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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. 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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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.

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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) 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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2. Drafting the work or revising it critically for important intellectual content;
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.

In addition to being accountable for the parts of the work he/she has done, an author should be able to identify which co-authors are responsible for

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The Turkish Journal of Surgery requires and encourages the authors and the individuals involved in the evaluation process of the submitted manuscripts to disclose any existing or potential conflicts of interests, including financial, consultant, and institutional. Any financial grants or other support received for a submitted study from individuals or institutions should be disclosed to the Editorial Board. To disclose a potential conflict of interest, the ICMJE Potential Conflict of Interest Disclosure Form should be filled in and submitted by all contributing authors. Cases of a potential conflict of interest of the editors, authors, or reviewers are resolved by the journal's Editorial Board within the scope of COPE and ICMJE guidelines.

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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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- Author Contributions Form, and
- ICMJE Potential Conflict of Interest Disclosure Form (should be filled in by all contributing authors)

INSTRUCTIONS TO AUTHORS

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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.

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In memory of Prof. Dr. Ahmet Çınar Yastı

On December 22, 2023, Turkish Surgery bid a fond farewell to an extremely valuable name. After serving tirelessly on the Turkish Surgical Association Board of Directors for seven years, Prof. Dr. Ahmet Çınar Yastı passed away, leaving behind invaluable memories and significant services.

Prof. Dr. Ahmet Çınar Yastı was born in Mersin in November 1968, as the second of four children born to pharmacist parents, according to his curriculum vitae. Following his boarding secondary education in Konya Anatolian High School and Ankara Science High School, he graduated with honors from Hacettepe University Faculty of Medicine and began practicing medicine.

Academic Career

At Ankara Numune Training and Research Hospital, he completed his training in general surgery. He was named an Associate Professor in 2008, an Intensive Care Sub-Branch Specialist in 2013, and a Professor in 2014. Established in 1969 as Türkiye's first burn clinic, the Ankara Numune Burn Unit named him the responsible physician in 2009.

Prof. Dr. Yastı, the Ministry of Health's Chairman of the Burn Science Board, oversaw the research on the 2010 Regulation on the Establishment and Operation of Burn Treatment Units in Inpatient Health Facilities and took part in its revision studies in 2011 and 2019.

Under the direction of Ankara Numune Training and Research Hospital and Ankara Bilkent City Hospital Burn Treatment Center, over 400 nurses and over 100 specialist physicians received training. Furthermore, many foreign medical professionals -including doctors and nurses- have received training.

In Numune Hospital Akyurt Integrated Unit, he established and defined Türkiye's first inpatient chronic wound unit in 2011. He led the legislative studies on the competency and physical requirements needed for the opening of hyperbaric centers and took part in the construction and legislation of the Akyurt Hyperbaric Medicine Application Center installation works. In his capacity as the Ministry's Türkiye Chronic Wound Coordinator, he made sure that the first Chronic Wound Care Services Circular was defined in legislation and helped bring it to print in 2021.

From 2012 to 2017, he pursued his education at Çorum Hitit University and Ankara Numune Hospital. In 2019, Prof. Dr. Yastı, who was teaching at the University of Health Sciences, was named the Burn Treatment Center's physician-in-charge at Ankara Bilkent City Hospital.

For his work on burns, he was awarded State Orders of Appreciation in both Azerbaijan and Romania. He took an active part in the Karabakh War, helping to treat burn patients. The Ministry of Health took part in service and training events as part of the Ministry of Health's Health Weeks in numerous nations, including Bangladesh, Afghanistan, Mongolia, Kyrgyzstan, Azerbaijan, Gagauzia, Kosovo, Mauritania, Djibouti, Yemen, and Sudan.

Not only has he been a consistent member of the Turkish Surgery Board of Directors since 2016, but he has also been the association's Secretary General for the past five years. Deniz Elif is the daughter of Prof. Dr. Ahmet Çınar Yastı, whom he loves. Ahmet Çınar Yastı was just a close friend of mine when we first met in 1983 in Ankara Science High School. We attended our boarding school for nearly three years. My 40-year friend Çınar and I ran into each other again at Ankara Numune Hospital General Surgery Clinic. Çınar became a very important friend of mine and we entered into a crucial partnership when the General Surgery assistant fellowship was added to the boarding school fellowship. We were aware of our mutual dependability in times of need. Even in circumstances I did not anticipate, he did everything in his power to support me. Naturally, Çınar extended his helping hand to all of us who knew him, not just to me. His social intelligence was extremely high; he was able to make friends with people of all social levels and communicate with them in a natural way. He was so kind to so many people. He was a person who looked out for his team, was gregarious and friendly, offered his helping hand to those in need and asked for assistance, and provided whatever assistance he could at no cost. I want to express my gratitude to my beloved brother for leaving us with so many priceless works and memories. Respectfully, I bow in remembrance of Prof. Dr. Ahmet Çınar Yastı.



Prof. Dr. Ahmet Çınar Yastı (1968-2023).

Prof. Dr. Barış Zülfiaroğlu



FROM THE EDITOR'S DESK

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Dear readers of the Turkish Journal of Surgery,

First of all, I am deeply saddened to share the news of the recent passing of a valued colleague within our surgical community. Ahmet Çınar Yastı, who served as Secretary General of the Turkish Surgical Association, was a warm and inspiring personality as well as a successful professional. His contributions to the surgery, especially to the burn therapy, were immense, and his absence will be profoundly felt. We extend our heartfelt condolences to their family, friends, and colleagues. Ahmet Çınar Yastı will be remembered for their passion, expertise, and the lasting impact they made on the surgical community.

As we gather for the final issue of 2023, it is a moment of reflection, gratitude, and remembrance.

In the ever-evolving field of surgery, this year has been marked by exceptional strides, groundbreaking research, and unwavering dedication from our contributors. Our 2023 volume summarizes the culmination of these efforts and presents the latest insights and developments in surgical practice that promise to shape the future of our discipline.

In a move toward embracing innovative educational formats, we introduced a new section to our journal - Video Articles. This addition aimed to provide a dynamic and immersive platform for the presentation of surgical techniques, case studies, and educational content. This new format has attracted great interest from both authors and readers. We believe that this multimedia approach will enhance the learning experience for our readers and contribute to the dissemination of practical knowledge in the surgical community.

In the spirit of reflection, I wish to express my sincere appreciation to all the authors who entrusted us with their valuable research and insights. Your dedication to advancing surgical knowledge has been essential to the success of our journal. I would also like to express my gratitude to each member of our editorial team for their hard work, dedication and passion for the field of surgery. Together we have overcome challenges, celebrated successes and continued to encourage a community dedicated to the pursuit of excellence in surgical research and practice.

I would also like to express our sincere thanks to our publisher, Bilimsel Tıp Yayınevi, and our technology partner, Yazılım Parkı, for their support and dedication to the smooth production and distribution of our journal.

Looking ahead to the new year, 2024 holds the promise of further innovation, collaboration, and breakthroughs in the world of surgery. May the coming year bring health, happiness, and continued success to each of you, our esteemed readers, contributors, and partners.

On behalf of the editorial team of TJS I wish for a Merry Christmas for our international readers and Happy New Year for all!

Warm regards,

Kaya SARIBEYOĞLU

Editor-in-Chief

Turkish Journal of Surgery



Prophylactic negative pressure wound therapy in patients with closed surgical wound: An integrative review

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ABSTRACT

Surgical site infection is the leading healthcare-associated infection and a major contributor to rising healthcare costs. Implementation of measures to reduce this problem, particularly the prophylactic use of negative pressure wound therapy, may be an effective and promising method to reduce the risk of surgical site infection in patients with closed surgical wounds. The aim of the study was to identify the effectiveness of negative pressure wound therapy as a prophylactic measure in reducing the risk of surgical site infection in patients with a closed surgical wound. Whittemore and Knaff's five-step integrative review framework was carried out using three electronic databases. MEDLINE with Full-text, CINAHL with Full-text and Academic Search Complete were searched through the EBSCOhost Web platform. Articles search publication date was between 2018 and 2022. Nine studies were identified that addressed the effectiveness of prophylactic negative pressure wound therapy in reducing the risk of surgical site infection in the patient with a closed surgical wound. There was also evidence of effectiveness in reducing surgical wound dehiscence, drainage output and drainage time, as well as reducing the incidence of hospital readmissions and the need for wound debridement. Prophylactic negative pressure wound therapy can be an effective treatment option, among others, in reducing the risk of surgical site infection in patients with a closed surgical wound. This evidence promotes improved clinical practice regarding the management of the closed surgical wound, promoting health gains for patients.

Keywords: Negative-pressure wound therapy, nursing, prevention and control, surgical wound infection

INTRODUCTION

Surgical site infection (SSI) is an infection that arises at or near the surgical site or surgical incision during the first 30 days after surgery, or for one year if a non-human device (prosthesis) has been implemented (1). It is the leading healthcare-associated infection (HAI) reported in developing countries and among the most common at the European level (2). The European Centre for Disease Prevention and Control (ECDC) revealed that, out of 15.000 HAI's reported in Europe, the most frequent was SSI, accounting for 19.6% (3). Economic costs associated with SSI at the European level are thought to be between €1.47-19.1 billion.

It increases the length of stay by approximately 6.5 days and it costs three times as much to treat a patient with SSI, making it clear that it is essential to reduce this risk as much as possible (2,4).

