN correctly predicted the negative lymph node status of the patient. Upstaging rate was defined as number of patients who turned node positive after advanced histopathology and IHC of patients who were node negative on conventional histopathology.

### Statistical Analysis

Statistical analysis-The data for the study was collected using structured pro forma. The results were expressed as mean and standard deviation (SD) or median and interquartile range (IQR) and for continuous variables. The categorical variables were expressed as % frequency distribution. Fisher's exact test was used for categorical variables. A p value <0.05 with two tailed test would be considered as statistically significant. The analysis was carried by using statistical package for social sciences (SPSS 20<sup>th</sup> version). Proportion test and MedCalc was used for outcomes analysis between T1/T2 and T3/T4 groups.

### RESULTS

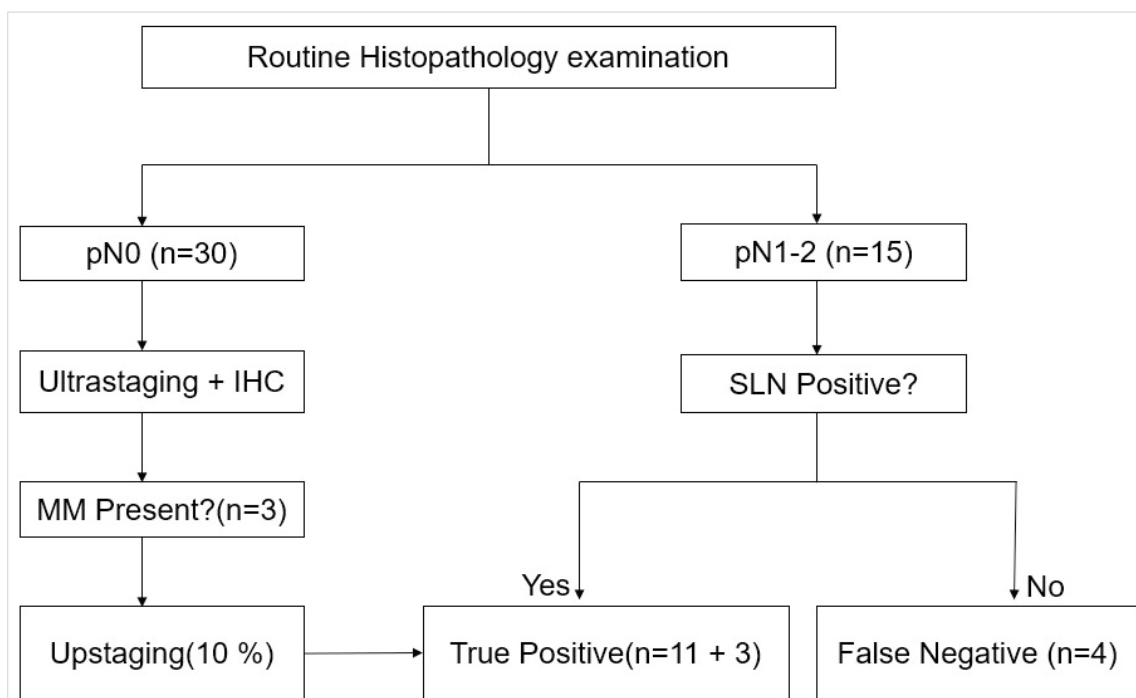
Total 136 patients of carcinoma colon presented to our institute during the study period i.e June, 2020 to June, 2022. Of these 136 patients, 24 patients had metastatic disease precluding curative resection, 64 patients had locally advanced disease with gross lymph node invasion on preoperative imaging or intraoperative staging and were excluded from the study.

Forty-eight patients were recruited. Thirty-two patients underwent colonoscopic ICG injection during laparoscopic resection and 16 patients underwent subserosal injectons during open resections. SLN could not be detected in three patients. Two patients had intraperitoneal spillage of the dye leading inability to identify the lymph nodes and one patient had a very fatty mesocolon. Therefore, detection rate was 93.75%. The demographic and pathological characteristics are depicted in Table 1. The location of primary tumour was sigmoid colon (24%), ascending colon (20%), caecum (16%), hepatic flexure (16%), transverse colon (11%), splenic flexure (9%) and descending colon (4%). The most common T stage was T3 (44.44%), followed by T2 (42.22%), T1 (11.11%) and T4a (2.22%). N staging was N0 (67%), N1a (7%), N1b (11%), N2a (11%) and N2b (4%).

Thirty patients were node negative (pN0) i.e. TN after conventional histopathological examination. Advanced histopathological examination and IHC revealed micrometastasis in three patients who were upstaged and considered as node positive. The upstaging rate was 10% (three in 30 patients) (Figure 2).

**Table 1.** Demographic and procedural characteristics of the study population

n= 45	Mean (SD)
Age (yrs)	59.7 (12.54)
Sex (M/F)	62.2%/37.8%
BMI (kg/m <sup>2</sup> )	24.8 (4.09)
Total no of LN	20.2 (10.06)
Total no SLN	2.08 (1.27)
Time to imaging (mins)	8.2 (3.68)



**Figure 2.** Overview of the pathological analysis.

**Table 2.** Outcomes in early (T1/T2) versus late (T3/T4) tumours

	T3/T4 (n=21)	T1/T2 (n=24)	P
Sensitivity	62.5%	90%	0.068
Accuracy	85.71%	95.85%	0.508
Negative predictive value	81.25%	93.33%	0.439
Upstaging rate	7.41%	11.76%	0.586

Total no of patients with positive SLN (TP) was 14 (11 on conventional H & E staining and three patients on ultrastaging and IHC). SLN was negative in four (FN) with positive non-sentinel lymph nodes. In 27 patients (TN), both the non-sentinel lymph nodes and sentinel lymph nodes were negative even after ultrastaging and IHC. Therefore, the sensitivity, negative predictive value, and accuracy of the procedure in our study were 77.77% (14/18), 87.09% (27/31) and 91.11% (26/30), respectively. Specificity and positive predictive value for the procedure was 100% as there were no false positive patients in the study.

There was no significant difference in sensitivity another outcome measures between the submucosal (n= 30) and subserosal groups (n= 15). There was a non-significant trend towards higher sensitivity in early (T1/T2) tumour when compared to late (T3/T4) tumours as depicted in Table 2.

One patient with a hepatic flexure carcinoma had an aberrant lymph node drainage at the splenic flexure paracolic node

which was harvested separately but non-metastatic on pathological examination, ultrastaging and IHC. Hence, the aberrant lymph node drainage rate was 2.22%.

## DISCUSSION

In this study we evaluated role of sentinel lymph node biopsy by indocyanine green in patients with carcinoma colon who underwent oncological resections with curative intent.

In our study the detection rate was 93.75%. SLN could not be detected in three patients due to intraperitoneal spillage of dye and fatty mesocolon. Previously, Anderson et al. had described intraperitoneal spillage of dye during sub-serosal injections but did not attribute it to cause false negative lymph nodes (13). Currie et al. have also described intraperitoneal spillage of dye during colonoscopic submucosal injections (14). In our study, the intraperitoneal spillage can be attributed to the learning curve involved in mastering the colonoscopic sub-mucosal injection technique. Multiple authors have described a learning



curve of 5-30 cases for ICG injection (15-17).

Previous meta-analysis has not shown any difference between submucosal and sub-serosal techniques of ICG injection (18,19). On the contrary, Ankersmit et al. in their single centre study found the detection rate higher with submucosal injection and opined that uptake of dye by tumour draining lymphatics is more efficient after submucosal injection (6). Carrara et al. in their study of 95 patients with non-metastatic colorectal cancer described a detection rate 96.8% with peritumoral laparoscopic injections (20). There was no significant difference in primary and secondary outcomes between the submucosal and subserosal techniques during our study. Our study was not designed or adequately powered to evaluate differences between the two techniques. Additionally, the subserosal injections were given in open surgeries where tactile feedback helped in correct positioning and limiting spillage compared to a previous study where laparoscopic access was used.

The mean time to detection was  $8.2 \pm 3.68$  minutes and the average number of SLN identified was  $2.08 \pm 1.27$ . A larger number of sentinel lymph nodes identified during the procedure is undesirable but analysing lymph nodes with serial sections and IHC is expensive and time-consuming. Watanabe et al. studied 31 patients of carcinoma splenic flexure of colon with 2.5 mg ICG peritumoral submucosal injections and observed lymph flow after 30 minutes resulting in a very high SLN yield of  $10.4 \pm 4.73$  which is undesirable (10). Therefore, it has been opined that lymphatic flow should be followed in real time after ICG injection to minimize the number of lymph nodes identified (6).

The upstaging rate in our study was 10% (three in 30 patients). Our upstaging rate is comparable to a recently published meta-analysis which had shown a pooled upstaging rate of 15% among five high quality studies (range 6% to 23%) (6). On the other hand a recently published study from Italy of 95 patients had an upstaging rate of only 1.08% (1 in 95 patients) (20). Desguetz et al. in their meta-analysis of 1794 patients (1201 colon, 332 rectum) in 33 studies found a micrometastasis rate of 9% (18,21).

The sensitivity, negative predictive value, and accuracy of the procedure in our study was 77.77%, 87.09% and 91.11%, respectively. Overall sensitivity in our study was relatively lower in our study at 77.77% due to the high number of T3/T4 tumours (46.66%) in the study population. Emile et al. conducted a meta-analysis of 12 studies with 248 patients where the median sensitivity and accuracy rates were 73.7% and 75.7% respectively with a pooled sensitivity and specificity of 71% and 84.6% (18). The percentage of patients with early-stage CRC

varied among the studies from 30 to 100% (median= 41%). In six studies, patients with early-stage tumors comprised less than 50% of the sample size and the median sensitivity, specificity, and accuracy rates were 76%, 87.2%, and 68.8%, respectively which was relatively lower than studies with >50% early-stage tumors.

Sensitivity for T1/T2 tumours was 90% which is comparable to other published literature. Other authors have also opined that SLNB procedure has better sensitivity for early stage procedures than advanced carcinoma (93.1% vs. 58.8%) (22,23).

In vivo approach for SLN mapping can help to identify aberrant lymph node drainage. Some authors have used it to modify the mesocolic resection margins (10,13,24,25). We identified aberrant lymph node drainage in one (2.22%) patient in our study.

Additionally, in vivo SLN approach in early tumour may enable us to identify patients who might benefit from a local segmental excision if the SLN are negative for metastasis thus decreasing the morbidity associated with extensive resection (26). In the future, well planned large sample size randomized controlled trials should be done to address this issue.

The limitations of our study were the small sample size with relatively higher number of advanced lesions.

## CONCLUSION

ICG guided sentinel lymph node biopsy in colon cancer is a promising tool to enable clinicians identify patients with lymph nodal metastasis in colon cancer. It has a high sensitivity for early (T1/T2) patients in the Indian population which confirms the findings of previous publications. Early (T1, T2) colon cancer patients might benefit from upstaging and subsequent adjuvant in this setting. Additionally, limited segmental resections might be considered for early tumours which are sentinel node negative. Further trials are needed to confirm this hypothesis.

**Ethics Committee Approval:** This study was approved by Asian Institute of Gastroenterology Institutional Ethics Committee (Decision no: AIG/IEC-Post BH&R 02/12.2019/ER-01, Date: 10.01.2020).

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - ZA, SP, AS; Design - ZA, SP; Supervision - PR, GVR, AS; Data Collection and/or Processing - ZA, SP; Analysis and/or Interpretation - ZA, SP, AS; Literature Review - ZA, PR, GVR; Writer - ZA; Critical Review - All of authors.

**Conflict of Interest:** The authors have no conflicts of interest to declare.

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

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## ORJİNAL ÇALIŞMA-ÖZET

Türk J Surg 2023; 39 (3): 190-196

**İndosiyenin yeşili rehberliğinde sentinel lenf nodu biyopsisi erken (T1/T2) kolon kanseri için yüksek duyarlılığa sahip olabilir: Hintli hastalarda prospektif bir çalışma**Zeeshan Ahmed<sup>1</sup>, Sanjeev M Patil<sup>1</sup>, Anuradha Sekaran<sup>2</sup>, Pradeep Rebala<sup>1</sup>, GV Rao<sup>1</sup><sup>1</sup> Asya Gastroenteroloji Enstitüsü, Gastroenteroloji Bölümü, Haydarabad, Hindistan<sup>2</sup> Asya Gastroenteroloji Enstitüsü, Patoloji Bölümü, Haydarabad, Hindistan**ÖZET**

**Giriş ve Amaç:** İndosiyenin yeşili (ICG) boya rehberliğinde yakın kızılötesi floresan (NIR) görüntüleme, lenfatikleri haritalamak için umut verici bir araçtır. Bu çalışmanın amacı, Hintli kolon kanseri hastalarında ICG rehberliğinde SLN biyopsisinin rolünü değerlendirmektir.

**Gereç ve Yöntem:** Klinik olarak evrenilmiş T1-T3 düğümü negatif kolon kanseri olan 48 hastaya laparoskopik/açık rezeksiyon uygulandı. Hastalara laparoskopik (n= 32) için kolonoskopik peritümöral submukozal ICG enjeksiyonları ve açık rezeksiyonlar için subserozal enjeksiyonlar (n= 16) yapıldı, ardından NIR kamera kullanılarak SLN saptandı. SLN'lere ek seri kesitleme ve pansitokeratin antikoru için immünohistokimya (ultra evreleme) ile geleneksel hematoksilen ve eozin (H & E) evrelemesi uygulandı. Tespit oranı ve ileri evreleme oranı birincil son noktalarıdır.

**Bulgular:** Kırk sekiz hasta çalışmaya alındı. Kırk beş hastada, ortalama 8,2 ± 3,68 dakikada ortalama 2,08 ± 1,27 SLN saptandı ve tespit oranı %93,75 idi. Ortalama yaş ve ortalama VKİ sırasıyla 59,7 ± 12,54 yıl ve 24,8 ± 4,09 kg/m<sup>2</sup> idi. On sekiz hastada nod pozitif hastalık vardı ve bu hastaların dördünde SLN yanlış negatifti ve T1-T2 tümörleri için daha yüksek duyarlılığa doğru bir eğilimle birlikte %77,77'lik bir duyarlılıkla sonuçlandı (%90'a karşı %62,5, p= 0,068). Evreleme oranı %10 idi. Negatif prediktif değer (NPV) ve işlemin doğruluğu sırasıyla %87,09 ve %91,11 idi.

**Sonuç:** ICG rehberliğinde SLN biyopsisi, kolon kanseri hastalarında erken (T1/T2) tümörler için nispeten daha yüksek hassasiyetle H & E evrelemesinde gözden kaçabilen metastatik lenf nodlarını belirleyebilir.

**Anahtar Kelimeler:** Sentinel lenf nodu, kolorektal neoplazmalar, İndosiyenin yeşili

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# Risk factors affecting oncological outcomes of surgical resections for middle and lower rectal cancer

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## ABSTRACT

**Objective:** In our study, it was aimed to evaluate the factors affecting oncological outcomes in resections for rectal cancer.

**Material and Methods:** Between January 2010 and December 2014, patients with rectal tumors were analyzed retrospectively. Demographic and pathological data and oncological outcomes were analyzed as disease-free survival, overall survival, and local recurrence.

**Results:** A total of 158 patients' data were obtained. Median age was 60 (22-83). Fifty-three patients were older than 65 years of age (138). Ninety-five (60%) patients were males, and 63 (40%) were females. Eighty patients (50.4%) had middle rectal, and 78 (49.6) patients had lower rectal cancer. There was no effect of tumor localization on oncological outcomes. Univariate analyses revealed the effects of age ( $p=0.003$ ), operation type ( $p<0.001$ ), nodal status ( $p<0.001$ ), malignant lymph node ratio ( $p<0.001$ ), stage of the disease ( $p<0.001$ ), distal resection margin ( $p=0.047$ ), perineural invasion ( $p<0.001$ ), lymphatic invasion ( $p<0.001$ ), venous-vascular invasion ( $p=0.025$ ), local recurrence ( $p<0.001$ ) and distant metastasis ( $p<0.001$ ) on overall survival rates. Univariate analyses revealed the effects of nodal status ( $p=0.007$ ), malignant lymph node ratio ( $p=0.005$ ), stage of the disease ( $p=0.008$ ), perineural invasion ( $p=0.004$ ) and venous-vascular invasion ( $p<0.001$ ) on disease-free survival rates. Univariate analyses revealed the effects of anastomotic leak ( $p=0.015$ ) and venous-vascular invasion ( $p=0.001$ ) on local recurrence rates.

**Conclusion:** Older age, advanced nodal status, and distant metastasis were detected as independent risk factors for overall survival. Perineural and venous-vascular invasion were detected as independent risk factors for disease-free survival. Lastly, anastomotic leak and venous-vascular invasion were detected as independent risk factors for local recurrence.

**Keywords:** Rectal cancer, rectal surgery, survival, local recurrence

## INTRODUCTION

Heald published the definition of total mesorectal excision (TME) in 1982 that started the modern rectal cancer surgery era (1). Five-year disease-free survival of 80% and 4% local recurrence rates published by Heald were spectacular (2). Heald proposed that the principle of TME is to preserve the "Holy Plan" in harmony with embryological principles and to perform resection with sharp dissection in this space (3). Additionally, evidence was presented that TME not only improved oncological outcomes but also significantly ameliorated quality of life. Significant decreases were shown in urinary and sexual autonomic dysfunctions in the postoperative period with the preservation of hypogastric nerves (4).

In the following years, the importance of reaching tumor-negative margins during rectal surgery was appreciated since adjuvant treatment, applied in cases with positive surgical margins, had not shown the effectiveness of resection with negative surgical margins (5). Furthermore, Swedish and Dutch studies revealed the importance of neoadjuvant therapy in the treatment of rectal cancer (6-8). Current guidelines emphasize the crucial role of neoadjuvant chemoradiotherapy in obtaining negative surgical margins in patients with T3 and T4 tumors detected by preoperative imaging techniques (9). Although there have been plenty of ongoing developments in rectal surgery for over a century; the main goals should be summarized as reaching tumor-free surgical margins, reducing loco-regional recurrences, increasing survival and disease-free survival times, and maintaining the quality of life are still the constant intentions (1).

In our study, it was aimed to evaluate the factors affecting oncological outcomes in resections for middle and lower rectal cancer.

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## MATERIAL and METHODS

Following the receipt of ethics committee's approval (2016-14/18), patients who underwent surgery had been followed with the diagnosis of rectal cancer in our center between January 1, 2010, and December 31, 2014 were included in the study. To make the patient groups homogeneous, patients who were operated under emergency conditions with bleeding or intestinal obstruction and/or whose resection material was not suitable for pathological examination were excluded. Likewise, cases with distant metastases and considered unresectable at the time of diagnosis or during surgery were also excluded from the study. Patients with any pathological diagnosis without adenocarcinoma were also excluded (Figure 1).

Age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, tumor location (distal rectum or middle rectum), and the existence of upfront neoadjuvant therapy history were evaluated in the preoperative period. According to the type of resections performed during the operation, the patients were divided into two groups those who underwent abdominoperineal resection (APR) or anterior resection (AR). Low anterior resection (LAR), very low anterior resection (VLAR), and Hartmann's procedures were evaluated within the AR group. In the postoperative period, the following parameters were analyzed; anastomotic leakage, dimensions of tumor (T stage), nodal status (N stage), malignant lymph node ratio (MLNR), pathological TNM staging, tumor grade, circumferential resection margin (CRM) involvement, distal resection margin (DRM) involvement, TME integrity in the pathology specimens, presence of a mucinous component in the tumor, presence of perineural invasion, presence of lymphatic invasion, presence of venous-vascular invasion, survival time, disease-free survival, local recurrence and existence of distant metastasis. For the evaluation of TME, pathology specimens were divided into three groups.

1- Complete TME: The mesorectal fascial plane has a smooth surface, and minor irregularities and defects are less than 5 mm in depth.

2- Near Complete TME: There are one or more defects greater than 5-mm deep in the mesorectum, but a macroscopic muscular layer is not observed in the defect area. Mesorectal defects are moderate.

3- Incomplete TME: Defects in the mesorectum reach the muscularis propria, and the removed mesorectal tissue is inadequate.

All procedures were performed by two experienced surgeons working in the colorectal surgery unit. All specimens were freshly evaluated by the same pathologist. In addition to TME integrity, CRM and DRM were also evaluated in the specimens. TNM classification, which was determined by the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC) in 1954 and was last revised in 2010, was used for oncological evaluation and postoperative treatment planning (10).

Patients' survival time was calculated as the period between the date of surgery and the day of death. The time to the recurrence of local and/or distant metastasis after the operation was identified as disease-free survival. Minimum and maximum follow-up periods were 23 and 81 months, respectively. Date of death data were obtained from the Turkish Ministry of Health death notification database.

Data conformity to normal distribution was evaluated with the Shapiro-Wilk test. The Kaplan-Meier test was used to evaluate survival times. Variables found to be significant in the Kaplan-Meier analysis were evaluated in terms of independent risk factors with stepwise forward Cox regression analysis. Cox regression analysis was used for the analysis of local recurrence.

## RESULTS

A total of 158 patients, 63 (40%) females, with a median age of 60 (22-83) years, were included in the study. In terms of body mass index (BMI), 47 (30%) patients were found to have a BMI of 30 and above. In terms of ASA scores, there were 44 (27.8%) patients for ASA-I, 109 (69%) patients for ASA-II, and only five (3.2%) patients for ASA-III (Table 1). Tumors of 80 patients were located in the middle rectum. Seventy-eight patients had a distal located rectal tumor. Considering the number of surgeries performed, anterior resection (AR) was performed in 119 (75.5%) patients and APR was performed in 39 (24.5%) of the patients.

Mean number of harvested lymph nodes per patient was  $14.6 \pm 9$ . Malignant lymph nodes were not detected in 94 (59.5 %) patients (N0). Thirty-four (21.5 %) patients had 1-3 malignant lymph nodes (N1). Four or more malignant lymph nodes were detected in 30 (18.9 %) patients (N2).

Mean follow-up time was  $63 (\pm 11.2)$  months. Mean overall survival time was  $63 (\pm 5.4)$  months and mean disease-free survival time was  $54.3 (\pm 2.5)$  months. There were 21 (13.2%)

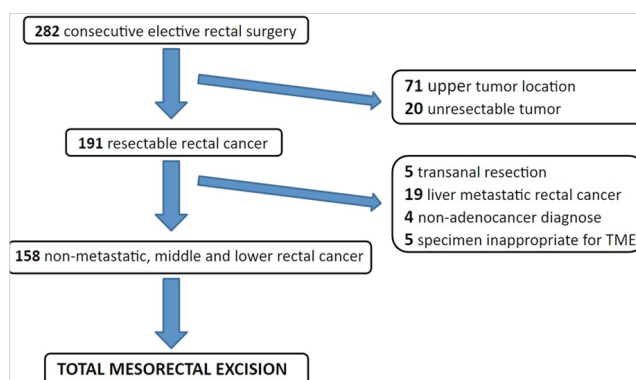


Figure 1. Flow-chart diagram.



**Table 1.** Demographics and perioperative data of the patients

	n	%
Age		
<65	105	66.5
≥65	53	33.5
Sex		
Female	63	39.9
Male	95	60.1
ASA Score		
1	44	27.8
2	109	69.0
3	5	3.2
Obesity		
BMI< 30	111	70.3
BMI≥ 30	47	29.7
Tumor Status		
0	23	14.6
1	10	6.3
2	26	16.5
3	94	59.5
4	5	3.2
Nodal Status		
0	94	59.5
1	34	21.5
2	30	19.0
Stage		
0	22	13.9
1	29	18.4
2A	43	27.2
2B	1	.6
2C	1	.6
3A	5	3.2
3B	41	25.9
3C	16	10.1

ASA: American Society of Anesthesiologists, BMI: Body mass index.

patients with local recurrence. Mean duration to local recurrence was 18.4 (± 11.2) months. There were 27 (17.1%) patients with distant metastasis. When the distribution of metastases was examined, 17 lung, 10 liver, six bone, one brain and one breast metastases were documented.

### Factors Affecting Overall Survival

Sex, ASA score, obesity, tumor level, neoadjuvant therapy, anastomotic leak, T stage of the tumor, adjuvant therapy, CRM involvement, TME integrity, tumor grade, and mucinous component of the tumor did not have a statistically significant effect on overall survival. However, older age, APR, advanced N stage, high malignant lymph node ratio (MLNR), advanced TNM stage, 10 mm or less DRM, perineural invasion, lymphatic invasion, venous-vascular invasion, local recurrence development, and distant metastases had a statistically significant effect on overall survival time. In Kaplan-Meier analysis, when the factors affecting survival time were examined

by Cox regression analysis, it was determined that older age, advanced N stage and development of distant metastases were independent risk factors (Table 2, Figures 2-4).

### Factors Affecting Disease-Free Survival

Age, sex, ASA score, obesity, tumor level, neoadjuvant therapy, anastomosis leak, surgery type, tumor T stage, adjuvant therapy, CRM involvement, DRM distance, TME integrity, tumor grade, a mucinous component of the tumor and lymphatic invasion did not have a statistically significant effect on disease-free survival. However, advanced N stage, MLNR, advanced TNM stage, presence of perineural invasion and venous-vascular invasion were statistically significant for disease-free survival. In the Kaplan-Meier analysis, when the factors affecting disease-free survival were examined by Cox regression analysis, it was determined that perineural invasion and venous-vascular invasion were independent risk factors (Table 3, Figures 5,6).

### Factors Affecting Local Recurrence

Age, sex, ASA score, tumor level, neoadjuvant therapy, type of surgery, tumor N stage, MLNR, TNM stage, adjuvant treatment, CRM involvement, DRM distance, TME integrity, tumor grade, mucinous component of the tumor, the perineural and lymphatic invasion did not show a statistically significant effect on the development of local recurrence. In the Kaplan-Meier analysis, it was found that anastomotic leak and venous-vascular invasion were factors affecting local recurrence. Moreover, Cox regression analysis revealed that both anastomotic leak and venous-vascular invasion were independent risk factors (Table 4).

## DISCUSSION

Colorectal cancer is the third most common type of cancer among men and the second most common among women worldwide (11). As a result of all the developments in rectal cancer surgery, the combination of total mesorectal excision with neoadjuvant and adjuvant approaches has become the main treatment strategy for rectal cancer today. In our study, factors affecting the oncological outcomes of resections for rectal cancer were evaluated.

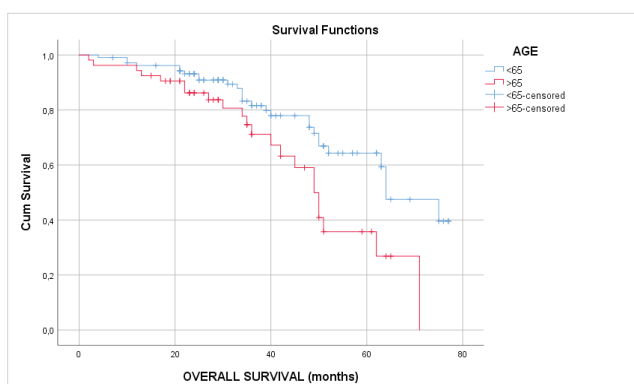
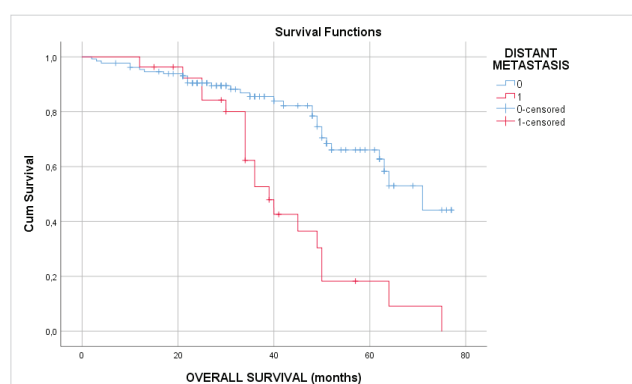
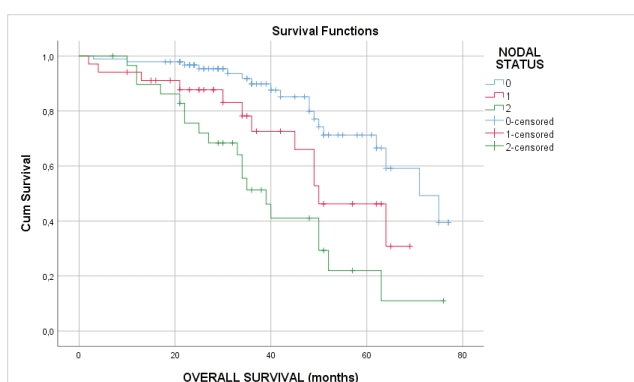
The effect of age on survival is still controversial in the literature (12,13). In our study, we observed that the survival of patients over 65 years of age decreased significantly compared to younger counterparts. Furthermore, in accordance with Tilly et al., we showed that sex had no effect on oncological outcomes (13). Yet, according to Shin et al., while the male sex was found to have a significant positive effect on survival, no effect on disease-free survival was demonstrated (14). Anatomical differences between male and female pelvises and differences in intraabdominal fat tissue distribution may have led to different results in different studies (15).



**Table 2.** Factors on overall survival

	n= 158	Univariate Analysis		Multivariate Analysis	
		Median (SEM)	Sig.	Hazard Ratio (%95 CI)	Sig.
Age					
<65	105	71.88 (3.09)	p= 0.003	1	p= 0.001
≥65	53	53.22 (3.75)		2.511 (1.455-4.333)	
Nodal Status					
0	94	76.67 (2.97)	p< 0.001	1	p= 0.002
1	34	54.45 (5.29)		2.248 (1.110-4.550)	p= 0.024
2	30	47.60 (5.26)		3.347 (1.684-6.652)	p= 0.001
Distant Metastasis					
No	122	74.89 (2.84)	p< 0.001	1	p< 0.001
Yes	36	43.26 (4.0)		3.630 (2.035-6.473)	

SEM: Standard estimated mean.

**Figure 2.** Kaplan-Meier graphics; age on overall survival (months).**Figure 4.** Kaplan-Meier graphics; distant metastasis on overall survival.**Figure 3.** Kaplan-Meier graphics; nodal status on overall survival (months).

Removal of at least 12 lymph nodes in rectal surgery is recommended for adequate oncological evaluation and proper management of adjuvant therapies (16). Our pathology results met this target recommended in the AJCC guidelines for lymph node dissection (10). In our study, advanced N stage was found to be a poor prognostic factor as expected.

After neoadjuvant chemoradiotherapy had become the standard in the treatment of locally advanced rectal cancer, the

number of lymph nodes that could be removed decreased (17). For this reason, MLNR, calculated by dividing the number of malignant lymph nodes removed by the number of all lymph nodes removed, plays a key role in determining the prognosis in these patients (18,19). In the study of Rosenberg et al., including 3026 patients, it has been shown that the MLNR may be a better tool in effectively directing decision-making compared to the current TNM evaluation (20). Since our series included patients receiving neoadjuvant therapy, MLNR was also examined in addition to the number of malignant lymph nodes. When the patients were analyzed in three different groups as 0.0-0.20 and 0.20-1.0 according to their lymph node ratio, it was shown that MLNR had a significant effect on overall survival ( $p < 0.001$ ) and disease-free survival ( $p = 0.005$ ). Higher MLNR was found to be associated with worse survival times.

Our results revealed the negative effects of the perineural invasion on overall survival and disease-free survival. Moreover, multivariate analysis showed that perineural invasion is an independent risk factor for disease-free survival. On the other hand, Kanso et al. have found no effect of perineural invasion on survivals (21). In the study of Allaix et al., the overall survival and disease-free survival times of patients with lymphatic invasion have

**Table 3.** Factors on disease-free survival

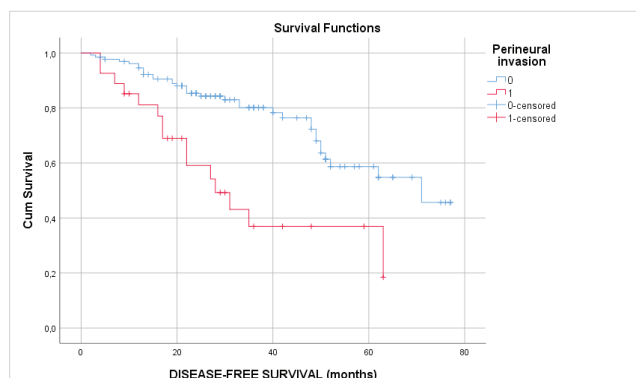
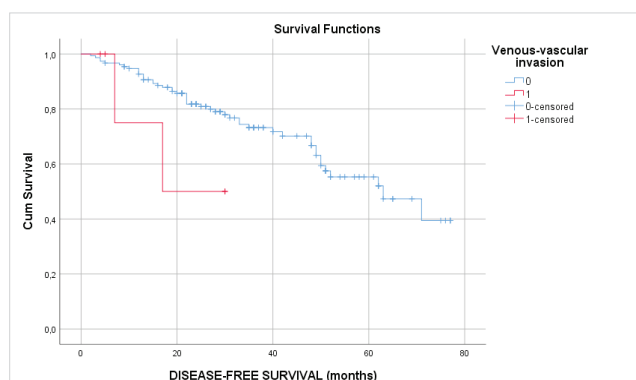
	n= 158	Univariate Analysis		Multivariate Analysis	
		Median (SEM)	Sig.	Hazard Ratio (%95 CI)	Sig.
Perineural Invasion					
No	131	58.68 (2.58)	p= 0.004	1	p= 0.010
Yes	27	35.11 (4.84)		2.263 (1.211-4.231)	
Venous-Vascular Invasion					
No	152	57.08 (2.46)	p< 0.001	1	p= 0.001
Yes	6	14.00 (3.88)		5.289 (2.061-13.570)	

SEM: Standard estimated mean.

**Table 4.** Factors on local recurrence

	n= 158	Univariate Analysis		Multivariate Analysis	
		Median (SEM)	Sig.	Hazard Ratio (%95 CI)	Sig.
Anastomotic Leak					
No	154	68.38 (1.85)	p= 0.015	1	p= 0.019
Yes	4	41.33 (11.98)		5.83 (1.34-25.40)	
Venous-Vascular Invasion					
No	152	68.88 (1.79)	p= 0.001	1	p= 0.003
Yes	6	30.67 (8.73)		6.59 (1.91-22.73)	

SEM: Standard estimated mean.

**Figure 5.** Kaplan-Meier graphics; perineural invasion on disease-free survival.**Figure 6.** Kaplan-Meier graphics; venous-vascular invasion on disease-free survival.

been found to be significantly shorter (12). They observed that lymphatic invasion was a negative risk factor for overall survival, but not for disease-free survival. Our results are similar to these.

Venous-vascular invasion is considered a negative prognostic factor although its specific relation with overall survival and disease recurrence in patients with rectal cancer is still unknown (22). While venous-vascular invasion is useful in evaluating the risk of disease recurrence, it may also give an idea about whether the patient will benefit from neoadjuvant and/or adjuvant treatments (23,24). We determined that the presence of venous-vascular invasion was an unfavorable prognostic factor for overall survival. Moreover, venous-vascular invasion was found to be an independent risk factor for disease-free survival and local recurrence.

Anastomotic leak was detected as a risk factor for local recurrence (LR) in our study. Four patients underwent low anterior resection, complicated with anastomotic leak and two (50%) of them experienced LR. Other 19 local recurrences occurred in 154 patients without anastomotic leak (12.4%). These findings correlated with a current, specific-designed study (25). Koedam et al. have proven that an anastomotic leak increases the 2.96-fold risk of local recurrence. On the other hand, there are three other current trials proposing no increased risk for LR for patients with anastomotic leaks (26-28).

Major limitation of this study is its retrospective nature. The fact that the minimum follow-up period of five years has not been completed for fully evaluating the oncological results is another

weakness of this research. However, homogenous data from a subspecialized center give this study its clinical values.

## CONCLUSION

In conclusion; older age, advanced nodal status, and distant metastasis were detected as independent risk factors for overall survival. Perineural and venous-vascular invasion were detected as independent risk factors for disease-free survival. Lastly, anastomotic leak and venous-vascular invasion were detected as independent risk factors for local recurrence.

**Ethics Committee Approval:** This study was approved by Uludağ University Faculty of Medicine Clinical Research Ethics Committee (Decision no: 2016-15/18, Date: 09.08.2016).

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - ATY, İT; Design - ATY; Supervision - Öl, ATY; Data Collection and/ or Processing - İT; Analysis and/or Interpretation - İT; Literature Search - İT, Öl-; Writing Manuscript - All of authors; Critical Reviews - Öl, ATY

**Conflict of Interest:** The authors have no conflicts of interest to declare.

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### ORJİNAL ÇALIŞMA-ÖZET

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## Orta ve distal yerleşimli rektum kanserinin cerrahi rezeksiyonlarında onkolojik sonuçlara etkili faktörler

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### ÖZET

**Giriş ve Amaç:** Çalışmamızda rektum kanseri rezeksiyonlarında onkolojik sonuçları etkileyen faktörleri değerlendirmeyi amaçladık.

**Gereç ve Yöntem:** Ocak 2010 ile Aralık 2014 tarihleri arasında rektum tümörü olan ve ameliyat edilen hastalar retrospektif olarak incelendi. Demografik ve patolojik verilerin yanında onkolojik sonuçlar, hastalısız sağkalım, genel sağkalım ve lokal nüks olarak incelendi.