The measures to prevent/reduce SSI should be implemented as early as possible and maintained throughout the perioperative period (consisting of three distinct periods: pre, intra and postoperative), aiming to improve the quality and safety of the care provided to patients (5,6). In this sense, international organizations have developed measures that should be respected and implemented. These are divided into the preoperative period (e.g., glycemic control, preoperative bath with antiseptic solutions, treatment of pre-existing infections, trichotomy only if strictly necessary, antiseptic preparation of the surgical team members, antimicrobial prophylaxis), intraoperative period (e.g., oxygenation, maintenance of normothermia, sterilization of surgical instruments, clothing of surgical team members, asepsis and surgical technique) and postoperative (e.g. surgical wound care) (2,4,7).

More recently, negative pressure wound therapy (NPWT) has begun to be used as

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a prophylactic measure in closed surgical wounds to reduce the risk of SSI and other possible associated complications (2,8,9). Until relatively recently, it has been mainly used for the treatment of complex, difficult-to-heal wounds, such as pressure ulcers, diabetic ulcers, burns, surgical wound dehiscence's, wounds with high amounts of exudate, among others. This therapy was initially tested prophylactically in orthopedic surgery and due to its success in reducing SSI in this specialty, NPWT began to be tested in other surgical specialties, increasing exponentially (9,10). Although several studies have reported a significant reduction in the rate of SSI after the use of prophylactic NPWT, its overall benefit is still under debate as its use is not fully consensual. This is because some studies, although in a minority part, do not prove its efficacy or do not find significant differences between it and traditional treatment (9,10).

Considering that NPWT is per se a therapy with a high monetary cost (11), and despite evidence showing its overall cost-saving potential versus control therapies to be effective (12), it is important that its efficacy is irrefutably proven, leading to the need for further studies to corroborate and demonstrate its cost-effectiveness (2,11,12).

Thus, to contribute to the increase of knowledge based on scientific evidence and improve the clinical practice of health professionals, particularly nurses, regarding its prophylactic use in reducing the risk of SSI in patients with closed surgical wound, this integrative literature review was developed to address this issue.

MATERIAL and METHODS

Integrative literature review design has an international reputation in nursing research and evidence-based practice, and this one summarizes empirical literature about the effectiveness of NPWT as a prophylactic measure in reducing the risk of SSI in patient with a closed surgical wound (13).

Integrative literature reviews have the potential to advance nursing science, enabling future research, clinical practice, and health policy initiatives, as well as the inclusion of several methodologies with direct applicability to practice and health policies. The methods used are based on Whittemore and Knafl's five stages, which are problem identification, literature search, data evaluation, data analysis and data presentation (14).

Problem Identification

The research problem emerged during the academic and clinical training of health professionals working in medical-surgical nursing. In the search for the best evidence related to nursing care, specifically for surgical patients, the aim was to improve quality, efficiency, and effectiveness, to obtain health gains and progressively improve the level of health indicators. To this end, the authors used the available literature and formulated the research question using the PICOD methodology [population

(P), intervention (I), comparison (C), outcomes (O) and study design (D)]. Thus, the guiding question was as follows: "What is the effectiveness of prophylactic NPWT (outcomes) in reducing the risk of surgical site infection (intervention) in people with a closed surgical wound (population)?"

Literature Search

The electronic platform EBSCOhost Web was used to search for articles using the MEDLINE with Full-Text, CINAHL with Full-Text and Academic Search Complete databases during the month of April 2022. Thus, articles' search publication date was between 2018 and April of 2022.

First, the descriptors to be used during the search were validated in the Medical Subject Headings (MeSH). The following descriptors were used: "negative wound pressure therapy"; "surgical wound"; "surgical wound infection"; "surgical procedures, operative"; "laparotomy". They were organized using the Boolean operators "OR" and "AND", according to the following search strategy:

[(Negative Wound Pressure Therapy)] AND

[(Surgical Wound) OR (Surgical Wound Infection)] AND

[(Surgical Procedures, Operative) OR (Laparotomy)].

As a result of the search, a total of 67 articles were obtained, which were exported to Mendeley Reference Manager: Twenty-seven articles were available in MEDLINE with Full Text; 14 articles in CINAHL with Full Text; and 26 articles in Academic Search Complete. After the removal of duplicates, manually and through Mendeley, 49 articles remained, which were submitted to title and abstract analysis to determine whether they met the remaining inclusion and exclusion criteria. After this selection phase, 27 articles were excluded for being Opinion studies and literature reviews ($n=10$), studies addressing postoperative measures ($n=8$), and studies without prophylactic NPWT ($n=9$). The remaining 20 articles were read in full and assessed regarding the methodological design and objectives, and 11 articles were excluded. Thus, nine articles were selected to be included in this review.

To make the selection process more understandable, a flowchart (Figure 1) was developed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow 2020 diagram (15).

Data Evaluation

Articles were assessed for their authenticity, methodological design, and informational value. The level of evidence of each article was analyzed through the contributions of the Joanna Briggs Institute (JBI) (16). JBI's approach considers the best available evidence, the context in which care is delivered, the individual patient and the professional judgement and expertise of the health professional (17).

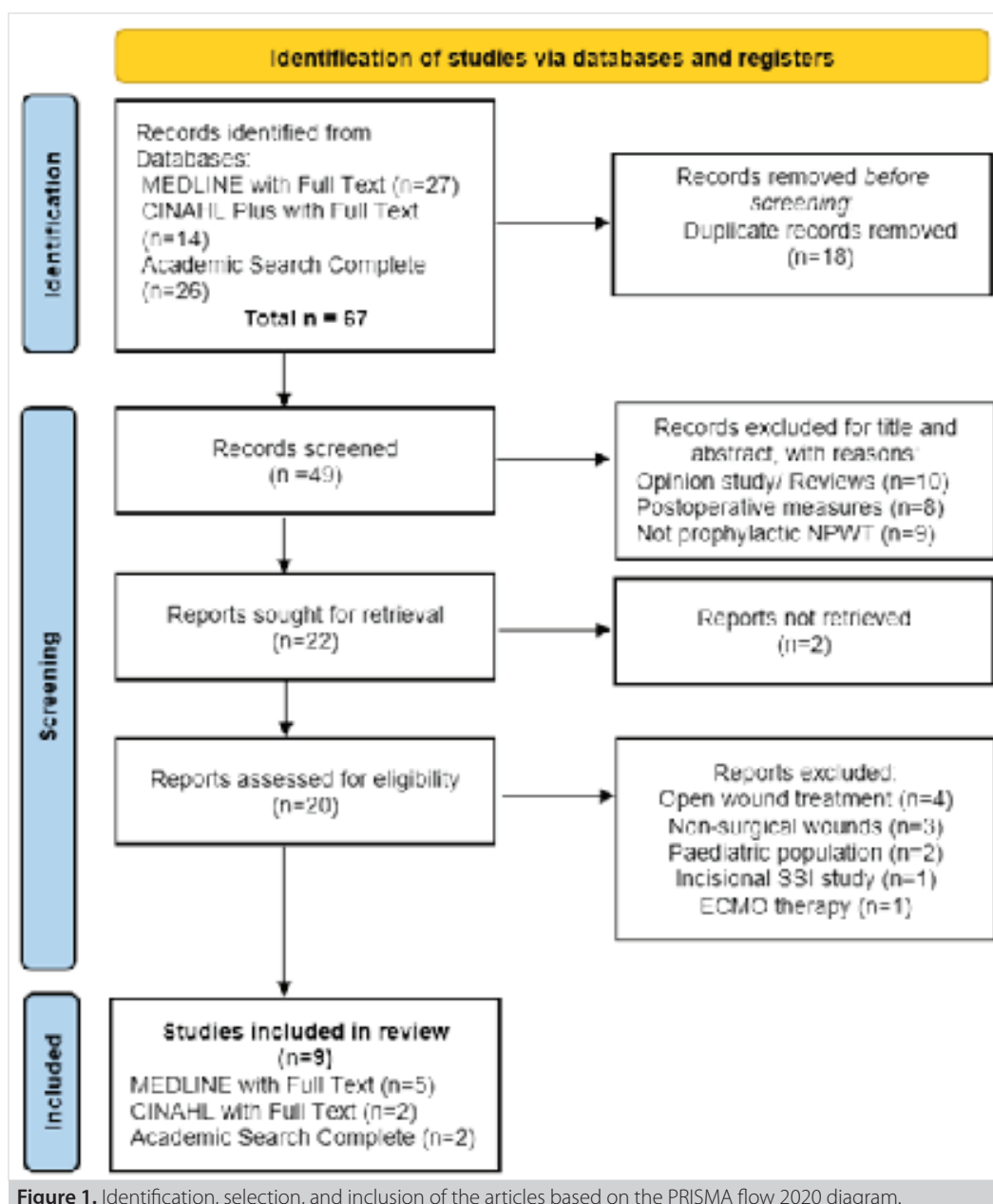


Figure 1. Identification, selection, and inclusion of the articles based on the PRISMA flow 2020 diagram.

Preference was given to experimental and observational studies, in full-text, and written in Portuguese or English. In addition, editorials, opinion studies and literature reviews were excluded. Articles that did not answer the research question, that may present ambiguous methodology, that had participants from the paediatric population and that were duplicated in the databases used were excluded.

Articles that validated the reduction of surgical wound complications, more specifically the association of NPWT with the reduction of SSI, were only advanced from abstract reading to full-text review.

Full-text records that did not comply with the assessment process were excluded from the review. Also, the relevant references of the selected articles were reviewed.

Data Analysis

The selection and analysis process were performed by two independent blinded-review researchers. For data extraction and analysis, an excel sheet was created by the authors of this study with the following information: authors, year, country of origin, level of evidence, objectives, participants/sample and main results/conclusions.

The authors individually analyzed the articles regarding the type of associated surgery (e.g., elective or emergency, contaminated, clean); the incidence of SSI in the postoperative period; several postoperative complications (e.g., seroma, surgical wound dehiscence); and the inherent technique, only NPWT or its comparison with other treatments.

RESULTS

Of the analyzed studies, four articles were developed in the United States of America, two studies were produced in Australia, one study was conducted in the United Kingdom, one was achieved in India and one in Europe, more specifically in the Netherlands.

Regarding the number of participants, 718 patients underwent prophylactic NPWT on the closed surgical wound and 1080 patients received standard or conventional surgical dressing/treatment/techniques, making a total of 1798 participants studied. The year with the most publications was 2021, 2020 and 2018 ($n=2$), and regarding the levels of evidence, most were level 3.c: Cohort study with control group ($n=5$) and level 1.c: Randomized controlled trial ($n=2$).

To answer the above-mentioned research question, we began the content analysis of the selected articles. The results of this analysis are shown below (Table 1) to facilitate the reader's reading and understanding. The table presents the results corresponding to all articles, where the information mentioned in the "Data Analysis" chapter is explained.

DISCUSSION

Given the results explained above, it is possible to observe that the articles have quite similar objectives. Somehow, they verify the effectiveness of prophylactic NPWT in reducing the risk of SSI, and other wound complications, when applied to the patient with closed surgical wound. Thus, it is found that all studies can answer the previously formulated research question and bring relevant contributions to clinical practice regarding the treatment of closed surgical wound.

Addressing the results obtained, regarding SSI, the results of the studies are mostly unanimous. In the study by Chung et al., which involved 474 patients undergoing emergency laparotomy, the incidence of SSI was approximately $\frac{1}{4}$, with a higher rate in the group receiving standard surgical dressing compared to the group undergoing NPWT, observed both the rate of superficial and deep infections (18). Despite this, organ/space infection rates were higher in the group submitted to NPWT, because it is directed to the abdominal wall, having no effect beyond the fascial layer, so it is not expected to have influence at this level. The use of standard surgical dressing and emergency colorectal surgery were associated with a higher risk of developing SSI. In the results of Mondal et al., the group that received NPWT also had fewer patients developing SSI than

the control group (19). However, in this study, where participants were intervened due to presenting incisional hernia, all documented SSIs were considered superficial. Similarly, in the study of De Rooij et al. 28.0% of the patients in the NPWT group developed postoperative wound complications, compared to only 18.9% in the control group [OR= 1.67 (95% CI= 0.77-3.63), $p=0.199$] (26). However, these wound complications involved surgical site infections, which showed a higher SSI with the use of NPWT in the study of De Rooij et al. (Control group 18.0% vs. NPWT 26.0%) (26). Previous studies demonstrate that these results are relatively high when compared to the SSI rate found in other research using closed-incision negative pressure therapy (8.6-16.9%) (18,21,22,24).

In the study developed by Schurtz et al., the results indicate that 14 patients developed SSI after exploratory laparotomy in the context of trauma (20). Only three belonged to the group that received NPWT, which goes against the results mentioned by the aforementioned authors. Curran et al., who in their study included patients at high risk of infection who underwent open abdominal colorectal surgery, revealed that, of the 315 participants, 41 developed SSI and, like the articles already mentioned, its incidence was higher in the control group (21). This study also observed the time elapsed until the diagnosis of SSI. However, this proved to be superior in the experimental group, which enjoyed NPWT, highlighting the need for greater surveillance of the surgical wound. In addition to this, the authors also mention that patients were associated with increased SSI the longest operative time, the fact that they depend on dialysis in the preoperative period and present a stoma in the preoperative or postoperative period. Conversely, the use of NPWT was associated with a decrease in SSI. In the study by Liu et al., regarding the time elapsed until the diagnosis of SSI, the results were different from those found by Curran et al., which was similar in both groups (21,22). Regarding the development of SSI, it corroborates the results of the studies already mentioned, and the rate of this was higher in the control group compared to the experimental group (33 patients in the control group, versus six patients in the NPWT group). The same authors also report that in all patients undergoing emergency laparotomy, NPWT obtained greater benefit in wounds classified as clean-contaminated, contaminated, and dirty.

Hall et al., observed that all SSI occurred in wounds classified as contaminated, making this event interesting, since in it there are also wounds classified as dirty (23). However, it should be noted that this presents a difference in relation to all others included in the literature review: 18 of the 20 patients with wound classified as dirty received first NPWT on the open surgical wound, with subsequent closure of the same, before receiving prophylactic NPWT on the closed surgical wound. That is, the wounds had the opportunity to form granulation tissue before being closed.

Table 1. Summary of the articles included in the literature review

Authors	Year	Country	Level of Evidence (15)	Objective	Study Population/ Sample	Main Results/Conclusions
Chung, Ali, Hawthornthwaite, Watkinson, Blyth, McKigney, Harji & Griffiths (18)	2021	United Kingdom	Level 3.c: Cohort study with control group	To compare the SSI rates in patients who underwent prophylactic NPWT on the closed surgical wound and those who received the standard dressing following emergency laparotomy.	n= 474 patients (n= 237 with NPWT and n= 237 standard dressing)	The incidence of SSI was 25.3%. In the group with NPWT it was 16.9%, while in the group receiving standard surgical dressing it was 33.8%. The use of a standard surgical dressing and the fact that the patient had undergone emergency colorectal surgery were associated with a higher risk of developing SSI.
Mondal, Ali, Galidevara & Arumugam (19)	2022	India	Level 1.c: Randomized controlled trial	To compare the effectiveness of prophylactic NPWT on the closed surgical wound with conventional gauze dressing in reducing postoperative complications after mesh placement in incisional hernia repair.	n= 64 patients (n= 30 with NPWT and n= 34 conventional dressing)	In both groups, SSI were considered superficial. As for the mean drained output, the group that received NPWT showed a statistically significant reduction in drained volume compared to the group that received conventional gauze dressing and the mean duration of wound drainage.
Schurtz, Differding, Jacobson, Maki & Ahmeti (20)	2018	United States of America	Level 3.d: Case - controlled study	To compare the complication rate of postoperative wounds following laparotomies performed in a trauma and acute care setting between prophylactic NPWT on closed surgical wound, provided by a Surgical Incision Management System (SIMS), and conventional wound care.	n= 96 patients (n= 48 with NPWT and n= 48 conventional dressing)	A lower rate of SSI was recorded in the group receiving SIMS compared to the control group. The same occurred regarding hospital readmissions, with only one readmission in the SIMS group and seven readmissions in the control group.
Curran, Alvarez, Valle, Cataldo, Poylin & Nagle (21)	2018	United States of America	Level 3.c: Cohort study with control group	To evaluate the impact of prophylactic NPWT on the closed surgical wound on the incidence of SSI in a group of high-risk patients undergoing open colorectal surgery.	n= 315 patients (n= 77 with NPWT and n= 238 standard dressing)	Overall, the incidence of SSI was 13%. In the group receiving NPWT, the rate of SSI was lower. Preoperative dialysis dependence, longer operative time, and the presence of pre or postoperative stoma were associated with increased SSI. Regarding hospital readmissions, their frequency was half in the experimental group 8%, and in the control group 16%.
Liu, Cheng, Islam, Tacey, Sidhu, Lam & Strugnell (22)	2020	Australia	Level 3.c: Cohort study with control group	To verify whether the use of prophylactic NPWT on the closed surgical wound reduces wound complications following emergency laparotomies.	n= 227 patients (n= 70 with NPWT and n= 238 standard dressing)	Around 17.2% patients developed SSI after emergency laparotomy: 8.6% of the group receiving NPWT and 21% of the control group. The usefulness of NPWT was most evident in clean and contaminated wounds. The group that received NPWT had a shorter length of stay and no surgical wound related readmissions. Increasing age, body weight above 75 kg and wound contamination were observed to be independent predictors associated with wound complications. Contrary to these, the use of NPWT reduced SSI and surgical wound dehiscence.

Table 1. Summary of the articles included in the literature review (continue)