**Bulgular:** Toplam 158 hasta çalışmaya dahil edildi. Ortanca yaş 60 (22-83) idi. Elli üç hasta 65 yaşından büyüktü (138). Hastaların 95'i (%60) erkek, 63'ü (%40) kadın idi. Seksen (%50,4) hastada orta, 78 (49,6) hastada alt rektum kanseri vardı. Tümör lokalizasyonunun onkolojik sonuçlar üzerinde etkisi yoktu. Tek değişkenli analizlerde sağkalıma etkili faktörler yaş ( $p=0,003$ ), operasyon tipi ( $p<0,001$ ), nodal durum ( $p<0,001$ ), malign lenf nodu oranı ( $p<0,001$ ), hastalığın evresi ( $p<0,001$ ), distal rezeksiyon sınırı ( $p=0,047$ ), perinöral invazyon ( $p<0,001$ ), lenfatik invazyon ( $p<0,001$ ), venöz-vasküler invazyon ( $p=0,025$ ), lokal nüks ( $p<0,001$ ) ve uzak metastaz ( $p<0,001$ ) olması saptandı. Tek değişkenli analizlerde hastalısız sağkalım için etkili faktörler; ileri nodal durum ( $p=0,007$ ), malign lenf nodu oranı ( $p=0,005$ ), hastalığın evresi ( $p=0,008$ ), perinöral invazyon ( $p=0,004$ ) ve venöz-vasküler invazyon ( $p<0,001$ ) olması saptandı. Tek değişkenli analizlerde lokal nükse etkili faktörler olarak anastomoz kaçacağına ( $p=0,015$ ) ve venöz-vasküler invazyonun ( $p=0,001$ ) olması saptandı.

**Sonuç:** İleri yaş, ileri nodal durum ve uzak metastaz gelişmesi genel sağkalım için bağımsız risk faktörleri olarak saptandı. Perinöral ve venöz-vasküler invazyon hastalısız sağkalım için bağımsız risk faktörleri olarak tespit edildi. Son olarak anastomoz kaçacağı gelişmesi ve venöz-vasküler invazyon olması lokal nüks için bağımsız risk faktörleri olarak tespit edildi.

**Anahtar Kelimeler:** Rektum kanseri, rektum cerrahisi, sağkalım, lokal nüks

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# Hospital teaching status and patient outcomes in intestinal obstruction surgery: A comparative analysis

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## ABSTRACT

**Objective:** Surgery at large teaching hospitals is reportedly associated with more favourable outcomes. However, these results are not uniformly consistent across all surgical patients. This study aimed to assess potential disparities in clinical outcomes by hospital type for patients with intestinal obstruction.

**Material and Methods:** 2018 NIS was queried for all adult non-elective admissions for intestinal obstruction. Hospitals were classified as either small-medium non-teaching hospitals or large teaching hospitals. Multivariate regression analyses were used to assess the association between hospital type and inpatient mortality, access to surgery, admission duration, non-home discharges, hospital costs, and postoperative complications.

**Results:** After adjustments, admission to large teaching hospitals was not associated with a reduction in inpatient mortality (AOR= 0.73; 95% CI= 0.41-1.31; p= 0.29), lower likelihood of surgery (AOR= 0.93; 95% CI= 0.58-1.48; p= 0.76) or increased chance of early surgery (p= 0.97). Patients admitted to large teaching hospitals had shorter hospital stays (p= 0.002) and were less likely to be discharged to other acute care hospitals (AOR= 0.94; 95% CI= 0.80-0.94; p= 0.04). Admission to large teaching hospitals was not associated with a reduction in perioperative complications (AOR= 1.04; 95% CI= 0.80-1.28; p= 0.91) or significantly higher hospital costs (mean increase= 1518; 95% CI= 1891-4927; p= 0.38).

**Conclusion:** Admission to large teaching hospitals does not necessarily result in better patient outcomes. Merely considering the teaching status of the hospital in isolation cannot explain the diverse outcomes observed for this condition.

**Keywords:** Intestinal obstruction, hospital teaching status, inflammatory bowel diseases, bands and adhesions

## INTRODUCTION

Intestinal obstruction surgery and care is often an emergency with multifactorial etiopathogenesis, including malignant bowel obstruction (MBO); and its management is complex and costly. The emergence of new technologies and treatments has further increased the complexity and cost of care (1,2). Patient outcomes, as with any other surgical procedure, can vary substantially across hospital types. For instance, mortality rates have been reported to differ up to fourfold between hospitals for patients undergoing cancer surgery (3).

Despite evidence suggesting superior outcomes among patients admitted to large teaching hospitals (LTHs) (4), patients often worry about having a resident, intern, or medical student involved in their care, fearing that this might jeopardize their safety or compromise positive surgical outcomes. Previous reports have indicated that up to 60% of surgical patients lack confidence in the level of training of surgical residents, and up to 11% of surgical patients do not want residents involved in their care (5). Additionally, teaching hospitals (THs) are often considered more expensive than community hospitals (6,7), and intestinal obstruction care is already a significant financial burden to patients and payers (8,9). Therefore,

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it is important to investigate whether patient outcomes differ between teaching and non-teaching hospitals (NTHs).

The present study endeavored to explore four critical inquiries using national-level data. Primarily, we aimed to determine the extent to which mortality rates for intestinal obstruction diverge between THs and their non-teaching counterparts. Secondly, we aimed to investigate the variances in surgical accessibility, duration of hospitalization, total hospital expenses, and discharge status between teaching and NTHs. Thirdly, we aimed to examine whether postoperative complications were less prevalent in THs relative to NTHs. Finally, we endeavored to identify any autonomous predictors of unfavorable outcomes for patients admitted to LTHs.

## MATERIAL and METHODS

### Data Source

We conducted a retrospective cohort study using the 2018 Nationwide Inpatient Sample (NIS) database. NIS serves as a comprehensive collection of all inpatient stays across the United States (U.S.). NIS contains a collection of clinical and resource utilization information that is typically included in discharge abstracts. Given its large sample size, NIS offers a unique opportunity for a detailed investigation of medical conditions, treatments, and patient groups. Additionally, NIS encompasses data from 47 states and the district of Columbia, effectively representing over 97% of the U.S. populace and almost 96% of discharges from community hospitals (10). It provides information on all hospital stays, regardless of the expected payer. Notably, NIS includes Medicare advantage patients, a cohort that is frequently absent from Medicare claims data but accounts for up to 30% of Medicare beneficiaries (11).

### Ethical Consideration

The U.S. Agency for Healthcare Research and Quality (AHRQ) designs and maintains NIS through its Healthcare Cost and Utilization Project (HCUP), ensuring compliance with HIPAA (The Health Insurance Portability and Accountability Act of 1996) and the removal of 16 direct patient- and hospital-level identifiers as specified in the privacy rule for all HCUP databases. The use of limited data sets such as the NIS under HIPAA does not require review by an institutional review board (IRB) (12,13).

### Inclusion Criteria and Study Variables

All adult non-elective admissions for intestinal obstruction were identified using the International Classification of Diseases, Tenth Revision, Clinical Modification/Procedure coding system (ICD-10-CM/PCS) and sub-classified into malignant bowel obstruction (MBO) and obstruction caused by non-malignant

factors (NMFs). Study variables encompassed patients' demographic information such as age, sex, race, and median annual income. Hospitals were classified as small-medium non-teaching hospitals (SMNTHs) and LTHs. A hospital is classified as a teaching hospital if it meets any of the following criteria: approval for residency training by the Accreditation Council for Graduate Medical Education (ACGME), membership in the Council of Teaching Hospitals (COTH), or a full-time equivalent interns and residents to beds ratio of 0.25 or higher. Hospital size categories are based on the number of beds and are customized to the hospital's region, location, and teaching status. To adjust for the burden of chronic medical conditions, the Charlson comorbidity index (CCI) was utilized.

### Outcome Measures

Primary outcome was inpatient mortality. Secondary outcomes were rate and time to procedures, hospital length of stay (LOS), rates and odds of non-home discharge (discharge to a skilled nursing home and other acute care facilities), mean total hospital charges, and postoperative complications. Prolonged LOS was defined as a diagnosis-specific length of stay above the median (7-12 days) reported in previous studies (14,15) or in the top decile of the index study population.

### Statistical Analysis

Stata, v.17.0BE (StataCorp LLC, College Station, Texas, USA) was used for statistical analysis. Unadjusted odds ratios (ORs) were calculated for the primary outcome using univariate logistic regression analyses, incorporating all variables and comorbidities listed in Table 1. Variables with p-values less than 0.1 were selected for a subsequent multivariate logistic regression model. Through a thorough review of the existing literature, established confounders of primary and secondary outcomes such as anemias, deconditioning and frailty, metabolic disorders, higher CCI scores, and concurrent bowel gangrene were identified and added to the multivariate regression. Frailty was defined as a score of 3 or more using the Johns Hopkins Adjusted Clinical Groups clusters (16,17). Fisher's exact test was used to compare proportions, while Student's t-test was used for continuous variables. The log-rank test was utilized to calculate p-values. Significance level for multivariate analysis was set at p-values less than 0.05. Categorical and continuous variables were reported as proportions or mean with standard deviation, while regression outcomes were reported as adjusted odds ratios (AORs) or  $\beta$  coefficients with 95% confidence intervals (CIs). To account for confounders in the secondary outcomes, we used multivariate logistic and linear regression models that included all confounders identified from the literature and all variables listed in Table 1.

**Table 1.** Patient and hospital characteristics by hospital teaching status

	SMNTHs, n= 19.243 (72.1%)	LTHs, n= 7.446 (27.9%)	p
Patient characteristics			
Female (%)	47.1	48.3	0.73
Race/Ethnicity (%)			0.36
White	72.6	70.8	
Black	14.1	16.2	
Hispanic	9.4	8.1	
Asian or Pacific Islander	1.6	2.1	
Native American	0.5	0.6	
Other	1.8	2.2	
Mean age (years)	63.6 ± 0.3	61.6 ± 0.5	<0.001
Charlson comorbidity index score (%)			<0.001
0	36.8	33.2	
1	22.4	19.9	
2	15.3	15.7	
≥3	25.5	32.0	
Median annual income in patient's zip code, US\$ (%)			<0.001
1-45.999	32.0	30.6	
46.000-58.999	29.1	24.9	
59.000-78.999	22.0	24.5	
≥79.000	17.0	20.0	
Insurance type (%)			0.04
Medicare	62.2	58.7	
Medicaid	12.7	13.7	
Private including HMO	21.8	25.0	
Uninsured	3.3	2.6	
Surgery <24 hr after admission (%)	1.7	1.9	0.61
Hospital region (%)			<0.001
Northeast	13.8	13.7	
Midwest	23.7	29.7	
South	45.6	33.5	
West	16.9	23.1	
Hospital bed size (%)			0.004
Small	13.5	22.6	
Medium	32.1	33.1	
Large	54.4	44.3	
Weekend admission (%)	27.9	28.4	0.71
Malignant bowel obstruction (%)	64.9	35.1	
Large bowel cancers	36.5	27.5	0.17
Small bowel cancers	2.0	2.5	0.82
Rectosigmoid cancers	12.8	20	0.15
Anal cancers	0.7	2.5	0.25

**Table 1. (continue)** Patient and hospital characteristics by hospital teaching status

	SMNTHs, n= 19.243 (72.1%)	LTHs, n= 7.446 (27.9%)	p
Endometrial cancer	2.0	6.3	0.10
Pancreatic cancer	12.8	17.5	0.35
Gastric cancer	2.0	3.8	0.43
Other cancers <sup>†</sup>	31.2	22.4	0.15
Non-malignancy-related causes (%)	72.3	27.7	
Strangulated hernias	0.5	0.1	0.08
Mechanical obstruction <sup>‡</sup>	0.9	0.5	0.13
Inflammatory bowel disease	30.7	39.1	0.10
Radiation	0.03	0.1	0.13
Adhesions and bands	2.4	5.5	0.06

SMNTHs: Small-medium non-teaching hospitals, LTHs: Large teaching hospitals, MBO: Malignant bowel obstruction, NMFs: Non-malignancy-related factors obstruction, HMO: Health maintenance organization.

All proportions are reported in percentages of the total study population except for NMFs and MBO variables where proportions are reported as percentages of NMFs and MBO subpopulations respectively.

All p values are rounded up and reported in two decimals.

<sup>†</sup>: Defines less common primary tumors like ovarian, gastrointestinal stromal tumors, splenic, uterine, and prostatic cancers, and other secondary neoplasia with peritoneal or retroperitoneal involvement e.g., metastatic breast cancer or melanoma causing bowel obstruction.

<sup>‡</sup>: Volvulus, intussusception, gallstone ileus, and impaction.

## RESULTS

### Baseline Patient and Hospital Characteristics

There were 26,690 adult admissions for intestinal obstruction included in the study. Of these, 4.3% (1,140) were attributed to MBO, while 95.7% (25,550) were caused by NMFs. Large bowel cancers were the most frequently observed malignancies associated with bowel obstruction in both teaching and non-teaching hospitals, with rates of 36.5% and 27.5%, respectively. Inflammatory bowel diseases (IBDs) were the most prevalent NMFs causing bowel obstruction in both THs and NTHs, with rates of 10.7% and 9.1%, respectively. The study population was predominantly admitted to SMNTHs (72.1%) as opposed to LTHs (27.9%). Table 1 outlines the baseline demographic, socio-economic, and clinical characteristics of the study population by hospital type.

Average age in the study population was 63 years (SD 0.3). The primary payer for most patients was Medicare, with private insurers being the second most common. More than half of the patients resided in a zip code with an annual median income ranging from \$1 to \$58,999.

### Inpatient Mortality by Hospital Type

About 365 (1.4%) deaths were recorded in the study population. Of these, 95.9% (350) were recorded among the NMFs population. Mortality rates were similar for SMNTHs and LTHs (1.4% and 1.2%, respectively). Similar results were obtained when mortality was compared among NMFs and MBO subpopulations.

Compared to patients who had surgery during index hospitalization, overall mortality was higher among patients managed conservatively (1.2% vs. 0.2%). However, mortality rates among patients managed surgically were slightly higher at SMNTHs compared to LTHs (1.6% vs 1.1%, respectively).

One point two percent of the patients who were admitted at SMNTHs and had surgery within the first 24 hours died during the index hospitalization. No deaths were recorded for similar patients in LTHs. About 2.6% of the patients who had initial conservative management (time from admission to surgery of five days or more) died during the index admission. All in-hospital mortality following initial conservative management in this study was recorded in SMNTHs.

Patients who stayed at LTHs for more than 12 days had a slightly higher mortality rate (5.6%) compared to those admitted at SMNTHs, where the rate was 5.2%. After adjustments for patient and hospital-level factors, admission to LTHs was not associated with a statistically significant reduction in the odds of in-hospital mortality (AOR= 0.73; 95% CI= 0.41-1.31; p= 0.29) (Table 2). A similar finding was obtained when regression models were built for both NMFs and MBO subpopulations. Independent predictors of increased in-hospital mortality were found to include: a higher Charlson comorbidity index, concurrent bowel gangrene, older age, and the presence of anemias (Table 2). Performing surgery within 24 hours of admission or after initial conservative management, the presence of metabolic disorders, and frailty were not associated with a statistically significant change in the odds of mortality in this study.

**Table 2.** Adjusted odds of mortality by hospital size/teaching status

Variables	AOR	Standard error	p	(95% CI)
In-hospital mortality				
Large teaching hospital	0.739	0.214	0.298	0.42-1.31
Weekend admission	1.305	0.360	0.335	0.76-2.24
Age	1.041	0.012	0.001	1.02-1.07
Female sex	1.181	0.311	0.529	0.70-1.98
Median annual income in patient's zip code, US\$				
46.000-58.999	1.005	0.332	0.988	0.53-1.92
59.000-78.999	0.706	0.258	0.342	0.35-1.43
≥79.000	0.649	0.286	0.327	0.27-1.54
Race				
Black	1.012	0.421	0.98	0.45-2.29
Hispanic	0.966	0.413	0.94	0.42-2.24
Higher Charlson index	1.249	0.062	<0.001	1.13-1.38
Early surgery (<24 hrs of admission)	1.064	1.594	0.967	0.06-20.09
Prolonged LOS (≥12 days)	1.524	0.73	0.38	0.60-3.90
Any surgery	1.267	0.705	0.671	0.43-3.77
Delayed surgery (≥5 days from admission)	1.708	1.981	0.644	0.18-16.59
Bowel gangrene <sup>Φ</sup>	27.725	11.405	<0.001	12.38-62.11
Anemias	2.151	0.576	0.004	1.27-3.64
Frailty	1.364	1.104	0.701	0.28-6.67

LOS: Length of hospital stay, AOR: Adjusted odds ratio, CI: Confidence interval.  
<sup>Φ</sup>: Including bowel damage with or without peritonitis.

### Rate and time to Procedures

Of the study population, 5.1% (1.361) had at least one surgical procedure performed in the index admission. The number of surgeries for bowel obstruction was higher in SMNTHs than in LTHs (984 vs. 377). A total of 44 patients in the MBO subpopulation had surgery to relieve bowel obstruction (24 in non-teaching and 20 in LTHs). 1.317 surgeries (960 vs. 354 in SMNTHs and LTHs respectively) were performed in the NMFs subpopulation. Overall, bowel de-rotation and decompression via colonoscopy or open surgery made up the bulk of all procedures performed (76.5%). Others included: Bowel resection and anastomosis (6.6%), Hernia repair (6.6%), Adhesiolysis (7%), and Hartmann's colostomy (3.3%).

The unadjusted odds of any procedure in LTHs were: 0.94 in the overall study population (95% CI= 0.72-1.22; p= 0.64), 1.51 among the MBO subpopulation (95% CI= 0.40-5.74; p= 0.55), and 0.92 in the NMFs subgroup (95% CI= 0.70-1.21; p= 0.57). After adjustments, admission to LTHs was not associated with a statistically significant reduction in the odds of surgery (AOR= 0.93; 95% CI= 0.58-1.48; p= 0.76). However, admission lasting ≥12 days was associated with a significant increase in the likeli-

hood of surgery, irrespective of hospital size or teaching status (AOR= 3.14; 95% CI= 1.58-6.20; p= 0.001).

Mean time to surgery in the total study population was 3.61 ± 0.26 days (3.71 ± 0.32 vs. 3.33 ± 0.45 days for SMNTHs and LTHs respectively). In the MBO population, mean time to surgery was 3.60 ± 1.93 vs. 0.75 ± 0.22 days in SMNTHs and LTHs respectively. In the NMFs subgroup, patients had similar times from admission to surgery across both hospital types (3.71 ± 0.32 vs. 3.49 ± 0.47 days). After adjustments, admission to LTHs was not associated with a significant increment in the chance of early surgery (AOR= 1.01; 95% CI= 0.64-1.57; p= 0.97).

### Length of Hospital Stay

Mean LOS in the total study population was 4.5 ± 0.1 and 5.2 ± 0.2 for SMNTHs and LTHs respectively. Among patients who had any surgery during the index admission, at least 380 and 199 patients (38.6% and 52.7%) respectively, were admitted for longer than six days in both hospitals. After multivariable adjustments, patients admitted to LTHs were likely to be discharged half to one day earlier than those admitted to SMNTHs (β= 0.54; 95% CI= 0.21-0.88; p= 0.002). Similar results were obtained for the NMFs subgroup (β= 0.48; 95% CI= 0.14-0.83; p= 0.006).

However, admission for MBO was found to significantly affect LOS in LTHs ( $\beta = 1.58$ ; 95% CI= 0.21-0.88;  $p = 0.03$ ).

Initial conservative management (first five days of admission) was found to significantly increase LOS in LTHs ( $\beta = 9.15$ ; 95% CI= 6.82-11.47;  $p < 0.001$ ). When adjusted for the effect of delayed surgery, patients admitted to LTHs were found to stay at least 0.59 days shorter than those admitted to SMNTHs. Performing surgery within the first 24 hours of admission did not significantly reduce overall LOS for patients admitted to LTHs ( $\beta = 1.71$ ; 95% CI= 0.22-3.20;  $p = 0.02$ ). Factors found to independently increase LOS were the presence of anemias ( $p < 0.001$ ), concurrent bowel gangrene at admission ( $p < 0.001$ ), and a higher Charlson index ( $p \leq 0.001$ ).

### Rates of Non-Home Discharges

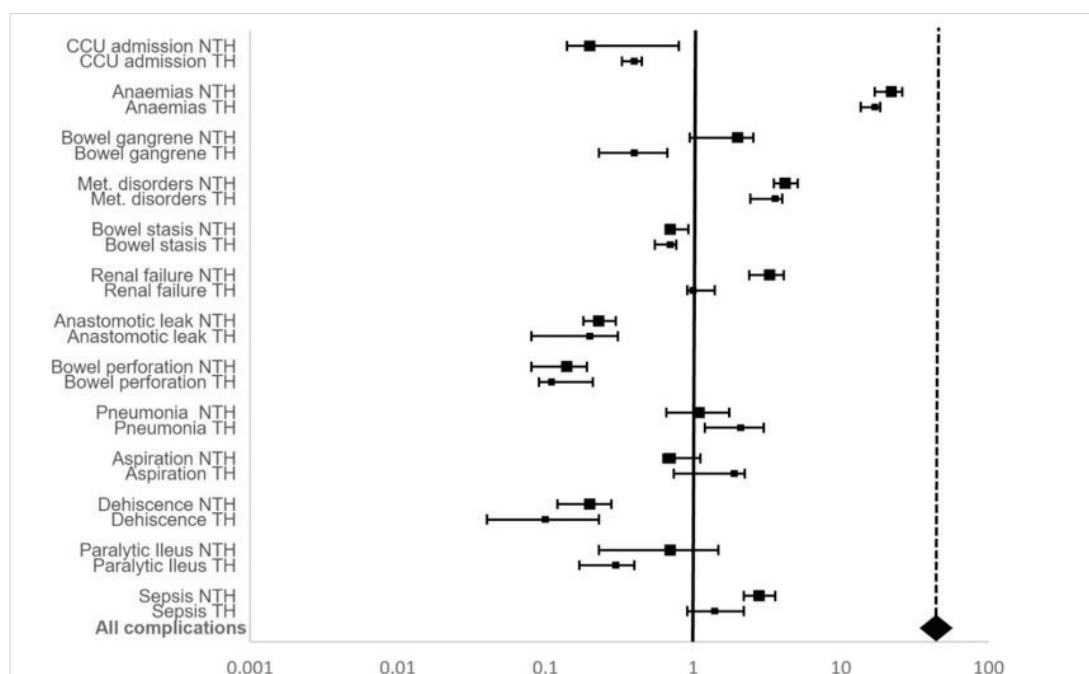
About 8.4% of the study population were admitted from other acute care hospitals to small-medium non-teaching hospitals compared to 14.4% admitted into LTHs. Twenty-five percent of the overall study population was discharged to another acute care hospital, home health care, or skilled nursing home from small-medium non-teaching hospitals compared to 9.9% from LTHs. Routine home discharge rates were 64.9% in SMNTHs and 64.6% in LTHs.

After adjustments, admission into a large teaching hospital was associated with a 6% reduction in the likelihood of non-home discharge (AOR= 0.94; 95% CI= 0.80-0.94;  $p = 0.04$ ). Other factors found to independently increase the odds of non-home discharges included higher Charlson comorbidity index, older age, white race, anemias, concurrent bowel gangrene at admission, physical frailty, previous admission from an acute care hospital, and prolonged hospital stay ( $p < 0.001$ ).

### Postoperative Complications

Figure 1 summarizes the frequency of perioperative complications in the study by hospital teaching status. At least 60.1% of the total study population experienced one complication in the index admission while 21% of the study population developed more than one complication in the index admission. Anemias were found to be the most prevalent complication (39%) and were more common in SMNTHs (22% vs. 17%). Critical care unit admissions and incidences of nosocomial and aspiration pneumonia were more prevalent in the LTHs (0.4%, 2.1%, and 1.9%, respectively), while the development of sepsis, renal failure, wound dehiscence, and metabolic disorders was found to be more prevalent in the SMNTHs.

The unadjusted odds of developing any complication among patients admitted to LTHs was 1.06 ( $p = 0.55$ ). After multivariable



**Figure 1.** Frequency of perioperative complications by hospital type.

NTH: Non-teaching hospital, TH: Teaching hospitals, CCU: Critical care unit, Met. disorders: Metabolic disorders, Aspiration: Aspiration pneumonia.

Pneumonia refers to patients who acquired nosocomial pneumonia in the index hospitalization.

Dehiscence refers to postoperative wound breakdown.



adjustment, admission to a large teaching hospital was not associated with a significant reduction in the likelihood of perioperative complications (AOR= 1.04; 95% CI= 0.80-1.28;  $p= 0.91$ ).

### Total Hospital Costs

Mean hospital charge for patients admitted to SMNTHs was \$36,534.43 while patients admitted to LTHs paid \$40,498.6 on average. Patients admitted to the MBO subgroup paid more on average compared to patients admitted to the NMFs subpopulation (\$42,399.1 vs. \$37,435.05). Compared to patients managed conservatively, patients who had any surgery in the index admission paid more in mean hospital expenses (\$90,496.71 vs \$34,863.25). Any complication was associated with a mean increase of \$38,294 in total hospital expenses.

When adjusted for any surgery, complications, prolonged hospital stay ( $\geq 12$  days), delayed surgery ( $\geq 5$  days from admission), early surgery (within 24 hours of admission), and other patient and hospital-level variables, admission to a large teaching hospital was not associated with significantly higher hospital charges (mean increase= 1518; 95% CI= 1891-4927;  $p= 0.38$ ). Factors found to independently increase total hospital charges included high Charlson comorbidity index, any complication such as anemia, pneumonia, or bowel gangrene, black race, higher median income in the patient's ZIP code ( $\geq \$59,000$ ), and prolonged hospital stay ( $p < 0.001$ ). Performing surgery within 24 hours of admission or initial conservative management (first five days of admission) did not significantly reduce or increase mean hospital expenses for patients admitted to LTHs.

### DISCUSSION

The results of this study suggest that there is no significant difference in the odds of mortality for patients with intestinal obstruction between SMNTHs and LTHs. Previous research suggesting that teaching status independently improves mortality odds contrasts with these findings (18-20). Recent advances in technology and medical knowledge have made it possible for non-teaching hospitals to provide care that is similar in quality to that of THs (21). Additionally, NTHs may have a smaller patient load per hospital, which could allow for more personalized care and similar patient outcomes.

Empirical evidence has demonstrated that bowel gangrene at admission, low hemoglobin levels, late presentation, postoperative complications, leukocytosis, elevated urea, metabolic disorders, and comorbidity were independent predictors of postoperative mortality in intestinal obstruction (22,23). Despite accounting for these factors in the index study, it was not possible to establish a meaningful connection between hospital teaching status and improved mortality rates. This suggests that the outcomes attributed to teaching status in prior studies may have been influenced by other patient factors that were not taken into consideration.

Admission to LTHs did not significantly reduce the odds of surgery or increase the chance of early surgery compared to SMNTHs. These findings indicate that THs may not necessarily provide better access to surgery for patients with intestinal obstruction. The comparable odds of surgery between LTHs and SMNTHs imply similar access to surgical care for patients irrespective of hospital teaching status. From the results, both types of hospitals can provide timely surgical care for patients with intestinal obstruction. However, mean time to surgery was slightly longer in SMNTHs. This alludes to longer waiting times for surgical procedures or different criteria for determining the need for surgery at SMNTHs. Likewise, comparable conservative care outcomes between the two hospital types imply no particular advantage for patients receiving conservative surgical care in teaching hospitals.

Patients admitted to LTHs were discharged half to one day earlier than those admitted to SMNTHs. One possible explanation for this difference in LOS could be the quality of care provided in THs or access to more resources and expertise than in NTHs, leading to shorter hospital stays. However, the study also found that admission into LTHs for MBO significantly increased LOS likely due to the complexities of treating other problems related to the underlying malignancy (24,25). Taken together, these findings suggest that patients with intestinal obstruction may benefit from early home discharges in LTHs when surgery is not delayed. However, the benefits may not extend to patients with more severe causes of intestinal obstruction.

Patients admitted to LTHs were 6% more likely to be discharged to their homes, which may reflect the higher level of expertise or intensive care available in these hospitals. The study also highlights the need to identify and address factors that increase the likelihood of non-home discharge, such as older age, comorbidities, and prolonged hospital stays in NTHs (26).

The results suggest that the higher prevalence of certain complications in LTHs, such as nosocomial and aspiration pneumonia, may reflect the higher acuity of patients and the greater use of critical care resources in these hospitals. On the other hand, the higher prevalence of sepsis, renal failure, wound dehiscence, and metabolic disorders in SMNTHs may reflect the challenges of managing complex patients in resource-limited settings. Patient factors such as age, comorbidities, and severity of illness may be more important predictors of perioperative complications than hospital teaching status. Future research could explore the relative contributions of patient and hospital factors to perioperative outcomes for patients with intestinal obstruction.

The current study is not without limitations. One noteworthy constraint pertains to the study's retrospective and predefined data source, which rendered the authors incapable of con-

trolling for all possible confounding variables. Also, the research only examined the prevalence of the most recognized causes of intestinal obstruction. Furthermore, the sample only comprised patients who had undergone surgery for intestinal obstruction, thereby constraining the generalizability of the findings to other surgical patients.

## CONCLUSION

This study concludes that there are no notable differences in the quality-of-care indicators, including access to care and clinical outcomes, for intestinal obstruction between SMNTHs and LTHs. Teaching status alone does not independently improve the outcomes for this patient population. Both types of hospitals can provide timely surgical care for patients with intestinal obstruction, with comparable outcomes. Patients admitted to LTHs may benefit from earlier discharge and a higher likelihood of home discharge. However, the benefits may not extend to patients with more severe causes of intestinal obstruction. Drawing upon the preceding discussion, it is advisable to encourage patients who share similar surgical conditions to promptly seek care at the hospitals located closest to their vicinity rather than postponing hospital visits in preference for specific academic medical centers.

**Ethics Committee Approval:** This study was approved by JOS University Teaching Hospital Institutional Health Research Ethical Committee (Decision no: JUTH/DCS/ADM/127/XIX/5111, Date: 08.03.2023).

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### ORJİNAL ÇALIŞMA-ÖZET

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## Bağırsak tıkanıklığı cerrahisinde hastanenin akademik durumu ve hasta sonuçları: Karşılaştırmalı bir analiz

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### ÖZET

**Giriş ve Amaç:** Büyük eğitim hastanelerindeki cerrahinin daha olumlu sonuçlarla ilişkili olduğu bildirilmektedir. Bununla birlikte, bu sonuçlar tüm cerrahi hastalarda aynı şekilde tutarlı değildir. Bu çalışmada, bağırsak tıkanıklığı olan hastalar için hastane tipine göre klinik sonuçlardaki olası farklılıkları değerlendirmeyi amaçladık.

**Gereç ve Yöntem:** 2018 NIS, bağırsak tıkanıklığı nedeniyle başvuran ve elektif olmayan tüm yetişkinlerde sorgulandı. Hastaneler, küçük-orta eğitim dışı hastaneler veya büyük eğitim hastaneleri olarak sınıflandırıldı. Hastane tipi ile yatan hasta mortalitesi, cerrahiye erişim, yatış süresi, evde olmayan taburculuklar, hastane maliyetleri ve postoperatif komplikasyonlar arasındaki ilişkiyi değerlendirmek için çok değişkenli regresyon analizleri kullanıldı.

**Bulgular:** Büyük eğitim hastanelerinde tedavi, yatan hasta mortalitesinde bir azalma (AOR= 0,73; %95 CI= 0,41-1,31; p= 0,29), daha düşük ameliyat olasılığı (AOR= 0,93; %95 CI= 0,58-1,48; p= 0,76) veya artmış erken cerrahi şansı (p= 0,002) ile ilişkili değildi. Büyük eğitim hastanelerine kabul edilen hastaların hastanede kalış süreleriye daha kısaydı (p= 0,002) ve diğer akut bakım hastanelerine taburcu edilme olasılıkları daha düşüktü (AOR= 0,94; %95 CI= 0,80-0,94; p= 0,04). Büyük eğitim hastanelerine kabul, perioperatif komplikasyonlarda bir azalma (AOR= 1,04; %95 CI= 0,80-1,28; p= 0,91) veya önemli ölçüde daha yüksek hastane maliyetleri (ortalama artış= 1518; %95 CI= 1891-4927; p= 0,38) ile ilişkili bulunmadı.

**Sonuç:** Büyük eğitim hastanelerine kabul, mutlaka daha iyi hasta sonuçlarıyla sonuçlanmaz. Hastanenin eğitim durumunu tek başına ele almak, bu durum için gözlemlenen farklı sonuçları açıklayamaz.

**Anahtar Kelimeler:** Bağırsak tıkanıklığı, hastane akademik durumu, enflamatuvar bağırsak hastalıkları, bantlar ve adezyonlar

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# Evaluation of breast cancer awareness in female patients diagnosed with schizophrenia

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## ABSTRACT

**Objective:** In this study, it was aimed to investigate the awareness of female patients diagnosed with schizophrenia about breast cancer and to evaluate whether there was a difference in this awareness between the control group and individuals diagnosed with schizophrenia. Secondly, the frequency of breast cancer screenings of patients diagnosed with schizophrenia and the control group was compared.

**Material and Methods:** Individuals between 18 and 65 years of age who were literate and voluntarily gave informed consent to participate after being informed about the study were included. The research study group comprised of 82 individuals, 35 patients with schizophrenia and 47 healthy individuals. Patients with schizophrenia were required to have no clinically severe disease picture (CGI-S score of 3 or below). Individuals were given the Breast Cancer Awareness Scale (B-CAS) to fill in.

**Results:** The patient group had less awareness of breast cancer than the control group; conversely, they faced more barriers in breast cancer screening. The number of those who stated that they did not know about breast cancer early diagnosis methods was higher in the patient group than in the control group. In the evaluation of health attitudes toward breast cancer, it was found that the healthy control group was better than the patient group in performing regular breast self-exam.

**Conclusion:** Educating individuals with schizophrenia about the signs and symptoms of cancer and adapting healthcare systems to facilitate rapid and early cancer diagnosis may result in cost-effective and applicable cancer control strategies for curable cancers.

**Keywords:** Breast cancer, schizophrenia, awareness

## INTRODUCTION

Evidence from epidemiological studies suggests that compared to the general population, mental illness is associated with a higher risk of and worse outcomes for cancer (1-4). Although an increased risk of cancer-related mortality has been found especially in individuals with severe mental illnesses such as schizophrenia, this group has been relatively neglected in cancer-related healthcare research (1,3,5,6). Moreover, to reduce mortality rates in schizophrenia patients, many treatment guidelines in recent years recommend monitoring cardiovascular and metabolic health, while there is no clear recommendation for cancer screening (2).

It has been suggested in the literature that several factors play a role in the increased risk of cancer in mental illnesses and the detection of more negative consequences: genetic factors, less use of preventive care in individuals with mental illnesses (e.g., cancer screening), behavioral factors (e.g., higher smoking rates, unhealthy lifestyle behaviors), postponing or not adhering to cancer treatment as a result of impaired compliance due to disease-related characteristics, side effects of antipsychotic drugs, high prolactin levels, both the risks associated with mental illness and high obesity caused by antipsychotic drug side effects, diabetes mellitus, cardiovascular comorbidity prevalence, nulliparity, low breastfeeding incidence, insufficient patient-physician interaction (1,7).

At this point, the increased risk of cancer in mental illnesses and the scarcity of cancer screening; one of the factors associated with more negative outcomes, are important issues to be considered. Screening is one of the best public health policies as it effectively reduces cancer incidence and mortality and creates early diagnosis-treatment options. Patients diagnosed with schizophrenia and other psychotic disorders are less likely to participate in cancer screenings, and studies

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show that the likelihood of screening for breast cancer is about half of the general population (4,8). The limited participation of patients diagnosed with schizophrenia in screening for breast cancer may cause the disease to be undetected in the early stages (9). The fact that women with a psychiatric diagnosis generally receive breast cancer diagnosis and treatment at a later stage than breast cancer patients without a psychiatric diagnosis also shows that this group is not screened to the same extent as other women (3,10). Whatever the reason, 15% of cancer deaths can be attributed to the interaction between breast cancer and serious mental illness (11).

Identifying the factors that affect the low participation of patients with schizophrenia in cancer screening can increase the benefit of these patients from screening services.

Numerous barriers to participation in cancer screening have been identified in this group. Among these factors are loss of interest and motivation specific to patients with schizophrenia, lack of a primary care physician that they follow up regularly, lack of general knowledge of the patient about screening programs, appointments given for a long time, absence of annual reminders, lack of optimal cooperation between the patient and healthcare professionals, diagnostic overshadowing, against patients with schizophrenia prejudiced attitude of health personnel (12,13). Among the reasons for the lower rates of cancer screening in patients with schizophrenia are the problems in predicting health risks in these patients or their cognitive symptoms (for example, impaired attention and executive function) that make it difficult to plan effectively forward, and the lack of awareness of the benefits of screening due to their lack of awareness of cancer (6,12). Increasing awareness of cancer is considered the first step in the fight against cancer. Low awareness of breast cancer and barriers to accessing health services are considered to be important causes of delay in screening/treatment (4,14). Because beliefs about cancer and cancer screenings are directly related to the behavior of participating in cancer screenings, physicians should improve their knowledge about cancer and cancer screening, especially in patients with schizophrenia, and eliminate misunderstandings (12,15).

This study, considering the high prevalence of breast cancer and its promising prognosis when diagnosed early, aimed to investigate the awareness of female patients diagnosed with schizophrenia about breast cancer and to evaluate whether there is a difference in this awareness between the control group and individuals diagnosed with schizophrenia (3,8). Secondly, in our study, the frequency of breast cancer screenings of schizophrenia patients and the control group is compared. We hypothesize that individuals diagnosed with schizophrenia have less awareness about and fewer breast cancer screenings. It is believed that evaluating the awareness of

patients will contribute to the literature in understanding the current situation and developing the necessary interventions.