Authors	Year	Country	Level of Evidence (15)	Objective	Study Population/Sample	Main Results/Conclusions
Hall, Regner, Abernathy, Isbell, Isbell, Kurek, Smith & Frazee (23)	2019	United States of America	Level 3.e: Observational study without a control group	To verify if the use of prophylactic NPWT on the closed surgical wound in emergency general surgery patients would result in low rates of superficial SSI.	n= 81 patients with NPWT	In 7.4% of patients, superficial SSI occurred, requiring antibiotherapy or wound reopening. All SSI occurred in wounds classified as contaminated. The application of NPWT resulted in acceptable rates of SSI in patients undergoing emergency general surgery.
Di Re, Wright, Toh, El-Khoury, Pathmanathan, Gosselink, Khanijaun, Raman & Ctercteko (24)	2021	Australia	Level 1.c: Randomized controlled trial	To assess the incidence of post-laparotomy SSI by comparing the use of prophylactic NPWT on the closed surgical wound with a standard surgical dressing.	n= 124 patients (n= 61 with NPWT and n= 63 specialized wound dressings)	A higher percentage of superficial SSI was observed in the control group (20.6%). NPWT group of 9.8%. Superficial wound dehiscence was 9.5% in the control group and did not occur in the experimental group. The use of standard postoperative surgical dressing (Cutiplast Dressing: Smith & Nephew, Watford, UK; or Comfeel Dressing: Coloplast, Humlebaek, Denmark) was associated with increased risk of superficial SSI. NPWT was not associated with a decrease in superficial SSI.
Chambers, Morton, Lampert, Yao, Debernardo, Rose & Vargas (25)	2020	United States of America	Level 3.c: Cohort study with control group	To determine whether prophylactic NPWT on the closed surgical wound is associated with reduced SSI in gynecological cancer patients undergoing laparotomy compared with standard surgical dressing.	n= 256 patients (n= 64 with NPWT and n= 192 standard dressing)	The group that received NPWT was associated with a significant reduction of any complication with the surgical wound (20.3% NPWT group and 40.1% control group). Of these complications, the lower rate of superficial (9.4% NPWT group and 29.7% control group) and deep (0% NPWT group and 6.8% control group) SSI stands out. The use of NPWT was associated to a lower probability of superficial and deep SSI.
De Rooij, van Kuijk, van Haaren, Janssen, Vissers, Beets & van Bastelaar (26)	2021	Netherlands	Level 3.c: Cohort study with control group	To estimate the incidence post-operative complications following the use of the NPWT, in non-high risk closed incisions in patients undergoing mastectomy.	n= 161 patients (n= 50 with NPWT and n= 111 control group with a conventional wound dressing)	28.0% of the patients in the NPWT group developed postoperative wound complications, compared to 18.9% in the control group (OR= 1.67 (95% CI= 0.77-3.63), p= 0.199). This research indicates that using Avelle negative pressure wound therapy for mastectomy wounds doesn't result in a reduction in postoperative wound complications. It also doesn't lead to fewer patients requiring unplanned visits or fewer patients developing clinically significant seromas.
NPWT: Negative pressure wound therapy, SIMS: Surgical Incision Management System, SSI: Surgical site infection.						

In this study, where all patients were submitted to emergency surgery and NPWT, of 81 patients, only six had superficial SSI, requiring antibiotic therapy, or reopening the wound. It is reported that the development of enterocutaneous fistula was the cause of SSI in a patient. The authors claim that they included ostomies in the same, because they were associated with a higher risk of developing SSI. However, 16 of the wounds classified as clean-contaminated presented stoma closures, but SSI was not observed in none.

Among the articles analyzed, only Di Re et al. and De Rooij et al. did not corroborate the same results (24,26). The De Rooij et al. study showed that one patient in the control group developed wound necrosis that required surgical debridement (26).

Di Re et al. included 124 patients undergoing open abdominal surgery and reported that after 30 days there was a higher rate of superficial SSI in the control group, compared to the group undergoing NPWT (24). However, they clarify that their percentage value was not statistically significant (20.6% versus 9.8%). On days five and seven, the incidence of superficial SSI was also higher in the control group but, again, it was not statistically significant (13.1% versus 7.9%). In this study, the use of standard surgical dressing was associated with a higher risk of developing superficial SSI and, once again, the authors do not consider it to be statistically relevant. Thus, the study by Di Re et al. considers that NPWT was not associated with a decrease in superficial SSI (24). It should be noted that, despite the information described, the authors admit that the study has several limitations.

In the same line of evidence, Chambers et al. supported the remaining studies, explaining that the group that was subjected to NPWT was associated with a significant reduction of any complication associated with the surgical wound, the lower rate of superficial and deep SSI, which shows once again the effectiveness of NPWT in this context (25). Regarding organ/space SSI, the difference between the groups was not significant, being 0% in the group subject to NPWT. In this study, which included 256 patients who underwent laparotomy due to diagnosis or suspicion of gynecological neoplasm, the use of NPWT was associated with a reduction in the incidence of superficial SSI and a lower probability of superficial and deep SSI.

In addition to SSI, the studies highlight the dehiscence of the surgical wound as a postoperative complication, being addressed in four studies (22,24-26). In the study by Liu et al., NPWT reduced wound dehiscence because, of the 24 patients where it was observed, only three patients belonged to the NPWT group (22). Di Re et al. share the same opinion since in their study superficial wound dehiscence was only found in the group that did not enjoy NPWT (24). The study by Chambers et al. revealed that, although there was a decrease in dehiscence in the group submitted to NPWT, this was not considered significant (25). Furthermore, De Rooij et al. displayed that 10% of the

patients in the NPWT group, compared to 3.6% of the patients in the control group, developed wound dehiscence requiring wound treatment with vacuum assisted closure [OR= 2.97 (95% CI= 0.76-11.58), $p=0.116$] (26). However, no beneficial effect of NPWT was found regarding wound necrosis and wound dehiscence.

Another of the conclusions found when analyzing the articles was the formation of seroma. Regarding this postoperative complication, Mondal et al. and Chambers et al. agree since both studies showed that the difference was not statistically significant between the two groups (19,25). In De Rooij et al. study, during NPWT, the mastectomy wound surface was under external nominal negative pressure of 80 mmHg by the NPWT pump during seven days, and the results should point to a favorable effect on seroma formation. However, there was a higher proportion of patients with clinically significant seroma in the NPWT group than in the control group, 24.0% versus 14.0%. This difference was not statistically significant, but a difference of this magnitude could be clinically relevant, as well as, the lower mean total drain output in the NPWT group (26).

Regarding hematoma associated with surgical wound, two studies addressed this complication (22,25). The study by Liu et al. reported that this was observed in two patients in the experimental group (undergoing NPWT) and four patients in the control group (22). The study by Chambers et al. did not find a statistically significant difference between the two groups (25).

Duration of surgery was also addressed in the article by Mondal et al. and by Chambers et al. (19,25). Both studies consider that the differences between the two groups are not statistically important or not significant. Mondal et al. also refer to the average drain rate and the average duration of wound drainage, being the only ones to address these results (19). Regarding the average drained flow, the authors indicate that the group submitted to NPWT revealed a statistically significant reduction in the drained volume, compared to the control group, with conventional gauze dressing. Regarding the average duration of wound drainage, this was also statistically significant, being 5.6 days in the NPWT group and 6.5 days in the control group.

The average length of stay was one of the most discussed results and was mentioned in six of the nine articles analyzed. In most studies, the authors reveal that the difference between the two groups studied was similar: it was not verified or statistically significant, except for Liu et al., where the group submitted to NPWT had a shorter hospitalization time when compared to the control group (22). Di Re et al., despite agreeing with most of the authors, add that, comparing patients undergoing elective or emergency surgery, those who underwent emergency surgery had a longer hospitalization period (24). In relation to hospital readmission, Schurtz et al. and Curran et al. stated that this was lower in the group subject to NPWT, and in the

first study mentioned there was only a hospital readmission in the experimental group and in the second study, readmission was double in the control group compared to the experimental group (20,21). Liu et al. reported that there was no hospital readmission related to the surgical wound in the experimental group (22). For Chambers et al. no significant differences were observed between both groups (25). Another result found in three of the articles analyzed was the need for surgical re-intervention. Both studies, Chung et al. and Chambers et al. stated that they did not identify significant differences between both groups (18,25). However, the study by Liu et al. stated that the four patients who presented dehiscence of the surgical wound needed to be re-intervened and in the study by De Rooij et al., one patient required surgical re-intervention, as a result of wound dehiscence (22,26).

Morbidity and mortality were also reported. In the study by Chung et al., no significant differences were identified between the groups (18). For Hall et al., these were 38% and 6%, respectively (23). Curran et al., referred only to the mortality rate, however, stated that this was similar between both groups studied (21).

Finally, the need for debridement of the surgical wound was addressed only by two articles. Chambers et al. found that this decreased significantly in the group submitted to NPWT, compared to the control group (25). In the other study, by De Rooij et al. the results showed that in the control group, there was a single patient who experienced wound necrosis necessitating surgical debridement (26).

CONCLUSION

Given the results presented above, it is concluded that prophylactic NPWT is one of a wide range of treatment options in reducing the risk of SSI in the person with closed surgical wound since the major control groups of the studies obtained a higher SSI rate in relation to the groups undergoing NPWT.

It was found that NPWT was associated with a reduction in dehiscence of the surgical wound and regarding seroma formation and hematoma associated with the wound, there is no evidence of the benefit of NPWT. It was verified that the NPWT obtained benefits in the considerable reduction of the drained flow and the duration of the drainage, respectively. Regarding the length of hospitalization, morbidity and mortality, the effect of NPWT was not proven.

As for a possible hospital readmission associated with the surgical context, it can also be concluded that participants undergoing NPWT were associated with a lower incidence, compared to participants undergoing conventional treatment. In this context, data on the need for surgical re-intervention were inconclusive.

Finally, regarding the need for debridement of the wound, the NPWT is associated with its significant decrease.

After this, we can conclude that prophylactic NPWT, in addition to reducing the risk of SSI in patients with closed surgical wound, also has efficacy in reducing the risk of several other complications associated, directly or indirectly, to the surgical wound. Economically NPWT is inherent in a higher cost than surgical dressing/treatment/standard or conventional techniques. However, since it can have several benefits as demonstrated, its use will compensate on a large scale, as it will reduce the costs associated with health care. In addition to this, it will increase the quality of life of the patient, following an elective or emergency surgical intervention.

It should be noted that, for the use of prophylactic NPWT to be effective, it is necessary that its benefits are consolidated in the body of knowledge and professional experience of health professionals in clinical practice, who apply and handle it. In this sense, training and professional updating should be a prerequisite for its implementation, particularly nurses, who provide care to patients with this therapy can maximize the efficiency of such procedure in line with scientific evidence.

Relevance to Clinical Practice

The results of the current study indicate that the prophylactic use of NPWT in patients with closed surgical wound is effective in reducing SSI, perhaps is necessary to consider other variables in clinical practice which were not addressed in this review.

The NPWT, in the form of several devices with differences in size, weight, type of therapy available, interface material, reservoir, technology and, more recently, the type of installation, allows its use not only in the hospital context, but also in the outpatient, being relevant in the average reduction of hospitalization time.

This review can guide the practice of care for the surgical patient with closed wound, for nurses or other health professionals, especially in the context of hospitalization.

Limitations

Although the search was conducted in credible electronic databases, studies in other databases may have been neglected. In addition, the full use of studies in English (the only alternative to the Portuguese language) and their divergent design were considered as limitations.

Since SSI is a multifactorial event, the timely identification of its potential risk factors is a fundamental necessity for the prevention of its occurrence. In the included studies, (internal and external) risk factors associated with their development were not addressed, thus it may have been another of the limitations that influenced the results.

Nevertheless, we want to emphasize that most of the studies included in this revision are in the emergency context and colorectal surgery, and only a few in clean surgeries. However, we do not have enough information to assess if there are benefits regarding in terms of infection risk.

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BÜTÜNLEYİCİ DERLEME-ÖZET

Turk J Surg 2023; 39 (4): 283-292

Kapalı cerrahi yarası olan hastalarda profilaktik negatif basınçlı yara tedavisi: Bütünleştirici bir inceleme

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ÖZET

Cerrahi alan enfeksiyonu, sağlık hizmeti ile ilişkili enfeksiyonların başında gelmekte ve artan sağlık hizmeti maliyetlerine önemli bir katkıda bulunmaktadır. Bu sorunu azaltmaya yönelik önlemlerin uygulanması, özellikle de negatif basınçlı yara tedavisinin profilaktik kullanımı, kapalı cerrahi yaraları olan hastalarda cerrahi alan enfeksiyonu riskini azaltmak için etkili ve umut verici bir yöntem olabilir. Bu çalışmanın amacı, kapalı cerrahi yarası olan hastalarda cerrahi alan enfeksiyonu riskini azaltmada profilaktik bir önlem olarak negatif basınçlı yara tedavisinin etkinliğini belirlemektir. Whittmore ve Knafl'ın beş adımlı bütünleştirici incelemesi üç elektronik veri tabanı kullanılarak gerçekleştirildi. MEDLINE with Full-text, CINAHL with Full-text ve Academic Search Complete EBSCOhost Web platformu üzerinden taranmıştır. Makale arama yayın tarihi 2018 ile 2022 yılları arasındaydı. Kapalı cerrahi yarası olan hastalarda cerrahi alan enfeksiyonu riskini azaltmada profilaktik negatif basınçlı yara tedavisinin etkinliğini ele alan dokuz çalışma tespit edildi. Ayrıca, cerrahi yara açılmasını, drenaj çıkışını ve drenaj süresini azaltmanın yanı sıra hastaneye tekrar yatış insidansını ve yara debridmanı ihtiyacını azaltmada etkili olduğuna dair kanıtlar vardı. Profilaktik negatif basınçlı yara tedavisi, kapalı cerrahi yarası olan hastalarda cerrahi alan enfeksiyonu riskini azaltmada diğerlerinin yanı sıra etkili bir tedavi seçeneği olabilir. Bu kanıt, kapalı cerrahi yaraların yönetimine ilişkin klinik uygulamaların iyileştirilmesini teşvik ederek hastalar için sağlık kazanımlarını desteklemektedir.

Anahtar Kelimeler: Negatif basınçlı yara tedavisi, hemşirelik, önleme ve kontrol, cerrahi yara enfeksiyonu

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Utility of positron emission tomography for determination of axillary metastasis of breast cancer

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ABSTRACT

Objective: The involvement of axillary lymph nodes plays a key role in breast cancer staging. Positron emission tomography is a promising modality for detecting axillary lymph node metastasis. In addition, nomograms are used to predict the status of axillary lymph nodes. In this study, the role of positron emission tomography in determining axillary metastasis and its correlation with the nomogram was evaluated.

Material and Methods: The axillary maximum standard uptake value (SUVmax) values of the patients in the preoperative period, the features in the perioperative and postoperative specimen and Memorial Sloan Kettering Cancer Center nomogram data were evaluated.

Results: As axillary SUVmax detected by Positron emission tomography in the preoperative period increased, so did the likelihood of lymph node involvement. Axillary SUVmax value were compared with Memorial Sloan Kettering Cancer Center nomogram data but no correlation was found. Age, lymph node number, histopathology results, mass diameter, presence or absence of lymphovascular invasion and/or perineural invasion, tumor type, estrogen receptor status, Ki67 and Cerb-B2 statuses were not correlated. However, axillary SUVmax was inversely correlated with grade and progesterone receptor status.

Conclusion: Results from positron emission tomography of axillary lymph nodes in breast cancer patients showed that SUVmax was only inversely related to cancer grade and progesterone receptor status while not correlating with other accepted parameters for tumor assessment. Thus there is insufficient reliability for the use of axillary SUVmax alone for accurate assessment of tumor characteristics at present.

Keywords: Axillary metastasis, breast cancer, positron emission tomography

INTRODUCTION

Breast cancer is the most common type of invasive cancer among women. The status of the axillary lymph nodes is important for staging and local control of the disease. Therefore, in breast cancer patients, axillary lymph node dissection (ALND) is performed in order to aid treatment decision-making and for prognostic purposes. Prognostic and predictive factors for breast cancer are various, including the number of axillary lymph nodes involved. Although patients with palpable tumor may have clinically negative axilla, approximately 30% are positive on histopathological assessment after axillary dissection, and this figure is 10% in non-palpable tumors. Thus, ALND is performed unnecessarily in the remaining 70% or 90% of patients each group, respectively. The low positivity rate after dissection in patients with clinically negative axilla has raised the question of the necessity of performing ALND in this group, which may be associated with many adverse effects and could be considered unnecessary overtreatment (1).

At the present time, breast-conserving surgery (BCS) is almost ubiquitous. In addition, many surgeons are more selective about performing ALND and may prefer sentinel lymph node biopsy (SLNB), and take Z011 clinical trial to attention.

Imaging methods including 18F-fluorodeoxyglucose tomography by combined positron emission tomography/computed tomography (PET/CT), are used to provide anatomical information for various disorders. While PET was only in research in the first years, PET/CT were developed with integration of CT and began to be used in routine clinical evaluations with high diagnostic potential in the following years.

Nomograms have been used in breast cancer diagnosis and can be used to predict axillary lymph node metastasis in the light of preoperative demographic and

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pathological findings. One of these is the Memorial Sloan Kettering Cancer Center (MSKCC) calculation chart. The MSKCC uses seven variables: tumor size, lymphatic invasion, tumor histology, nuclear grade, multifocality, estrogen receptor status and progesterone receptor status (2).

The aim was to determine the preoperative SUVmax value of axillary lymph nodes in PET/CT for predicting the axillary metastasis and to compare the findings with the MSKCC nomogram.

MATERIAL and METHODS

Patients

Patients who underwent surgery for breast cancer at our clinic between February 2015 and November 2016 were recruited to the study. The inclusion criteria were: clinically node negative, absence of any other primary neoplasm; and preoperative PET/CT performed. Patients were excluded if they had either diabetes mellitus or inflammatory breast cancer. A total of 70 patients were excluded from the study and the study was conducted with 51 patients (Figure 1). Ethics approval for the study was obtained from the clinical ethical committee of our university and our study has been performed with the appropriate participants' informed consent in compliance with the Helsinki Declaration.

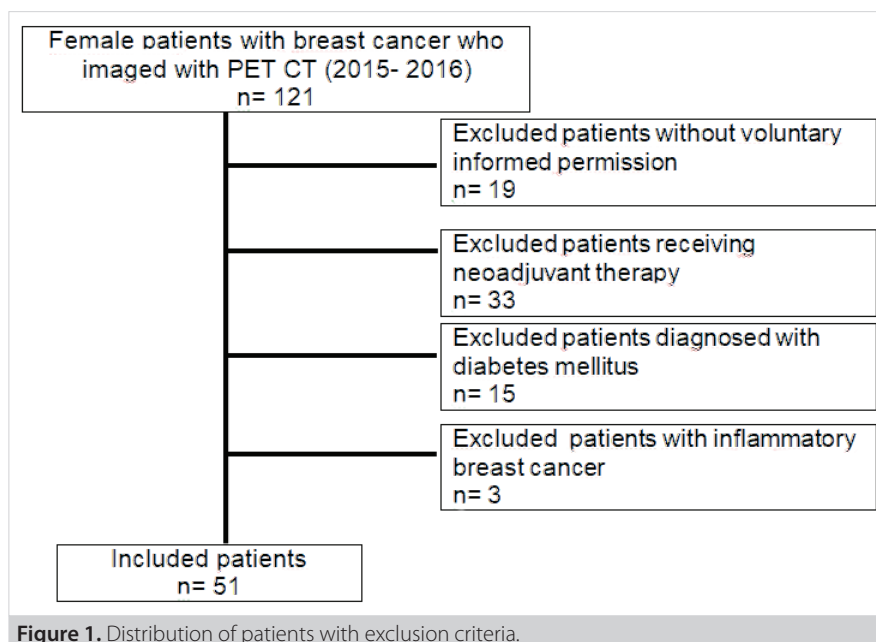
Mean age of the patients was 52.4 ± 12.4 . Forty-three patients were diagnosed with invasive ductal cancer, six patients with invasive lobular cancer, and the remaining patients with other rare breast tumors. Sentinel lymph node biopsy was evaluated as positive in pathology specimens of 38 patients. Eight patients were evaluated as grade 1, 28 patients as grade 2, and

17 patients as grade 3. Estrogen receptor (ER) in 36 patients and progesterone receptor (PR) in 32 patients were evaluated positive.