## MATERIAL and METHODS

This research was conducted in the Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital, Psychiatry Clinic and Community Mental Health Center (CMHC), and the Family Medicine Clinic of Ankara Training and Research Hospital. Patients diagnosed with schizophrenia from the Psychiatry Clinic and the control group (women with no history of mental illness) from the Family Medicine Clinic of Ankara Training and Research Hospital were included in the research. Individuals between the ages of 18 and 65 who were literate and voluntarily gave informed consent to participate after being informed about the study were included in the research. To fill out the forms appropriately, patients diagnosed with schizophrenia were required to have no clinically severe disease picture (CGI-S score of 3 or below) and having no psychiatric diagnosis or treatment was the criterion for inclusion in the control group. Schizophrenia patients with comorbid psychiatric disorders were not included in the research. Furthermore, individuals with cognitive and physical disabilities, which would prevent them from filling out the forms, for both groups were not included in the research.

Ethical approval was obtained from the Ethics Committee of Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital (Date: 18.04.2022 Number: 135/10). This study was carried out in accordance with the Helsinki Declaration.

Patients diagnosed with schizophrenia who met the inclusion criteria and volunteered to participate in the research were examined in the psychiatry clinic. Patients who met the inclusion criteria of the research constituting the control group were also examined in the family medicine clinic. Afterward, individuals were given the Breast Cancer Awareness Scale (B-CAS) to fill in.

## Scales

### Breast Cancer Awareness Scale (B-CAS)

The breast cancer awareness scale was developed by Rakkapao et al (2016) (16). It is a scale designed as a self-report tool for early detection and prevention of breast cancer that allows women to understand their level of awareness about breast cancer. It consists of 35 items. The scale consists of five subscales: 1) Knowledge of Risk Factors, 2) Knowledge of Signs and Symptoms, 3) Attitude to Breast Cancer Prevention, 4) Barrier of Breast Scanning, 5) Health Behavior Related to Breast Cancer Awareness. The Turkish reliability validity study of the scale was conducted by Altuntug et al (2021) (14). Six items were removed due to the analysis made in this research. Since the Turkish form of the scale was used in our study, the analysis was carried out on 29 items.



### Clinical Global Impression Scale (CGI)

The Clinical Global Impression Scale is a three-dimensional scale devised by Guy (1976) to evaluate the clinical course of psychiatric disorders (17). The severity of the disease is evaluated in the first dimension, recovery in the second dimension and the severity of the drug side effects in the third dimension. The first part (Clinical Global Impression-Disease Severity) is evaluated between 1 and 7 points according to the severity of the disease at the time of filling the scale.

### Statistical Analysis

In data analysis, descriptive statistical measures (frequency and percentages) and Cronbach's alpha coefficient were used to provide evidence for the reliability of the measurements obtained from the measurement tools. Parametric tests (independent samples t-test) were used in the difference analysis since there was a sufficient sample size. SPSS (version 25) package program was used in data analysis. For statistical significance, 0.05 alpha level was taken into account.

### RESULTS

The research study group consisted of 82 individuals, 35 patients with psychotic disorders and 47 individuals in the control group, who were selected by the convenient sampling method. Descriptive statistics on the socio-demographic information of both groups that participated in the research are shown in Table 1.

Descriptive statistics of the participants' knowledge about cancer and their attitudes to health are given in Table 2. While it was determined that both groups were similar regarding doing regular sports, having an HPV vaccination, getting a mammogram, having a family history of breast cancer, and the COVID-19 epidemic as an obstacle to breast cancer screening, other variables showed a statistically significant difference.

Finally, it was examined whether there was a difference between the groups regarding the answers to the breast cancer awareness scale (Table 3). In the examination of Table 3, it is seen that F3 and F5 factors and the total score do not have a statistically significant difference. In contrast, other sub-factors have a statistically significant difference in the groups. In the examination of the mean values for both groups, it was determined that the control group had higher values than the patient group in F1 and F2 sub-factors. The effect size was calculated for the practical significance of these differences, and it was determined that it had a great effect for F1 and F2 (18). For the F4 sub-factor, it was determined that the patient group was higher than the control group, and this difference was statistically significant. In the examination of the calculated effect size, it was seen that there was a difference with a large effect.

### DISCUSSION

In this study, we aimed to compare the individuals diagnosed with schizophrenia and the control group in terms of their awareness levels about breast cancer and their health attitudes towards breast cancer (such as self-examination, going for a check-up, and having mammography). Our data demonstrated that the patient group had less awareness of breast cancer (about breast cancer risk factors and symptoms) than the control group; on the other hand, they faced more barriers in breast cancer screening. The number of those who stated that they did not know about breast cancer early diagnosis methods was higher in the patient group compared to the control group. In the evaluation of the health attitudes toward breast cancer, it was found that the healthy control group was better than the patient group in terms of performing regular breast self-exam.

Many people with early-stage breast cancer can be treated with surgery alone without any systemic treatment. For this reason, "early diagnosis" is vital to reduce deaths from cancer (19). Knowledge and awareness of breast cancer, the ability to perform breast self-exams, detecting physical changes in the breast, and immediate consulting an expert are critical factors in the early breast cancer diagnosis (20,21).

The number of studies investigating breast cancer awareness is limited, and studies have different results (22). In studies conducted on this subject, the level of awareness about breast cancer symptoms was 51% (95% CI= 37-66%), and this rate was only 40% (95% CI= 24-56%) for risk factors (23). In a recent meta-analysis, it has been reported that the general awareness of breast cancer is 53% (95% CI= %42-64); in some countries it is as low as 16%, and general information about breast cancer symptoms, risk factors and awareness levels are low (23,24). The reasons related to the difference in awareness levels include the difference in the questionnaires applied, different ethnic origins in the study samples, religions, settlements, socioeconomic level differences, and lifestyle habits (23). Factors such as living in urban areas instead of rural areas, high socioeconomic and income levels, and having a job demonstrated a tendency to have higher awareness levels about breast cancer (23). Factors such as age, education, income level, and family history of cancer were also associated with knowledge and awareness levels about cancer (23,25). Education level seems to be an important determinant for the increase of cancer awareness, regardless of the development level of countries (23). Although older women have a higher risk of developing breast cancer, some studies have shown that younger women tend to have more awareness and knowledge about breast cancer. However, there are also study results showing that older women tend to have more information about breast cancer (23). Many studies have reported that married women have lower levels of breast cancer awareness than single women (23,26).

**Table 1.** Frequency and percentages of socio-demographic information of the control and patient groups

Categorical variables						
		Patient		Control		$\chi^2$ (Difference)
Variables	Variable levels	f	%	f	%	
Marital status	Single	19	54.3	4	8.5	29.13*
	Married	9	25.7	36	76.6	
	Divorced	3	8.6	3	6.4	
	Widowed	3	8.6	2	4.3	
	Missing data	1	2.9	2	4.3	
Cohabitants	Spouse and children	8	22.9	37	78.7	32.54*
	Parents	15	42.9	4	8.5	
	Living alone	3	8.6	2	4.3	
	Extended family	7	20.0	1	2.1	
	Missing data	2	5.7	3	6.4	
Having a child	Yes	13	37.1	40	85.1	22.80* (p= .000)
	No	22	62.9	7	14.9	
Education level	Literate	--	--	3	6.4	7.08 (p= .132)
	Primary school	8	22.9	14	29.8	
	Secondary school	5	14.3	8	17.0	
	High school	13	37.1	17	36.2	
	University/College degree	9	25.7	5	10.6	
Occupation	Student	1	2.9	1	2.1	18.30 <sup>1</sup> *
	Housewife	27	73.2	27	57.4	
	Worker/Civil servant	1	2.9	16	34.0	
	Retiree	4	11.4	--	--	
	Self-employed	1	2.9	--	--	
	Missing data	1	2.9	3	6.4	
Level of income	Low	10	28.6	9	19.1	1.04
	Average	18	51.4	30	63.8	
	High	5	14.3	6	12.8	
	Missing data	2	5.7	2	4.3	
Menopause status	Yes	5	14.3	13	27.7	2.74
	No	30	85.7	34	72.3	
Smoking	Yes	26	74.3	15	31.9	0.42
	No	9	25.7	32	68.1	
Alcohol usage	No	29	82.9	46	97.8	10.55*
	Yes	1	2.9	--	--	
	Missing data	5	14.2	1	2.1	
Total		35	100	47	100	
Continuous variables						
		Mean	SD	Mean	SD	t-values (difference)
Age (years)		41.26	9.25	44.02	11.65	1.14
Disease onset (year)		26.35	9.40	--	--	--
Height (cm)		160.86	6.55	162.24	5.54	0.95
Weight (kg)		75.31	17.23	69.93	14.08	1.49
Age of first menstruation (years)		13.65	1.34	13.30	1.15	1.19
*p< .05.						
<sup>1</sup> Fisher's exact test.						

**Table 2.** Frequencies and percentages related to knowledge about cancer and attitudes toward the health of both groups

Variables	Variable levels	Patient		Control		$\chi^2$ (Difference)
		f	%	f	%	
Doing sports regularly	Yes	11	31.4	13	27.7	0.30
	No	22	62.9	34	72.3	
	Missing data	2	5.7	--	--	
Healthy diet	Yes	28	80.0	28	59.6	3.87*
	No	7	20.0	19	40.4	
Do you know anything about breast cancer	I have enough information	5	14.3	12	25.5	24.25*
	I have some information	12	34.3	33	70.2	
	I have no information	18	51.4	2	4.3	
Information sources about breast cancer	Visual-print media	11	31.4	32	68.1	8.31 <sup>1</sup> *
	Physician	6	17.1	4	8.5	
	Nurse/Midwife	3	8.6	4	8.5	
	Friend-neighbor	--	--	3	6.4	
	Seminar/Meeting	4	11.4	2	4.3	
	Missing data	11	31.4	2	4.3	
Having knowledge about early diagnosis methods of breast cancer	No	27	77.1	5	10.6	41.59 <sup>1</sup> *
	Yes	8	22.9	42	89.4	
Performing regular breast self-examination	Yes	6	17.1	36	76.6	29.74*
	No	29	82.9	10	21.3	
	Missing data	--	--	1	2.1	
Mammography	Yes	9	25.7	21	44.7	3.39 <sup>1</sup>
	No	26	74.3	26	55.3	
Having regular mammography	Yes	5	14.3	16	34.0	4.24 <sup>1</sup>
	No	30	85.7	31	66.0	
Has COVID-19 prevented you from getting breast cancer screening?	No	30	85.7	42	89.4	0.95 <sup>1</sup>
	Yes	4	11.4	4	8.5	
	Missing data	1	2.9	1	2.1	
Family history of breast cancer	Yes	4	11.4	2	4.3	2.13 <sup>1</sup>
	No	31	88.6	45	95.7	
Total		35	100	47	100	

\*p< .05.  
<sup>1</sup>Fisher's exact test.

In our study, breast cancer awareness levels of the control group were found to be higher than the patient group in terms of breast cancer symptoms and risk factors dimensions. The similarity between the two groups regarding education, income level, mean age and family history of breast cancer suggests that these factors do not affect the difference we found between the groups.

On the other hand, the rate of having a job and being married in the control group was higher compared to the patient group. In the literature, having a profession has been found to be associated with higher awareness levels; and being married, on the contrary, has been associated with lower awareness levels (23,26). Therefore; the impact of these factors should be considered in interpreting our data.

**Table 3.** Independent samples t-test results of comparison of breast cancer awareness levels of the patient and control group

Subdimenstions/Total	Group	n	$\bar{X}$	SD	SD	t	$\eta^2$
F1	Patient	35	9.25	2.58	80	3.59*	.14**
	Control	47	11.22	2.37			
F2	Patient	35	13.00	3.28	54.19 <sup>1</sup>	3.05*	.14**
	Control	47	14.94	2.10			
F3	Patient	35	23.79	4.89	47.29 <sup>1</sup>	1.96	--
	Control	47	25.56	2.51			
F4	Patient	35	10.56	3.87	80	4.50*	.20**
	Control	47	7.15	3.00			
F5	Patient	35	9.69	2.81	80	0.83	--
	Control	47	9.22	2.26			
Total	Patient	35	66.29	8.52	80	1.12	--
	Control	47	68.09	5.98			

\* $p < .05$ ; d\* = small effect. d\*\* = great effect.<sup>1</sup>Equal variances not assumed.

F1: Knowledge of risk factors, F2: Knowledge of signs and symptoms, F3: Attitude to breast cancer prevention, F4: Barrier of breast scanning, F5: Health behavior related to breast cancer awareness.

It is necessary to raise awareness about breast cancer symptoms and risk factors in women. In this context, to increase knowledge and awareness about breast cancer, it is necessary to clearly understand the insufficient information and the factors associated with knowledge and awareness (23,27). In addition, standards are needed to assess awareness and knowledge about breast cancer. In our study, the rate of individuals reporting that they had knowledge of breast cancer early diagnosis methods was lower in the patient group compared to the control group. In addition, there was a difference between the two groups in terms of information sources on this subject. The rate of obtaining information through visual print media is higher in the control group compared to the patient group. In both groups, it is seen that obtaining information in this way has the highest rates compared to other information sources (physicians, nurses, friends, seminars, etc.). Our data provide information on ways to reach the target audience in awareness studies.

In addition to the lack of awareness, many women do not have appropriate health-related attitudes toward this disease, and it is reported that women do not participate in screening programs, especially in developing countries (28). Breast cancer is seen in one of every eight women in the general population, and this risk can be reduced by up to 20% with mammography screenings (29). Our study found that the rate of self-examination of patients diagnosed with schizophrenia was lower than that of the healthy control group. However, although the rates in the control group were higher than the patient group in terms of participation in mammography and regular mammography screenings, no statistically significant difference was

found between the groups. Similarly, in our study, no difference was found between the groups regarding the Attitude to Breast Cancer Prevention dimension in the breast cancer awareness scale. In this dimension, individuals were also asked about their thoughts on early cancer diagnosis through regular examinations by health personnel and mammography examinations. Contrary to our data in the literature, women with a past or present diagnosis of mental illness seem to be less likely to have mammography compared to the general population, and it is noteworthy that participation in screening studies is less than half of the control group (8,30). Although there is no significant difference between the groups in terms of mammography, it is observed that the patient group in our study reported more difficulties in terms of breast screening barriers compared to the control group. In this dimension, individuals are asked whether they know how to self-exam, whether they have time to go to a physician for cancer screening, whether they wait a long time to see a physician, and whether it is convenient for them to go to a physician. The fact that the majority of the patient group in our sample consisted of individuals followed in the CMHC may have been effective in the absence of differences in mammography scans between the two groups in our study. CMHCs provide holistic health services to individuals with severe mental illness and apply healing-oriented case treatment plans. The consultations of the individuals followed here to the required departments are planned by the consultant doctors. For this reason, individuals may be able to have the necessary examinations done even if they feel barriers to screening. However, in the light of our study data, it was thought that the group with the disease should receive training

on self-examination. The fact that our study sample consisted of a relatively young patient group may have provided limited data in terms of evaluating the attitude of having regular mammography, and it is recommended to conduct studies that include the older age group.

Due to the design of our study, the effect of cancer awareness could not be evaluated on the fact that the patients' self-examination rate is lower than that of the control group. Literature data indicate that the low level of awareness about cancer may have an effect on low breast cancer screenings in general (6). It was determined that the clinicians evaluated the difficulties in accessing care, social support, prioritization of psychiatric complaints, communication difficulties, and patients' concerns as effective factors in this group's low number of cancer screenings (31). The relative failure of individuals with serious mental illness to seek cancer screening is attributed to transportation problems, lack of reminders, and unfamiliarity with the process by patients or healthcare providers (12). It is also possible that physicians may underestimate the clinical significance of complaints from patients with psychotic disorders or attribute such complaints to psychotic phenomena (e.g., diagnostic overshadowing). This situation may result from the patients' communication difficulties and cognitive challenges or stigmatization, which is common among physicians. It has also been reported that patients diagnosed with schizophrenia have a high pain threshold, so they may not complain until the late stages of the disease. Patients may have a little family incentive to visit their physician even when symptoms occur (32,33). As a result of reduced screening and examinations, cancers come to medical attention at relatively late stages, are less amenable to treatment, and are more likely to lead to treatment-refractory and premature death (33).

Our study is important in terms of reflecting the data of Türkiye, but the single-center study and the low sample size are the limitations of our study. In our study, the difficulties individuals face in participating in self-examination and screening programs were not discussed in detail, and it is recommended to be investigated in further studies. Finally, although there was no difference in terms of age between the two groups, the fact that the evaluation of mammography screening was not limited to individuals over 40 in our study can be considered a limitation.

## CONCLUSION

Early diagnosis plays a crucial role in patient survival. Therefore, interventions should be implemented to increasing knowledge and awareness about breast cancer (34). Educating individuals about the signs and symptoms of cancer and adapting health-care systems to facilitate rapid and early cancer diagnosis may be cost-effective and applicable cancer control strategies for curable cancers (22). For the prevention of breast cancer, an

initial assessment should be made to classify the risk of breast cancer in women with schizophrenia, and antipsychotics that may increase prolactin levels and breast cancer risk should be avoided in high-risk women. Regular screening should be done, including imaging or biomarker testing. Awareness of cancer risk, more accurate risk detection, stronger connection with primary care, regular monitoring and screening, appropriate drug selection and low-dose antipsychotic treatment, use of cognitive and psychosocial therapies in addition to psychopharmacotherapy, recommending diet and exercise programs to individuals are very important in the fight against cancer (7). It is important for psychiatrists to be in contact with primary care physicians and help their patients be screened in order to maintain good patient care (10). In addition, every effort should be made to increase patient compliance with treatment and follow-up processes as well as prevention (35).

**Ethics Committee Approval:** This study was approved by T.C. Ministry of Health SBU Dışkapı Yıldırım Beyazıt Training and Research Hospital Clinical Research Ethics Committee (Decision no: 135/10, Date: 18.04.2022).

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**ORİJİNAL ÇALIŞMA-ÖZET**

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**Şizofreni tanılı kadın hastalarda meme kanseri farkındalığının araştırılması**

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**ÖZET**

**Giriş ve Amaç:** Bu çalışmanın amacı şizofreni tanılı kadın hastaların meme kanseri farkındalığını araştırmak ve kontrol grubu ile şizofreni tanılı bireyler arasında bu farkındalık açısından fark olup olmadığını değerlendirmektir. İkinci olarak şizofreni tanılı hastalar ile kontrol grubunun meme kanseri tarama sıklığı karşılaştırılacaktır.

**Gereç ve Yöntem:** On sekiz-65 yaş arası okuma yazma bilen ve araştırmaya gönüllü olarak bilgilendirilmiş onay beyanı vererek katılmayı kabul eden bireyler çalışmaya dahil edildi. Araştırmanın çalışma grubunu 35 şizofreni hastası ve 47 sağlıklı birey olmak üzere 82 kişi oluşturmuştur. Şizofreni hastalarının klinik olarak ciddi bir hastalık tablosuna sahip olmaması (CGI-S skoru 3 veya altında) istendi. Bireylere doldurmaları için Meme Kanseri Farkındalık Ölçeği (B-CAS) verildi.

**Bulgular:** Hasta grubu meme kanseri konusunda kontrol grubuna göre daha az farkındalığa sahiptir ve diğer taraftan meme kanseri taramasında daha fazla engelle karşılaşmaktadır. Meme kanseri erken tanı yöntemlerini bilmediğini belirtenlerin sayısı hasta grubunda kontrol grubuna göre daha fazlaydı. Meme kanserine yönelik sağlık tutumları değerlendirildiğinde, sağlıklı kontrol grubunun kendi kendine düzenli meme muayenesi yapma konusunda hasta grubuna göre daha iyi olduğu saptanmıştır.

**Sonuç:** Şizofreni tanısı olan bireyleri kanserin belirti ve semptomları konusunda eğitmek ve sağlık sistemlerini hızlı ve erken kanser teşhisini kolaylaştıracak şekilde düzenlemek, tedavi edilebilir kanserler için uygun maliyetli ve uygulanabilir kanser kontrol stratejileri olabilir.

**Anahtar Kelimeler:** Meme kanseri, şizofreni, farkındalık

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# Does mechanical bowel preparation really prevent complications after colorectal surgery depending on the lesion localization? A myth or fact?

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## ABSTRACT

**Objective:** Despite being routinely used before elective colorectal surgery in most surgical clinics, mechanical bowel preparation (MBP) remains controversial. This study aimed to investigate postoperative complications and outcomes of right, left, or rectosigmoid resection without MBP.

**Material and Methods:** Patients who underwent elective colorectal surgery without mechanical bowel preparation and oral antibiotics between January 2011 and December 2021 were included in the study. Patients were categorized according to the side of resection, and these subgroups were compared for anastomotic leakage, surgical site infections (SSI), and overall morbidity measured using the Clavien-Dindo complication grade.

**Results:** Data of 422 patients were analyzed. Overall anastomotic leakage was found in 14 patients (3.3%), SSI in 46 (10.9%), collection in 14 (3.3%), mortality in 18 (4.3%), and reoperation in 17 (4%) patients. Anastomotic leakage was observed in six (3.9%) in right colectomy, two (1.9%) in left colectomy, and in six (3.7%) patients in the rectosigmoid resection group when the groups were evaluated separately. There was no statistical difference between the groups ( $p=0.630$ ). Furthermore, there was no statistical difference between the groups regarding collection and reoperation ( $p$  values were  $p=0.31$ , and  $p=0.251$ , respectively).

**Conclusion:** Study results showed that anastomotic leakage, surgical site infection, intra-abdominal collection, reoperation, and mortality rates were similar to the current literature obtained from the studies with mechanical bowel preparation. In addition, these results were found to be similar according to the resection site.

**Keywords:** Preoperative bowel preparation, mechanical bowel preparation, infectious complications, surgical site infection, anastomotic leakage

## INTRODUCTION

Colorectal surgeons use various protocols for bowel preparation to prevent complications such as anastomotic leakage, intraabdominal abscess, and surgical site infections. These include oral antibiotics, intravenous antibiotics, rectal enemas, oral solutions, and combinations.

Despite having been used for nearly a century to reduce postoperative infectious complications and minimize the contamination of the operation area by reducing the colonic bacterial load (1,2), the usage of mechanical bowel preparation (MBP) is still questionable and the debate of the usage has been not to be finalized yet. Based on evidence-based studies, three different aspects are formed in clinical practice. Studies conducted in recent years have shown that complications such as anastomotic leakage, surgical site infection (SSI), and intraabdominal abscess are less common in patients with mechanical bowel preparation (3-6). On the other hand, some studies have shown that MBP does not affect postoperative infectious complications and anastomotic leakage rates (7-9). Other studies have paradoxically cited increased rates of infectious complications after MBP and also slower return of bowel function and increased rates of cardiac complications, electrolyte disturbances, and anastomotic leak (10-12).

The first questioning of the necessity and effectiveness of MBP was shown in a study by Hughes in 1972 (13). After this study, many studies have emerged exploring the potential benefits of MBP. However, various studies have shown that the

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reduction or prevention of SSI, intraabdominal abscess, and anastomotic leakage cannot be prevented after MBP (14,15). Furthermore, MBP is not recommended before colorectal surgery as it causes various side effects such as bloating, nausea, fatigue, electrolyte imbalance, abdominal discomfort, and perforation, especially in elderly patients (16,17).

The World Health Organization (WHO) and American Society of Colon and Rectal Surgeons (ASCRS) guidelines recommend oral antibiotics (OA) together with MBP (18,19). On the other hand, the Enhanced Recovery After Surgery (ERAS) guidelines in elective colorectal surgery assigned the low quality of evidence for MBP with OAs (20). Therefore, the ERAS guidelines still recommend that MBP should not be routinely used in colon surgery. Therefore, this study investigated the postoperative morbidity of resections in different colon regions in patients who had undergone elective colorectal surgery without MBP retrospectively.

The aim of this study was to investigate complications in patients who underwent colonic resection and anastomosis without performing MBP and comparing the outcomes of right, left or rectosigmoid resections with each other. The primary aim was to evaluate anastomotic leakage and surgical site infection in addition to the rate of SSI within 30 days after surgery and subcategories of SSI (superficial incisional, deep incisional, and organ/space). Secondary aim was to evaluate overall morbidity measured by using Clavien-Dindo complication grade.

## MATERIAL and METHODS

### Source of Data and Study Population

We conducted a retrospective single-center cohort study of patients from tertiary centers experienced in colorectal surgery. These patients underwent elective colorectal resections for benign and malignant diseases for ten years from January 2011 to December 2021. The ethics committee approved the study protocol of the university hospital (E-78017789-050.01.04-1647269/2021/347). A total of 767 consecutive patients were enrolled in this study. Exclusion criteria were accepted as follows: 1) patients who underwent emergent surgery (n= 87), 2) age under 18 years (n= 2), 3) patients with bowel obstruction (n= 14), 4) patients who underwent abdominoperineal resection with end stoma (n= 24), patients who performed laparoscopic surgery (n= 184) and 6) patients with no enough data available in the medical records (n= 34). Finally, four hundred and twenty-two patients who fulfilled the eligibility criteria were included in the study.

Patients were divided into three groups according to lesion localization and resection site. Of these, regions from the ileocolic region to the 2/3 proximal of the transverse colon were included in the right colectomy group; resections from the 1/3 distal part of the transverse colon to the distal sigmoid colon

were included in the left colectomy group, and resections from the distal sigmoid colon to the distal rectum were included in the rectosigmoid resection group.

Prophylactic intravenous antibiotic prophylaxis was routinely administered with 1500 mg of cefuroxime and 500 mg of metronidazole 30 minutes before the incision and was terminated on day one postoperatively. It was also repeated when the operation time exceeded four hours, and blood loss exceeded 1.5 liters. In addition, ciprofloxacin 500 mg was administered to patients with penicillin and cephalosporin allergy.

Demographic data (age, sex), ASA scores, transfusion needing, receiving neoadjuvant treatment, comorbidity status (Charlson Comorbidity Index), operation indication (malignant causes, benign causes), type of operation, protective ileotomy status and stage of the disease were recorded. In terms of postoperative results, anastomotic leakage, intraabdominal collection, mortality, reoperation and extraintestinal infection were recorded.

The primary and secondary aims of the study are stated in the manuscript. The primary aim was to evaluate the anastomotic leakage and surgical site infection. In addition, the rate of SSI within 30 days after surgery and subcategories of SSI (superficial incisional, deep incisional, and organ/space), as defined by the Centers for Disease Control and Prevention (21). Secondary outcomes included overall morbidity measured using the Clavien-Dindo complication grade (22).

### Statistical Methods

Descriptive findings were presented as numbers and percentages for categorical variables and as mean and standart deviation for continuous variables. The Kolmogorov-Smirnov test evaluated the conformity of continuous variables to normal distribution. In the comparisons of groups of three or more, those with normal distribution were analyzed with the ANOVA test, and those which did not show normal distribution were analyzed with the Kruskal Wallis test. Tukey equal variances for those who show equal variances when comparing binary groups and Tamhane's T2 post-hoc test was applied in those who did not. Pearson's chi-square test was used to compare categorical variables in independent groups. The exact test was applied in cases that did not meet the Pearson's chi-square test conditions. Multivariable logistic regression analysis was performed to evaluate the relationship between colon regions and complications with further analysis. The results were evaluated with a 95% confidence interval, with an alpha error of 0.05. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) for Windows 25.0 (IBM SPSS Inc., Chicago, IL).

## RESULTS

A total of 422 consecutive patients with a mean age of 59.9 ± 13.7 (range, 18-92) years were included in our study.

Male/Female ratio was 239 (56.6%)/183 (43.4%). A total of 252 (59.7%) patients were under 65 years, whereas 170 (40.3%) of the patients were 65 years or over. ASA score was I (+43.4%) or II (56.6%) in most of the patients. The Charlson comorbidity index score of the patients was similar in all groups, and the average was 3. Neoadjuvant treatment was applied in 39 (9.2%) the patients. The need for peri/post-operative blood transfusions was seen in 193 (45.7%) patients, while 229 (54.3%) patients did not need any transfusion. Three hundred and sixty-five (86.5%)

patients were operated for malignant reasons, and the remaining 57 (13.5%) of the patients were operated for benign reasons.

In the form of reconstruction after resection, colorectal anastomosis was performed in 234 (55.5%) patients, ileocolic anastomosis in 147 (34.8%) patients, and colocolic anastomosis in 41 (9.7%) patients. Protective ileostomy was applied to 108 (25.6%) patients. Clinicopathological and demographic features of the patients were summarized in Table 1.

**Table 1.** Clinicopathological and demographic features of the patients

	Right colon	Left colon	Rectosigmoid	p
<b>Age</b>	62.99 ± 13.03	56.18 ± 15.44	59.66 ± 12.50	<0.001
<b>Sex</b>				0.648
Female	70 (46.1)	46 (43.4)	67 (40.9)	
Male	82 (53.9)	60 (56.6)	97 (59.1)	
<b>ASA</b>				<0.001
ASA 1	25 (16.4)	28 (26.4)	62 (37.8)	
ASA 2	92 (60.5)	62 (58.5)	85 (51.8)	
ASA 3	29 (19.1)	15 (14.2)	15 (9.1)	
ASA 4	6 (3.9)	1 (0.9)	2 (1.2)	
<b>Transfusion</b>				0.593
No	85 (55.9)	53 (50)	91 (55.5)	
Yes	6 (1)	53 (50)	73 (44.5)	
<b>Comorbidity</b>				0.129
No	71 (46.7)	55 (51.9)	65 (39.6)	
Yes	81 (53.3)	51 (48.1)	99 (60.4)	
<b>Malignancy</b>				<0.001
Benign	17 (11.2)	35 (33)	5 (3)	
Malignant	135 (88.8)	71 (67)	159 (97)	
<b>Operation type</b>				<0.001
Ileocolic anastomosis	144 (94.7)	2 (1.9)	1 (0.6)	
Colocolic anastomosis	0 (0)	41 (38.7)	0 (0)	
Colorectal anastomosis	8 (5.3)	63 (59.4)	163 (99.4)	
<b>Stoma status</b>				<0.001
No stoma	143 (94.1)	84 (79.2)	87 (53)	
Protective ileostomy	9 (5.9)	22 (20.8)	77 (47)	
<b>Stage</b>				0.084
Stage 1	12 (10)	8 (13.8)	26 (17.1)	
Stage 2	36 (30)	15 (25.9)	24 (15.8)	
Stage 3	60 (50)	26 (44.8)	86 (56.6)	
Stage 4	12 (10)	9 (15.5)	16 (10.5)	
<b>NACRT</b>				<0.001
No	150 (98.7)	106 (100)	127 (77.4)	
Yes	2 (1.3)	0 (0)	37 (22.6)	

ASA: American Society of Anesthesiologists, NACRT: Neoadjuvant chemoradiotherapy.



When the three groups were evaluated in terms of mean age, it was seen that the mean age of the right colon patients was  $62.99 \pm 13.03$ , the left colon patients were  $56.18 \pm 15.44$ , and the rectum patients were  $59.66 \pm 12.50$  years, and a statistically significant difference was determined ( $p < 0.001$ ). In group comparisons, it was determined that the group that created a statistically significant difference was the mean age of the right and left colon ( $p < 0.001$ ).

Postoperative complication rates of the patients were analyzed according to the Clavien-Dindo complication grade and when all groups were evaluated, major complication (3b and above) was seen in 35 (8%) patients. Anastomotic leakage was observed in 14 (3.3%), intra-abdominal collection in 14 (3.3%), reoperation in 17 (4%), wound infection in 46 (10.9%), extraintestinal infection in 65 (15.4%), and mortality in 18 (4.3%) patients. Postoperative infective complications of the patients according to lesion localization are summarized in Table 2.

The patients were divided into three groups according to lesion localization and the resections performed: right colectomy group consisted of 152 (36.02%) patients, whereas left colectomy group included 106 (25.12%) patients, and rectosigmoid resection group had 164 (38.86%) of the patients. Anastomotic leakage was observed in six (3.9%) patients in the right colectomy group, two (1.9%) patients in the left colectomy group, and seven (4.3%) patients in the rectosigmoid resection group.

Intraabdominal collection rates were seen in six (3.9%) patients in the right colectomy, one (0.9%) in the left colectomy, and in seven (4.3%) patients in the rectosigmoid resection group. No statistically significant results were found between the three groups ( $p = 0.31$ ) in terms of intraabdominal collections. Reoperation was seen in nine (5.9%), two (1.9%), four (2.4%) patients in the right colectomy, left colectomy, and rectosigmoid resection groups, respectively. Wound infection was seen in 15 (9.9%), 10 (9.4%) and 21 (12.8%) patients in the right colectomy, left colectomy, and rectosigmoid resection groups, respectively. Extraintestinal infection was seen in 23 (15.1%), 11 (10.4%) and 31 (18.9%) patients in the right colectomy, left colectomy, and rectosigmoid resection groups, respectively. Mortality was observed in 13 (8.6%), one (0.9%), four (2.4%) patients in the right colectomy, left colectomy, and rectosigmoid resection groups, respectively. There was no statistically significant difference between the groups regarding anastomotic leakage, intraabdominal collection, reoperation, wound infection, extraintestinal infection, and p values were 0.093, 0.31, 0.251, 0.612, and 0.234, respectively. Considering the mortality rates, it was found to be higher in the right colectomy group compared to the other groups, and the p value was 0.003. In addition, multivariable logistic regression analysis of the clinicopathological data of the patients according to the lesion localization is shown in Table 3.

**Table 2.** Postoperative complications of the patients according to lesion localization

	Right colon	Left colon	Rectosigmoid	p
<b>Anastomotic leakage</b>				0.630
No	146 (96.1)	104 (98.1)	158 (96.3)	
Yes	6 (3.9)	2 (1.9)	6 (3.7)	
<b>Collection</b>				0.310
No	146 (96.1)	105 (99.1)	157 (95.7)	
Yes	6 (3.9)	1 (0.9)	7 (4.3)	
<b>Mortality</b>				0.003
No	139 (91.4)	105 (99.1)	160 (97.6)	
Yes	13 (8.6)	1 (0.9)	4 (2.4)	
<b>Reoperation</b>				0.251
No	143 (94.1)	104 (98.1)	158 (96.3)	
Yes	9 (5.9)	2 (1.9)	6 (3.7)	
<b>SSI</b>				0.612
No	137 (90.1)	96 (90.6)	143 (87.2)	
Yes	15 (9.9)	10 (9.4)	21 (12.8)	
<b>Extra intestinal infection</b>				0.234
No	129 (84.9)	95 (89.6)	133 (81.1)	
Yes	23 (15.1)	11 (10.4)	31 (18.9)	

SSI: Surgical site infection.

**Table 3.** Multivariable logistic regression analysis of the clinicopathological data of the patients according to the lesion localization

		B	Std. Error	Wald	p	OR	95% confidence interval for OR	
							Lower bound	Upper bound
Right colon	Intercept	0.082	1.789	0.002	0.964			
	Age	0.008	0.013	0.408	0.523	1.011	0.98	1.03
	Charlson comorbidity index	-0.084	0.069	1.49	0.222	0.92	0.80	1.05
	Albumin	-0.599	0.208	8.338	0.004	0.55	0.37	0.83
	ASA 1	-1.522	0.963	2.496	0.114	0.22	0.03	1.44
	ASA 2	-0.385	0.926	0.173	0.678	0.68	0.11	4.18
	ASA 3	-0.496	0.965	0.264	0.607	0.61	0.09	4.04
	ASA 4 (ref)							
	Benign (ref: malignant)	1.8	0.585	9.473	0.002	6.05	1.92	19.04
	NAKRT No (ref: yes)	1.453	0.829	3.072	0.08	4.28	0.84	21.71
	Alive (ref: ex)	-0.811	0.669	1.47	0.225	0.44	0.12	1.65
Left colon	Intercept	-17.035	2.066	68.013	0			
	Age	-0.015	0.013	1.419	0.234	0.99	0.96	1.01
	Charlson comorbidity index	0.011	0.07	0.023	0.879	1.01	0.88	1.16
	Albumin	-0.415	0.223	3.459	0.063	0.66	0.43	1.02
	ASA 1	-0.689	1.29	0.286	0.593	0.50	0.04	6.28
	ASA 2	0.352	1.261	0.078	0.78	1.42	0.12	16.84
	ASA 3	0.447	1.302	0.118	0.731	1.56	0.12	20.06
	ASA 4 (ref)							
	Bening (ref: malignant)	2.832	0.555	26.076	<0.001	16.9	5.73	50.37
	NACRT No (ref: yes)	-	-	-	-	-	-	-
	Alive (ref: ex)	1.405	1.171	1.44	0.23	4.08	0.41	40.49

The reference category is: Rectosigmoid.

ASA: American Society of Anesthesiologists, NACRT: Neoadjuvant chemoradiotherapy.

When multivariable logistic regression analysis of the colon regions and complications was performed, anastomotic leakage among the patients who underwent rectosigmoid resection ( $p=0.196$ , OR= 0.28, 95% CI for OR= 0.04-1.94) was found when the right colon was taken as a reference. For SSI ( $p=0.219$ , OR= 0.59, 95% CI for OR= 0.25-1.37), complication status ( $p=0.054$ , OR= 0.59, 95% CI for OR= 0.25-1.37), and collection ( $p=0.521$ , OR= 0.57, 95% CI for OR= 0.25-1.37), no statistical difference was observed. In addition, anastomotic leakage ( $p=0.462$ , OR= 0.41, 95% CI for OR= 0.04-4.36) and SSI ( $p=0.493$ , OR= 0.71, 95% CI for OR= 0.27-1.87) compared to the left colon region, again when the right colon is referenced (0.27-1.87), and complication status ( $p=0.183$ , OR= 0.13, 95% CI for OR= 0.01-2.59) and collection ( $p=0.559$ , OR= 2.14, 95% CI for OR= 0.17-27.36) showed no difference. These findings are shown in Table 4.