Methods

Axillary SUV (standard uptake value) values of the all patients were recorded. The prediction of lymph node metastasis with MSKCC nomograms was preoperatively performed. Nomogram data were taken as age, size of the mass according to the preoperative images, location of the tumor, and lymph vascular invasion status in the preoperative pathological specimen, the unifocality or multifocality feature, estrogen and progesterone receptor status. The probability of axillary involvement was calculated by entering these criteria to the MSKCC Breast Cancer nomogram. The preoperative axillary SUVmax values in PET/CT were recorded for each case.

The axillary SLNB with dual methods including preoperatively applied radioactive tracer and perioperative injections of methylene blue to the areola was performed according to guidelines and specimens handled following incision to axilla were evaluated by using the frozen section. Axillary lymph node dissection was performed to the patients whose SLNB results were reported as metastatic. Post-operative pathology reports of the patients were obtained and tumor mass size, tumor type, histological grade, lymphovascular invasion status, ER percentage, PR percentage, Cerb-B2 and Ki67 percentage were recorded as data. The data obtained were statistically compared with the prognostic and predictive values of the patients and their axillary lymph node status.



Main (primary) implications are the preoperative axillary SUVmax value for predicting axillary metastasis and comparison of it with MSKCC nomogram. Secondary implications: Determination of the relationship between preoperative axillary SUVmax value and ER, PR, HER2/neu, Ki67, tumor size, tumor grade, axillary status, molecular subgroups, lymphovascular invasion and age.

Statistical Analysis

Statistical evaluation was made with IBM SPSS 20.0 (SPSS Inc., Chicago, IL, USA) Package Program. The normal distribution test was done by using the Kolmogorov-Smirnov test. Numerical variables were given as mean \pm standard deviation and median (25th percentile-75th percentile) and frequency (percentiles). Differences between the groups were evaluated with the Mann-Whitney U test for numerical variables that did not have a normal distribution. The relationship between the numerical variables was evaluated using Spearman correlation analysis. $p < 0.05$ was considered enough for statistical significance. In addition, ROC analysis was performed to evaluate axilla SUVmax uptake by positron emission tomography.

RESULTS

SUVmax values of the axilla were examined with PET/CT in the preoperative period and the postoperative axillary sentinel lymph node status. It was observed that the possibility of sentinel lymph node involvement in the axilla increased when the SUVmax value was high in preoperative PET/CT ($p = 0.000$). According to ROC analysis, its sensitivity was calculated as 80.95%, specificity 88.89%, positive predictive value 97.1%, and negative predictive value 50%. The cut-off value for axillary SUVmax was 2.3 (Figure 2).

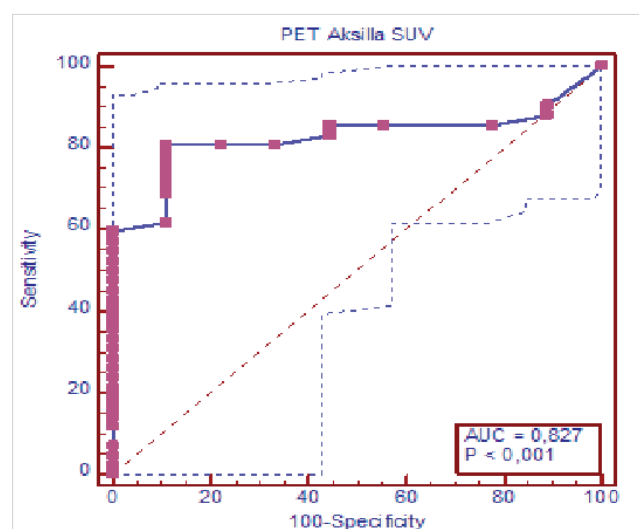


Figure 2. ROC analysis for PET/CT axillar SUVmax value.

The comparison of MSKCC nomogram data with axilla PET/CT SUVmax value was done. In the correlation analysis, it was seen that the increase in the axillary SUVmax value was not statistically similar to the increase in the percentage of the nomogram ($p = 0.061$). SUVmax values were evaluated according to age and parameters reported in pathology reports. With the comparison of age and axillary SUVmax value, there was no significant relation ($r = -0.125$, $p = 0.382$). With the correlation analysis, the number of metastatic lymph nodes and axillary SUVmax value were found to be insignificantly different ($r = -0.070$, $p = 0.660$). In other words, the increase in the number of metastatic lymph nodes did not affect the SUVmax values. When the pathological tumor size and axillary SUVmax value were compared, the correlation between them was not found significant ($r = -0.176$, $p = 0.217$). It means that the increase of tumor size did not increase the axillary SUVmax value. The correlation analysis between grade and axillary SUVmax value showed significant changes ($r = 0.439$, $p = 0.001$). The high tumor grade showed to be related with the high axillary SUVmax value (Figure 3).

With the evaluation of data, it was observed that the relationship between lymphovascular invasion and axillary SUVmax value was insignificant ($r = -0.231$, $p = 0.315$), the axillary SUVmax values were insignificant, when compared with histological tumor types ($r = 0.075$, $p = 0.603$). With correlation analysis, comparison of ER positivity and axillary SUVmax value was found to be insignificant (true $r = -0.157$, $p = 0.270$) (code $r = -260$, $p = 0.065$). There was significant and inverse difference between PR and axillary SUVmax values (true $r = -0.285$, $p = 0.043$) (code $r = -0.302$, $p = 0.031$) (Figure 4). So, while the PR level decreased, the axillary SUVmax value increased.

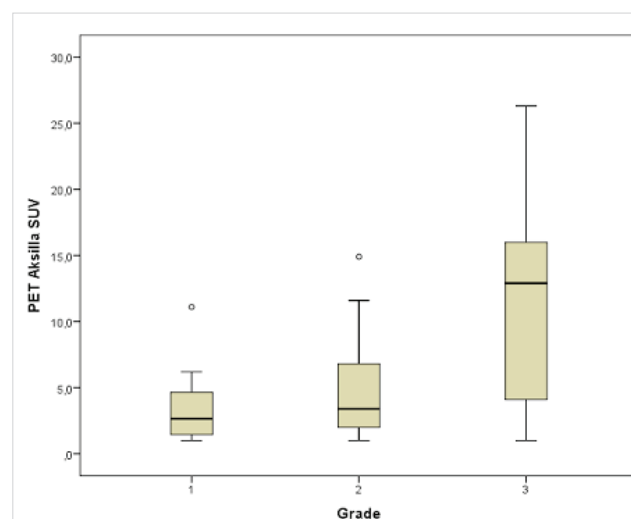


Figure 3. Correlation analysis between grade and axillary SUVmax value.

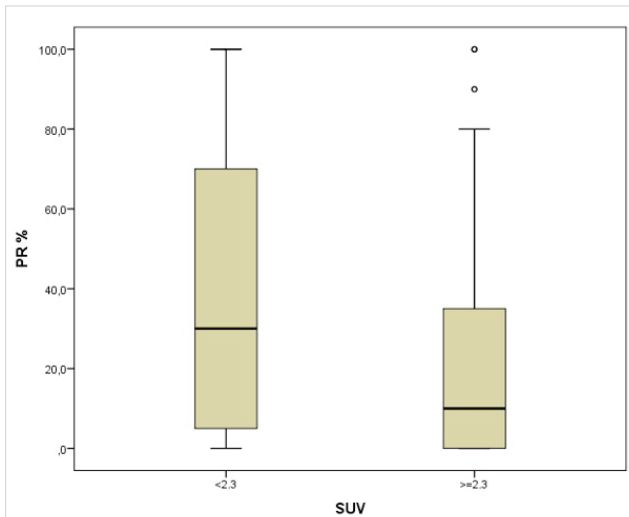


Figure 4. Correlation analysis between PR with axillary SUVmax value.

There was not any significant relation between Ki67 results and axillary SUVmax values when compared ($r = -0.220$, $p = 0.167$). The correlation analysis between Cerb-B2 positivity and axillary SUVmax value was also similarly insignificant ($r = -0.082$, $p = 0.569$). Statistical analysis also showed that there was no relationship between perineural invasion and axillary SUVmax values ($r = 0.143$, $p = 0.625$) (Table 1).

DISCUSSION

Determining axillary lymph node involvement in breast cancer patients is still one of the most controversial issues today. It is known that breast cancer can spread first to regional axillary lymph nodes and then to other body parts (bone, liver, lung, brain). Therefore, determining the metastasis status in axillary lymph nodes is important in terms of staging, treatment planning and prediction of prognosis for breast cancer.