## DISCUSSION

The present study evaluated postoperative outcomes in patients who underwent elective colorectal surgery without mechanical bowel preparation. The role of mechanical bowel

preparation in colorectal surgery is still controversial. The negative effect on infection rates, the lack of effectiveness of mechanical preparation, and its use have led to a decrease (23). In line with the evidence of randomized trials and meta-analyses conducted in recent years, it has been understood that mechanical bowel preparation has no benefit on postoperative results (24,25).

While SSI is 11.4% in colorectal surgery, it varies between 5.4% and 23.2% (26). In the European results, depending on the ERAS protocol, SSI rates of >10% have been observed in patients who did not undergo mechanical bowel preparation (27). In the MOBILE trial investigating mechanical and oral antibiotic bowel preparation (MOABP) versus no bowel preparation (NBP) in the right and left colectomy, subgroup analysis has shown that the rate of SSI in patients who underwent right colectomy was similar in the MOABP and NBP groups, 7% and 10%, 9%, respectively (OR= 0.71, 95% CI= 0.26-1.95;  $p=0.510$ ). In addition, SSI has been found at a similar rate in the MOABP and NBP groups who underwent left colectomy and were 6% and 10%, respec-

**Table 4.** Multivariable logistic regression analysis of the colon regions and complications

		B	Std. Error	Wald	p	OR	95% confidence interval for OR	
							Lower bound	Upper bound
Rectosigmoid	Intercept	-1.896	1.227	2.387	0.122			
	Anastomotic leak (ref: yes)	-1.278	0.989	1.668	0.196	0.28	0.04	1.94
	Collection (ref: yes)	-0.568	0.885	0.413	0.521	0.57	0.10	3.21
	Alive (ref: ex)	3.459	1.313	6.947	<b>0.008</b>	31.80	2.43	416.49
	Reoperation (ref: yes)	3.392	1.512	5.034	<b>0.025</b>	29.74	1.54	575.87
	SSI (ref: yes)	-0.533	0.434	1.508	0.219	0.59	0.25	1.37
	Minor complication (ref: major complication)	-2.521	1.31	3.705	0.054	0.08	0.01	1.05
Left colon	Intercept	-4.492	2.016	4.963	0.026			
	Anastomotic leak (ref: yes)	-0.884	1.203	0.54	0.462	0.41	0.04	4.36
	Collection (ref: yes)	0.759	1.301	0.341	0.559	2.14	0.17	27.36
	Alive (ref: ex)	3.914	1.772	4.878	0.027	50.11	1.55	1616.11
	Reoperation (ref: yes)	2.759	1.792	2.37	0.124	15.79	0.47	529.75
	SSI (ref: yes)	-0.336	0.491	0.47	0.493	0.71	0.27	1.87
	Minor complication (ref: major complication)	-2.022	1.517	1.777	0.183	0.13	0.01	2.59

The reference category is: Right colon. SSI: Surgical site infection.

tively (OR= 0.57, 95% CI= 0.18-1.82; p= 0.338) (28). The SSI rates in the current study were 10.9%. When we evaluated it as a subgroup, the rates of 9.9%, 9.4%, and 12.8% were observed in those who underwent right colectomy, left colectomy, and rectosigmoid resections, respectively.

Anastomotic leakage is among the most important causes of mortality after colorectal surgery. Anastomotic leakage rates reported in colorectal surgery vary between 1.8% and 19% (29). The present study also evaluated the effect of NBP on anastomotic leakage. In a study evaluating patients with and without MBP, anastomotic leakage rates were 2.3% and 2.6%, respectively; and there was no statistical difference (30). In addition, similar results are supported by other studies (31,32). As demonstrated in a prospective randomized trial, there was no difference in anastomotic leakage between MBP and NBP among 249 patients who underwent rectal surgery. Anastomotic leakage rates were 4.2% and 2.3%, respectively (33). In our study, the rate of anastomotic leakage was 2.8%. In subgroup analysis, it was found as 3.9% in right colon surgery, 1.9% in left colon surgery, and 3.7% in patients with rectosigmoid surgery.

In a meta-analysis evaluating the effect of mechanical bowel preparation on postoperative outcomes in elective colorectal surgery, when MBP was compared with no MBP, there was no difference in the incidence of anastomotic leak (OR = 0.90, 95% CI= 0.74 to 1.10, p= 0.32) also in terms of SSI. When the studies were evaluated, no difference existed between those who underwent MBP and those who did not. Also, intraabdominal

collection (OR = 0.86, 95% CI= 0.63 to 1.17, p= 0.34), reoperation (OR= 0.91, 95% CI= 0.75 to 1.12, p= 0.38) and mortality (OR= 0.50, 95% CI= 0.34 to 0.74, p= 0.0005) rates were evaluated in this meta-analysis, and effectiveness of MBP was observed on it (34). In our study, similar to this meta-analysis, when we performed and evaluation according to the resection sites of the colon, the rates of intraabdominal collection (p= 0.31) and reoperation (p= 0.251) were similar, but mortality rates (p= 0.003) were not different from the patients who underwent MBP, unlike this meta-analysis.

When the studies conducted in recent years are evaluated, there is discrepancy in meta-analyses on mechanical bowel preparation, oral antibiotic use and IV antibiotic use before elective colorectal surgery. In a meta-analysis involving 5107 patients in 10 randomized controlled trials, patients have been grouped as IV antibiotics only, MBP with IV antibiotics, IV and oral antibiotics and MBP with oral antibiotics. Although there was no difference in terms of anastomotic leakage; SSI was seen to be reduced by more than 50% in patients who did not undergo MBP (35). In another meta-analysis, the analysis included a total of 22 studies involving 8852 patients. Patients were divided into two groups as MBP alone and MBP with oral antibiotics. As a result, the incidence of AL was significantly lower in the group treated with MBP plus OAB compared with MBP alone (OR= 0.43, 95% CI= 0.23-0.81, p= 0.009, I<sup>2</sup>= 73%). In addition, SSI was significantly lower in the MBP plus oral antibiotics group (OR= 0.38, 95% CI= 0.32-0.46, p< 0.0001, I<sup>2</sup>= 24%) (36).

The effect of gut microbiota composition on postoperative infectious complications after colorectal surgery has been demonstrated (37). When MBP is combined with oral antibiotics, both the microbiome and pathobionts are affected. MBP with oral antibiotics causes the disruption of the delicate balance between pathogen proliferation and natural suppression by rearrangement of the normal microbiota (38). In addition, the importance of the gut microbiota in its influence on gut sensorimotor function, which is associated with postoperative recovery of gut function, has been demonstrated in recent animal studies (39).

Although this study had several limitations, it also included some powerful features. The first significant limitation was the retrospective and single-center design. Although many studies evaluate the effectiveness of MBP, a vital aspect of the study was that the first study evaluated the outcomes of right and left hemicolectomy and anterior resection without MBP and compared them. Another strength of this study might be the large sample size. In addition, some patients need neoadjuvant chemotherapy, which is expected to increase postoperative complications. Nevertheless, the results of this study showed that using neoadjuvant chemotherapy might not increase postoperative infective complications under the condition of non-mechanical bowel preparations.

## CONCLUSION

Surgical site infections are in an Achilles heel condition after colorectal surgery. Within the framework of the ERAS protocols, mechanical and oral antibiotic bowel preparations have been abandoned for decades. However, the rate of anastomotic leakage, one of the most feared complications after colorectal surgery, has not changed. Contrary to dogma and popular belief, data from patients who did not undergo mechanical bowel preparation were analyzed and discussed with the current literature in this study. Surgical site infection, postoperative mortality, intraabdominal collection rates, and anastomotic leakage were similar.

**Ethics Committee Approval:** This study was approved by Mersin University Rectorate Clinical Research Ethics Committee (Decision no: IEC/GMC/Cat C/2021/448, Date: 13.02.2021).

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## ORJİNAL ÇALIŞMA-ÖZET

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**Mekanik bağırsak hazırlığı lezyon lokalizasyonuna bağlı olarak kolorektal cerrahi sonrası komplikasyonları gerçekten önler mi? Bir efsane mi, gerçek mi?**Sami Benli<sup>1</sup>, Deniz Tikici<sup>2</sup>, Caner Baysan<sup>3</sup>, Mehmet Özgür Türkmenoğlu<sup>4</sup>, Tahsin Çolak<sup>4</sup><sup>1</sup> Evliya Çelebi Eğitim ve Araştırma Hastanesi, Cerrahi Onkoloji Kliniği, Kütahya, Türkiye<sup>2</sup> Gazi Yaşargil Eğitim ve Araştırma Hastanesi, Gastroenterolojik Cerrahi Kliniği, Diyarbakır, Türkiye<sup>3</sup> İzmir Demokrasi Üniversitesi Tıp Fakültesi, Halk Sağlığı Anabilim Dalı, İzmir, Türkiye<sup>4</sup> Mersin Üniversitesi Tıp Fakültesi, Cerrahi Anabilim Dalı, Kolorektal Cerrahi Bilim Dalı, Mersin, Türkiye**ÖZET**

**Giriş ve Amaç:** Mekanik bağırsak hazırlığının (MBP) cerrahi kliniklerin çoğunda elektif kolorektal cerrahiden önce rutin olarak kullanılmasına rağmen, MBP kullanımı tartışmalıdır. Bu çalışma, MBP yapılmadan sağ, sol veya rektosigmoid rezeksiyonların postoperatif komplikasyonlarını ve sonuçlarını araştırmayı amaçladı.

**Gereç ve Yöntem:** Ocak 2011 ile Aralık 2021 tarihleri arasında mekanik bağırsak hazırlığı yapılmadan elektif kolorektal cerrahi uygulanan hastalar çalışmaya dahil edildi. Hastalar rezeksiyon tarafına göre kategorize edildi ve bu alt gruplar, Clavien-Dindo sınıflaması kullanılarak ölçülen anastomoz kaçağı ve cerrahi alan enfeksiyonları (CAE) ve genel morbidite açısından karşılaştırıldı.

**Bulgular:** Dört yüz yirmi iki hastanın verileri retrospektif olarak analiz edildi. Toplam anastomoz kaçağı 14 (%3,3), cerrahi alan enfeksiyonu 46 (%10,9), batın içi koleksiyon 14 (%3,3), mortalite 18 (%4,3), reoperasyon 17 (%4) hastada saptandı. Gruplar ayrı ayrı değerlendirildiğinde sağ kolektomide altı (%3,9), sol kolektomide iki (%1,9) ve rektosigmoid rezeksiyon grubunda altı (%3,7) hastada anastomoz kaçağı görüldü. Gruplar arasında istatistiksel fark yoktu ( $p=0,630$ ). Ayrıca toplama ve tekrar operasyon açısından gruplar arasında istatistiksel fark yoktu;  $p$  değerleri sırasıyla  $p=0,31$  ve  $p=0,251$  idi.

**Sonuç:** Çalışmanın sonuçları; anastomoz kaçağı, cerrahi alan enfeksiyonu, karın içi sıvı toplanması, tekrar operasyon ve ölüm oranlarının mekanik bağırsak hazırlığıyla yapılan çalışmalardan elde edilen mevcut literatürle benzer olduğunu gösterdi. Ayrıca bu sonuçlar rezeksiyon bölgesine göre benzer bulunmuştur.

**Anahtar Kelimeler:** Preoperatif bağırsak hazırlığı, mekanik bağırsak hazırlığı, enfeksiyöz komplikasyonlar, cerrahi alan enfeksiyonu, anastomoz kaçağı

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# RIPASA versus Alvarado score in the assessment of acute appendicitis: A prospective study

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## ABSTRACT

**Objective:** This study aimed to compare Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) and Alvarado scoring to accurately identify acute appendicitis.

**Material and Methods:** A cross-sectional prospective study was carried out in the department of surgery. Patients were enrolled and scored using RIPASA and Alvarado scoring systems. Appendectomy was done, and the specimen was sent for histopathology examination, which was used as the gold standard for diagnosis. Among 400 recruits, 11 patients were lost to follow-up, giving us a sample size of 389 patients. The cut-off value for RIPASA and Alvarado scores was 7.5 and 7.0, respectively. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy in diagnosing acute appendicitis of both scores were analyzed using SPSS.

**Results:** Among 389 patients, 256 (66%) were males, and 277 (71%) were under the age of 40 years. RIPASA was more than 7.5 in 345 cases, while Alvarado was more than 7.0 in 261 patients. RIPASA score had a sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 95.8%, 87.9%, 98.9%, and 65.9%, respectively. In contrast, the ALVARADO score was 71.1% sensitive and 75.8% specific. RIPASA had a diagnostic accuracy of 95.12%, while Alvarado was only 71.46% accurate in diagnosing acute appendicitis.

**Conclusion:** Compared to the Alvarado scoring system, RIPASA is a better tool in terms of accuracy, sensitivity, and specificity for diagnosing acute appendicitis.

**Keywords:** Appendicitis, diagnostic technique, RIPASA score, Alvarado score, diagnostic accuracy

## INTRODUCTION

Acute appendicitis is the most common surgical emergency presenting to hospitals, with a lifetime prevalence of roughly 7% (1). In males, the incidence of acute appendicitis is higher compared to women (2). Several acute abdominal pathologies tend to mimic acute appendicitis' clinical symptomatology. However, appendectomy remains the gold-standard management for acute appendicitis (3). Even though appendicitis is a common problem that hospital patients come in with, diagnosis is still difficult and primarily clinical, with some laboratory findings, such as raised white blood cells (WBC) count, offering some assistance (4).

Grading systems have historically been used to aid physicians in making a more precise diagnosis and preventing unnecessary appendectomies due to the wide variety of reasons for right iliac fossa pain and clinical presentations for appendicitis. In the recent past, imaging modalities such as CT scans have helped with diagnostic challenges (5). In contexts where ordering frequent CT scans would result in extra resources and cost restrictions, clinical scoring criteria are nevertheless regarded as essential diagnostic auxiliary tools (6). The most prominent scoring system in this regard historically has been the Alvarado score, followed by the modified Alvarado score. These scoring systems were developed in the West, but when they were applied to other populations, particularly those in Asia, they did not show the same sensitivity and specificity (7,8). In order to stratify the risk of acute appendicitis among Asians, the Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) score system, developed in Brunei Darussalam in 2008, has proven to be beneficial (9). The parameters that make up the RIPASA grading system sum into a total score of 17.5 (9). This grading system requires just two routine investigations (WBC count and urine R/E) that are easily reported, yielding results that have a high

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negative predictive value that could reduce hospital costs by preventing negative appendectomy rates (10).

Some centres still utilize the Alvarado score to determine the likelihood of acute appendicitis despite the mounting evidence in favour of RIPASA. Owing to its decreased sensitivity and specificity, there is still a chance of making an inaccurate diagnosis and receiving subpar treatment. Untreated appendicitis can result in worse outcomes such as perforation, peritonitis, or abscess formation (11). Therefore, our study aims to compare the two scoring systems, RIPASA and Alvarado, to accurately identify acute appendicitis in our population.

### MATERIAL and METHODS

A cross-sectional prospective study was carried out at the department of surgery spanning over a time course of one year from January 2022 to December 2022. Approval was obtained from the ethical review board of the institute (Date: 16.12.2021), and informed consent was taken from all the participants. The study included all individuals who were clinically suspected to have acute appendicitis with the aid of an ultrasonography examination. The study eliminated participants who were under the age of 15, pregnant, had an appendicular mass, or had peritonitis-like symptoms. All patients who met the study eligibility requirements underwent RIPASA and Alvarado scoring by the same surgical team. Tables 1 and 2 describe the detailed parameters of the Alvarado and RIPASA grading system. The Alvarado score threshold was set at 7, while the RIPASA score cut-off was set at 7.5, and the scores were deemed positive when they were over 7 and 7.5, respectively. The appendectomies performed on the recruited patients were followed by specimens being sent for histopathology. Upon their discharge, patients were monitored for any postoperative problems and then had a follow-up assessment one week later. After that, histopathology results were recorded to distinguish between positive and negative appendectomies, and the outcomes were then associated with both scores.

**Table 1.** Alvarado grading system

Parameters	Score
Migratory pain	01
Anorexia	01
Nausea	01
Tenderness in right iliac fossa	02
Rebound tenderness	01
Elevated temperature	01
Raised WBC count	02
Shift to left	01
<b>Total score</b>	<b>10</b>

**Table 2.** RIPASA grading system

Parameters	Score
Male	1.0
Female	0.5
Age <40 years	1.0
Age >40 years	0.5
Pain-Right iliac fossa	0.5
Migratory pain	0.5
Anorexia	1.0
Nausea/Vomiting	1.0
Length of symptoms <48 hrs.	1.0
Length of symptoms >48 hrs.	0.5
Tenderness in right iliac fossa	1.0
Guarding in right iliac fossa	2.0
Rebound tenderness	1.0
Rovsing's sign	2.0
Elevated temperature	1.0
Raised WBC count	1.0
Unremarkable urinalysis	1.0
Foreign nationality	1.0
<b>Total score</b>	<b>17.5</b>

### Statistical Analysis

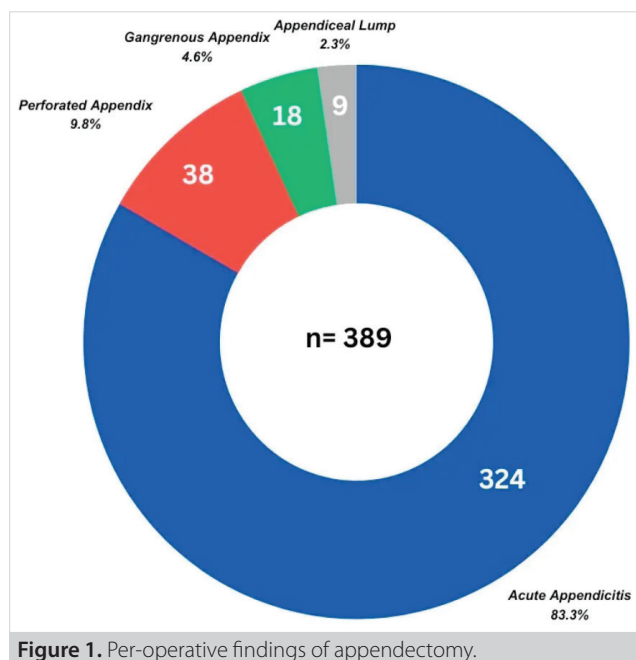
The data was entered and analysed using Statistical Package for Social Sciences (SPSS) version 23. Frequency and percentages were calculated for age, gender, duration of symptoms, histopathology, RIPASA and the Alvarado scores. The chi-square test was used to compare categorical variables, and the results were tabulated. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of both the scores were calculated. A p-value of 0.05 or lower was deemed significant.

### RESULTS

During the course of the study, 400 patients between the ages of 15 and 65 were enrolled in the study out of which 11 were lost to follow-up, leaving 389 patients for final evaluation. Of the recruited population, 71.2% (n= 277) were younger than 40 years, while 28.8% (n= 112) were older than 40 years. Out of 389 patients, 65.8% (n= 256) were males while 34.2% (n= 133) were females. Of patients, 75.8% (n= 295) had a duration of symptoms of less than 48 hours, while 24.2% (n= 94) had symptoms that lasted more than 48 hours. Out of 389 subjects, 345 (88.7%) had RIPASA scores greater than 7.5, while 261 (67.1%) cases had Alvarado scores greater than 7, as shown in Table 3. The participant's peroperative findings are shown in Figure 1.

**Table 3.** Characteristics of the study participants

Parameters	Frequency, n (%)
Gender	
Male	256 (65.8%)
Female	133 (34.2%)
Age	
<40 years	277 (71.2%)
>40 years	112 (28.8%)
Duration of symptoms	
<48 hrs.	295 (75.8%)
>48 hrs.	94 (24.2%)
Histopathology	
Positive	356 (91.5%)
Negative	33 (8.5%)
Alvarado	
>7	261 (67.1%)
<7	128 (32.9%)
RIPASA	
>7.5	345 (88.7%)
<7.5	44 (11.3%)

**Figure 1.** Per-operative findings of appendectomy.

Of the 345 patients with RIPASA >7.5, 341 had appendicitis on the histopathology report and four patients had histopathology reporting negative for appendicitis. A RIPASA score of less than 7.5 was seen in 44 (11.3%) individuals, of whom 15 had positive histopathology results and 29 had negative histopathology reports. Out of 261 patients, 253 cases were histopa-

thology-proven positive with an Alvarado score >7.0, whereas it was less than 7.0 in 128 patients, 103 of whom tested positively and 25 were negative on histopathology results, shown in Tables 4 and 5.

The RIPASA score was 95.8% sensitive and 87.9% specific in diagnosing acute appendicitis with a positive predictive value (PPV) and a negative predictive value (NPV) of 98.9% and 65.9%, respectively. The sensitivity, specificity, PPV, and NPV of the Alvarado score were 71.1%, 75.8%, 96.9%, and 19.5%, respectively. The diagnostic accuracy of the RIPASA and Alvarado scoring systems was 95.12% and 71.46%, respectively as shown in Tables 4 and 5.

## DISCUSSION

Across the world, acute appendicitis is a common condition with which patients present to the hospital, especially individuals under the age of 40 years. Appendectomy is a common procedure carried out in emergency services accounting for approximately 10% of the surgical procedures carried out for abdominal pathology (12-14). The most crucial factor in a surgeon's clinical evaluation is seen to be the ability to diagnose acute appendicitis. Appendectomy rates of 15-30% come from basing one's choice to operate only on a clinical approach (15,16). Despite the high levels of sensitivity and specificity that contrast-enhanced computed tomography (CECT) scans may attain, it is not always feasible to expose all individuals who may have acute appendicitis to CECT, especially in underdeveloped nations (17).

In this context, a variety of scoring systems have been created, with RIPASA and Alvarado being the most widely utilized. This study compared the two scoring methods among Asian people to identify a superior score with higher diagnostic accuracy. In our investigation, the RIPASA score sensitivity and specificity were determined to be 95.8% and 87.9%, respectively, whereas the Alvarado score was 71.1% sensitive and 75.8% specific. RIPASA score has a PPV and NPV of 98.88% and 97.67% compared to the Alvarado scores of 96.84% and 21.82%. The RIPASA and Alvarado scores' diagnostic accuracy was 97.67% and 69.33%, respectively.

Chisthi et al. have conducted a study in India which reported RIPASA as 87.78% sensitive, 76.47% specific with a diagnostic accuracy of 85.98% (8). Another study conducted in Saudi Arabia by Maksoud et al. have shown a phenomenal RIPASA sensitivity of 96% which was comparable to our results i.e., 95.8% sensitive (18). Regar et al. have conducted a study in India that revealed results comparable to our study, however, with a significantly low specificity of RIPASA (3). Chavan et al. have compared the two scoring systems i.e., Alvarado versus RIPASA and reported results comparable to our study (19). Noor et al. have conducted a study in Peshawar, Pakistan recruiting

**Table 4.** Diagnostic value of RIPASA scoring system

RIPASA	Histopathology		Total
	Positive	Negative	
>7.5	341	4	345
<7.5	15	29	44
	356	33	389
Parameters	Estimates*		Confidence interval (95%)
Sensitivity	95.8% (p= 0.000)		93.4-97.6
Specificity	87.9% (p= 0.000)		74.0-96.1
PPV	98.9% (p= 0.000)		97.3-99.6
NPV	65.9% (p= 0.000)		51.3-78.7
Diagnostic accuracy	95.12%		

\*p-value of  $\leq 0.05$  is considered statistically significant.  
PPV: Positive predictive value, NPV: Negative predictive value.

**Table 5.** Diagnostic value of Alvarado scoring system

Alvarado	Histopathology		Total
	Positive	Negative	
>7	253	8	261
<7	103	25	128
	356	33	389
Parameters	Estimates*		Confidence interval (95%)
Sensitivity	71.1% (p= 0.000)		66.2-75.6
Specificity	75.8% (p= 0.000)		59.6-88.1
PPV	96.9% (p= 0.000)		94.4-98.6
NPV	19.5% (p= 0.000)		13.3-27.0
Diagnostic accuracy	71.46 %		

\*p-value of  $\leq 0.05$  is considered statistically significant.  
PPV: Positive predictive value, NPV: Negative predictive value.

300 participants revealed the RIPASA sensitivity and specificity at 98.5% and 90%, respectively (20). These values are comparable and slightly better from the results reported in our study. A study recently conducted in Karachi has evaluated 384 patients and shown RIPASA score sensitivity, specificity, and diagnostic accuracy of 95.98% (95% CI 93.36-97.59), 91.67% (95% CI 78.17-97.13) and 95.57% (95% CI 93.03-97.22) (21). RIPASA specificity reported in this study is slightly better but overall results are comparable to our study.

This study was conducted at a single centre, which may limit the generalizability of the findings. It is recommended that future studies with larger sample sizes should be conducted at multiple centres to further investigate this topic. Moreover, the research focused on individuals who underwent an appendectomy procedure. Cases that did not involve surgery were not

taken into account during the study, thus restricting the applicability of the findings to only those who received surgical treatment. Consequently, the outcomes cannot be universally applied to all patients who presented with symptoms of pain in the right lower quadrant.

## CONCLUSION

Compared to the Alvarado scoring system, the RIPASA grading system is superior in terms of accuracy, sensitivity, and specificity providing a reliable predictor for the diagnosis of acute appendicitis. Frequent implementation of the RIPASA grading system in our setting will lessen patient morbidity, shorten hospital stays, and lower the burden of healthcare costs. It can also prevent the need for expensive imaging examinations, which is especially advantageous for the public system in a country with a lower-middle income level.



**Ethics Committee Approval:** This study was approved by Federal Government Polyclinic Ethics Committee (Decision no: FGPC.1/12/2020, Date: 16.12.2021).

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**ORİJİNAL ÇALIŞMA-ÖZET**

Türk J Surg 2023; 39 (3): 231-236

**Akut apandisit değerlendirilmesinde RIPASA vs. Alvarado skoru: Prospektif bir çalışma**Syed Shams Ud Din<sup>1</sup>, Inayat Ullah Baig<sup>1</sup>, Mirza Tassawar Hussain<sup>1</sup>, Abdullah Sadiq<sup>1</sup>, Talha Humayun<sup>1</sup>, Umair Ahmad<sup>1</sup>, Aqsa Syed<sup>2</sup><sup>1</sup> Federal Hükümet Poliklinik Hastanesi, Cerrahi Kliniği, Islamabad, Pakistan<sup>2</sup> Akbar Niazi Eğitim Hastanesi, Cerrahi Kliniği, Islamabad, Pakistan**ÖZET**

**Giriş ve Amaç:** Bu çalışma, akut apandisiti doğru bir şekilde tanımlamak için Raja Isteri Pengiran Anak Saleha Apandisit (RIPASA) ve Alvarado puanlamasını karşılaştırmayı amaçladı.

**Gereç ve Yöntem:** Cerrahi anabilim dalında kesitsel prospektif bir çalışma yapıldı. Hastalar kaydedildi ve RIPASA ile Alvarado skorlama sistemleri kullanılarak skorlandı. Apendektomi sonrası örnekler tanıda altın standart olarak kullanılan histopatoloji incelemesine gönderildi. Dört yüz hasta arasında 11 hasta takipte kaybedildi, bu da 389 hastadan oluşan bir örneklem büyüklüğü sağladı. RIPASA ve Alvarado skorları için kesme değeri sırasıyla 7,5 ve 7,0 idi. Her iki skorun da akut apandisit tanısındaki duyarlılığı, özgüllüğü, pozitif prediktif değeri (PPV), negatif prediktif değeri (NPV) ve doğruluğu SPSS kullanılarak analiz edildi.

**Bulgular:** Üç yüz seksen dokuz hastanın 256'sı (%66) erkek, 277'si (%71) 40 yaşın altındaydı. RIPASA 345 vakada 7,5'in üzerindeyken, Alvarado 261 hastada 7,0'ın üzerindeydi. RIPASA skorunun sırasıyla %95,8, %87,9, %98,9 ve %65,9'luk bir duyarlılığı, özgüllüğü, pozitif öngörü değeri (PPV) ve negatif öngörü değeri (NPV) vardı. Buna karşılık, Alvarado skoru %71,1 duyarlı ve %75,8 spesifikti. RIPASA'nın tanısıl doğruluğu %95,12 iken, Alvarado akut apandisit tanısında yalnızca %71,46'lık bir doğruluğa sahipti.

**Sonuç:** Alvarado puanlama sistemiyle karşılaştırıldığında RIPASA, akut apandisit tanısında doğruluk, duyarlılık ve özgüllük açısından daha iyi bir araçtır.

**Anahtar Kelimeler:** Apandisit, tanı tekniği, RIPASA skoru, Alvarado skoru, tanısıl doğruluk

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# The effect of surgery and hormone therapy on quality of life in breast cancer patients receiving radiotherapy

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## ABSTRACT

**Objective:** The aim of this study was to examine the effect of surgery type and hormone therapy on the general quality of life in breast cancer patients receiving radiotherapy.

**Material and Methods:** A total of 109 patients were included in the study. As data collection tools in the research, a form stating the demographic and clinical features was used in the first part, and in the second part, "EORTC QLQ-C30" developed by the European Organization for Research and Treatment of Cancer and "EORTC QLQ-BR23" Turkish quality of life forms specific to breast cancer were used. The patients were asked to fill in the questionnaire forms on the first day, the last day of radiotherapy and three months after the end of the treatment.

**Results:** Mean age of this study was  $54.8 \pm 12.1$  years. In the questionnaires made on the first day, last day and three months after radiotherapy, the highest score according to the EORTC QLQ-C30 scale was in social and cognitive function, and in sexual life on the EORTC QLQ-BR23 scale. According to multiple comparison test and comparing the first day of radiotherapy and three months after radiotherapy, there was a significant difference in patients' physical function average ( $p=0.049$ ), future expectation ( $p=0.033$ ), sexual life ( $p=0.029$ ), sexual satisfaction ( $p<0.001$ ), and hair loss ( $p=0.011$ ), and arm related problems ( $p<0.001$ ). According to the analysis of variance in repeated measurements, physical function, sexual life, side effects, hair loss, dyspnea, and future expectation were statistically significant according to the type of surgery, and for hormone therapy, sexual life, hair loss, constipation and financial difficulty were found statistically significant.

**Conclusion:** It was observed that other than radiotherapy, hormone therapy and surgical techniques were also effective on the quality of life in patients receiving radiotherapy for breast cancer.

**Keywords:** Breast cancer, radiotherapy, hormone therapy, surgery, quality of life, QLQ-C30, QLQ-BR23

## INTRODUCTION

Breast cancer is the most common type of cancer diagnosed in women, apart from skin cancers. It affects approximately 2.1 million women each year (1). Although the incidence of breast cancer is higher in developed countries, the diagnosis of breast cancer is increasing in almost every country. In Türkiye, according to the 2016 data of the Ministry of Health, breast cancer ranks first among the top ten most common cancer types in women (2,3). Although breast cancer-related mortality is decreasing gradually in many countries, it is the most common cause of cancer-related deaths among women (1-3).

Due to the developments in the diagnosis and treatment of cancer in recent years, breast cancer is diagnosed at an early stage. Accordingly, the concept of quality of life in patients has begun to come to the fore as a result of prolongation of survival and therefore long-life expectancy. Breast cancer treatment includes surgery, radiotherapy, chemotherapy, hormone therapy and targeted therapies. Some side effects seen in these treatments negatively affect the general quality of life in women (4). Radiotherapy is usually started after the end of adjuvant chemotherapy or 3-8 weeks after surgery when wound healing is complete. The aim of radiotherapy is to provide the best local tumor control with low complication rates. As with all treatment types, some side effects are seen in radiotherapy. Radiotherapy can cause fatigue, nausea, vomiting, esophagitis, and therefore a decrease in work force can be observed. In addition, hair loss, drying and discoloration of the skin can be seen in some changes in the skin area within the radiotherapy area. Nerves entering the treatment area may also be adversely affected by radiation, loss of

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sensation and weakness may occur in the area where the nerves are dispersed. The surgical technique applied or the combined hormone therapy/chemotherapy drugs may cause an increase in these side effects. It is important to determine and treat the factors affecting the quality of life in this group of patients (5).

Various quality of life evaluation modules have been developed in order to objectively evaluate the general quality of life of the patients. Headquartered in Brussels, Belgium, the European Organization for Research and Treatment of Cancer (EORTC) is one of the leading organizations in cancer treatment and research in Europe. It carries out studies on the treatment of cancer and attaches importance to the quality of life of patients receiving this treatment. With the questionnaires it has developed, it provides the opportunity to question the quality of life of the patients in an international common language. The most widely used module among the questionnaires developed by EORTC is the Quality of Life Questionnaire-Core30 (QLQ-C30) general quality of life questionnaire. In addition, EORTC has many other surveys on different body parts and organs. In patients with breast cancer, the EORTC QLQ-BR23 questionnaire is widely used (6-9).

Based on the knowledge that breast cancer is the most common cancer among women and that the treatments applied will affect the quality of life, this study was planned to determine the effect of the type of surgery and hormone therapy on the quality of life in patients with breast cancer who received radiotherapy.

## **MATERIAL and METHODS**

### **Method of Study**

This study was conducted as a descriptive, prospective, and analytical study to determine the effect of radiotherapy on general quality of life in patients with breast cancer.

### **Ethical Aspect of the Study**

Permission was obtained from the ethics committee for this study.

### **Location of the Study and Sampling Group**

It consisted of 109 patients who came to receive adjuvant radiotherapy for breast cancer. Radiotherapy was started 3-8 weeks after the operation in patients who had received neoadjuvant chemotherapy. In patients who received adjuvant chemotherapy, adjuvant radiotherapy was applied after chemotherapy had been finished.

Selection criteria of cancer patients included in the study were as follows:

- a. 18 years of age and older,
- b. Willing to participate,
- c. Able to answer questions,
- d. The patient or one of her relatives is literate,
- e. Without patients receiving psychological support,
- f. Without neurological or psychiatric disorders that prevent the completion of the questionnaire,
- g. With a Karnofsky performance score of  $\geq 50$ , 1-3. patients with a diagnosis of stage 1-3 breast cancer who voluntarily agreed to participate in the study were included in the study.

### **Data Collection Tool**

Patients were asked to fill out the questionnaires on the first and last day of radiotherapy and three months after radiotherapy. Written informed consent was obtained from the individuals participating in the study, explaining the purpose, plan, and benefits of the study. The questionnaire form was composed of two parts. In the first part, information about the patient's age, marital status, educational status, and family history of cancer was included. These questions were asked to the individuals by the researcher and recorded. In the second part, clinical information about the disease was recorded by learning from the patient's file, whether the patient received surgery, chemotherapy and hormone therapy, tumor location, pathological diagnosis, receptor status and stage. The Turkish versions of the EORTC QLQ-C30 and EORTC QLQ-BR23 scales were used.

### **EORTC QLQ-C30 scale**

This scale is known as general quality of life and includes 30 questions. These consist of three sub-dimensions: functional functions (physical, role, cognitive, emotional, social), symptom scale (fatigue, pain, nausea/vomiting, dyspnea, insomnia, anorexia, constipation, diarrhea, financial difficulty) and general well-being. The first 28 of the scale questions are four-point Likert type. The answers given; not at all (1 point), a little (2 points), quite (3 points), a lot (4 points). High scores from the first 28 questions indicate low quality of life, and low scores indicate high quality of life. The 29<sup>th</sup> and 30<sup>th</sup> questions of the scale constitute the general quality of life area. In the 29<sup>th</sup> question of the scale, the patient is asked to evaluate her general health in the past week, and in the 30<sup>th</sup> question, the quality of life of the last week, with the scores given from one to seven as very bad (1 point), very good (7 points). Low scores in this section indicate low quality of life, and high scores indicate high quality of life.

The scale consists of three basic sub-dimensions. Although each basic sub-dimension also contains sub-dimensions, there are a total of 15 sub-dimensions in the whole scale (Table 1).

**Table 1.** EORTC QLQ-C30 cancer quality of life scale

Scales	Materials
<b>Functional status</b>	
Physical function	1-5
Role function	6-7
Emotional function	21-24
Cognitive function	20, 25
Social function	26-27
Global health status (general well-being)	29-30
<b>Symptom scale</b>	
Weakness	10, 12, 18
Nausea-Vomiting	14-15
Ache	9, 19
Dyspnea	8
Insomnia	11
Loss of appetite	13
Constipation	16
Diarrhea	17
Financial difficulty	28

Scoring of the scale is made according to the hundredth system. Scores ranging from 0-100 are obtained from each sub-dimension. There are formulas applied to find the equivalent of the scores obtained from the scale in the hundredth system. Functional score, Symptom score, and General Health score are calculated with the following formulas:

Calculation of the functional score (FS): The patient's total score from 15 questions is divided by the total number of questions (15) and the Raw score (RS) was calculated. The range value, on the other hand, gave the value of three, which is the difference between the highest score (4) and the lowest score (1) given to the answers. With these values, FS is calculated with the formula  $FS = \{1 - (RS - 1)/range\} \times 100$ .

Calculation of social function score (SFS): Raw score (RS) is calculated by dividing the total score of the patient from questions 26 and 27 by two, which is the total number of questions. Then the range value is found as in FS. With these values, SFS is calculated with the formula  $SFS = \{1 - (RS - 1)/range\} \times 100$ .

Symptom score (SS): Raw score (RS) is calculated by dividing the total score from 13 questions by the total number of questions (13). Then the range value is found as in FS. With these values, SS is calculated with the formula  $SS = \{(RS - 1)/range\} \times 100$ .