Table 1. Patient characteristics in low- and high-zinc groups

	Axillary SUVmax< 2.3	Axillary SUVmax> 2.3	p
Age	54.0 (50-64)	51 (43-60.75)	0.391
Number of metastatic lymph nodes	5.50 (3.00-7.75)	5.50 (2.75-9.00)	0.987
Pathology mass diameter (mm)	30.00 (22.00-35.00)	30.00 (17.00-44.25)	0.756
Grade			
1	3 (20%)	5 (13.9%)	0.001
2	9 (60%)	17 (47.2%)	
3	3 (20%)	14 (38.9%)	
Lymphovascular invasion			
No	2 (40%)	7 (43.7%)	0.315
Yes	3 (60%)	9 (56.2%)	
Perineural invasion			
No	3 (100%)	5 (45.5%)	0.625
Yes	0 (0%)	6 (54.5%)	
Tumor type			
Invasive ductal	14 (93.3%)	29 (80.6%)	0.603
Invasive lobular	1 (6.7%)	5 (13.9%)	
Other	0 (0%)	2 (5.6%)	
ER			
Positive	12 (80%)	24 (66.7%)	0.065
Negative	3 (20%)	12 (33.3%)	
PR			
Positive	12 (80%)	20 (55.6%)	0.031
Negative	3 (20%)	16 (44.4%)	
Ki67			
Positive	9 (60%)	21 (58.3%)	0.563
Negative	6 (40%)	15 (41.7%)	
Cerb-B2			
0	11 (73.3%)	25 (69.4%)	0.837
1	0 (0%)	1 (2.8%)	
2	0 (0%)	2 (5.6%)	
3	4 (26.7%)	8 (22.7%)	

The best clinical procedure to determine the metastasis status in lymph nodes is still ALND. However, it is known that adverse events occur due to ALND including lymphedema, limitation of arm and shoulder movements, numbness in the upper arm, etc. in 20% of patients. On the other hand, in patients with T1 and T2 breast cancer, only 3-20% of those who undergo routine ALND is reported to have metastases. This means that routine axillary lymph node dissection is unnecessary for the most of the patients (3,4). In the light of this information, SLNB has been developed over the years and entered clinical practice. With the introduction of the SLNB to the clinical use, unnecessary ALND were significantly reduced and unnecessary complications were prevented. Sentinel lymph node evaluation requires a multidisciplinary approach with participation at nuclear medicine specialist, surgeon, and an experienced pathologist (5,6).

The success of SLNB depends on the experience of the surgeon (7). Despite all care, there is 10-15% false negativity in SLNB (8). This situation has led to the development of some non-invasive, simple, easy-to-use and reproducible imaging methods to detect axillary and other lymph node metastases (9,10).

PET/CT, one of the modern imaging methods, is one of the noninvasive techniques in detecting lymph nodes and other organ metastases in cancer patients. This technique has been shown to be useful in the detection of many subclinical metastases in cancer patients. PET/CT has been found useful in showing metastasis to normal size and anatomical lymph nodes when compared to other radiological methods (11). A preclinical study showed that PET/CT was a feasible method to show lymph node metastases (12). Although various clinical studies have been conducted to evaluate axillary staging with PET/CT in patients with breast cancer, these studies have conflicting results (13,14). The study of the Milan Cancer Institute encouraged use of PET/CT for preoperative evaluation. In the evaluation made in this study, PET/CT was performed preoperatively in 167 patients who were previously decided to undergo axillary lymph node dissection and compared with the patients' existing pathologies. In the study, the accuracy of PET/CT in axillary lymph node staging was 94.4% and its positive predictive value was 84%. False negativity was expressed as result of patients with a low tumor burden or microscopic lymph node metastasis (15). Utech et al. correctly detected the axillary status of 44 patients with stages 1-3 breast cancer with PET/CT and reported the sensitivity as 100% (14). In the other studies, sensitivity ranged between 70% and 100% (16,17).

There were few studies that compared SLNB and PET/CT. In 100 PET/CT with negative axillary involvement; Zornosa et al. reported 17 positive axillary metastasis with SLNB (sensitivity

84%) (18). In our study, as the axillary SUVmax value in PET/CT increased, so did the possibility of axillary sentinel lymph node metastasis. The sensitivity was calculated as 80.95% and positive predictive value as 97.1%.

Greco et al. suggested that the sensitivity of PET/CT for detection of axillary lymph node metastasis was 98% if tumor size was 21-50 mm, and 84% in tumors with a diameter of 10 mm or less. On the other hand, negative predictive and positive predictive values were respectively 93.5-97.5% and 54.5%-94.1% (15). In present study, we did not observe any significant relationship between the diameter of the pathological mass and the axillary SUVmax value.

As known, invasive lobular cancers have significantly lower FDG uptake and higher false negativity than those of invasive ductal cancers. This was reported to be associated with low GLUT1 expression and low proliferation rate of this type cancer cells (19). On the other hand, invasive ductal carcinoma has higher SUVmax values than other types of breast cancers (20). In our study, axillary SUVmax values were compared for different types of breast cancer and we suggested that the difference of axillary SUVmax values due to tumor types was statistically insignificant.

Yoon HJ et al. reported that SUVmax values for ER and PR negative breast cancer were approximately 50% higher than the positive cases in their study where they included 43 patients with large or locally advanced invasive ductal cancer (21). Other studies have also shown higher SUVmax values for ER and PR negative breast cancers (22,23). We also determined that ER positivity did not affect the axillary SUVmax value, but there was an inversely significant relationship between the PR receptor value and axillary SUVmax value, consistent with previous studies.

Groheux et al. found that SUVmax values of the primary lesion for 132 preoperative breast cancer patients were higher in patients without ER, PR negative and *Cerb-B2* expression. *Cerb-B2* positivity indicates tumor aggressiveness and is a sign of hormone and chemotherapy resistance and poor prognosis (24). A positive relationship between *Cerb-B2* positivity and F-FDG uptake was reported (25,26), but some of publications did not support this significant relationship (23). We also demonstrated that *Cerb-B2* positivity did not affect the axillary SUVmax value.

Ekmekçioğlu et al. compared prognostic factors in 140 breast cancer cases, primary tumor F-FDG uptake was determined by histological type, histological grade, pleomorphism, mitosis number, lymphatic invasion, necrosis, estrogen receptor negativity, high Ki-67 level, axillary lymph node involvement that it has a high correlation (27). In our study, the relationship between axillary SUVmax value and histological grade of

primary tumor was statistically significant. However, there was no relationship between lymphovascular invasion, and Ki67 level with axillary SUVmax. As it is known, the usage of nomograms is easy and helpful in many conditions. Any study comparing nomogram and axillary SUVmax values was not found in the literature. In this study, when the MSKCC nomogram and axillary SUVmax value were compared statistically, there was not any significant relationship between them.

CONCLUSION

Today, use of PET/CT in the axillary evaluation of breast cancer is among the promising non-invasive methods. Its usability can be evaluated in new nomograms to be developed in the future. Its reliability may increase with new and sophisticated development in the future due to advances in techniques. Unfortunately, its reliability alone is currently debatable.

Ethics Committee Approval: This study was approved by the Kocaeli University Noninvasive Clinical Research Ethics Committee (Decision no: GOKA-EK 2016, Date: 30.11.2016).

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Author Contributions: Concept - GP, AG; Design - GP; Supervision - NZC; Data Collection and/or Processing - GP, SAG; Analysis and/or Interpretation - GP, SAG; Literature Search - GP, AG; Writing Manuscript - GP; Critical Reviews - TŞ, NZC.

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ORİJİNAL ÇALIŞMA-ÖZET

Türk J Surg 2023; 39 (4): 293-299

Meme kanserinin aksiller metastazının belirlenmesinde pozitron emisyon tomografisinin kullanılabilirliği

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ÖZET

Giriş ve Amaç: Aksiller lenf nodlarının tutulumu meme kanseri evrelemede anahtar rol oynar. Pozitron emisyon tomografisi, aksiller lenf nodu metastazını saptamak için umut verici bir yöntemdir. Ek olarak, aksiller lenf nodlarının durumunu tahmin etmek için nomogramlar kullanılır. Bu çalışmada pozitron emisyon tomografisinin aksiller metastaz belirlemedeki rolü ve nomogram ile ilişkisi değerlendirildi.

Gereç ve Yöntem: Hastaların preoperatif dönemde aksiller maksimum standart uptake (SUVmax) değerleri, peroperatif ve postoperatif spesimenlerdeki özellikler ve Memorial Sloan Kettering Cancer Center nomogram verileri değerlendirildi.

Bulgular: Pozitron emisyon tomografisi ile preoperatif dönemde saptanan aksiller SUVmax arttıkça lenf nodu tutulumu olasılığı da arttı. Aksiller SUVmax değeri Memorial Sloan Kettering Cancer Center nomogram verileri ile karşılaştırıldı ancak korelasyon bulunamadı. Yaş, lenf nodu sayısı, histopatoloji sonuçları, kütle çapı, lenfovasküler invazyon ve/veya perinöral invazyon varlığı veya yokluğu, tümör tipi, östrojen reseptör durumu, Ki67 ve Cerb2 durumları korele değildi. Bununla birlikte, aksiller SUVmax, tümörün derecesi ve progesteron reseptör durumu ile ters orantılıydı.

Sonuç: Meme kanseri hastalarında aksiller lenf nodlarının pozitron emisyon tomografisinden elde edilen sonuçlar, SUVmax'ın kanser derecesi ve progesteron reseptör durumu ile sadece ters orantılı olduğunu ve tümör değerlendirmesi için kabul edilen diğer parametrelerle korele olmadığını gösterdi. Bu nedenle, şu anda tümör özelliklerinin doğru bir şekilde değerlendirilmesi için aksiller SUVmax'ın tek başına kullanımı için yeterli güvenilirlik yoktur.

Anahtar Kelimeler: Aksiller metastaz, meme kanseri, pozitron emisyon tomografisi

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A comparative analytical study on outcome of secondary peritonitis using Mannheim's peritonitis index in geographically diverse Indian patients

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ABSTRACT

Objective: Secondary peritonitis is caused by infection of the peritoneal cavity due to perforation of the alimentary tract. Mannheim's peritonitis index (MPI) is a prognostic scoring system that predicts outcomes in peritonitis. Increasing MPI scores correlate with poor outcomes and mortality. The objective of this study is to evaluate the effectiveness of MPI-based prognosis and its impact on Indian patients with secondary peritonitis.