Calculation of the fatigue score (FAS) in the symptom scale: The raw score (RS) is calculated by dividing the total score of the patient from questions 10, 12 and 18 by the total number of questions. The difference (3) range value between the highest score (4) and the lowest score (1) given to the answers is found. With these values, FAS is calculated with the formula  $= \{(RS - 1)/range\} \times 100$ .

Calculation of general health score (GSS): Raw score (RS) is calculated by dividing the total score from the last two questions by the total number of questions (2). The difference between the highest score (7) and the lowest score (1) in these two questions is calculated as the range value (6). These values are calculated with the formula  $GSS = \{(RS - 1)/range\} \times 100$ .

The European Organization for Research and Treatment of Cancer periodically renews the EORTC QLQ-C30 with different versions. According to these, studies investigating the validity and reliability in Turkish have been carried out. In the study of Demirci et al., Cronbach's alpha value for body image and sexual function sub-dimensions was 0.88, Cronbach's alpha for treatment side effects sub-dimension was 0.73, and Cronbach's alpha for breast symptoms sub-dimension was 0.66 (9).

#### EORTC QLQ-BR23 scale

It is a quality-of-life questionnaire prepared specifically for breast cancer. This questionnaire is divided into two subgroups as functional and symptom scales and consists of 23 questions. On the functional scale, body image, sexual function, sexual satisfaction, and future expectation are measured, and on the symptom scale, systemic treatment side effects, breast-related problems, arm-related problems, and discomfort related to hair loss are measured. In the QLQ-BR23, each parameter has a score between 0 and 100. A high score on the functional scale indicates good health, and a high score on the symptom scale indicates an excess of symptoms (Table 2).

**Table 2.** EORTC QLQ-BR23 breast cancer specific scale

Scales	Materials
<b>Functional scale</b>	
Body image	39-42
Future expectation	43
Sex life	44-45
Sexual satisfaction	46
<b>Symptom scale</b>	
Side effect	31-34, 36-38
Hair loss	35
Arm related problems	47-49
Breast related problems	50-53



### Analysis of Data

While the findings obtained in the study were evaluated, statistical analyzes were carried out in computer environment using TURCOSA (Turcosa Analitik Çözümler LTD. ŞTİ., www.turcosa.com.tr) statistical software. The results were socio-demographic and disease-related characteristics; given as numbers, percentages, and averages. Quality of life scale scores were calculated using the above-mentioned formulas: The conformity of the data to normal distribution was evaluated with the Shapiro-Wilk test. Homogeneity of variance was evaluated with Levene's test. Hormone therapy and surgical status of the patients on the EORTC QLQ-C30 and EORTC QLQ-BR23 scales were evaluated by one-way repeated measure ANOVA (post-hoc test: Bonferroni) and Student's t test analysis. The results were evaluated at the 95% confidence interval, and the significance level was  $p < 0.05$ .

### Limitation of the Study

The limitation of the study is that the study was conducted with a specific patient group in only one center.

### Strengths of the Research

The strength of the study is that the sample group was carried out by a single physician and the results were monitored.

### RESULTS

Sociodemographic and clinical characteristics of the patients are given in Table 3. Mean age was  $54.8 \pm 12.1$  years. The most common surgery was breast conserving surgery, and the most common type of pathology was invasive ductal carcinoma. Of the patients, 62.4% were postmenopausal, and pT3 was 47.7%, pN3 was 45.9%, chemotherapy was 97.2%, and hormone therapy was 85.3%.

In the questionnaires made on the first day, the last day and three months after radiotherapy, the highest score according to the EORTC QLQ-C30 scale was in social and cognitive function, and in sexual life on the EORTC QLQ-BR23 scale. In our study, according to multiple comparison of the repeated measure ANOVA test results, the result was significant for the physical function ( $p = 0.049$ ) variable between the time groups receiving radiotherapy (first day, last day, and three months later) (Table 4). These analyses for the EORTC QLQ-BR23 scales were investigated for future expectation ( $p = 0.033$ ), sexual life ( $p = 0.029$ ), sexual satisfaction ( $p < 0.001$ ), hair loss ( $p = 0.011$ ) and arm related problems ( $p < 0.001$ ) are found statistically significant (Table 5).

According to the repeated measure ANOVA of the EORTC QLQ-C30 scale, surgical status of the patients who underwent BCS was found to be significant for the variable of physical function ( $p^* = 0.008$ ) at three different times (first, last day and three months after radiotherapy). There was a significant difference in the measurement of dyspnea ( $p^* = 0.047$ ) on the last day of

**Table 3.** Sociodemographic and clinical characteristics of the patients participating in the study

Quantitative variables	$\bar{x} \pm SD$
Age	$54.86 \pm 12.17$
	<b>Median (min-max)</b>
	<b>54.00 (24.00-84.00)</b>
Qualitative variables	n (%)
<b>Work at work</b>	
No	99 (90.8)
Yes	10 (9.2)
<b>Marital status</b>	
Single	15 (14.3)
Married	90 (85.7)
<b>Education status</b>	
No	26 (23.9)
Yes	83 (76.1)
<b>Cancer in the family</b>	
No	83 (76.1)
Yes	26 (23.9)
<b>Menopause</b>	
Pre	41 (37.6)
Post	68 (62.4)
<b>Additional disease</b>	
No	72 (66.1)
Yes	37 (33.9)
<b>Breast location</b>	
Left	67 (61.5)
Right	42 (38.5)
<b>Pathology type</b>	
Invasive ductal carcinoma	95 (87.2)
Others (mucinous, etc)	14 (12.8)
<b>Tumor Stage (AJCC 2009 stage)</b>	
1	11 (10.1)
2	38 (34.9)
3	52 (47.7)
4	8 (7.3)
<b>Lymph node (AJCC 2009 stage)</b>	
0	11 (10.1)
1	6 (5.5)
2	42 (38.5)
3	50 (45.9)
<b>Stages</b>	
1	1 (0.9)
2	13 (12.0)
3	94 (87.1)

**Table 3.** Sociodemographic and clinical characteristics of the patients participating in the study (continue)

Quantitative variables	$\bar{x} \pm SD$
<b>Estrogen status</b>	
Negative	16 (14.7)
Positive	93 (85.3)
<b>Progesterone status</b>	
Negative	27 (24.8)
Positive	82 (75.2)
<b>HER status</b>	
Negative	96 (88.1)
Positive	13 (11.9)
<b>Surgical condition</b>	
Modified radical mastectomy	37 (33.9)
Breast conserving surgery	72 (66.1)
<b>Chemotherapy</b>	
No	3 (2.8)
Yes	106 (97.2)
<b>Hormone therapy</b>	
No	16 (14.7)
Yes	93 (85.3)

$\bar{x}$ : Arithmetic mean, SD: Standard deviation.

radiotherapy by Student's t test, compared to patients with BSC who had surgical intervention MRM. In addition, the measurements of constipation ( $p^* = 0.032$ ) of the patients who did not receive hormone therapy were significant in terms of the time they received radiotherapy. According to the multiple comparison test of the constipation and financial difficulty variable, the measurement of the patients who did not receive hormone therapy three months after radiotherapy was also significant compared to the measurement of radiotherapy on the first day (Tables 6-10).

In the analyses performed on the EORTC QLQ-BR23 scale, mean differences of body image, future expectation and sexual life scales were not found statistically significant in terms of the time (first day, last day, three months later) patients with MRM and BSC received radiotherapy. The variables of future expectation ( $p^* = 0.021$ ) of the patients with surgical intervention for BSC and sexual life ( $p^* = 0.013$ ) of the patients who received hormone therapy were found to be statistically significant in terms of the time they received radiotherapy (Table 11). The variable of sexual satisfaction ( $p^* = 0.019$ ) of the patients with MRM was statistically significant, meanwhile patients with surgical intervention BSC had sexual satisfaction ( $p^* = 0.011$ ), side effects ( $p^* = 0.030$ ), and hair loss ( $p^* = 0.045$ ). The hair loss ( $p^* = 0.007$ ) variable of the patients who did not receive hormone therapy was found to be statistically significant, and at the same time, the variable of sexual satisfaction ( $p^* = 0.002$ )

**Table 4.** Comparison of the mean scores of the EORTC QLQ-C30 cancer quality of life scale of the patients participating in the study

Variables	When receiving radiotherapy			p
	First day (n= 109) $\bar{x} \pm SD$	Last day (n= 109) $\bar{x} \pm SD$	Three months later (n= 109) $\bar{x} \pm SD$	
Physical function	61.47 $\pm$ 23.31 <sup>a</sup>	60.86 $\pm$ 22.02 <sup>ab</sup>	54.13 $\pm$ 25.90 <sup>b</sup>	<b>0.049</b>
Role function	68.83 $\pm$ 23.14	64.35 $\pm$ 19.66	62.81 $\pm$ 19.68	0.114
Emotional function	72.48 $\pm$ 21.71	67.13 $\pm$ 19.99	72.09 $\pm$ 19.09	0.122
Cognitive function	78.86 $\pm$ 23.96	81.64 $\pm$ 18.22	76.70 $\pm$ 22.55	0.282
Social function	81.04 $\pm$ 21.81	75.99 $\pm$ 22.16	76.61 $\pm$ 19.66	0.177
General health perception	55.35 $\pm$ 20.05	56.57 $\pm$ 17.86	55.89 $\pm$ 20.30	0.883
Weakness	42.20 $\pm$ 28.28	43.12 $\pm$ 18.62	40.57 $\pm$ 18.48	0.709
Nausea	22.94 $\pm$ 25.13	22.02 $\pm$ 24.31	23.39 $\pm$ 27.04	0.927
Ache	20.64 $\pm$ 21.62	18.81 $\pm$ 21.17	20.64 $\pm$ 21.98	0.772
Dyspnea	24.46 $\pm$ 26.70	24.46 $\pm$ 26.70	29.05 $\pm$ 27.25	0.395
Insomnia	33.95 $\pm$ 29.39	26.29 $\pm$ 29.42	30.89 $\pm$ 29.64	0.193
Loss of appetite	30.58 $\pm$ 28.01	29.97 $\pm$ 26.43	29.66 $\pm$ 24.15	0.970
Constipation	20.18 $\pm$ 27.97	26.30 $\pm$ 27.99	27.52 $\pm$ 31.38	0.138
Diarrhea	24.46 $\pm$ 23.41	23.85 $\pm$ 18.20	20.49 $\pm$ 18.65	0.298
Financial difficulty	17.13 $\pm$ 25.51	14.98 $\pm$ 22.45	18.96 $\pm$ 21.45	0.326

According to the multiple comparison test result (Bonferroni), the difference in alphabetical exponents indicates statistically significant.

$\bar{x}$ : Arithmetic mean, SD: Standard deviation.

**Table 5.** Comparison of the mean score of the EORTC QLQ-BR23 scale of the patients participating in the study

Variables	When receiving radiotherapy			p
	First day (n= 109) $\bar{x} \pm SD$	Last day (n= 109) $\bar{x} \pm SD$	Three months later (n= 109) $\bar{x} \pm SD$	
Body image	86.25 $\pm$ 21.54	83.82 $\pm$ 22.62	84.95 $\pm$ 24.14	0.748
Future expectation	68.81 $\pm$ 35.80 <sup>a</sup>	67.28 $\pm$ 42.31 <sup>ab</sup>	79.51 $\pm$ 34.22 <sup>b</sup>	<b>0.033</b>
Sex life	83.18 $\pm$ 23.52 <sup>a</sup>	88.69 $\pm$ 16.02 <sup>b</sup>	89.91 $\pm$ 18.57 <sup>b</sup>	<b>0.029</b>
Sexual satisfaction	76.76 $\pm$ 29.22 <sup>a</sup>	89.91 $\pm$ 18.43 <sup>b</sup>	86.85 $\pm$ 21.76 <sup>b</sup>	<b>&lt;0.001</b>
Side effects	35.74 $\pm$ 21.23	41.74 $\pm$ 24.39	34.98 $\pm$ 21.95	0.058
Hair los	33.95 $\pm$ 29.39 <sup>a</sup>	43.12 $\pm$ 26.95 <sup>b</sup>	33.95 $\pm$ 27.21 <sup>a</sup>	<b>0.011</b>
Arm related problems	12.35 $\pm$ 17.34 <sup>a</sup>	8.33 $\pm$ 10.20 <sup>b</sup>	4.42 $\pm$ 8.17 <sup>c</sup>	<b>&lt;0.001</b>
Breast related problems	43.27 $\pm$ 14.72	41.67 $\pm$ 11.89	44.34 $\pm$ 13.51	0.339

According to the multiple comparison test result (Bonferroni), the difference in alphabetical exponents indicates statistically significant.  
 $\bar{x}$ : Arithmetic mean, SD: Standard deviation.

of the patients who received hormone therapy was found to be statistically significant. According to Table 12, sexual satisfaction, side effects, and hair loss scales of the patients with surgical interventions for MRM and BSC, and those who received and did not receive hormone therapy, for each measurement at the time of radiotherapy (first day, last day, three months later) in the Student's t test was not statistically significant mean differences. Otherwise, the mean difference of hair loss measurement ( $p=0.036$ ) three months after radiotherapy was found to be statistically significantly higher in those who received hormone therapy compared to those who did not. The results were significant in terms of arm-related problems ( $p<0.001$ ) in patients with surgical intervention for BSC and arm-related problems ( $p<0.001$ ) in patients receiving hormone therapy when they received radiotherapy (Tables 11-13).

## DISCUSSION

While treatment and supportive treatment in breast cancer are the main goals, increasing the quality of life has been added to these goals in recent years. Since breast cancer is the most common cancer among women and the adverse effect of breast loss on patient identity, it is observed that quality of life is evaluated more frequently than in the past. However, it is not possible to talk about a scale that has yet been developed that can be considered as the gold standard today. Quality of life can vary from individual to individual, from society to society, and from culture to culture, and is affected by many factors. Therefore, it is very difficult to measure and evaluate quality of life. The reason is that the questions in the quality scales do not fully cover the concept of quality of life, and the answers given by the patients are subjective. In addition, the role of quality of life in determining the treatment method to be given to the patient is not clear (6-12).

Quality of life in breast cancer, as in other cancers, refers to general health status, physical functionality, severity of

symptoms, psychosocial adjustment of the patient and satisfaction with life. Studies show that cancer disease and its treatment negatively affect the quality of life. While symptoms related to illness and treatment, anxiety, anxieties about the individual and her environment, changes in body image negatively affect the quality of life, factors such as adequate social support systems, comfort, belief in recovery, and economic adequacy can affect positively (5,7,8,10-12). In this study, it was observed that the change in body image, the surgical technique applied, and the use of radiotherapy combined hormone therapy affected the quality of life. In addition, it was observed that the quality of life was lower in the first month after the diagnosis compared to the following months, and the quality-of-life score started to follow a certain line from three months after the treatment. In a study, it has been shown that the quality of life of cancer patients is very low in the first six months after diagnosis (12). Lee et al. have reported that quality of life improve seven months after radiotherapy (13).

The most common problems experienced by breast cancer patients during treatment are symptoms such as pain, weakness, nausea, loss of appetite, alopecia, dyspnea, diarrhea, and insomnia. All these problems cause difficulties in the functional lives of individuals with cancer. In our study, in the questionnaires made on the first day, last day and three months after radiotherapy, physical function was affected according to the EORTC QLQ-C30 scale, and in the QLQ-BR23 scale, it was observed that future expectation, sexual life, sexual satisfaction, hair loss and arm-related problems were affected. These results were found to be affected by the timing of radiotherapy. According to the results of another study conducted in our country to determine the quality of life of patients who received radiotherapy for breast cancer, the most determining subscales on general health in the QLQ-C30 were emotional

**Table 6.** Comparison of surgical technique and hormone therapy status and the mean score of EORTC QLQ-C30 cancer quality of life scale in the study

Variables	Physical function			p*	Role function			p*	Emotional function			p*
	First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$		First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$		First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$	
Surgery												
MRM (n= 37)	63.60 $\pm$ 23.96	55.50 $\pm$ 23.89	59.82 $\pm$ 25.55	0.342	72.52 $\pm$ 22.64	61.26 $\pm$ 16.69	64.86 $\pm$ 20.33	0.080	72.97 $\pm$ 18.26	70.27 $\pm$ 19.69	69.14 $\pm$ 20.68	0.702
BCS (n= 72)	60.37 $\pm$ 23.06 <sup>a</sup>	63.61 $\pm$ 20.63 <sup>a</sup>	51.20 $\pm$ 25.76 <sup>b</sup>	<b>0.008</b>	66.90 $\pm$ 23.32	65.69 $\pm$ 20.98	61.74 $\pm$ 19.39	0.333	72.22 $\pm$ 23.40	65.51 $\pm$ 20.09	73.61 $\pm$ 18.18	0.064
p#	0.495	0.068	0.100		0.233	0.291	0.381		0.865	0.241	0.249	
Hormone therapy												
No (n= 16)	61.67 $\pm$ 28.02	59.58 $\pm$ 21.97	43.75 $\pm$ 27.96	0.117	63.54 $\pm$ 22.13	62.50 $\pm$ 21.52	63.54 $\pm$ 21.27	0.988	69.27 $\pm$ 28.50	61.98 $\pm$ 24.15	75.00 $\pm$ 19.72	0.438
Yes (n= 93)	61.43 $\pm$ 22.58	61.08 $\pm$ 22.14	55.91 $\pm$ 25.25	0.220	69.75 $\pm$ 23.30	64.67 $\pm$ 19.43	62.68 $\pm$ 19.51	0.084	73.03 $\pm$ 20.46	69.01 $\pm$ 19.20	71.60 $\pm$ 19.04	0.216
p#	0.971	0.804	0.083		0.324	0.733	0.827		0.525	0.267	0.512	

According to the multiple comparison test result (Bonferroni), the difference in alphabetical exponents indicates statistically significant.

p\*: Repeated measure analysis of variance, p#: Student's t test,  $\bar{x}$ : Arithmetic mean, SD: Standard deviation, BCS: Breast conserving surgery, MRM: Modified radical mastectomy.**Table 7.** Comparison of surgical technique and hormone therapy status and the mean score of EORTC QLQ-C30 cancer quality of life scale in the study

Variables Surgery	Cognitive function			p*	Social function			p*	General health perception			p*
	First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$		First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$		First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$	
Surgery												
MRM (n= 37)	77.78 $\pm$ 24.88	81.53 $\pm$ 17.91	78.83 $\pm$ 20.66	0.741	79.73 $\pm$ 20.46	78.38 $\pm$ 20.36	75.23 $\pm$ 20.27	0.629	58.33 $\pm$ 17.24	53.83 $\pm$ 19.50	58.78 $\pm$ 19.64	0.451
BCS (n= 72)	79.40 $\pm$ 23.65	81.48 $\pm$ 18.46	75.69 $\pm$ 23.39	0.293	81.71 $\pm$ 22.58	74.77 $\pm$ 23.07	77.31 $\pm$ 19.44	0.174	53.82 $\pm$ 21.30	57.99 $\pm$ 16.93	54.40 $\pm$ 20.60	0.320
p#	0.742	0.989	0.493		0.655	0.423	0.602		0.268	0.252	0.287	
Hormone therapy												
No (n= 16)	76.04 $\pm$ 27.20	79.17 $\pm$ 18.76	70.83 $\pm$ 23.96	0.633	79.17 $\pm$ 27.55	70.83 $\pm$ 27.55	82.29 $\pm$ 22.33	0.459	52.60 $\pm$ 25.59	53.65 $\pm$ 21.51	50.52 $\pm$ 18.63	0.913
Yes (n= 93)	79.34 $\pm$ 23.49	82.07 $\pm$ 18.20	77.72 $\pm$ 22.28	0.421	81.36 $\pm$ 20.83	76.88 $\pm$ 21.14	75.63 $\pm$ 19.12	0.147	55.82 $\pm$ 19.07	57.08 $\pm$ 17.24	56.81 $\pm$ 20.52	0.879
p#	0.613	0.581	0.255		0.712	0.315	0.212		0.555	0.480	0.254	

According to the multiple comparison test result (Bonferroni), the difference in alphabetical exponents indicates statistically significant.

p\*: Repeated measure analysis of variance, p#: Student's t test,  $\bar{x}$ : Arithmetic mean, SD: Standard deviation, BCS: Breast conserving surgery, MRM: Modified radical mastectomy.

**Table 8.** Comparison of surgical technique and hormone therapy status and the mean score of EORTC QLQ-C30 cancer quality of life scale in the study

Variables	Weakness			p*	Nausea			p*	Ache			p*
	First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$		First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$		First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$	
Surgery												
MRM (n=37)	36.34 $\pm$ 19.54	42.64 $\pm$ 18.43	40.54 $\pm$ 19.28	0.351	22.97 $\pm$ 26.16	26.13 $\pm$ 26.51	21.62 $\pm$ 25.11	0.769	20.27 $\pm$ 20.84	19.37 $\pm$ 19.84	18.47 $\pm$ 18.75	0.935
BCS (n= 72)	45.22 $\pm$ 31.56	43.36 $\pm$ 18.85	40.59 $\pm$ 18.19	0.529	22.92 $\pm$ 24.77	19.91 $\pm$ 23.01	24.31 $\pm$ 28.10	0.592	20.83 $\pm$ 22.16	18.52 $\pm$ 21.95	21.76 $\pm$ 23.51	0.666
p#	0.121	0.849	0.990		0.991	0.207	0.626		0.898	0.844	0.462	
Hormone therapy												
No (n= 16)	50.69 $\pm$ 52.58	49.31 $\pm$ 20.27	40.97 $\pm$ 22.12	0.742	30.21 $\pm$ 28.03	18.75 $\pm$ 21.84	28.13 $\pm$ 32.04	0.431	23.96 $\pm$ 29.79	20.83 $\pm$ 30.12	30.21 $\pm$ 19.45	0.662
Yes (n= 93)	40.74 $\pm$ 21.75	42.06 $\pm$ 18.23	40.50 $\pm$ 17.92	0.841	21.68 $\pm$ 24.55	22.58 $\pm$ 24.78	22.58 $\pm$ 26.20	0.966	20.07 $\pm$ 20.05	18.46 $\pm$ 19.42	19.00 $\pm$ 22.06	0.858
p#	0.195	0.151	0.926		0.212	0.563	0.451		0.509	0.681	0.059	

According to the multiple comparison test result (Bonferroni), the difference in alphabetical exponents indicates statistically significant.

p\*: Repeated measure analysis of variance, p#: Student's t test,  $\bar{x}$ : Arithmetic mean, SD: Standard deviation, BCS: Breast conserving surgery, MRM: Modified radical mastectomy.

**Table 9.** Comparison of surgical technique and hormone therapy status and the mean score of EORTC QLQ-C30 cancer quality of life scale in the study

Variables	Dyspnea			p*	Insomnia			p*	Loss of appetite			p*
	First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$		First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$		First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$	
Surgery												
MRM (n= 37)	23.42 $\pm$ 25.90	31.53 $\pm$ 29.34	25.23 $\pm$ 26.53	0.473	35.14 $\pm$ 27.16	31.53 $\pm$ 30.37	24.32 $\pm$ 27.94	0.319	32.43 $\pm$ 26.63	31.53 $\pm$ 27.16	26.13 $\pm$ 23.75	0.561
BCS (n= 72)	25.00 $\pm$ 27.26	20.83 $\pm$ 24.67	31.02 $\pm$ 27.59	0.090	33.33 $\pm$ 30.64	23.61 $\pm$ 28.77	34.26 $\pm$ 30.11	0.077	29.63 $\pm$ 28.83	29.17 $\pm$ 26.20	31.48 $\pm$ 24.31	0.874
p#	0.772	0.047	0.295		0.763	0.185	0.098		0.623	0.660	0.275	
Hormone therapy												
No (n= 16)	22.92 $\pm$ 23.47	25.00 $\pm$ 25.82	39.58 $\pm$ 25.00	0.170	33.33 $\pm$ 32.20	29.17 $\pm$ 34.16	35.42 $\pm$ 30.96	0.861	33.33 $\pm$ 34.43	37.50 $\pm$ 29.50	33.33 $\pm$ 27.22	0.925
Yes (n= 93)	24.73 $\pm$ 27.32	24.37 $\pm$ 26.98	27.24 $\pm$ 27.34	0.763	34.05 $\pm$ 29.07	25.81 $\pm$ 28.71	30.11 $\pm$ 29.51	0.197	30.11 $\pm$ 29.95	28.67 $\pm$ 25.82	29.03 $\pm$ 23.69	0.931
p#	0.803	0.931	0.094		0.929	0.675	0.511		0.672	0.219	0.513	

According to the multiple comparison test result (Bonferroni), the difference in alphabetical exponents indicates statistically significant.

p\*: Repeated measure analysis of variance, p#: Student's t test,  $\bar{x}$ : Arithmetic mean, SD: Standard deviation, BCS: Breast conserving surgery, MRM: Modified radical mastectomy.



**Table 10.** Comparison of surgical technique and hormone therapy status and the mean score of EORTC QLQ-C30 cancer quality of life scale in the study

Variables	Constipation			p*	Diarrhea			p*	Financial difficulty			p*
	First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$		First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$		First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$	
Surgery												
MRM (n= 37)	20.72 $\pm$ 28.71	30.63 $\pm$ 31.80	27.93 $\pm$ 28.88	0.345	25.23 $\pm$ 19.88	20.72 $\pm$ 21.30	20.72 $\pm$ 18.18	0.475	18.02 $\pm$ 25.57	17.12 $\pm$ 24.37	18.92 $\pm$ 21.57	0.918
BCS (n= 72)	19.91 $\pm$ 27.78	24.07 $\pm$ 25.77	27.31 $\pm$ 32.78	0.301	24.07 $\pm$ 25.16	25.46 $\pm$ 16.30	20.37 $\pm$ 19.02	0.334	16.67 $\pm$ 25.64	13.89 $\pm$ 21.49	18.98 $\pm$ 21.54	0.318
p#	0.886	0.249	0.924		0.809	0.199	0.927		0.795	0.480	0.989	
Hormone therapy												
No (n= 16)	12.50 $\pm$ 23.96 <sup>a</sup>	25.00 $\pm$ 31.03 <sup>ab</sup>	41.67 $\pm$ 41.28 <sup>b</sup>	0.032	16.67 $\pm$ 17.21	27.08 $\pm$ 18.13	22.92 $\pm$ 20.07	0.290	18.75 $\pm$ 24.25	18.75 $\pm$ 27.13	8.33 $\pm$ 14.91	0.314
Yes (n= 93)	21.51 $\pm$ 28.51	26.52 $\pm$ 27.61	25.09 $\pm$ 28.93	0.759	25.81 $\pm$ 24.14	23.30 $\pm$ 18.25	20.07 $\pm$ 18.48	0.162	16.85 $\pm$ 25.83	14.34 $\pm$ 21.65	20.79 $\pm$ 21.93	0.068
p#	0.236	0.842	0.050		0.150	0.445	0.575		0.784	0.470	<b>0.008</b>	

According to the multiple comparison test result (Bonferroni), the difference in alphabetical exponents indicates statistically significant.

p\*: Repeated measure analysis of variance, p#: Student's t test,  $\bar{x}$ : Arithmetic mean, SD: Standard deviation, BCS: Breast conserving surgery, MRM: Modified radical mastectomy.**Table 11.** Comparison of the mean score of the EORTC QLQ-BR23 breast cancer-specific scale according to the surgical status and hormonal therapy in the study

Variables	Body image			p*	Future expectation			p*	Sex life			p*
	First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$		First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$		First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$	
Surgery												
MRM (n= 37)	87.84 $\pm$ 18.38	86.71 $\pm$ 22.94	85.19 $\pm$ 18.59	0.875	67.57 $\pm$ 36.42	74.77 $\pm$ 38.81	77.48 $\pm$ 39.33	0.516	86.49 $\pm$ 17.50	91.89 $\pm$ 13.39	91.44 $\pm$ 16.49	0.249
BCS (n= 72)	86.34 $\pm$ 22.52	81.67 $\pm$ 22.32	84.90 $\pm$ 26.48	0.657	69.44 $\pm$ 35.71 <sup>ab</sup>	63.43 $\pm$ 43.75 <sup>a</sup>	80.56 $\pm$ 31.52 <sup>b</sup>	0.021	81.48 $\pm$ 26.02	87.04 $\pm$ 17.07	89.12 $\pm$ 19.61	0.095
p#	0.728	0.273	0.955		0.797	0.186	0.659		0.295	0.135	0.539	
Hormone therapy												
No (n= 16)	83.85 $\pm$ 22.66	82.81 $\pm$ 20.74	89.29 $\pm$ 17.73	0.643	70.83 $\pm$ 38.25	60.42 $\pm$ 45.90	79.17 $\pm$ 34.16	0.472	80.21 $\pm$ 32.90	86.46 $\pm$ 22.13	81.25 $\pm$ 25.73	0.797
Yes (n= 93)	87.37 $\pm$ 20.95	83.52 $\pm$ 22.97	84.34 $\pm$ 24.81	0.575	68.46 $\pm$ 35.57	68.46 $\pm$ 41.81	79.57 $\pm$ 34.41	0.059	83.69 $\pm$ 21.70 <sup>a</sup>	89.07 $\pm$ 14.85 <sup>b</sup>	91.40 $\pm$ 16.78 <sup>b</sup>	<b>0.013</b>
p#	0.542	0.909	0.475		0.808	0.485	0.966		0.587	0.550	<b>0.043</b>	

According to the multiple comparison test result (Bonferroni), the difference in alphabetical exponents indicates statistically significant.

p\*: Repeated measure analysis of variance, p#: Student's t test,  $\bar{x}$ : Arithmetic mean, SD: Standard deviation, BCS: Breast conserving surgery, MRM: Modified radical mastectomy.

**Table 12.** Comparison of the mean score of the EORTC QLQ-BR23 breast cancer-specific scale according to the surgical status and hormonal therapy in the study

Variables	Sexual satisfaction			Side effect			Hair loss			p*
	First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$	First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$	First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$	
Surgery										
MRM (n= 37)	75.68 $\pm$ 27.94 <sup>a</sup>	90.09 $\pm$ 19.03 <sup>b</sup>	88.29 $\pm$ 19.59 <sup>b</sup>	35.60 $\pm$ 19.42	37.14 $\pm$ 23.29	35.65 $\pm$ 23.02	36.63 $\pm$ 26.50	40.54 $\pm$ 26.22	34.23 $\pm$ 28.85	0.174
BCS (n= 72)	77.31 $\pm$ 30.04 <sup>a</sup>	89.81 $\pm$ 18.25 <sup>b</sup>	86.11 $\pm$ 22.90 <sup>ab</sup>	35.32 $\pm$ 22.17 <sup>a</sup>	43.98 $\pm$ 24.76 <sup>b</sup>	34.66 $\pm$ 21.57 <sup>a</sup>	35.65 $\pm$ 30.81 <sup>ab</sup>	44.44 $\pm$ 27.41 <sup>a</sup>	33.80 $\pm$ 26.53 <sup>b</sup>	<b>0.045</b>
p#	0.783	0.942	0.623	0.751	0.155	0.930	0.401	0.476	0.937	
Hormone therapy										
No (n= 16)	68.75 $\pm$ 33.26	89.58 $\pm$ 20.07	81.25 $\pm$ 27.13	36.90 $\pm$ 24.62	44.94 $\pm$ 25.43	36.01 $\pm$ 18.48	31.25 $\pm$ 30.96 <sup>ab</sup>	52.08 $\pm$ 27.13 <sup>a</sup>	20.83 $\pm$ 23.96 <sup>b</sup>	<b>0.007</b>
Yes (n= 93)	78.14 $\pm$ 28.44 <sup>a</sup>	89.96 $\pm$ 18.25 <sup>b</sup>	87.81 $\pm$ 20.73 <sup>b</sup>	35.53	$\pm$ 20.72	41.18 $\pm$ 24.31	0.117	34.41 $\pm$ 29.26	41.58 $\pm$ 26.76	36.20 $\pm$ 27.21
p#	0.237	0.940	0.267	0.818	0.557	0.810	0.693	0.151	<b>0.036</b>	

According to the multiple comparison test result (Bonferroni), the difference in alphabetical exponents indicates statistically significant.

p\*: Repeated measure analysis of variance, p#: Student's t test,  $\bar{x}$ : Arithmetic mean, SD: Standard deviation, BCS: Breast conserving surgery, MRM: Modified radical mastectomy.

functionality, and the authors have stated that, among the QLQ-BR23 scales, there were systemic treatment side effects, perspective on the future, and discomfort with hair loss (9). In other studies, it has been reported that adjuvant radiotherapy did not affect the quality of life in patients with breast cancer (11,14).

It has been reported that removal of all or part of the breast often causes women to experience distress and difficulties such as depression and affective disorders, loss of sexual desire, deterioration in body image, loss of femininity, and difficulty in finding suitable clothes (15,16). In our study, the results of the quality-of-life questionnaire were found to be better in the BCS group. These values were found to be significant for physical function, future expectation, and dyspnea variables. The reason for the higher incidence of dyspnea in patients who underwent MRM was attributed to the entry of the lung into the treatment area. In our study, it was thought that the statistical significance in other parameters, that is, the fact that most of them were not significant, was because the operation types were not equal in number.

Radiation damages both the lymph nodes and indirectly the lymphatic vessels, reducing the carrying capacity of the lymphatic system and causing the development of lymphedema. Especially, patients who receive radiotherapy after radical mastectomy are stated to be at the highest risk in terms of lymphedema (9,12). In our study, it was seen that the problems related to the arm were higher in patients with MRM than in the BSC group. In addition, it was observed that future expectations were lower. The results of the study of Montazeri et al. are similar to the results of our study (17). In a study conducted by Pyzel et al. with the EORTC QLQ-C30 quality of life scale, they have reported that patients with arm edema have more physical, mental and social status disorders, and that pain and fatigue are felt more (18).

In our study, in the findings related to the QLQ-BR23 quality of life scale, it was determined that the scores of the subjects in the subgroups of future expectation, sexual satisfaction, hair loss, and arm-related problems increased significantly. Body image and high future expectations suggest that the individual wishes to meet his/her social needs throughout his/her life. In a study, it was reported that 55% of existing psychosexual disorders occur after surgery, 24% after chemotherapy and 1% after radiotherapy. These results show that invasive surgical treatment methods deeply affect the psychosexual lives of Turkish women. Possible reasons for the low rate of psychosexual disorders in Turkish women may be low sexual expectation and shyness in answering the questionnaire due to cultural and social characteristics (19).

**Table 13.** Comparison of the mean score of the EORTC QLQ-BR23 breast cancer-specific scale according to the surgical status and hormonal therapy in the study

Variables	Arm related problems			p*	Breast related problems			p*
	First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$		First day $\bar{x} \pm SD$	Last day $\bar{x} \pm SD$	Three months later $\bar{x} \pm SD$	
Surgery								
MRM (n= 37)	8.95 $\pm$ 11.52	6.17 $\pm$ 8.99	5.25 $\pm$ 9.00	0.230	43.69 $\pm$ 12.17	42.79 $\pm$ 13.35	45.05 $\pm$ 14.36	0.787
BCS (n= 72)	14.04 $\pm$ 19.47 <sup>a</sup>	9.41 $\pm$ 10.66 <sup>a</sup>	4.01 $\pm$ 7.76 <sup>b</sup>	<0.001	43.06 $\pm$ 15.95	41.09 $\pm$ 11.13	43.98 $\pm$ 13.14	0.413
p#	0.151	0.098	0.510		0.831	0.481	0.699	
Hormone therapy								
No (n= 16)	17.36 $\pm$ 23.30	11.11 $\pm$ 12.83	4.86 $\pm$ 9.04	0.148	44.27 $\pm$ 14.50	41.67 $\pm$ 13.61	43.75 $\pm$ 12.36	0.842
Yes (n= 93)	11.47 $\pm$ 16.09 <sup>a</sup>	7.85 $\pm$ 9.68 <sup>a</sup>	4.35 $\pm$ 8.06 <sup>b</sup>	<0.001	43.10 $\pm$ 14.83	41.67 $\pm$ 11.66	44.44 $\pm$ 13.76	0.380
p#	0.212	0.227	0.801		0.770	1.000	0.850	

According to the multiple comparison test result (Bonferroni), the difference in alphabetical exponents indicates statistically significant.

p\*: Repeated measure analysis of variance, p#: Student's t test,  $\bar{x}$ : Arithmetic mean, SD: Standard deviation, BCS: Breast conserving surgery, MRM: Modified radical mastectomy.

When the literature was examined, no study was found examining the quality of life of hormone therapy. In our study, it was seen that hormone therapy had an effect only on constipation according to the EORTC QLQ-C30 questionnaire. Other parameters were found to be affected. On the other hand, in QLQ-BR23 breast scale, positive results were obtained in sexual satisfaction and arm related problems. It was thought that hormone therapy could increase the problems related to the arm due to radiotherapy.

## CONCLUSION

As a result, radiotherapy has an important place in the treatment of breast cancer. As with all treatment methods, radiotherapy also has side effects. Radiotherapy can cause fatigue, nausea, and vomiting, and therefore, a decrease in work force and a decrease in quality of life can be observed. As seen in this study, other than radiotherapy, hormone therapy and surgical techniques were found to be effective on quality of life. Thanks to this information obtained, it will be easier to make the necessary medical and social interventions to achieve a better quality of life.

**Ethics Committee Approval:** This study was approved by Erciyes University Clinical Research Ethics Committee (Decision no: 2016/177, Date: 04.03.2016).

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## ORJİNAL ÇALIŞMA-ÖZET

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### Radyoterapi alan meme kanseri hastalarında cerrahi ve hormon tedavisinin yaşam kalitesine etkisi

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#### ÖZET

**Giriş ve Amaç:** Bu çalışmanın amacı radyoterapi alan meme kanserli hastalarda cerrahi tipi ve hormon tedavisinin genel yaşam kalitesi üzerine etkisini incelemektir.

**Gereç ve Yöntem:** Meme kanseri nedeniyle adjuvan radyoterapi uygulanan toplam 109 hasta çalışmaya alındı. Prospektif gözlemsel bir çalışma olarak planlandı. Araştırma için etik kurul onayı alındı. Araştırmada veri toplama aracı olarak birinci bölümde demografik ve klinik özellikleri belirten form, ikinci bölümde ise Avrupa Kanser Araştırma ve Tedavi Teşkilatı tarafından geliştirilmiş "EORTC QLQ-C30" ve meme kanserine özgü "EORTC QLQ-BR23" Türkçe yaşam kalitesi formları kullanıldı. Bu veriler hastalarla yüz yüze görüşülerek toplandı. Hastalardan radyoterapinin birinci günü, son günü ve tedavi bitiminden üç ay sonra anket formlarını doldurmaları istendi.

**Bulgular:** Bu çalışmanın yaş ortalaması  $54,8 \pm 12,1$  yılı. En sık yapılan ameliyat meme koruyucu cerrahi idi. Hastaların %85,3'ü hormon tedavisi alıyordu. Radyoterapi birinci günü, son günü ve üç ay sonra yapılan anketlerde EORTC QLQ-C30 ölçeğine göre en yüksek puan sosyal ve kognitif fonksiyonda, EORTC QLQ-BR23 ölçeğinde ise cinsel yaşamda görüldü. Çoklu karşılaştırma testine göre ilk gün radyoterapi alan hastaların radyoterapiden üç ay sonraki ölçümlerine göre fiziksel fonksiyon ortalaması ( $p=0,049$ ), gelecek beklentisi ( $p=0,033$ ), cinsel yaşam ( $p=0,029$ ), cinsel tatmin ( $p<0,001$ ), saç dökülmesi ( $p=0,011$ ) ve kola bağlı sorunlar ( $p<0,001$ ) değişkenlerinin ortalama farkları anlamlı bulundu. Tekrarlı ölçümlerde varyans analizine göre cerrahi tipine göre fiziksel fonksiyon, cinsel yaşam, yan etkiler, saç dökülmesi, dispne ve gelecek beklentisi; hormon tedavisinde ise cinsel yaşam, saç dökülmesi, kabızlık ve ekonomik zorluk istatistiksel olarak anlamlı idi.

**Sonuç:** Meme kanseri nedeniyle radyoterapi alan hastalarda yaşam kalitesi üzerinde radyoterapiden başka hormon tedavisi ve yapılan cerrahi tekniklerin de etkili olduğu görüldü.

**Anahtar Kelimeler:** Meme kanseri, radyoterapi, hormon tedavisi, cerrahi, yaşam kalitesi, QLQ-C30, QLQ-BR23

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# How good is lobectomy for the Turkish population with papillary thyroid cancer? A clinicopathological evaluation

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## ABSTRACT

**Objective:** In modern practice, there is an increasing recommendation for higher utilization of lobectomy in the management of papillary thyroid cancer (PTC). However, in this decision where the optimal balance of locoregional recurrence and complication burden should be achieved, there are still conflicting results in the literature. The aim of this study was to evaluate the effect of high-risk factors in the Turkish population with PTC on the decision of hypothetical lobectomy.

**Material and Methods:** In this study, 96 PTC patients undergoing total thyroidectomy were retrospectively analyzed. Preoperative and postoperative evaluation differences and the impact of high-risk factors (tumor size, multifocality, extrathyroidal extension and central lymph node metastasis) on the decision for hypothetical lobectomy were investigated.

**Results:** In all patients and lobectomy-eligible patients, postoperative evaluations of multifocality, contralateral multifocality, and central lymph node metastases were significantly higher than preoperative evaluations. Consequently, postoperative evaluation revealed that completion thyroidectomy would be required in 52.9% of 51 patients who were hypothetically suitable for lobectomy. Furthermore, comparisons of tumor size-based grouping in lobectomy and total thyroidectomy suitable patients showed similar high-risk factor distribution except for central lymph node metastasis for tumors <10 mm and contralateral multifocality between 11-20 mm.

**Conclusion:** Completion thyroidectomy will be required in approximately half of the patients evaluated as suitable for lobectomy in the treatment of PTC in the Turkish population. In the treatment decision, in which many patient- and surgeon-related factors are influential, each patient should be considered separately.

**Keywords:** Papillary thyroid carcinoma, thyroid, thyroid cancer, thyroidectomy

## INTRODUCTION

Thyroid cancer is the 9<sup>th</sup> most common type of cancer seen today according to recent epidemiological data (1). The three-fold increase in incidence rates over the past three decades is mainly attributed to the overdiagnosis of thyroid nodules resulting from the increased use and improved sensitivity of thyroid ultrasonography (2-4). Although thyroid cancer has a low disease-related mortality rate, locoregional recurrence (LRR), which has an impact on patients' quality of life, is still a major treatment concern (5,6). The overall recurrence rate of thyroid cancer varies between 8-28%, and reducing the frequency of LRR requires more aggressive or recurrent surgical interventions and additional radioactive iodine (RAI) treatments (2,7).

In the low-risk patient group, locoregional recurrence rate is low and reported to be around 2% (8). Routine use of total thyroidectomy, prophylactic central lymph node dissection (CLND), and RAI is still a subject of debate in this low-risk group although total thyroidectomy and prophylactic CLND are known to provide more accurate staging (9). When referring to the widely accepted 2015 treatment guidelines by the American Thyroid Association (ATA), it is stated that in cases of papillary microcarcinoma and papillary cancer measuring between 1-4 cm, thyroid lobectomy might be sufficient for patients with low recurrence risk (8). The low-risk group is defined as intrathyroidal tumors (T1-2) with the presence of no more than five metastatic central lymph nodes measuring less than 2 mm, according to the ATA's 2015 guidelines (8). Especially with the consideration of active surveillance as an alternative in papillary microcarcinoma, there has been an increase in the

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frequency of lobectomy and a decrease in the use of prophylactic central lymph node dissection following the 2015 ATA recommendations (10). However, the utilization of guideline recommendations varies among surgeons worldwide due to several factors. Although minimally invasive treatment alternatives are more commonly used nowadays, aggressive surgical interventions have not lost their significance due to the impact of high-risk factors on LRR (11,12). There are studies in the literature reporting that even in the cN0 low-risk patient group, when prophylactic central lymph node dissection is performed, the rate of detecting metastatic lymph nodes is around 50-80% (13-15). Similarly, depending on prognostic factors determined through pathological evaluation, approximately half of the patients who undergo lobectomy may eventually require completion thyroidectomy (12,16). While a more aggressive approach might detect more significant disease, we do not know whether it has an impact on LRR or disease-related survival. Furthermore, depending on surgeon experience, total thyroidectomy is potentially associated with a higher risk of complications compared to lobectomy. Despite the lower rates of complications observed in high-volume centers in thyroid surgery, high-volume surgeons tend to perform lobectomy more frequently compared to low-volume surgeons (17). Therefore, personal and regional differences are also observed in treatment preferences (18,19).

Consequently, there is no consensus on treatment approaches that should be used for the low-risk patient group. Since optimal treatment should aim for the lowest possible rates of LRR and complications, the selection of an individualized treatment considering patient-related factors as well as local surgical practices becomes crucial (20,21). The aim of this study was to evaluate the feasibility of hypothetical lobectomy based on preoperative assessment and pathological outcomes in patients who had undergone total thyroidectomy in a Turkish thyroid cancer patient population.

## MATERIAL and METHODS

This retrospective study included 96 patients who were operated by a single surgeon (CK) in the Department of General Surgery, Ankara University Faculty of Medicine, between February 2020 and May 2022, with histopathological confirmation of papillary thyroid carcinoma (PTC). The study was approved by the Ankara University Faculty of Medicine Ethics Committee (Decision No: İ04-236-23). In addition to demographic data and operative details, preoperative clinical factors influencing surgical indication, postoperative pathological examinations, and complications were recorded.

Risk factors determining the type of surgery (total thyroidectomy vs. lobectomy) were defined as tumor size, unilateral and contralateral multifocality, presence/number and size of central

lymph node metastasis, and extrathyroidal extension (ETE). Tumor size and metastatic lymph node size were identified preoperatively by ultrasonography and postoperatively by pathological examination and were recorded based on the largest diameters measured. Patients were classified into four groups according to tumor size as  $\leq 10$  mm, 11-20 mm, 21-39 mm, and  $\geq 40$  mm.

In the preoperative ultrasound evaluation of the patients, lesions that are distinct from the primary cancer focus and suspected to have a high malignant potential (TIRADS 4 and 5) were categorized as either multifocal or contralateral multifocal foci, regardless of biopsy confirmation. Similarly, lymph nodes located in the central region, showing sonographic evidence of metastases, were classified as metastatic. Lesions with a primary cancer diagnosis were recorded as positive for ETE if they demonstrated sonographic evidence of exceeding the thyroid capsule boundary or if such an extension was suspected. During the postoperative pathological assessment, only the involvement of primary cancer focus capsule was considered as capsule invasion, while cases showing extension into the soft tissue beyond the capsule were classified as ETE positivity.

All patients included in this study underwent total thyroidectomy. Central lymph node dissection (CLND) was performed in all patients except those with a preoperative cytology result classified as Bethesda 3. Based on preoperative clinical evaluations, we formed a hypothetical patient group as "suitable for lobectomy" with tumors measuring less than 4 cm, without contralateral multifocality, without extrathyroidal extension (ETE), and evaluated as cN0. Patients in this group were further analyzed for a hypothetical need for "completion thyroidectomy" based on their pathology results. We compared the preoperative and postoperative rates of those risk factors determining the type of surgery and calculated the number of patients who would need a completion thyroidectomy if they had been suitable for lobectomy in the preoperative evaluation.

## Statistical Analysis

Descriptive statistics are presented as counts and percentages for categorical variables, mean and standard deviations for normally distributed continuous variables, and median (interquartile range) for ordinal or non-normally distributed continuous variables. The Mann-Whitney U test was used to test the difference between two groups in terms of ordinal or non-normally distributed continuous variables. The differences in categorical variables were compared by using the Chi-square or Fisher's exact test, where appropriate. Intragroup comparison, in terms of categorical variables, was tested by the McNemar test. *p* value less than 0.05 was considered significant. The R programming language 4.2.0 was used for statistical analysis.



## RESULTS

Ninety-six papillary thyroid cancer patients were included in the study. Baseline characteristics of the patients are presented in Table 1. Mean age of the patients was  $43.8 \pm 13.1$  years, and 81.3% of the patients were females. Mean preoperative tumor

**Table 1.** Baseline information of the patients

	n= 96
Age (years)	$43.8 \pm 13.1$
Sex (female/male)	78 (81.3)/18 (18.8)
BMI (kg/m <sup>2</sup> )	$27.50 \pm 5.65$
Graves' disease (yes/no)	3 (3.1)/93 (96.9)
Hashimoto's disease (yes/no)	42 (43.8)/54 (56.3)
Bethesda classification	
3	9 (9.4)
4	8 (8.3)
5	17 (17.7)
6	62 (64.6)
Presence of nodules other than the primary site of cancer	
None	35 (36.5)
Unilateral	11 (11.5)
Bilateral	50 (52.1)
Thyroid volume (mL)	17.50 (14.00)
Pathological aggressive variant (yes/no)	11 (11.5)/85 (88.5)
Capsule invasion (yes/no)	29 (30.2)/67 (69.8)
Central lymphatic dissection	
None	9 (9.4)
Unilateral	63 (65.6)
Bilateral	24 (25.0)
Number of harvested central lymph nodes	12.00 (12.00)
RLN paralysis	
None	96 (100)
Temporary (<12 months)	0 (0)
Permanent (>12 months)	0 (0)
Hypoparathyroidism	
None	73 (76)
Temporary-Short term (<1 month)	18 (18.8)
Temporary-Long term (<12 months)	5 (5.2)
Permanent (>12 months)	0 (0)
Neck hematoma (yes/no)	0 (0)/96 (100)

BMI: Body mass index, RLN: Recurrent laryngeal nerve.  
All data are represented as either mean  $\pm$  SD or median (IQR) or number (percentage).

size was  $15.65 \pm 11.91$  mm. While 41 (42.7%) patients were suspected to have micropapillary thyroid cancer, only five (5.2%) patients had a preoperative tumor size of  $\geq 40$  mm. Contralateral multifocal tumor was considered probable in nine (9.4%) patients and ETE in 12 (12.5%) patients at the preoperative evaluation. The number of patients with cN1 in central lymph node evaluation was 31 (32.3%) (Table 2).

In the postoperative pathological evaluation, aggressive subtypes of papillary thyroid cancer were detected in 11 (11.5%) patients, which included tall cell variant in nine (9.4%) and diffuse sclerosing variant in two (2.1%). Mean postoperative tumor size was  $15.25 \pm 12.96$  mm, and 38 (39.6%) patients had papillary microcancer while only three (3.1%) patients had a tumor size of  $\geq 40$  mm. ETE was present in 10 (10.4%) patients. Unilateral or bilateral CLND was performed in 90.6% of the patients, and central lymph node metastasis was detected in 46 (47.9%) (Table 2).

In terms of postoperative complications, no cases of recurrent laryngeal nerve (RLN) paralysis, permanent hypoparathyroidism, or postoperative neck hematoma were observed. However, temporary hypoparathyroidism developed in 23 (24%) and only five (5.2%) had hypoparathyroidism lasting for more than one month (Table 1).

The rate of risk factors influencing the decision on the type of surgery (lobectomy vs. total thyroidectomy) as multifocality, contralateral multifocality, presence of central lymph node metastasis, and number of central metastatic lymph nodes were significantly different between preoperative and postoperative evaluations. There were significantly higher rates of multifocality, contralateral multifocality, presence of central lymph node metastasis, and number of central metastatic lymph nodes in postoperative examination when compared to preoperative evaluation (Table 2). The number of patients preoperatively determined to be suitable for lobectomy significantly decreased from 51 (53.1%) to 24 (25%) when postoperative pathological examination was carried out ( $p < 0.001$ ). The rate of ETE and the size of central metastatic lymph node were similar between preoperative and postoperative evaluations (Table 2). When the differences in those prognostic factors were analyzed pre- and postoperatively in the "hypothetical" suitable for lobectomy patient group only ( $n = 51$ ), significant differences were observed in multifocality, contralateral multifocality, presence of central lymph node metastasis, number of metastatic central lymph nodes, and size of metastatic central lymph nodes (Table 2). If lobectomy had been performed in those 51 patients according to the preoperative evaluation results, 27 (52.9%) patients would have required a completion thyroidectomy based on postoperative findings.

**Table 2.** The characteristics of changes in high-risk factors in preoperative and postoperative evaluations in all patients and patients suitable for lobectomy

		Preoperative evaluation	Postoperative evaluation	p
All patients (n= 96)	Tumor size (mm)	11.70 (12.00)	12.00 (11.75)	0.336
	≤10 mm	41 (42.7)	38 (39.6)	0.278
	11-20 mm	34 (35.4)	37 (38.5)	
	21-39 mm	16 (16.7)	18 (18.8)	
	≥40 mm	5 (5.2)	3 (3.1)	
	Multifocality	18 (18.8)	45 (46.9)	<0.001
	Contralateral multifocality	9 (9.4)	36 (37.5)	<0.001
	ETE	12 (12.5)	10 (10.4)	0.824
	Central lymph node metastasis	31 (32.3)	46 (47.9)	0.014
	Metastatic central lymph node count	0.00 (1.00)	0.00 (3.00)	<0.001
	Metastatic central lymph node size (mm)	0.00 (5.00)	0.00 (2.50)	0.655
	Number of patients eligible for lobectomy	51 (53.1)	24 (25.0)	<0.001
Lobectomy eligible patients (n= 51)	Tumor Size (mm)	11.00 (12.00)	11.00 (13.00)	0.483
	≤10 mm	25 (49)	23 (45.1)	0.337
	11-20 mm	16 (31.4)	17 (33.3)	
	21-39 mm	7 (13.7)	10 (19.6)	
	≥40 mm	3 (5.9)	1 (2)	
	Multifocality	4 (7.8)	19 (37.3)	<0.001
	Contralateral multifocality	0 (0)	13 (25.5)	<0.001
	ETE	0 (0)	3 (5.9)	0.083
	Central lymph node metastasis	0 (0)	16 (31.4)	<0.001
	Metastatic central lymph node count	0.00 (0.00)	0.00 (1.00)	<0.001
	Metastatic central lymph node size (mm)	0.00 (0.00)	0.00 (0.80)	<0.001

ETE: Extrathyroidal extension.

All data are represented as either median (IQR) or number (percentage).

To determine whether preoperative tumor size had an impact on surgical selection, patients were grouped based on preoperative tumor size (≤10 mm, 11-20 mm, 21-39 mm) to compare for the postoperative presence of high-risk factors.

When preoperative tumor sizes were ≤10 mm, postoperative presence, number and size of central lymph node metastasis were higher in the total thyroidectomy eligible group compared to the lobectomy eligible group, while they had similar postoperative rates of multifocality, contralateral multifocality, capsule invasion, ETE and the presence of an aggressive variant (Table 3). No significant differences in the postoperative presence of any of the high-risk factors were found between the “lobectomy eligible” and “total thyroidectomy eligible” groups, with the exception of a higher rate of contralateral multifocality in the 11-20 mm group in total thyroidectomy eligible patients (Table 3).

## DISCUSSION

In our study, we found that if hypothetical lobectomy had been performed in eligible patients according to preoperative evaluation, 52.9% of those patients would have required a completion thyroidectomy based on postoperative findings. To the best of our knowledge, this is the first study in the Turkish population that compares high-risk factors as multifocality, contralateral multifocality, ETE and central lymph node metastasis in the preoperative assessment as an indicator of proper surgical selection.

In our study, we determined rates of high-risk factors in the postoperative evaluation of our patient population. We found that mean tumor size was 15.25 mm and multifocality was present in 46.9%, contralateral multifocality in 37.5%, capsule invasion in 30.2%, ETE in 10.4%, and central lymph node metastasis in 47.9% of our cases. In a study examining 20 years

**Table 3.** Comparison of postoperative tumor characteristics in patients eligible for hypothetical lobectomy and total thyroidectomy based on preoperative tumor sizes

Postoperative presence of	Lobectomy eligible patients			Total thyroidectomy eligible patients			*p1	**p2	***p3
	≤10 mm, n= 25	11-20 mm, n= 16	21-39 mm, n= 7	≤10 mm, n= 16	11-20 mm, n= 18	21-39 mm, n= 9			
Multifocality	12 (48.0)	5 (31.3)	1 (14.3)	7 (43.8)	11 (61.1)	6 (66.7)	0.790	0.082	0.060
Contralateral multifocality	8 (32.0)	3 (18.8)	1 (14.3)	5 (31.3)	10 (55.6)	6 (66.7)	0.960	<b>0.028</b>	0.060
Capsule invasion	7 (28.0)	5 (31.3)	2 (28.6)	3 (18.8)	7 (38.9)	4 (44.4)	0.712	0.642	0.633
ETE	1 (4.0)	2 (12.5)	0 (0.0)	1 (6.3)	4 (22.4)	2 (22.2)	1.000	0.660	0.475
Presence of pathological aggressive variant	4 (16.0)	0 (0.0)	1 (14.3)	3 (18.8)	2 (11.1)	1 (11.1)	1.000	0.487	1.000
Central lymph node metastasis	8 (32.0)	5 (31.3)	3 (42.9)	12 (75)	11 (61.1)	6 (66.7)	<b>0.007</b>	0.082	0.615
Metastatic central lymph node count	0.00 (1.00)	0.00 (1.00)	0.00 (2.00)	2.00 (4.00)	2.00 (4.00)	5.00 (8.00)	<b>0.007</b>	0.117	0.142
Metastatic central lymph node size (mm)	0.00 (0.80)	0.00 (0.50)	0.00 (4.00)	2.30 (3.58)	0.55 (3.50)	2.20 (8.00)	<b>0.001</b>	0.095	0.252

ETE: Extrathyroidal extension.  
 All data are represented as either median (IQR) or number (percentage).  
 \*p1: LT vs TT in ≤10 mm.  
 \*\*p2: LT vs TT in 11-20 mm.  
 \*\*\*p3: LT vs TT in 21-39 mm.

of pathological data on PTC in the Turkish population and with demographic data closely resembling our study, an average tumor size of 12 mm has been reported in 726 PTC patients, and the rates of multifocality, capsule invasion, ETE, and central lymph node metastasis have been reported as 31%, 24%, 13%, and 7.9%, respectively (22). However, in this study, 85% of PTC patients underwent total thyroidectomy and 7.9% underwent CLND. In a similar study comparing the characteristics of familial and sporadic PTC in the Turkish population, it has been reported that in all patients who underwent total thyroidectomy, the rate of multifocality was 42.6%, bilateral multifocality was 29.1%, ETE was 19.0%, and central lymph node metastasis was 22.1% (23). Furthermore, in another study examining the relationship between BRAF mutation and clinicopathological factors in the Turkish population, the rate of multifocality has been reported as 52%, while the rates of ETE, capsule invasion, and central lymph node metastasis have been reported to be lower compared to our study (24). While these studies are comparable in terms of primary tumor characteristics, the variability in multifocality and central lymph node metastasis might be attributed to different rates of total thyroidectomy (the extent of thyroidectomy) and CLND applied to the patients in each study. In this regard, we believe that our study reflects a more reliable data in the Turkish population due to the use of total thyroidectomy in every patient and the higher rate of CLND carried out.

In our study, central lymph node metastasis was observed in almost every other patient (47.9%) in the pathological evaluation, and contralateral multifocality was observed in one out of every three (37.5%) patients. Furthermore, significant differences were observed between the preoperative and postoperative evaluations of all patients, specifically in those who were suitable for lobectomy, in terms of multifocality, contralateral multifocality, presence and the number of central lymph node metastasis. Clinical reflection of lower detection rates of those game changer high-risk factors is the necessity of completion thyroidectomy. We determined that a total of 52.9% of the patients would have required a completion thyroidectomy if they had undergone a lobectomy based on their preoperative evaluation. Several studies in the literature have reported consistent results with our findings. In a study including 30.180 papillary thyroid microcarcinoma (PTMC) cases, where CLND was performed in 52%, there was a 19% incidence of high-risk factors identified through pathological evaluation (11). In another study evaluating 301 low-risk PTC patients with tumor sizes between 1-4 cm, 15% of the patients transitioned from the low-risk group to the intermediate or high-risk group based on postoperative evaluation (25). Similarly, in another study including 1513 patients with tumor sizes between 1-4 cm, 42.8% of patients had unknown high-risk factors identified postoperatively (26). Bakkar et al. have reported that among 245 patients with tumor sizes between

1-4 cm who were suitable for lobectomy, the rate of identifying one or more high-risk factors requiring completion thyroidectomy was 59% (12). In a recent study including 152 patients meeting the criteria for lobectomy according to the ATA guidelines and of whom 72.4% underwent total thyroidectomy, it has been reported that 61.8% of the patients had high-risk factors detected in postoperative evaluation. Accordingly, the authors have suggested that preoperative staging was inadequate in identifying those factors and recommended a more frequent use of total thyroidectomy (20). In a study by Wouter et al. involving 287 lobectomy-eligible patients with tumor sizes between 1-4 cm and without CLND, 43% of the patients required completion thyroidectomy based on lobectomy pathology (16). In another study reporting the need for completion thyroidectomy in 43.5% of cases, the authors have argued that total thyroidectomy, when performed in high-volume centers, remains a valid treatment option with low complication rates for low-risk patients with tumor sizes between 1-4 cm (27). These findings suggest that despite the advancements in technology and techniques, we still cannot accurately stage patients during the preoperative period and eliminate the need for a completion thyroidectomy.

In our study, when patients eligible for lobectomy and total thyroidectomy were compared for the postoperative presence of high-risk factors based on preoperative tumor sizes, no significant differences were found between the groups in terms of multifocality, ETE, or the presence of pathological aggressive variants. In the total thyroidectomy eligible group, when compared to the lobectomy eligible group, the frequency of central lymph node metastasis was higher in tumors measuring 10 mm and below, and the frequency of contralateral multifocality was higher in tumors measuring 11-20 mm. In the comparison of patients with PTMC, similar postoperative high-risk factors were observed between patients suitable for lobectomy and those suitable for total thyroidectomy, except for the rate of central lymph node metastasis and the number of metastatic lymph nodes. This finding supports the idea that the postoperative presence of most high-risk factors is irrelevant to tumor size for tumors under 40 mm. It also implies that the preoperative staging criteria are insufficient because they attempt to group patients with similar risk factors. This result is consistent with the recent discussion on the categorization of tumor size as a prognostic factor in the literature. For instance, Barbaro et al.'s review, which utilizes studies cited as references in the guidelines, highlights that the literature supports the use of lobectomy for PTMC, indicating that a "grey zone" still exists for tumors between 1-2 cm in size, and emphasizing an increased risk of LRR in tumors sized between 2-4 cm (28). In the study by Kiss et al., it has been reported that tumor size, except for angioinvasion, was not a significant predictor for the presence of postoperative risk factors (20). In another study

evaluating 906 patients with PTC and pathologic N1 metastasis, it has been reported that total thyroidectomy was associated with better survival outcomes compared to lobectomy in patients with more than five lymph node metastases and metastatic lymph node sizes between 2-5 mm (29). In a Korean study analyzing data from 3282 patients with tumor sizes below 2 cm, it has been found that patients who underwent lobectomy had higher rates of long-term recurrence in cases where the tumor size was larger than 18 mm, there were two or more lymph node metastases, or bilateral tumors were present. Based on these findings, total thyroidectomy has been suggested as a potential approach to prevent reoperations in these patients (30).

Aggressive interventions may be associated with a higher rate of complications. Our study results show that none of the patients experienced neck hematoma, permanent hypoparathyroidism, or temporary or permanent RLN paralysis. Additionally, the rate of temporary hypoparathyroidism lasting longer than one month was only 5.2%. These findings support the suggestion that in high-volume centers like ours, aggressive surgical interventions can be performed with low complication rates. A similar topic has been discussed in a review by Liu et al., which included treatment guidelines, and it has been stated that high-volume surgeons have significantly lower complication rates compared to intermediate and low-volume surgeons. According to the review, total thyroidectomy is emphasized for 1-4 cm tumors by high-volume surgeons in Europe and Korea, while the Japanese guidelines recommending lobectomy clarify that they are not intended for experts. Therefore, they have highlighted that in the decision-making process of surgery, which is influenced by many factors, a personalized approach for each patient is more appropriate (21). Certainly, the complication rate alone cannot be considered as the sole determinant in this decision.

The guideline recommendations on surgical selection are molded by local surgical practices as well as patient-related factors. In a multidisciplinary survey conducted by Makay et al. in Türkiye, it has been reported that total thyroidectomy was more prominent in patients with PTMC, while routine central neck dissection was not commonly preferred by general surgeons. The authors have reported that there were differing opinions among disciplines regarding these variable preferences in the country (18). In a study examining the impact of the 2015 ATA guidelines, Conroy et al. have found there was an increase in the incidence of lobectomy, but total thyroidectomy was still recommended in 67.9% of low-risk patients after the publication of the 2015 ATA guidelines (10). Moreover, a recent review suggests that total thyroidectomy should be favored in cases where high-risk factors cannot be meticulously evaluated (31). The diversity of surgical approaches

in the literature emphasizes the importance of a tailored treatment for each individual patient in each different setting. Considering that recurrences and repeated surgical interventions are the most common issues affecting the quality of life in patients with thyroid cancer, and that approximately two-thirds of patients after lobectomy require replacement therapy to maintain TSH levels below 2.0 µIU/mL, it might be suggested that total thyroidectomy performed in high-volume centers may offer a more reliable treatment option with lower complication rates than lobectomy (31,32).

The study exhibits several strengths, including the consistent implementation of total thyroidectomy in all patients and a high rate of CLND (90.6%). These factors are expected to yield more reliable results when evaluating pathological high-risk factors compared to studies that adopt lobectomy or have a lower rate of CLND. The single-surgeon approach also ensures standardization in thyroidectomy technique and the extent of lymphatic dissection. However, certain limitations should be acknowledged. Due to the study design, it was not possible to explore the relationship between high-risk factors and LRR or disease-free survival. Additionally, the lack of information on patients' family history of thyroid cancer and BRAF mutation status restricted the investigation of their impact on pathological risk factors. Moreover, as surgical procedures were solely performed by a single high-volume surgeon, thus the overall complication rates associated with total thyroidectomy might not be entirely represented.

## CONCLUSION

Our findings indicate that nearly half of the patients undergoing lobectomy would require a completion thyroidectomy and that the patient population categorized as low risk based on certain criteria may not differ significantly from the group that does not meet the indications for lobectomy. Therefore, total thyroidectomy remains a safer option compared to lobectomy, particularly in high-volume centers for tumors measuring less than 40 mm. In each context, surgical and patient specific criteria must be considered individually to make a tailored surgical decision.

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## ORİJİNAL ÇALIŞMA-ÖZET

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## Papiller tiroid kanseri tedavisinde lobektomi Türk popülasyonuna ne kadar uygun? Klinikopatolojik bir değerlendirme

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### ÖZET

**Giriş ve Amaç:** Günümüzde, papiller tiroid kanseri (PTK) tedavisinde lobektominin daha sık kullanımı önerilmektedir. Fakat lokorejyonel rekürens ve komplikasyon yükünün optimal dengesinin sağlanması gereken bu durumda literatürde halen çelişkili sonuçlar bulunmaktadır. Bu çalışmanın amacı total tiroidektomi uygulanmış PTK'li Türk popülasyonunda saptanan yüksek risk faktörlerinin varsayımsal olarak uygulanacak lobektomi kararına etkisinin değerlendirilmesidir.

**Gereç ve Yöntem:** Bu çalışmada PTK nedeniyle total tiroidektomi yapılmış 96 PTK hastasının verileri retrospektif olarak incelendi. Preoperatif ve postoperatif değerlendirme farklılıkları ve yüksek risk faktörlerinin (tümör boyutu, multifokalite, ekstratiroidal yayılım ve santral lenf nodu metastazı) varsayımsal olarak uygulanacak lobektomi kararı üzerindeki etkisi araştırıldı.

**Bulgular:** Tüm hastalarda ve lobektomiye uygun hastalarda multifokalite, kontralateral multifokalite ve santral lenf nodu metastazlarının karşılaştırılmasında postoperatif değerlendirmeler, preoperatif değerlendirmelere göre anlamlı daha yüksek saptandı. Sonuç olarak, varsayımsal lobektomiye uygun olan 51 hastanın %52,9'unda postoperatif değerlendirme sonunda tamamlayıcı tiroidektomi gerekeceği gözlemlendi. Ayrıca, lobektomi ve total tiroidektomiye uygun hastalarda tümör boyutuna dayalı gruplandırmanın karşılaştırmalarında, <10 mm tümörler için santral lenf nodu metastazı ve 11-20 mm arasında kontralateral multifokalite farklılığı dışında benzer yüksek risk faktörü dağılımı saptandı.

**Sonuç:** Türk popülasyonunda PTK tedavisinde lobektomiye uygun olarak değerlendirilen hastaların yaklaşık yarısında tamamlayıcı tiroidektomi gerekeceği gözlemlenmiştir. Hasta ve cerrahla ilgili birçok faktörün etkili olduğu tedavi kararında her hasta ayrı ayrı değerlendirilmelidir.

**Anahtar Kelimeler:** Papiller tiroid karsinomu, tiroid, tiroid kanseri, tiroidektomi

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# Feasibility of totally extraperitoneal inguinal hernia repair in patients with previous prostatectomy

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## ABSTRACT

**Objective:** Laparoscopic totally extraperitoneal inguinal hernia repair (TEP) surgery technique includes three key steps: reaching the preperitoneal space, reducing hernias, and placement of mesh. However, reaching the preperitoneal space can be complicated in patients with previous lower abdominal surgeries. This study aimed to assess the feasibility of laparoscopic inguinal TEP in patients with previous prostatectomies.

**Material and Methods:** Inguinal hernia patients who underwent laparoscopic TEP between January 2015 and February 2021 at Koç University Faculty of Medicine, Department of General Surgery, were included in this retrospective study. The operations were performed by five senior surgeons experienced in laparoscopy. Patients were divided into two study groups, as the radical prostatectomy (RP) group which included patients with previous prostatectomy non-RP which included patients without previous radical prostatectomy. Operative time (OT), length of hospital stay (LOS), and postoperative complications were compared within two groups.

**Results:** Three hundred and forty-nine patients underwent laparoscopic TEP, and 27 had previous prostatectomies. Among them, 190 patients had unilateral inguinal hernias, and 159 had bilateral inguinal hernias. Mean age of the patients in the non-RP and RP groups was  $58.1 \pm 14.7$  and  $73.9 \pm 9.6$  years, respectively. Only one (3.7%) case was complicated with urinary tract infection in the RP group, and 10 (3.1%) were complicated in the non-RP group. Complications for the non-RP group include hematomas in six cases, urinary tract infection in three cases, and urinary retention in one case. No significant difference in mean operative time was seen between non-RP and RP groups ( $p=0.43$ ). There was no significant difference in the means of the length of hospital stay between the two groups ( $p=0.7$ ).

**Conclusion:** Laparoscopic TEP in patients with a previous prostatectomy can be performed safely without prolonging the operative time and increasing the length of hospital stay.

**Keywords:** Inguinal hernia, laparoscopic inguinal hernia surgery, benign prostate hyperplasia, totally extraperitoneal hernia repair

## INTRODUCTION

Inguinal hernia (IH) is the most prevalent type of abdominal wall hernia, accounting for 75% of all cases. It is a frequent part of daily general surgery practice, with the lifetime risk of developing an IH standing at 27% for men and 3% for women (1). Risk factors include male sex, advanced age, patent processus vaginalis, chronic cough-induced increases in intraabdominal pressure, systemic connective tissue disorders, benign prostatic hyperplasia, constipation, smoking, and lower midline incision surgery (2-4).

Prostate cancer ranks one of the most common cancers among men worldwide, including Türkiye, where 19.444 new cases were diagnosed in 2020 (5). Open-laparoscopic or robotic radical prostatectomy (RP) is the primary treatment for non-metastatic prostate cancer (6). Due to its proximity and shared anatomy, there is an inevitable causal relationship between RP and IH. Previous studies have revealed that RP can quadruple the long-term incidence of IH, with incidence rates varying based on the surgical approach: 13.7% post-open surgery, 7.5% post-laparoscopic surgery, and 7.9% post-robotic surgery (7,8).

Recent guidelines highlight the laparo-endoscopic technique, incorporating totally extraperitoneal (TEP), and transabdominal preperitoneal (TAPP), as one of the most effective approaches to treat IH (9). These techniques have replaced open techniques due to advantages such as lower risk of postoperative pain and numbness, shorter recovery time, and earlier return to work (10-12). However, studies have indicated that patients with a history of abdominal surgery, such as prostatectomy, may face a higher risk of post and perioperative complications when

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undergoing endo-laparoscopic surgery (13-15). On the other hand, some studies attempted to prove the feasibility of endo-laparoscopic techniques in a patient with previous lower abdominal surgery (16,17).

Therefore, data in the literature about the feasibility of laparoscopic TEP in patients with prostatectomy is still controversial, and there is no consensus on the optimal technique. In addition, reported data in the literature come from studies with surgeons at various levels of expertise, which might impact the results of such a technically challenging procedure (13,18-20). In this study, it was aimed to present the results of TEP done by experienced surgeons on patients with a previous history of prostatectomy and compare the outcomes to those without a prostatectomy.

## MATERIAL and METHODS

This single-center, retrospective study was conducted at the Department of General Surgery, Koç University Faculty of Medicine, between January 2015 and January 2021. Male patients who underwent TEP due to IH in the study period were included in this study. Patients undergoing concurrent surgery and those found to have other concomitant groin hernias (femoral, sportsman) intraoperatively were excluded. Five experienced laparoscopic surgeons (>50 cases/year) performed all operations. Patients with a history of prostatectomy and those without a history of prostatectomy or any other abdominal surgery (non-RP) were compared.

Patient demographics (sex, age, BMI and comorbidities), perioperative outcomes (hernia location, operative time, and intraoperative complications), and postoperative results (length of the hospital stay, recurrence of the hernia, postoperative complications such as hematoma formation, urinary tract infection, and mesh infection) graded in Clavien-Dindo classification were noted for both groups. The primary outcome was peri/postoperative complications; the secondary outcome was the length of the hospital stay (LOS) and operative time (OT). Operative time is defined as the duration from the initiation of anesthesia until extubation.

The study protocol was approved by the local institutional review board of Koç University (approval code: 2022.440. IRB1.166). This study was conducted in accordance with the 1964 Helsinki Declaration. Written informed consent was obtained from all subjects before their participation, and all methods were carried out per our institutional review board's relevant guidelines and regulations.

Descriptive statistics were used to identify the mean and standard deviation groups. Operative time and LOS were tested for normality using the Shapiro-Wilk test, and both parameters were non-normally distributed. Non-parametric Mann-Whitney U test was used to compare two groups in means of LOS and

OT separately for bilateral and unilateral IH. The Chi-square test was used to compare postoperative complications between the two groups. A p-value <0.05 was considered statistically significant.

The surgical procedure was performed as follows: A short oblique incision just inferolateral to the umbilicus on the hernia site was made, and the anterior rectus sheath was opened with the help of S retractors. Ten mm trocar was inserted, and a 30° 10 mm laparoscope was introduced. Two 5 mm operating ports were placed in the lower abdominal midline just above the pubis and in-between via the linea alba. Telescopic dissection under direct vision was used to reduce the possibility of peritoneal tearing due to scarring. The surgical technique was similar, independent of the prior history of prostatectomy. A combination of sharp and blunt dissection was employed to clear the area until reaching the subumbilical area superiorly, space of Retzius inferiorly, and psoas muscle inferolateral. Iliac vessels were carefully dissected. A polypropylene mesh of appropriate size was fixed to the periosteum of the superior pubic ramus using penetrative titanium tacs. Lateral fixation was not employed to allow any subsequent mesh contraction without impediment. The decision for drain placement was based on the surgeon's experience and the risk of bleeding.

## RESULTS

From 2014 to 2021, 414 patients underwent laparoscopic IH repair at our single-center institution. Among them, 36 (8.6%) patients were treated directly with TAPP procedures, while 378 (91.4%) initially underwent TEP. During the TEP procedure, the operation was converted to open or TAPP in 29 (5.2%) patients, specifically 17 to open and 12 to TAPP. There was no significant difference between the two groups in conversion rate ( $p=0.72$ ). Successful TEP was carried out from initiation to completion in 349 patients. Subsequently, these TEP patients were classified as right-sided ( $n=107$ , 32.4%), left-sided ( $n=82$ , 22.9%), and bilateral ( $n=160$ , 44.7%).

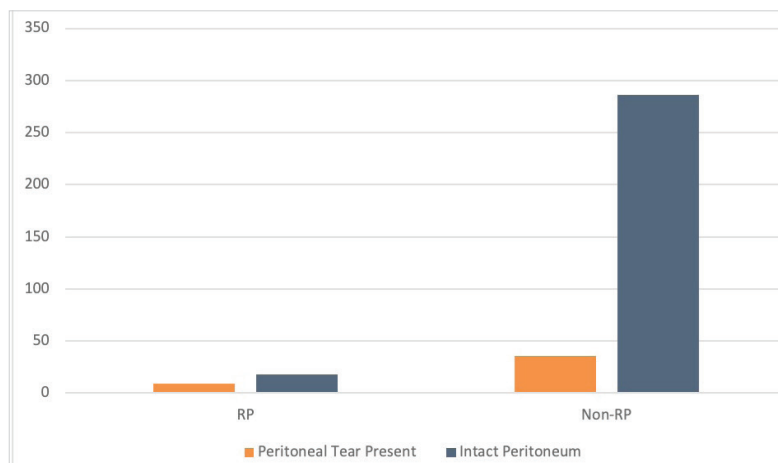
The first group, RP, comprised 27 (7.5%) patients, whereas the control group, non-RP, encompassed 322 (92.5%) patients. Of the 27 patients in the RP group, 20 underwent minimally invasive surgery while seven patients underwent open prostatectomy. For the 20 patients (out of the 27) for whom data is available, the average duration between radical prostatectomy and inguinal hernia repair is 44.5 months, with a standard deviation of 20.51 months. The RP group demonstrated a significantly higher mean age compared to the non-RP group, while a higher BMI was notably prevalent in the non-RP group (Table 1).

In terms of perioperative complications, the RP group exhibited a statistically significant increase in peritoneal tear rates (33.3%) compared to the non-RP group (11.2%) (Figure 1).

**Table 1.** Patient characteristics

Parameters	Non-RP (n= 322)	RP (n= 27)	p
Age	58.1 ± 14.7	73.9 ± 9.6	<0.001
BMI	26.5 ± 3.4	25.5 ± 2.1	0.024
<b>ASA score</b>			
1	174 (53.9%)	7 (25.9%)	0.018
2	130 (40.5%)	17 (63%)	
3	18 (5.6%)	3 (11.1%)	
<b>Clavien-Dindo score</b>			
1	311 (96.5%)	25 (92.6%)	0.481
2	10 (3.1%)	2 (7.4%)	
3	1 (0.3%)	0	
<b>Comorbidities</b>			
COPD presence	7 (2.2%)	2 (7.4%)	0.099
DM presence	62 (19.3%)	9 (33.3%)	0.081
Hypertension presence	111 (34.5%)	14 (51.9%)	0.070
<b>Repair location</b>			
Unilateral	175 (54.2%)	15 (55.6%)	0.892
Bilateral	147(45.8%)	12 (44.4%)	
<b>Postoperative complication</b>	10 (3.1%)	1 (3.7%)	0.869
Hematoma	6	0	
Urinary tract infection	3	1	
Urinary retention	1	0	
Conversion	27 (8.3%)	2 (7.4%)	0.722
Length of hospital stay	1.1	1.2	0.673
Operative time	82.4 ± 40.4	83.7 ± 36.5	0.438

ASA: American Society of Anesthesiologists, BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, DM: Diabetes mellitus.



**Figure 1.** Peritoneal tear was found statistically correlated with the presence of prior prostatectomy ( $p < 0.001$ ).

RP: Radical prostatectomy, Non-RP: Non-radical prostatectomy.

**Table 2.** Operative time comparison in terms of prostatectomy and peritoneal tear

	Peritoneal tear	Intact peritoneum	p
RP	104 ± 47	73 ± 26	<b>0.022</b>
Non-RP	133 ± 54	76 ± 33	<b>&lt;0.001</b>

RP: Radical prostatectomy, Non-RP: Non-radical prostatectomy.

Postoperative complication rates were comparable between the two groups, with rates of 3.1% in the non-RP group and 3.7% in the RP group, respectively ( $p=0.869$ ).

No statistically significant association was identified between the location of the IH and a history of radical prostatectomy ( $p=0.892$ ). Furthermore, no statistical significance was found in LOS and OT, with respective  $p$ -values of 0.673 and 0.438. For patients with a history of prostatectomy: mean operative time for unilateral hernia repairs was  $75.5 \pm 34.6$  minutes, and for bilateral hernia repairs, it was  $90.9 \pm 44.5$  minutes. The difference between these times was found to be statistically significant ( $p=0.023$ ).

A separate analysis for the presence of a peritoneal tear in both RP and non-RP groups showed statistical significance with respect to OT. In the RP group, OT was  $104 \pm 47$  minutes with a peritoneal tear and  $73 \pm 26$  minutes without ( $p=0.022$ ). Similarly, in the non-RP group, OT was significantly longer in the presence of a peritoneal tear ( $133 \pm 54$  minutes) than without ( $76 \pm 33$  minutes) ( $p<0.001$ ) (Table 2).

## DISCUSSION

Endo-laparoscopic hernia repair approaches typically fall into two categories: TEP and TAPP procedures. Prior studies comparing the two techniques have shown that each procedure has advantages and disadvantages, yet there is no clear indication of superiority based on outcomes (21,22). At our institution, we have primarily chosen TEP as the preferred technique for IH repair due to its lower invasiveness, non-exposure of intra-abdominal organs, and more accurate anatomical visualization. While TEP and TAPP are accepted as suitable options for hernia recurrence and chronic pain, many surgeons often choose TEP to avoid peritoneal entry (23).

However, performing TEP can present challenges in patients with a history of lower abdominal surgery, such as RP, due to extensive preperitoneal scarring and adhesion. This has resulted in the ongoing discourse on the appropriateness of minimally invasive IH repair in patients with prior RP (18-20). A study by Prassas et al. has demonstrated inferior outcomes in intra- and postoperative complications for patients with a history of abdominal surgery undergoing TEP compared to those without such a history, suggesting a possible preference for open techniques due to higher complication rates (14). Our findings also indicated an increased perioperative complication risk in

patients with a history of prostatectomy, although it did not achieve statistical significance. However, this heightened risk may not solely result from the previous prostatectomy; mean age of the RP group was 73, and advancing age is a recognized risk factor for peri- and postoperative complications following any surgery. Our results regarding postoperative complications were in alignment with the study by Trawa et al (15). In comparison to our findings, the variability in surgeon familiarity and experience, along with the number of experienced surgeons, could partially explain discrepancies in the results. These factors contribute to the diversity of outcomes and increase the likelihood of external validation. Further, recent studies have validated the feasibility of TEP in patients with a history of prostatectomy, suggesting that experienced surgeons can effectively perform the TEP procedure in this population (13,15,16,18-20).

Studies have also indicated that OT is significantly longer in patients with a history of prostatectomy (21,22,24). Compared to reported operative times of  $82.4 \pm 40.4$  and  $83.7 \pm 36.5$  for non-RP and RP groups, respectively, our operative times were more protracted. This discrepancy may be attributed to our recording of OT from the initiation of anesthesia to extubation. Additionally, consistent with Prassas et al., we note that a wide range of operative times is documented in the literature (14,18,19). However, we were able to corroborate findings from previous studies demonstrating longer operative times in patients experiencing peritoneal tears during surgery (16,17,19).

The incidence of peritoneal tear during surgery appears to be elevated in patients with a history of prostatectomy. Moreover, if a peritoneal tear occurs during the TEP procedure, it is likely to extend the OT, regardless of the patient's prostatectomy history. Peritoneal tears during TEP repair can introduce complications, and the altered anatomy and scarring in the pelvic region of patients with a history of prostatectomy may heighten this risk (25). The presence of adhesions and fibrosis in the pelvic area can make the dissection of the preperitoneal space more challenging and increase the risk of inadvertent peritoneal tear (25). In addition, a peritoneal tear can be a marker of underlying factors that contribute to increased OT. For example, peritoneal tears may be more common in patients with a history of prostatectomy due to altered anatomy and scarring in the pelvic region. These factors can make the dissection and repair of peritoneal tears more challenging, leading to increased OT.

Despite its limitations, our study offers valuable insights. It is a single-center, retrospective observational study with a relatively limited patient number ( $n=349$ ), and the three-month follow-up period may not be sufficient for detecting postoperative IH recurrence, a significant complication. Subgroup analysis could not be performed due to the limited number of previous prostatectomies. Nevertheless, this study's robustness derives from the IH repairs performed by experienced surgeons, which enhances the variability and external validation of peri- and postoperative complications. Further studies with more cases are needed to evaluate the safety and feasibility.

## CONCLUSION

This study demonstrated that laparoscopic TEP IH repair in patients with a prior prostatectomy history is safe, effective, and efficient when performed by experienced laparoscopic surgeons.

## Acknowledgements

The preliminary results from this study were presented in 15. Ulusal Endoskopik Laparoskopik Cerrahi Congress in 2021.

**Ethics Committee Approval:** This study was approved by Koç University Ethics Committee (Decision no: 2022.440.IRB1.166, Date: 05.12.2022).

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**Author Contributions:** Concept - İHÖ, SS, SK, BKK, MK, OA; Design - İHÖ, SS, EB; Supervision - İHÖ, EB, OA, DSU, EB, EÖ, FC; Data Collection and/or Processing - SS, SK, BKK, MK, FC, EÖ, EB, DSU; Analysis and/or Interpretation - İHÖ, EÖ, EB, DSU, OA; Literature Search - FC, SS, SK; Writing Manuscript - İHÖ, EÖ, MK, BKK; Critical Reviews - İHÖ, EÖ, EB, OA, EB, DSU.

**Conflict of Interest:** The authors have no conflicts of interest to declare.

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### ORJİNAL ÇALIŞMA-ÖZET

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## Daha önce prostatektomi yapılmış hastalarda total ekstraperitoneal kasık fıtığı onarımının uygulanabilirliği

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### ÖZET

**Giriş ve Amaç:** Laparoskopik total ekstraperitoneal kasık fıtığı onarımı (TEP) üç temel adımı içerir: preperitoneal boşluğa ulaşmak, fıtık kesesini düşürmek ve mesh yerleştirmek. Ancak daha önce alt karın ameliyatı geçirmiş hastalarda preperitoneal boşluğa ulaşmak karmaşık olabilir. Bu çalışma, daha önce prostatektomi geçirmiş hastalarda laparoskopik TEP ameliyatının uygulanabilirliğini değerlendirmeyi amaçladı.

**Gereç ve Yöntem:** Koç Üniversitesi Tıp Fakültesi Genel Cerrahi Anabilim Dalında Ocak 2015 ile Şubat 2021 tarihleri arasında laparoskopik TEP ameliyatı yapılan kasık fıtığı hastaları bu retrospektif çalışmaya dahil edildi. Operasyonlar laparoskopi konusunda deneyimli beş kıdemli cerrah tarafından gerçekleştirildi. Hastalar, daha önce radikal prostatektomi yapılmamış grup (non-RP) ve prostatektomi geçirmiş grup (RP) olarak iki çalışma grubuna ayrıldı. Ameliyat süresi (OT), hastanede kalış süresi (LOS) ve ameliyat sonrası komplikasyonlar iki grup arasında karşılaştırıldı.

**Bulgular:** Üç yüz kırk dokuz hastaya laparoskopik TEP uygulandı ve 27 hastanın daha önce prostatektomi öyküsü vardı. Bunların 190'ında tek taraflı kasık fıtığı, 159'unda ise iki taraflı kasık fıtığı vardı. RP olmayan ve RP grubundaki hastaların yaş ortalaması sırasıyla  $58,1 \pm 14,7$  ve  $73,9 \pm 9,6$  yıldı. RP grubunda sadece bir (%3,7) olguda idrar yolu enfeksiyonu gelişirken, RP olmayan grupta 10 (%3,1) olguda komplikasyon gelişti. RP dışı grup için komplikasyonlar arasında altı olguda hematoma, üç olguda idrar yolu enfeksiyonu ve bir olguda idrar retansiyonu yer almaktadır. RP olmayan ve RP grupları arasında ortalama ameliyat süresi açısından anlamlı fark görülmedi ( $p=0,43$ ). İki grup arasında hastanede kalış süresi ortalamaları açısından anlamlı fark yoktu ( $p=0,7$ ).

**Sonuç:** Prostatektomi geçirmiş hastalarda laparoskopik TEP, ameliyat süresini ve hastanede kalış süresini uzatmadan güvenle yapılabilir.

**Anahtar Kelimeler:** Kasık fıtığı, laparoskopik kasık fıtığı cerrahisi, benign prostat hiperplazisi, total ekstraperitoneal fıtık onarımı

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# Metabolic and surgical factors affecting postoperative quality of life in patients with total pancreatectomy with or without splenectomy: Single center results

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## ABSTRACT

**Objective:** Pancreatic resection may be required in the treatment of patients with pathologies of the pancreas. Total pancreatectomy is a major surgical procedure with serious risk of mortality and morbidity, and patient selection is important for prognosis. The endocrine and exocrine pancreatic insufficiency that develops in patients after total pancreatectomy can lead to a serious decrease in the quality of life of the patients due to pain, diarrhea, vomiting etc. Our aim was to evaluate the effect of total pancreatectomy with spleen preservation as well as splenectomy on the quality of life of the patients.

**Material and Methods:** In our study, we retrospectively analyzed the data of patients diagnosed with pancreatic cancer, intrapapillary mucinous neoplasia, pancreatic neuroendocrine tumors, and chronic pancreatitis undergoing from partial to total pancreatic resections in our clinic between 12/2017 and 12/2022. Quality of life was compared using the EORTC QLQ-C30 scale.

**Results:** A total of 47 total pancreatectomy patients, 30 (63.8%) males and 17 (36.2%) females, were included in the study. Mean age of the patients was 61.38 (39-83) years. Five (35.7%) patients underwent perioperative total pancreatectomy because of high risk of pancreatic fistula development due to hard parenchyma and narrow pancreatic duct. Patients had a perioperative blood loss of 500 mL or more, and there was a statistically significant increase in perioperative blood loss compared to patients without vascular resection ( $p < 0.001$ ). Forty (85.1%) patients used enzyme preparations to replace pancreatic enzymes.

**Conclusion:** After total pancreatectomy, quality of life of the patients is reduced both by surgical factors and by metabolic factors due to endocrine and exocrine insufficiency in the postoperative period.

**Keywords:** Total pancreatectomy, pancreatic insufficiency, splenectomy, quality of life

## INTRODUCTION

The pancreas is a vital organ in the regulation of metabolism with both endocrine and exocrine functions (1). Pancreatic resection may be required in the treatment of patients with pathologies such as solid or cystic tumors of the pancreas, pancreatic trauma, chronic hereditary pancreatitis (2-4). The resection of the pancreas can be partial or total, depending on the pathology.

After the first successful total pancreatectomy was performed by the Viennese surgeon Theodor Billroth in 1884, there have been many developments in pancreatic surgery over the last century, but the high mortality and morbidity rates have made surgeons hesitant about pancreatic surgery (5). However, there has been an increase in the number of pancreatic surgeries and total pancreatectomies in the last 2-3 decades due to new treatment modalities, surgical techniques, surgeons' experience and knowledge, and the increase in the number of health care institutions with high technology and facilities.

Total pancreatectomy is a major surgical procedure with serious risk of mortality and morbidity, and patient selection is important for prognosis. Patient's age, performance status, and comorbidities are the determinants of perioperative and postoperative mortality and morbidity, and it is important to operate on the patient with the correct indication (6). Common indications for elective total pancreatectomy include chronic pancreatitis that is refractory to medical management, premalignant lesions (intraductal papillary mucinous neoplasms) where partial resection is not sufficient, pancreatic neuroendocrine tumors, and

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malignant tumors of the pancreas (2-4). In addition, conversion total pancreatectomy is performed in patients who are scheduled for partial pancreatectomy but considered to be at high risk of developing pancreatic fistula in the postoperative period, and completion total pancreatectomy is also performed after complications such as postoperative bleeding and abscess development after partial pancreatectomy (7-9).

Another reason for the high mortality and morbidity rates in pancreatic surgery is the anatomical location of the pancreas and the multiple gastrointestinal system (GIS) reconstructions after resection. The retroperitoneal location of the pancreas, its close proximity to the duodenum, its proximity to major vascular structures, and its proximity to almost all organs in the upper abdomen make the operation technically difficult (10,11). GI resections and anastomoses, biliary anastomosis and vascular resections performed together with pancreatic resection increase the possibility of complications in the postoperative period and thus prolong the follow-up process (10,12). Splenectomy is also performed together with pancreatectomy in some patients due to the close proximity of the spleen and its vascular structures. Patients who undergo splenectomy are at risk for infectious diseases, such as encapsulated bacterial infections, in which the spleen plays a protective role in the postoperative period (13).

The exocrine pancreas is one of the most important organs in the absorption of nutrients with the digestive enzymes it produces. As a result, patients who undergo total pancreatectomy develop exocrine pancreatic insufficiency and may experience malnutrition, weight loss, persistent diarrhea and vomiting, which can reduce quality of life and even lead to serious morbidity and mortality (14,15). The endocrine pancreas is responsible for the production and release of hormones that regulate metabolism, and after total pancreatectomy, patients will not produce insulin and will develop diabetes. Endocrine pancreatic insufficiency leads to increased comorbidities, continuous diet and medication use, and serious morbidities in uncontrolled diabetes (16).

The endocrine and exocrine pancreatic insufficiency that develops in patients after total pancreatectomy can lead to a serious decrease in the quality of life of the patients due to these reasons. Therefore, frequent follow-up, pain relief, appropriate pancreatic enzyme replacement, and diabetic treatment plans should be established in the postoperative period to reduce mortality and morbidity and prevent decreased quality of life (17-19).

## **MATERIAL and METHODS**

### **Patient Selection and Data Collection**

In our study, we retrospectively analyzed the data of patients diagnosed with pancreatic cancer, intrapapillary mucinous

neoplasia, pancreatic neuroendocrine tumors, and chronic pancreatitis undergoing from partial to total pancreatic resections in our clinic between 12/2017 and 12/2022. Demographic data, preoperative, perioperative and postoperative data, pathological data, current complaints if any, insulin use and prognosis of the patients were evaluated, and performance status was determined by the Eastern Cooperative Oncology Group (ECOG) performance status scale, and comorbidities were determined by the American Society of Anesthesiologists (ASA) physical status score (20,21). Postoperative complications were determined according to the Clavien-Dindo classification (22). Quality of life was compared using the EORTC QLQ-C30 scale (23). Emergency total pancreatectomies were not included in the study. Patients were called and asked about severe diarrhea, persistent vomiting, symptoms of weight loss suggesting exocrine pancreatic insufficiency, use of pancreatic enzymes, and use of insulin to assess endocrine insufficiency status. Early postoperative period was defined as the first 30 days. Relatives of the patients with late excitus were also called and asked about the pre-excitus period. Quality of life scale was administered to the surviving patients to assess both the preoperative period and the postoperative period.

### **Perioperative Data**

All operations were performed by the same team of surgeons with a high level of experience in hepatobiliary surgery. Perioperative blood loss was assessed in all patients, and there were patients in which vascular resections were performed. Patients with adhesions to the spleen and splenic vascular structures or tumors invading the spleen underwent concomitant splenectomy. Patients who underwent partial resection and had a high risk of pancreatic fistula underwent total pancreatectomy at the discretion of the surgeon.

### **Statistical Analysis**

Microsoft Office Excel 2023 was used for data collection, and SPSS version 26 (IBM, Armonk, New York, USA) was used for analysis. Independent samples t-test (for normally distributed data) and Mann-Whitney U test (for abnormally distributed data) were used to compare continuous variables between the study groups. Chi-square test was used for categorical variables.  $p < 0.05$  was considered statistically significant.

The study was conducted in accordance with the tenets of the Declaration of Helsinki, and ethical approval was granted by the Ethics Committee of Ege University Hospital with document number 23-9.1T/26.

## **RESULTS**

A total of 47 total pancreatectomy patients, 30 (63.8%) males and 17 (36.2%) females, were included in the study. Mean age of the patients was 61.38 (39-83) years. According to performance status, 16 (34%) patients were ECOG1, 24 (51.1%)

patients were ECOG2, seven (14.9%) patients were ECOG3. Four (8.5%) patients were ASA1, 24 (51%) patients were ASA2, 18 (38.3%) patients were ASA3, and one (2.1%) patient was ASA4. While 14 (29.8%) patients had no comorbidity, several patients had multiple comorbidities as follows: 19 (40.1%) patients had diabetes mellitus (DM), 19 (40.1%) patients had hypertension, three (6.4%) patients had cerebrovascular disease, three (6.4%) patients had coronary artery disease, and one (2.1%) patient had liver cirrhosis in the preoperative period (Table 1). Mean preoperative body mass index was 23.7. Forty-four (90.7%) patients were operated for pancreatic mass, while three (9.3%) patients were operated for chronic pancreatitis. Localization of the tumor in the pancreas was in the head of the pancreas in 32 (68.1%) patients. Thirty-five (74.5%) patients underwent simultaneous splenectomy.

When the median survival of patients who underwent splenectomy was evaluated according to their performance, 10 (28.6%) patients were ECOG1, 19 (54.3%) patients were ECOG2 and six (17.1%) patients were ECOG3, and it was found that there was no significant effect on the median survival

( $p=0.717$ ). The same subgroup analysis for patients with splenectomy was made according to ASA scores, and it was found that three (8.6%) patients were ASA1, 18 (51.4%) patients were ASA2, 13 (37.1%) patients were ASA3 and one (2.1%) patient was ASA4, and there was no significant effect on median survival ( $p=0.973$ ) (Figure 1).

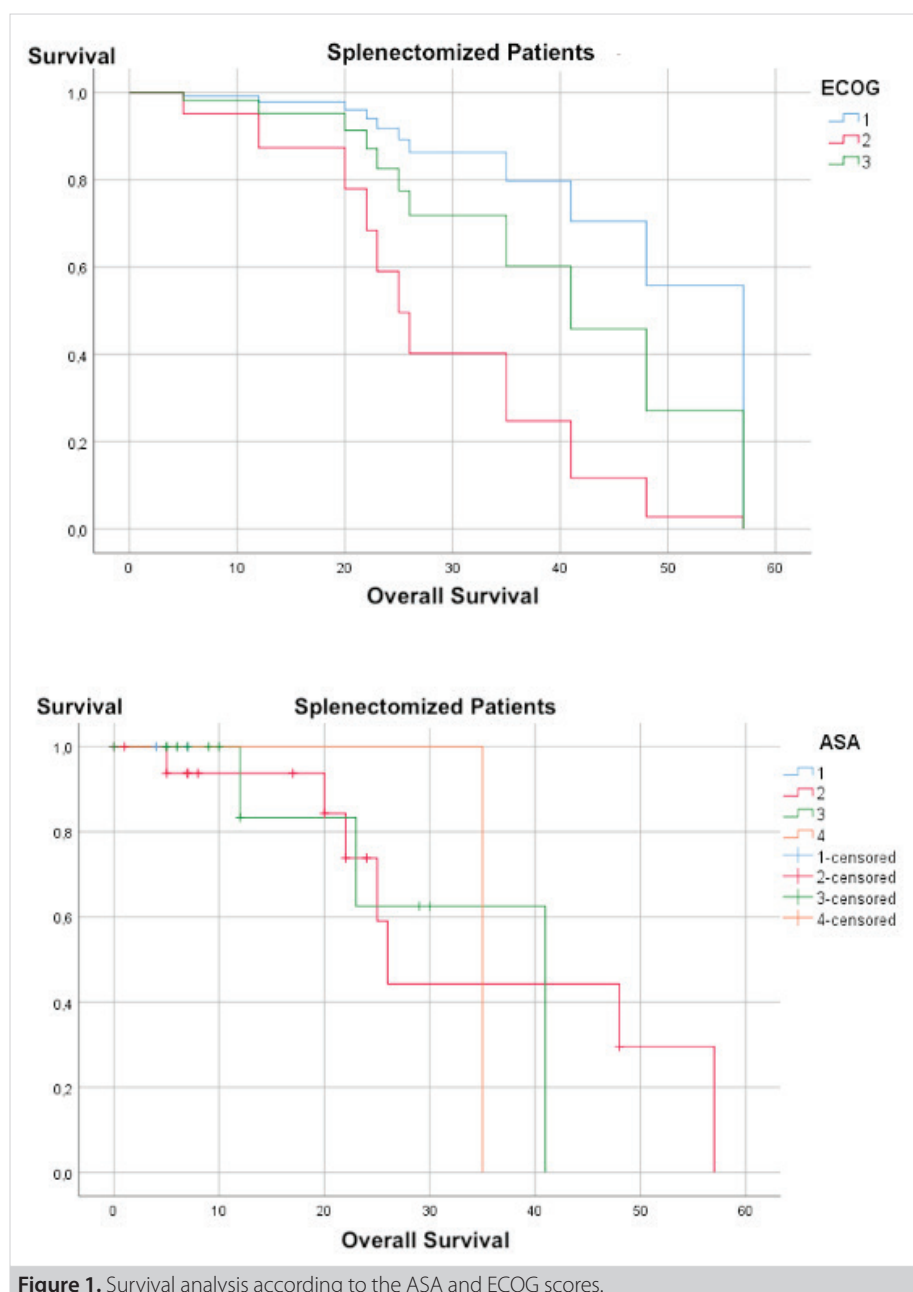
Perioperative blood loss of 500 mL or more was observed in 18 (51.5%) patients who underwent splenectomy and no significant difference was found compared to the non-splenectomy group ( $p=0.549$ ). According to the Clavien-Dindo classification of patients who underwent splenectomy, the patients were stratified as follows: twenty-three (65.7%) of them as stage 2, four (11.4%) of them as stage 3, three (8.6%) of them as stage 4 and finally three (8.6%) of them as stage 5. Complications that developed in these patients were intraabdominal abscess in three (8.6%) patients, bleeding in two (5.7%) patients, sepsis in three (8.6%) patients, and early mortality in one (2.9%) patient; no significant difference was found compared to the non-splenectomized group. Mean length of hospital stay was 24.89 days in patients who underwent splenectomy and 21.42 days in those who did not. No significant difference was observed between the two groups ( $p=0.449$ ). Mean survival time was 23.3 months in patients who underwent splenectomy and 26.25 months in patients who did not undergo splenectomy; no significant difference was found between the two groups ( $p=0.509$ ).

Fourteen (29.7%) patients underwent partial resection prior to total pancreatectomy. Nine (64.2%) of these patients underwent perioperative total pancreatectomy because of positive surgical margin after frozen section and five (35.7%) patients underwent perioperative total pancreatectomy because of high risk of pancreatic fistula development due to hard parenchyma and narrow pancreatic duct.

Vascular resection with pancreatectomy was performed in 17 (36.2%) patients. According to the Clavien Dindo classification, 12 (25.5%) patients were stage 2, two (4.2%) patients were stage 3, one (2.1%) patient was stage 4, and one (2.1%) patient was stage 5. All of these patients had a perioperative blood loss of 500 mL or more, and there was a statistically significant increase in perioperative blood loss compared to patients without vascular resection ( $p<0.001$ ). Intraabdominal bleeding was observed in two (11.7%) patients who underwent vascular resection in the postoperative period. The duration of postoperative hospital stay was 23.4 (6-60) days in patients who underwent vascular resection and 18.23 (4-61) days in those who did not; there was no statistically significant difference in the duration of hospital stay ( $p=0.086$ ). Overall survival was 26.3 (17-35) months in patients who underwent vascular resection. Vascular resection had a statistically significant effect on overall survival ( $p=0.019$ ).

**Table 1.** Characteristics and outcomes of the study group

	n= 47
Sex	
Male	30 (63.8%)
Female	17 (36.2%)
Age (mean)	61.38 (39-83)
ECOG	
1	16 (34%)
2	24 (51.1%)
3	7 (14.9%)
ASA	
1	4 (8.5%)
2	24 (51.1%)
3	18 (38.3%)
4	1 (2.1%)
Comorbidity	
HT	19 (40.1%)
DM	19 (40.1%)
CVD	3 (6.4%)
CAD	3 (6.4%)
CIRR	1 (2.1%)
Alcohol abuse	18 (38.2%)
Tobacco abuse	27 (57.4%)
Pancreas pathology	
Malignancy	37 (78.7%)
IPMN	4 (8.5%)
Pancreas NET	3 (6.4%)
CP	3 (6.4%)
Overall survival (month)	36.61 (0-57)
Exitus	35 (74.4%)
HT: Hypertension, DM: Diabetes mellitus, CVD: Cerebrovascular disease, CP: Chronic pancreatitis CAD: Coronary artery disease, CIRR: Cirrhosis.	



**Figure 1.** Survival analysis according to the ASA and ECOG scores.

Of the 17 patients who underwent vascular resection, one (5.8%) had arterial and 16 (94.2%) had venous vascular resection. Among the patients who underwent venous vascular resection, 12 (70.6%) patients underwent portal vein resection and four (29.4%) patients underwent superior mesenteric vein resection. The patient who underwent arterial resection underwent right hepatic artery resection. In this patient, the right hepatic artery originated from the superior mesenteric artery and reconstruction was performed by end-to-end anastomosis of the superior mesenteric artery and the gastroduodenal artery.

In three (75%) patients who underwent superior mesenteric vein resection, reconstruction was performed with end-to-end anastomosis, and in one (25%) falciform ligament was used as graft. In patients who underwent portal vein resection, eight (66.6%) underwent end-to-end anastomosis, one (8.35%) underwent primary repair, one (8.35%) underwent reconstruction with round ligament graft, one (8.35%) with splenic vein graft, and one (8.35%) with internal jugular vein graft.



**Table 2.** Consequences of pancreatic insufficiency

	<b>n= 45</b>
Persistent nausea and vomiting	23 (48.9%)
Diarrhea	17 (36.2%)
Weight loss	33 (70.2%)
Diabetes	45 (100%)
Pancreatic enzyme usage	40 (85.1%)
Insulin dependency	44 (97.7%)

In 24 (51.1%) patients, perioperative blood loss was less than 500 mL, in 20 (42.6%) patients, it was 500 to 1000 mL, and in three (6.4%) patients, it was more than 1000 mL. Perioperative blood loss of 500 mL or more was observed in 16 (48.4%) patients with comorbidities; there was no statistically significant difference between them and patients without comorbidities ( $p= 0.98$ ). Mean length of postoperative hospital stay was 20.69 (4-60) days in patients with perioperative blood loss of 500 mL or more and 18.23 (4-61) days in patients without perioperative blood loss. There was no statistically significant difference ( $p= 0.42$ ).

According to Clavien-Dindo classification, 32 (68.1%) patients developed stage 2, five (10.6%) stage 3, three (6.4%) stage 4 and four (8.5%) stage 5 complications in the postoperative period. Five (10.6%) patients had postoperative intraabdominal abscess, two (4.3%) patients had bleeding during follow-up and two (4.2%) patients had early postoperative mortality. Percutaneous drainage catheter was placed in two patients with intraabdominal abscess. Sepsis due to nosocomial infection was the cause of death in both patients. Surgical and percutaneous drainage catheters were removed before discharge in all patients, and no patient was discharged with a drain.

Mean postoperative hospital stay was 20.1 days. When the pathology results of the patients were analyzed, 37 (84.09%) of the 44 patients operated for pancreatic mass were operated for pancreatic adenocarcinoma. Fourteen (37.8%) patients had T3 stage tumors and 21 (56.7%) patients had T4 stage tumors. Seventeen (45.9%) patients had positive retroperitoneal surgical margins. Three (6.8%) patients were operated for pancreatic neuroendocrine tumor and four (9%) patients for IPMN.

In the postoperative follow-up period, all of the surviving 45 patients developed endocrine pancreatic insufficiency, and two exitus patients were not evaluated. Out of 45 patients, 23 (48.9%) patients had persistent attacks of nausea and vomiting, and 17 (36.2%) patients had persistent diarrhea. Weight loss of 15 kg or more was observed in 33 (70.2%) patients in the postoperative period. Forty (85.1%) patients used enzyme preparations to replace pancreatic enzymes. Mean age of the patients without symptoms due to loss of exocrine function was 63.9 (40-83) years, while mean age of the patients with

symptoms was 60.47 (39-79) years, and there was no significant difference ( $p= 0.33$ ). In the classification of patients with symptoms according to performance, there were 14 (38.9%) ECOG1, 15 (41.7%) ECOG2, seven (19.4%) ECOG3 patients. There was no significant effect of performance on the development of symptoms ( $p= 0.053$ ). Again, three (8.3%) ASA1, 19 (52.8%) ASA2, 13 (36.1%) ASA3, one (2.8%) ASA4 patients were observed, and no significant difference was observed between patients according to ASA score ( $p= 0.898$ ). Mean age of the patients not using pancreatic enzymes was 65.3 (59-68) years, while mean age of the patients using pancreatic enzymes was 60.5 (39-83) years, and this difference was statistically significant ( $p= 0.035$ ) (Table 2).

While all patients developed DM following total pancreatectomy, one (2.2%) of the 45 patients who were discharged had adequate oral antidiabetic therapy without requiring insulin. Of the 44 (97.8%) patients who were on insulin, four (9%) had an increase in the dose of insulin compared to the early postoperative period. Mean age of the patients whose insulin dose was increased in the late postoperative period was 69.2 (58-83) years, and mean age of the patients whose insulin dose was not increased was 60.3 (39-79) years; no significant difference was observed between these two groups ( $p= 0.104$ ). ASA and ECOG scores were not associated with increased insulin dose ( $p= 0.504$ ,  $p= 0.738$ ). One (2.5%) patient with preoperative DM had an increase in insulin dose. This was not statistically significant ( $p= 0.915$ ) (Table 2).

Preoperative and postoperative quality of life data were analyzed using the EORTC QLQ-C30 scale. The scale was applied to the living patients, one (7.1%) patient did not want to complete the scale. In 11 patients, preoperative and postoperative EORTC QLQ-C30 scores showed a significant decrease in physical function, role function, social function, and emotional function. There was also a statistically significant decrease in general health. Among the symptom scales, fatigue, pain, dyspnea showed a statistically significant increase, while nausea and vomiting, insomnia, loss of appetite, constipation and diarrhea showed no significant change (Table 3).

All splenectomized patients were vaccinated after the 14<sup>th</sup> postoperative day. No postsplenectomy infection was observed in any of the splenectomized patients.

When patients were divided into two groups according to their symptoms in the follow-up period as those who were symptomatic, and those who were not symptomatic, overall survival was calculated as 25.29 months ( $\pm 7.28$ ) in non-symptomatic group, 40.57 months ( $\pm 4.14$ ) in symptomatic group. The difference between groups in overall survival was found to be significant ( $p= 0.003$ ).



**Table 3.** EORTC QLQ-C30 quality of life scale scores

	Preoperative	Postoperative	p
Global health status	84.7 (75-100)	71.6 (58-83)	0.007
Physical functioning	87.2 (54-100)	70.5 (27-100)	0.005
Role functioning	85.1 (50-100)	73.5 (17-100)	0.042
Emotional functioning	79.5 (50-100)	56.1 (0-100)	0.007
Cognitive functioning	88.1 (50-100)	72.9 (34-100)	0.139
Social functioning	83.8 (50-100)	65.4 (0-100)	0.010
Fatigue	31 (0-66)	57 (0-100)	0.008
Nausea and vomiting	1.45 (0-16)	2.9 (0-16)	0.317
Pain	22.45 (0-50)	37.6 (0-83)	0.027
Dyspnea	6 (0-33)	39.2 (0-10)	0.031
Insomnia	21 (0-66)	33 (0-100)	0.102
Constipation	6 (0-33)	9 (0-66)	0.317
Appetite loss	21 (0-66)	24 (0-100)	0.661
Diarrhea	9 (0-100)	9 (0-100)	1.000

## DISCUSSION

In recent years, the frequency of total pancreatectomy has increased. As a result, patients with exocrine and endocrine pancreatic insufficiency develop pathologies that increase the frequency of hospitalization in the postoperative period, which decreases the patients' standard of living and quality of life. For this reason, many studies and research are being carried out in order to reduce the discomfort of the patients after total pancreatectomy and to increase the success of the treatment, as well as to reduce the surgical complications (24). Our study is the only study to investigate the quality of life after pancreatectomy in Türkiye.

Although indications for total pancreatectomy are limited due to the associated potential morbidity and mortality, potential indications for total pancreatectomy include chronic pancreatitis unresponsive to conventional therapies, surgical removal of precancerous pancreatic lesions, surgical resection of locally advanced pancreatic cancer, and the care of patients with exceptionally high-risk pancreatic texture after pancreaticoduodenectomy (25).

Likewise, in our series, patients who underwent partial resection were determined at the discretion of the surgeon as high risk of pancreatic fistula with a high-risk pancreatic texture or had locally advanced disease. Fourteen (29.7%) patients underwent partial resection prior to total pancreatectomy. Nine (64.2%) of these patients underwent perioperative total pancreatectomy because of positive surgical margin after frozen section and five (35.7%) patients underwent perioperative total pancreatectomy because of high risk of pancreatic fistula development due to

hard parenchyma and narrow pancreatic duct. Thirty-five (74.5%) patients underwent simultaneous splenectomy, 17 (36.2%) patients underwent vascular resection due to invasion. In patients who had vascular resection, 14 (82.3%) of them had splenectomy, and the remaining three of them (17.7%) were operated because of chronic pancreatitis.

Pancreatic anastomotic leakage is associated with postoperative complications such as intraabdominal collections, abscess formation, and pancreatic fistula formation after partial pancreatectomy. Perioperative evaluation of the pancreatic morphology and surgical technique can prevent the development of leakage. Pancreatic duct diameter, parenchymal tissue (hard, soft), pancreatic pathology (malignancy, pancreatitis, etc.) and perioperative blood loss, which are the parameters of pancreatic fistula risk scoring published by Callery et al., should be evaluated by the surgeon and the right decision should be made to achieve a good patient prognosis in patients with high fistula risk (7,8,26). In a single-center study conducted in Germany, the likelihood of leakage at the pancreatic duct anastomosis has been found higher in hard tissue than in soft tissue. The likelihood of leakage at the narrow duct anastomosis has also been reported to be higher (27). In an Italian study, it has been shown that deciding to perform total pancreatectomy in patients at high risk of developing pancreatic fistula reduces the risk of postoperative complications (9). In our study, five patients were decided to undergo perioperative total pancreatectomy due to high risk of developing pancreatic fistula, which was consistent with the literature.

In a meta-analysis by Ning Shi et al., it has been found that perioperative blood loss was higher in patients who underwent splenectomy with pancreatectomy than in patients who underwent spleen preserving surgery. In the same study, there was no significant difference between splenectomy and spleen-preserving pancreatectomy in terms of hospital stay and survival (28). However, a study by Lee et al. comparing patients who underwent distal pancreatectomy with splenectomy and with spleen preservation showed that longer operation time, increased perioperative blood loss, and more extensive surgical resection prolonged postoperative hospital stay and had a poor prognosis (29). According to our results, there was no significant difference in perioperative blood loss between splenectomy and spleen-preserving pancreatectomy groups, while the length of hospital stay and mean survival did not show a significant difference.

Some studies have shown that the spleen is the most effective organ for removing IgG-coated bacteria and is critical for clearance of encapsulated bacteria that are not opsonized by antibodies or complement (30). Therefore, vaccination is recommended for patients to prevent encapsulated bacterial infection after splenectomy. In our study, all patients were vaccinated after postoperative day 14, and no post-splenectomy infection was observed in any of the patients.

Another surgical factor that affects patient prognosis is vascular resection. Major arterial and venous structures are also included in the dissection margins in pancreatic surgery due to their proximity. In a study by Belfiori et al. that reviewed patients operated for pancreatic head malignancies, vascular resection has been shown to have no effect on survival (31). Similar results were found in a study by Marangoni et al. evaluating the outcomes of patients who underwent vascular resection during pancreatectomy (32). In our data, perioperative blood loss was higher in patients who underwent vascular resection compared to those who did not. However, this difference and the surgical technique did not have a significant effect on postoperative complications, prognosis, and median survival, similar to the literature.

It is known in the literature that endocrine failure can develop in 3-40% of the patients due to insulin deficiency after total pancreatectomy. Kusakabe et al. have reported the results of long-term follow-up of patients after pancreatectomy and found that 20.15% of patients developed postoperative endocrine insufficiency and 62.6% of these patients required insulin. While 19.7% of the patients included in the study used insulin in the preoperative period due to DM, it was observed that the need for insulin increased in the postoperative period (18). Stoop et al. have investigated the effect of exocrine and endocrine insufficiency on quality of life after total pancreatectomy and shown that patients had a very good

quality of life with appropriate endocrine treatment (17). In our study, we found that all patients developed DM postoperatively, while only one of the discharged patients had no need for insulin. However, we found that the need for insulin increased in the postoperative period in a small proportion of patients, and only one of the patients who used insulin in the preoperative period because of DM increased the insulin dose in the postoperative period.

Exocrine pancreatic insufficiency causes malabsorption of nutrients due to a deficiency of pancreatic enzymes in the gastrointestinal tract, resulting in symptoms such as nausea and vomiting, bowel dysfunction, malnutrition, and weight loss (26). There are many studies in the literature on exocrine insufficiency and its treatment due to the increasing number of pancreatic diseases and pancreatic surgeries. In a prospective study by Halloran et al, 76.9% of the patients have developed exocrine insufficiency at six weeks and 86.9% at one year after pancreatectomy (33). The largest US-based study in the literature with 1165 patients has shown that 34.7% of patients developed exocrine insufficiency after pancreatectomy (34). In our study, approximately 50% of the patients developed symptoms due to exocrine pancreatic insufficiency. Age and comorbidities did not affect the development of exocrine insufficiency.

It has been well established that both exocrine and endocrine pancreas insufficiency have a negative impact on quality of life, including physical and role function (35). In a single-center study of 34 patients by Billings et al., it has been shown that patients who underwent total pancreatectomy had a decreased quality of life (36). In the study by Müller et al. comparing patients who underwent Whipple procedure and total pancreatectomy, acceptable quality of life results have been obtained after Whipple procedure, whereas quality of life has decreased after total pancreatectomy (37). In a study from New York, although the quality of life of patients after total pancreatectomy was acceptable, most of the patients included in the study were operated for benign reasons, and it was shown that the quality of life after pancreatectomy also depends on the pancreatic pathology (38). In our study, in which we utilized the EORTC QLQ-C30 scale scores for both pre- and postoperative periods, patients who underwent total pancreatectomy and survived had a significant decrease in postoperative quality of life.

Early recognition of exocrine pancreatic insufficiency and initiation of pancreatic enzyme replacement therapy is critical to prevent the development of malabsorption-related morbidities in patients (39). In addition, enzyme replacement plays an effective role in improving patients' quality of life by alleviating their symptoms. It is recommended to start taking pancreatic enzymes soon after starting oral intake following

total pancreatectomy. Large-scale studies have shown that weight loss and malabsorption-related symptoms decreased after the use of pancreatic enzyme preparations in patients with exocrine pancreatic insufficiency (35,40,41). Our data showed that most of the patients we operated on used pancreatic enzyme supplements. Although age had no effect on the development of exocrine insufficiency symptoms, the mean age of patients who used enzyme preparations was lower than that of those who did not.

## CONCLUSION

After total pancreatectomy, patients are exposed to great stress in the postoperative period due to both surgical factors and metabolic factors related to endocrine and exocrine insufficiency, and these factors may lead to complications, morbidity, and mortality in the early and late postoperative period. In addition, the discomfort that develops especially in patients with exocrine insufficiency leads to a decrease in patients' quality of life. There are many studies in the literature evaluating both exocrine and endocrine insufficiency and quality of life after pancreatic resection. In the literature, many centers have reported a decrease in quality of life in the postoperative period in total pancreatectomy patients. In our study, we found that patients with endocrine and exocrine insufficiency showed similar results to the literature.

Limitations of our study were use of a single scale to assess quality of life, limited number of patients, and short duration of study. However, we believe that this study, which is the first in Türkiye to compare quality of life with preoperative and postoperative outcomes, will draw attention to the importance of follow-up and treatment planning for patients with total pancreatectomy. However, in our country, where the prevalence of pancreatic surgery is increasing, we believe that more meaningful results should be obtained by analyzing a larger number of patient data and by regulating the endocrinological and surgical follow-up and treatment of patients by conducting a multicenter study.

**Ethics Committee Approval:** This study was approved by Ege University Faculty of Medicine Medical Research Ethics Committee (Decision no: 23-9.1T/26, Date: 21.09.2023).

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - MZ, AU, TG, VU; Design - MZ, VU, EK; Supervision - MZ, AU, TG, VU; Data Collection and/or Processing - EK, RT, FB; Analysis and/or Interpretation - VU, RT, EK, FB; Literature Search - RT, EK, FB; Writing Manuscript - VU, TG, EK, RT; Critical Reviews - AU, VU.

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## ORİJİNAL ÇALIŞMA-ÖZET

Türk J Surg 2023; 39 (3): 264-273

**Splenektomili veya splenektomisiz total pankreatektomili hastalarda ameliyat sonrası yaşam kalitesini etkileyen metabolik ve cerrahi faktörler: Tek merkez sonuçlarımız**

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**ÖZET**

**Giriş ve Amaç:** Total pankreatektomi, pankreas patolojileri hastalarda gerekebilen ciddi mortalite ve morbidite riski taşıyan majör bir cerrahi işlemdir ve hasta seçimi prognoz açısından önemlidir. Total pankreatektomi sonrası hastalarda gelişen endokrin ve ekzokrin pankreas yetmezliği ağrı, ishal, kusma vb. nedenlerle hastaların yaşam kalitesinde ciddi düşüşe neden olabilmektedir. Amacımız dalak korunarak yapılan total pankreatektomi ve splenektominin hastaların yaşam kalitesi üzerine etkisini değerlendirmektir.

**Gereç ve Yöntem:** Çalışmamızda, 12/2017 ile 12/2022 tarihleri arasında kliniğimizde pankreas kanseri, intrapapiller müsinöz neoplazi, pankreatik nöroendokrin tümörler ve kronik pankreatit tanısıyla total pankreas rezeksiyonu yapılan hastaların verileri retrospektif olarak analiz edilmiştir. Yaşam kalitesi EORTC QLQ-C30 ölçeği kullanılarak karşılaştırılmıştır.

**Bulgular:** Çalışmaya 30 (%63,8) erkek ve 17 (%36,2) kadın olmak üzere toplam 47 total pankreatektomi hastası dahil edildi. Hastaların yaş ortalaması 1,38 (39-83) yıl idi. Beş (%35,7) hastaya sert parankim ve dar pankreatik kanal nedeniyle pankreatik fistül gelişme riski yüksek olduğu için perioperatif total pankreatektomi uygulandı. Hastaların perioperatif kan kaybı 500 mL veya daha fazlaydı ve vasküler rezeksiyon yapılmayan hastalara kıyasla perioperatif kan kaybında istatistiksel olarak anlamlı bir artış vardı ( $p < 0,001$ ). Kırk (%85,1) hasta pankreatik enzimlerin yerine enzim preparatları kullanmıştır.

**Sonuç:** Total pankreatektomi sonrasında hastaların yaşam kalitesi hem cerrahi faktörler hem de postoperatif dönemde endokrin ve ekzokrin yetmezliğe bağlı metabolik faktörler nedeniyle azalmaktadır.

**Anahtar Kelimeler:** Total pankreatektomi, pankreas yetmezliği, splenektomi, yaşam kalitesi

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# Coexisting of small bowel perforation and abdominal cocoon syndrome: A case report

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## ABSTRACT

Abdominal cocoon syndrome (ACS) is a rare situation and has an unknown etiology. Patients are characterized by the development of intraabdominal fibrotic tissue surrounding the small intestine as a result of chronic inflammation of the peritoneum. Small bowel perforations due to foreign bodies are not frequent in clinical practice. The coexistence of these two rare situations are extremely uncommon. In this article, the radiological findings and treatment process of the patient who presented with acute abdomen syndrome findings and the association of these two rare conditions are presented.

**Keywords:** Abdominal cocoon syndrome, fishbone, perforation, intestinal obstruction

## INTRODUCTION

Abdominal cocoon syndrome (ACS) is a rare clinical condition that causes intestinal obstruction. Syndrome is also known, such as peritonitis chronica fibrosa incapsulata, sclerosing encapsulating peritonitis (1). Although the physiopatology described in 1908 as the development of fibrosis with chronic inflammation in the peritoneum and subsequently enclosure of small intestines by this tissue, which causes partial or complete intestinal obstruction, the syndrome defined in detail on a case in 1978 (2). ACS is defined in two forms as primary in which etiological factors cannot be determined and secondary form in which underlying etiological causes determined (previous abdominal surgery, peritonitis, tuberculosis, sarcoidosis, or peritoneal dialysis) (3). Clinical presents with small bowel obstruction findings (nausea, vomiting, abdominal distension, and the inability of defecation) in acute condition, but after careful questioning is done, it is typical that such attacks are repeated occasionally, albeit lighter over the years. Small bowel obstructions are frequent all over the world, and the most common cause is adhesions. Obstructions due to foreign bodies (such as bezoars) are less frequent situations (4). Small bowel perforation due to accidentally ingested foreign bodies during meals has been reported in the literature, and in fact, fishbone has an essential place among these foreign bodies (5). Such cases are seen among seafarers or in geographic areas, that usually coast to the oceans where fishes which have larger and harder fishbones are consumed (6). This study aims to present the radiological findings and the treatment process of a case that has the concurrent occurrence of these two conditions, which are rare in the literature, were determined.

## CASE REPORT

A 63-year-old male patient admitted to the emergency department with abdominal pain, nausea, and vomiting lasting one week. At the time of admission, physical examination findings of the patient who had no history of comorbid disease and previous abdominal surgery were asymmetric abdominal distention and peritoneal irritation findings more prominent in the upper level of the umbilicus. Laboratory examinations were normal except leukocytosis (16.200 mm<sup>3</sup>/L). The patients whose conventional abdominal X-ray showed air-fluid levels, an abdominal com-

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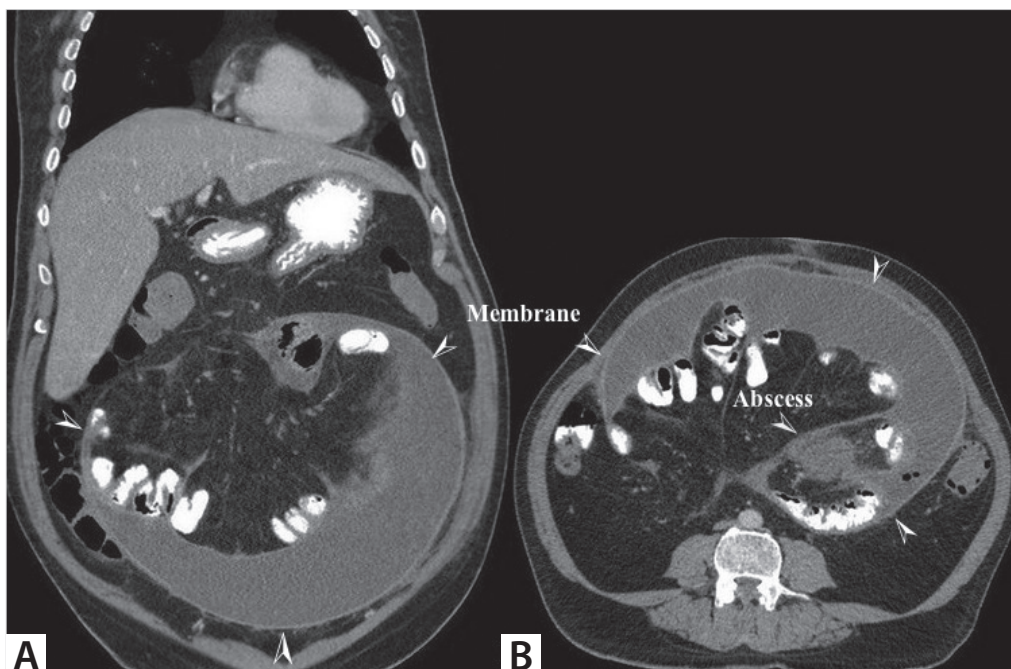
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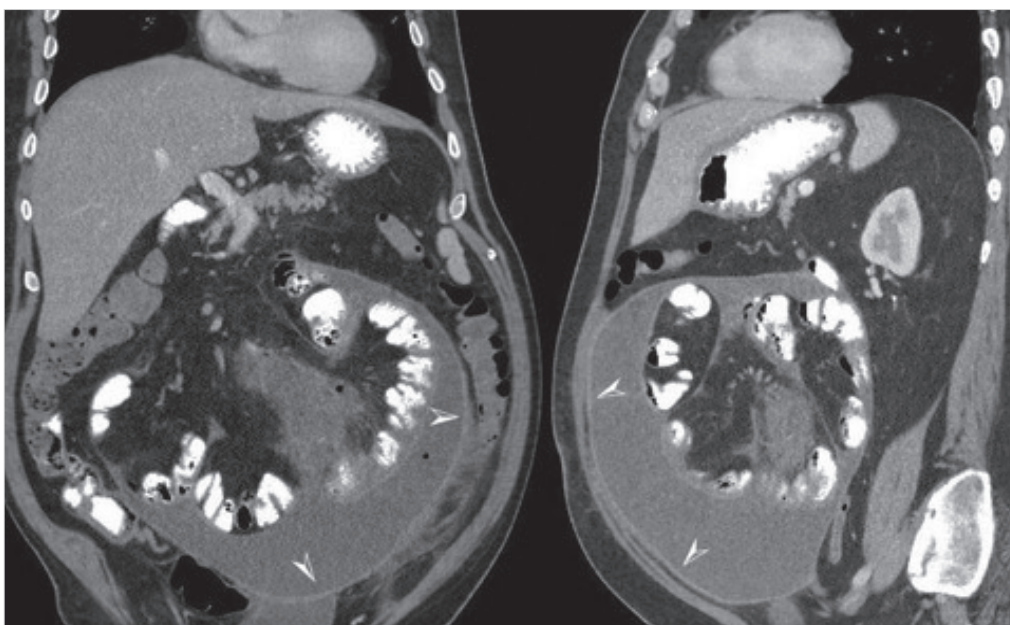


puted tomography (CT) examination revealed that a thin membrane surrounded the small intestines gathered in the periumbilical region (Figure 1A). Within this membranous structure, localized free fluid and free air particles were found around the small intestine segments. Also, a 3 x 6 cm abscess appearance was detected in the proximal jejunum mesentery localization (Figure 1B).

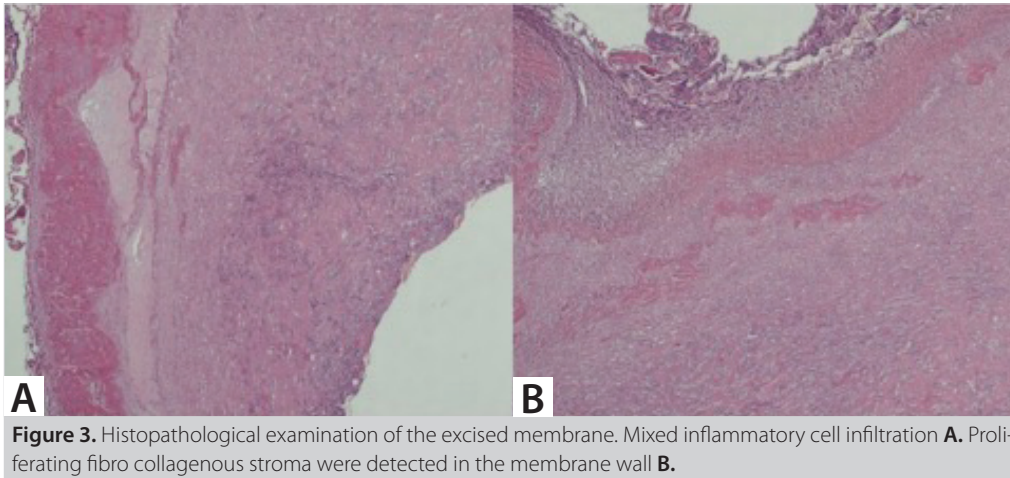
Laparoscopic exploration planned to the patient who has had an urgent surgery decision for due to peritoneal irritation findings. When the camera is entered tho the abdomen through the 10 mm port placed subumbilical, encountered with a smooth surfaced membrane surrounded by column segments seen, and it determined that all small intestine segments were settled in this membrane (Figure 2).



**Figure 1.** A thin membrane surrounded the small intestines gathered in the periumbilical region **A.** abscess appearance was detected in the proximal jejunum mesentery localization **B.**



**Figure 2.** All small intestine segments were settled in this membrane.



**Figure 3.** Histopathological examination of the excised membrane. Mixed inflammatory cell infiltration **A**. Proliferating fibro collagenous stroma were detected in the membrane wall **B**.

When the membrane was opened with a sharp dissection at the apex, purulent fluid was discharged. Intensive adhesions between the small intestine segments and the existing membrane were determined during the exploration, and conventional surgery was decided. A median incision was made to enter the abdomen, adhesions between the membrane and small intestine were dissected, abscess drained. In further exploration, it was determined that perforation existed in the small intestine 90 cm away from the Treitz ligament due to the foreign body, which was thought to be a fishbone. Following anastomosis after segmental resection, the membrane surrounding the small intestine was partially excised because of the intense adhesions. When the preoperative abdominal CT examination was re-evaluated, it was observed that the foreign body, which caused to perforation, could be observed on CT, but it was overlooked in the preoperative period. The postoperative period was uneventful, and the patient was discharged on the sixth day. At the histopathological examination of the excised membrane, mixed inflammatory cell infiltration, and proliferating fibro collagenous stroma were detected in the membrane wall (Figure 3). In the 10<sup>th</sup> month of follow-up, the patient is being followed up without any problems.

## DISCUSSION

ACS is a rare cause of intestinal obstruction, and it is challenging to diagnose clinically. According to Yip and Lee's article, small bowel obstruction without any other reason, similar history of attacks, unclear or asymmetric abdominal distention, and palpation of soft abdominal mass without abdominal tenderness were reported to be clinical signs of ACS (7). In our case, there were all findings above said except abdominal palpation. We think that we could not evaluate this finding due to the presence of peritoneal irritation findings at admission. However, these findings are non-specific and may be similar in patients with small bowel obstruction due to any cause. Therefore, we think that these findings may be useful only in patients who

are suspected to be abdominal cocoon. The disease is rare and presents with nonspecific symptoms; therefore, it is difficult to diagnose in the preoperative period. Small intestine conglomerations with membrane-covered loops at contrast-enhanced abdominal radiographs are typical, but the radiological diagnosis of ACS requires advanced experience (8). In a retrospective study in which 24 patients were analyzed, only 16% of the patients were diagnosed preoperatively. Diagnosis is usually made during surgery (9). The combination of careful clinical history, detailed physical examination, and radiological imaging results is the way of determination in the preoperative period, but most importantly, having met ACS previously. Thanks to our previous clinical experience, we were able to decide on surgery with ACS diagnosis preoperatively (10). Medical treatments such as steroids, immunosuppressive agents, and colchicine have been tried, but surgery is the main treatment modality (11). Although various comments have been made for the type and limits of the surgery to be performed in the literature, such as removal of the membrane totally by wide aggressive adhesiolysis, it is likely to encounter intense adhesions on the intestinal segments (12). Therefore, it should be kept in mind that extensive adhesions and total removal of the membrane may result in intestinal injuries or fistula development (13). Even though, recurrent intestinal obstruction attacks may be seen, albeit rarely, after limited adhesiolysis and partial excision of the membrane, it is not clear that these attacks, whether due to residual membrane or because of adhesions owing to previous abdominal surgery which are the most common cause of small bowel obstructions. In our case, we performed partial membrane excision and adhesiolysis due to severe adhesions, concurrently small bowel resection, because of the presence of a perforation.

## CONCLUSION

ACS is a rare clinical condition for which preoperative diagnosis is challenging. Diagnosis can be made by the combination of careful evaluation of the clinical history, questioning the recur-

rent character of the disease, careful physical examination, and careful radiological examinations. The necessity of early and rapid surgical treatment should be kept in mind.

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## OLGU SUNUMU-ÖZET

Turk J Surg 2023; 39 (3): 274-277

## İnce bağırsak perforasyonu ve abdominal cocoon sendromunun birlikte görülmesi: Bir olgu sunumu

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## ÖZET

Abdominal cocoon sendromu (ACS) nadir görülen ve nedeni bilinmeyen bir sendromdur. Hastalar peritonun kronik enflamasyonu sonucu ince bağırsakları saran intraabdominal fibrotik doku gelişimi ile karakterizedir. Yabancı cisme bağlı ince bağırsak perforasyonları da klinik pratikte sık karşılaşılan olgular değildir. Bu iki nadir durumun bir arada bulunması ise son derece ender bir durumdur. Bu yazıda, akut batın sendromu bulguları ile başvuran ve bu iki nadir durumun birlikteliği saptanan olgunun radyolojik bulguları ve tedavi süreci sunulmaktadır.

**Anahtar Kelimeler:** Abdominal cocoon sendromu, balık kılıcı, perforasyon, intestinal obstrüksiyonu

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# Percutaneous gas decompression can ease endoscopic derotation in sigmoid volvulus

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## ABSTRACT

Sigmoid volvulus is a disease of elderly and debilitated patients. In sigmoid volvulus patients, colonoscopic derotation is the most commonly applied approach as the first line treatment. However, colonoscopic derotation sometimes fail and then urgent surgery is required in these frail patients with high morbidity and mortality. Percutaneous colonic gas decompression has been described to sigmoid volvulus. In case of life-threatening increase intraabdominal pressure and as a primary attempt before colonoscopy. However, this technique did not find wide acceptance in the literature. Here, we aimed to present a 78-year-old male with sigmoid volvulus in whom colonoscopic derotation failed and following percutaneous gas decompression, endoscopic derotation could be done successfully. Evacuation of percutaneous colon gas in the sigmoid volvulus may facilitate endoscopic derotation when the first colonoscopic attempt failed.

**Keywords:** Colorectal, dolichocolon, ileus, bowel obstruction, endoscopy, decompression

## INTRODUCTION

Sigmoid volvulus most commonly occurs in elderly, frail patients. Emergency colonic surgery in those patients carry a substantial risk of morbidity and mortality. Nonoperative treatment by colonoscopic derotation risks and can be bridged the patients to a safe elective sigmoid resection (1). Derotation can be done by rigid or flexible colonoscopy. However, the success rate of colonoscopic derotation is not 100% and its failure compels the patients to an emergency and risky surgery.

In this case report, we presented a patient who has undergone a successful detorsion procedure by decompression of colonic gas percutaneously after a fail colonoscopic intervention.

## CASE REPORT

A 78-year-old male admitted to emergency department with abdominal pain, nausea, and vomiting lasting for three days. He had asymmetric abdominal distension and abdominal tenderness but no rigidity. There was no stool or blood in rectal examination. Plain abdominal X-ray showed a coffee bean sign that revealed the diagnosis of sigmoid volvulus (Figure 1). Laboratory values demonstrated that white blood cells 10.100/mm<sup>3</sup>, hemoglobin 13.4 g/dL, sodium 138 mmol/L, potassium 5.7 mmol/L and C-reactive protein (CRP) 0.9 mg/dL. The patient was admitted to the intensive care unit and monitored. Colonoscopic detorsion was tried but failed under sedation. Because the patient was elderly, we decided to retry colonoscopic detorsion. Informed consent was obtained from the patient and his relatives. Before the procedure, percutaneous gas decompression by 18G needle of the central venous catheter set (Figure 2). A needle was inserted from the top of the distention in the right upper quadrant of the abdomen, which is thought to be located after the rotation of the sigmoid colon. After the needle was entered, the sound of gas was heard, and the smell of stool came. If there was excessive bleeding, there was a smell of necrosis, if the patient had perforation peritonitis, the operation would be terminated, and emergency surgery would be planned. The colonoscopy was performed again successfully after percutaneous gas evacuation. Abundant gas and stool discharged after a rectal tube was placed, and the patient was followed for three days. Oral intake for liquid food was started on the first day after the pro-

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**Figure 1.** Coffee bean sign in the plain abdominal X-ray.



**Figure 2.** Percutaneous gas decompression technique by 18G needle.

cedure. On physical examination, the distention completely disappeared, and he discharged gas and stool. According to the visual analog scale, the pain score was 3, 3, 2 on the first, second and third days respectively (2). The patient was discharged on the fourth day because he denied an elective sigmoid resection surgery. At the eight-month follow-up of the patient, there was no sign of recurrence.

## DISCUSSION

It is considered as physiological that the sigmoid colon is twisted less than 180 degrees around itself. The degree of torsion should be greater than 180 degrees for obstruction and more than 360

degrees for gangrene development (3). After the sigmoid colon rotates around itself, the gas in the colon increases with hyperperistaltic movements. In addition, bacterial fermentation in closed loop intestine contributes to the increase of gas in the colon (4). The dilatation in the sigmoid colon segment further increases and there is not enough space to allow a detorsion procedure.

Successful endoscopic detorsion of the sigmoid volvulus is not always possible and the failure rate varies between 0-52% in different series (5-7). As a result of the delay in the admission to the hospital, dilatation in the colon increases. Increased tension in the wall of the colon increases the degree of obstruction in the twisted part of the sigmoid colon. This situation does not allow detorsion because the sigmoid colon in the abdomen occupies a large area. Most sigmoid volvulus patients are slim and elderly males. Therefore, percutaneous evacuation of the colon gas was thought to facilitate the detorsion procedure.

According to the National Institute for Health and Clinical Excellence (NICE) 2006 guidelines, different treatment options are available for the treatment of sigmoid volvulus. Percutaneous endoscopic colostomy is recommended as an alternative treatment option in elderly and debilitated patients whom the resection is contraindicated (8). We think that we should consider non-operative treatment options in patient groups with high mortality and morbidity.

In case of failure of endoscopic detorsion procedure in elderly and debilitated patients, emergency surgery is unavoidable. After percutaneous discharge of the colon gas, the success of the detorsion procedure increases and elective surgery can be performed. There is one prospective randomized study in the literature and this study consists of 41 patients (9). In this series, endoscopic detorsion was performed on 21 patients as a control group and as a study group endoscopic detorsion procedure was applied to 20 patients after percutaneous colon gas discharge. The success rate in the primary endoscopic detorsion group was 15/21 (75%). The success rate of endoscopic detorsion after percutaneous colon gas discharge was found as 100%. The addition of percutaneous colon gas prior to the first endoscopic detorsion significantly improved the success rate. Six patients in this series who underwent unsuccessful endoscopic detorsion were performed emergency surgery and none of these patients experienced with percutaneous gas decompression before laparotomy. Mortality was detected in five patients, two in elective colectomy and three in emergency colectomy patients all from control group. There was no mortality in endoscopic detorsion after percutaneous colon gas evacuation group. Wound infection was seen in one patient after elective surgery in the study group. Mortality was significantly lower in endoscopic detorsion after percutaneous colon gas discharge than in the other group ( $p=0.04$ ). There was no associated with any clinical or ultrasonic evidence of leakage of colonic contents.

In a case report, percutaneous colon gas evacuation was performed up on the development of abdominal compartment after sigmoid volvulus (10). In this case, the author used a 16 G needle and its aim was to reduce the pressure in the abdomen. By using this method, the patient's blood pressure was improved, and the patient was operated. There was no intraabdominal contamination in exploration.

Percutaneous colonic gas desufflation can be performed in patients without any sign of acute abdomen. During percutaneous gas discharge may develop colon perforation of the dilated colon segment. This situation can create fecal peritonitis in these patients. While trying to provide the possibility of elective surgery, mortality and morbidity risk may increase due to fecal peritonitis. Surgeons who will perform this technique should be careful about perforation. However there is no perforation in our patient and in the previously published series.

## CONCLUSION

Percutaneously evacuation of colon gas may facilitate endoscopic detorsion, in the sigmoid volvulus especially in unsuccessful endoscopic detorsion. Also, this technique may be performed for decompression by gas evacuation in patients with increased intraabdominal pressure and hemodynamic instability.

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## OLGU SUNUMU-ÖZET

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## Perkütan gaz dekompresyonu sigmoid volvulusta endoskopik derotasyonu kolaylaştırabilir

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## ÖZET

Sigmoid volvulus yaşlı ve düşükün hastaların bir hastalığıdır. Sigmoid volvulus hastalarında, birinci basamak tedavi olarak kolonoskopik derotasyon en sık uygulanan yaklaşımdır. Bununla birlikte, kolonoskopik derotasyon bazen başarısız olabilir ve yüksek morbidite ve mortalitesi olan bu zayıf hastalarda acil cerrahi gerekebilir. Perkütan kolonik gaz dekompresyonu, hayatı tehdit edecek kadar intraabdominal basıncın arttığı sigmoid volvulus hastalarında kolonoskopi öncesi ilk girişim olarak tarif edilmiştir. Hayatı tehdit eden durumlarda, intraabdominal basıncı ve kolonoskopi öncesi birincil girişim olarak artırılması literatürde geniş kabul görmemiştir. Burada, 78 yaşında, sigmoid volvuluslu, kolonoskopik derotasyonun başarısız olduğu ve perkütan gaz dekompresyonunu takiben endoskopik derotasyonun başarılı bir şekilde yapılabileceği bir erkek hasta sunuldu. Sigmoid volvulustaki perkütan kolon gazının boşaltılması, ilk kolonoskopik girişim başarısız olduğunda endoskopik derotasyonu kolaylaştırabilir.

**Anahtar Kelimeler:** Kolorektal, dolikokolon, ileus, bağırsak obstrüksiyonu, endoskopi, dekompresyon

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# Continuous saline irrigation during video-assisted liver transection: The 'Waterfall' technique

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## ABSTRACT

The use of a sealing device during video-assisted liver transection has gained a lot of popularity due to its advantages in operative and patient outcomes. However, it has some technical problems including tissue debris sticking to the instrument, excessive smoke production, and loss of pneumoperitoneum from suction. Herein, we describe a novel 'Waterfall' technique that uses continuous irrigation of saline directly on the transection plane. This technique washes away tissue particles and smoke, clears the operative view, and improves the effectiveness of tissue sealing.

**Keywords:** Hepatectomy, laparoscopic, liver transection, sealing device, video-assisted

Video link: <https://turkjsurg.com/img/UCD-6143-V1.mp4>



## INTRODUCTION

Video-assisted surgery has gained considerable momentum in all fields of surgery, including liver resection. Liver transection using a sealing device provides many advantages, including shorter operative time, decreased blood loss, and fewer complications (1). However, using a sealing device in video-assisted liver surgery has some technical problems including tissue debris sticking to the jaw of the device that requires frequent cleaning and reinsertion, excessive smoke production leading to a blurring of the camera, and excessive suction inducing loss of pneumoperitoneum which leads to more bleeding. Herein, it was aimed to describe a technique using continuous saline irrigation during video-assisted liver transection to mitigate these problems.

## Operative Technique

In this demonstrated case, we performed a laparoscopic left hepatectomy. The patient was lying in the French position. Five ports were used for this operation, which included three 11 mm and two 5 mm ports. After confirming resectability, the vascular inflow and outflow of the left lobe of the liver were individually controlled using a combination of a Foley catheter and an endo-mini retractor, which was described by our team (2). The planned transection plane was marked along the ischemic demarcation line that appeared. During liver transection, the operating surgeon uses a sealing device in the main hand and a suction-irrigation instrument in another. The sealing device acted as a clamp-crushing instrument for dividing the liver parenchyma while saline was continuously irrigated directly into the transection plane. A three-way connector is used for controlling the flow of water. Blood vessels or pedicles that are smaller than 7 mm were sealed securely using the sealing device. All bleeding points were first clearly visualized by irrigation, then secured using bi- or mono-polar cauterization. The main structures, which were the left hepatic duct and left hepatic vein, were individually secured using linear staplers.

## DISCUSSION

In this paper, we proposed a novel and simple 'Waterfall' technique to overcome common problems when using a sealing device during video-assisted liver transection.

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Continuous irrigation of saline washes away the cauterized tissue-particles from the jaw of the device and the transection plane, which in turn reduces the amount of smoke produced. This provided a clearer surgical field that requires less suctioning and reduces the number of times the device has to be removed for cleansing. The use of warm saline stabilizes intraabdominal temperature and prevents blurring of the camera lens. The incorporation of a three-way connector allows for more precise control of water flow and prevents splashing of water into the camera lens.

Better bleeding control could also be achieved with this technique. Firstly, having a flow of water on the transection plane enhances the bipolar function of the sealing device by acting as an electric current conduction media and provides a thermoprotective effect on the tissue (3). Secondly, this technique washes away the blood from the cut surface and aids in pinpointing the bleeding spot that needs to be sealed. Additionally, unlike the use of suction devices that would typically cause a loss of pneumoperitoneum and worsen the bleeding, saline irrigation helps maintain a high intraabdominal pressure.

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## VIDEO MAKALE-ÖZET

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## Video yardımcı karaciğer transeksiyonu sırasında sürekli salin irrigasyonu: 'Şelale' tekniği

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## ÖZET

Video yardımcı karaciğer transeksiyonu sırasında sızdırmazlık cihazı kullanımı, ameliyat ve hasta sonuçlarındaki avantajları nedeniyle oldukça popülerlik kazanmıştır. Bununla birlikte, alete yapışan doku artıkları, aşırı duman üretimi ve emme nedeniyle pnömoperiton kaybı gibi bazı teknik sorunları vardır. Bu yazıda, doğrudan transeksiyon düzleminde sürekli salin irrigasyonu kullanan yeni bir 'şelale' tekniği tanımlandık. Bu teknik doku partiküllerini ve dumanı yıkayarak uzaklaştırır, operatif görüşü temizler ve doku sızdırmazlığının etkinliğini artırır.

**Anahtar Kelimeler:** Hepatektomi, laparoskopik, karaciğer transeksiyonu, sızdırmazlık cihazı, video yardımcı

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