Material and Methods: For understanding the effectiveness of the MPI scoring system, a cross-sectional data analysis of published studies on secondary peritonitis from 10 geographical locations in India was performed. The 10-site study results were compared with unpublished in-house study data for individual MPI parameters to analyze any variations of MPI score-based predictions across a diverse Indian population. Patients were divided into risk groups on the basis of MPI scores: <21 mild, MPI= 21-29 moderate, MPI> 29 severe risk.

Results: We observed a significant correlation between mortality with age and gender as reported worldwide. Site of perforations were prevalent in the upper alimentary tract with the majority being gastro-duodenal for the Indian population as opposed to distal parts in the western population. Higher lethality in India is often associated with evolution time, organ failure, and sepsis due to delayed presentation and poor management.

Conclusion: MPI scoring is effective in predicting risk across geographically diverse Indian populations. The sensitivity and specificity of MPI scores are more reliable and a score >29 specifically recommends aggressive resuscitation & monitoring of patients, initiation of broad-spectrum antibiotics, and intensive care support to reduce mortality and morbidity.

Keywords: Secondary peritonitis, Mannheim's peritonitis index, infection, mortality

INTRODUCTION

Peritonitis is the inflammation of the peritoneum caused by the damage of intestinal lining and associated infection (1,2). Clinically, peritonitis is classified as primary, secondary, or tertiary peritonitis (1,3). Primary peritonitis is rare and often caused by extra peritoneal bacterial/foreign bodies' translocation and hematogenous dissemination (3,4). Secondary peritonitis is the most common form of peritonitis caused by spontaneous perforation of the gastrointestinal tract, intestinal ischemia or iatrogenic exposure resulting in direct contact with a peritoneal contaminant (1,2,5). Since abdominal integrity is compromised, secondary peritonitis is often associated with poly-microbial infection (5,6). Secondary peritonitis accounts for 1% of emergency admissions and is the second leading cause of sepsis resulting in a global mortality rate of 6% (2). Secondary peritonitis is a very common surgical emergency in India with a mortality rate of ~9% to 16% as per recent studies across India (7-9). Despite improved understanding of pathophysiology, advanced surgical techniques and antibiotic availability, mortality due to secondary peritonitis is higher in Indian population in comparison to western world (10,11). Consequently, identifying better scoring systems for early evaluation and categorization of the patients with secondary peritonitis is required for better resuscitative measures.

Here, we used Mannheim's peritonitis index (MPI), which had been developed and validated by Wacha et al. and others, for scoring the severity and outcomes of the study performed with 110 subjects of secondary peritonitis from the northeastern

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region of India (12-14). MPI based system is often advantageous over other scoring systems for better management of the disease, patient segregation, prognostic reliability and specificity (15,16). Additionally, we performed a comparative analysis of studies with secondary peritonitis throughout India using MPI based scoring parameters and provided a bird's eye view regarding risk factors of the disease (17-26). The purpose of the study was to understand the variability in outcome due to MPI score parameters across Indian patients with diverse background and predict the overall effectiveness of the MPI scoring system used for accessing risk groups in secondary peritonitis. We observed significant increase in morbidity and mortality in patients with increasing MPI scores. There is less variability among individual parameter score and outcomes in terms of mortality. Together, our study convenes an Indian subcontinent specific risk evaluation of secondary peritonitis and supports the usage of the MPI scoring system to predict patient outcomes.

MATERIAL and METHODS

Study Details

The Institute study protocol was reviewed and approved by REB (research ethics board). All methods were performed in accordance with the relevant guidelines and regulations. Informed consent was obtained by all subjects. The study was conducted in the department of surgery in a regional institute of the northeastern part of India as a cross sectional study for two years (2018-2020). Patients with a diagnosis of secondary peritonitis were placed under inclusion criteria. Exclusion criteria included patients with primary peritonitis, tertiary peritonitis, patients who had not undergone surgery, patients with post-operative anastomotic dehiscence or leak, peritonitis due to trauma to abdomen, patients with acute appendicitis (without perforation) and patients unwilling to take part in the study. One hundred and ten patients enrolled underwent exploratory laparotomy within the study period. Independent study variables for MPI scoring system included: age in

completed years, sex, malignancy (present/absent), organ failure (present/absent), evolution time (>24 hours/<24 hours), extension of peritonitis (localized/diffuse), origin of sepsis (non-colonic/colonic), character of exudates (clear/faecal/purulent) as described previously (12-14). We also curated available published data of MPI based studies from India for our comparative analysis (17-26).

Parameters for MPI Evaluation

A pre-designed, pre-tested proforma which consisted of particulars of the patients, symptomatology, general physical examination, abdominal findings & other systematic examinations, laboratory investigations, intra-operative findings & post-operative outcomes were taken into account for MPI scoring (Table 1). Criteria published by Deitch EA were utilized for organ failures. Renal failure assessment was determined as serum creatinine >177 mmol/L OR serum urea >16.7 mmol/L OR oliguria (urine output <20 mL/hr), pCO_2 > 50 mm Hg OR pO_2 < 50 mm Hg for respiratory failure, >24 hours of paralysis OR mechanical ileus for intestinal obstruction and systolic BP < 90 mmHg OR reduction > 40 mm Hg from baseline for shock. Malignancy was categorized as known malignancy or gross or histo-pathological features of malignancy including perforation of the malignant gastric ulcer, suspicious perforation of a colonic mass and obstruction due to distal malignant growth, perforation of proximal bowel. For evolution time criteria was set for <24 hours/>24 hours between onset and surgery. Source of perforation was demarcated as non-colonic/colonic based on exploratory laparotomy. Individual scores of each parameter of each patient were added to calculate MPI. Divisions of the patients into three categories were done as follows: MPI < 21: mild risk group, MPI = 21-29: moderate risk group, MPI > 29: severe risk group.

Biochemical and Radiological Study

Routine haematological and urine examinations were performed for secondary peritonitis patients. Diagnoses of secondary peritonitis were confirmed routinely by erect

Table 1. Representing study variables and adverse factors used for scoring Mannheim's peritonitis index for secondary peritonitis studies

Study variable	Adverse factors	Score	Favorable factors	Score
Age	>50 years	5	<50 years	0
Sex	Female	5	Male	0
Organ failure	Present	7	Absent	0
Evolution time	>24 hours	4	<24 hours	0
Malignancy	Present	4	Absent	0
Source of perforation	Non-colonic	4	Colonic	0
Extension of peritonitis	Diffuse	6	Localized	0
Character of exudate	Purulent fecal	6 12	Clear	0

radiograph of the abdomen. In selected cases, ultrasonography (USG) and axial computerised tomography (CT) scan of the whole abdomen were done.

Surgery and Follow Up

Initial resuscitative measures included keeping the patient nil per orally (NPO), intravenous fluid, antibiotics and analgesics, correction of electrolyte imbalance (if any), abdominal decompression by putting nasogastric tube and Foley's catheterisation. Patients who were fit for surgery were managed by exploratory laparotomy for peritoneal toileting and repair of perforation. Intra-operative finding of perforation in a patient with peritonitis were taken as gold standard for secondary peritonitis. Post-operatively, all of the patients were followed up until their discharge or death.

Statistical Analysis and Reproducibility

Collected data were tabulated using Microsoft Excel and analysed accordingly using Graphpad Prism version 8.3.02 (GraphPad Software, CA, United States). For comparative analysis, available data were treated as non-parametric for adverse factors. Independent t-test using Mann-Whitney method was used for statistical significance. One way-ANOVA using Kruskal-Wallis method for multiple groups was used for statistical significance. Chi-square test and Fisher's exact test were performed for correlation among MPI categories for statistical significance. For in-house study data, $n = 110$ patients. ROC curve was plotted using MedCalc® Statistical Software version 20.112 (MedCalc Software Ltd, Ostend, Belgium; <https://www.medcalc.org>; 2022). DeLong et al. method and binomial exact with 95% confidence interval regarding AUC were performed for statistical significance, and $p < 0.05$ was considered as statistically significant.

RESULTS

Occurrence and Associated Mortality Due to Secondary Peritonitis in India

In order to evaluate secondary peritonitis for a group of 110 patients from the study institute, we used Mannheim's peritonitis index (MPI) scoring system. We utilized an 8-parameter-based scale deployed in all studies for assessing MPI scores as described in study detail. In order to understand the prevalence and pattern of secondary peritonitis across India, we compared our in-house study with 10 other published studies that had used MPI scoring system from various states of India (17-26). Studies from different geographical locations were selected to have an idea about the epidemiological diversity of secondary peritonitis across India (Figures 1A, 1B). As we further subcategorized patients as per sex, we observed a preponderance of male patients compared to female that were significantly correlated in all studies (Figure 1C). We observed a higher lethality rate due to secondary peritonitis in

the Indian population up to ~32% in comparison to current lethality rate of 6% worldwide (Figure 1D) (2).

Correlation of Mortality with Factors Contributing to MPI Score Among Various Studies

We accessed the MPI based studies from 11 sites as stated above and categorized the outcome (percentage of death) against individual factors affecting MPI scores as per data availability. The parameter for age (<50 and >50 years), indicated significantly higher incidence of peritonitis in age groups lower than 50 (Figure 2A). As reported by others, we also observed an increased death rate (11-33%) in patients group with age >50 years (Figure 2B) (27-29). Interestingly, we found significant association between increased duration of hospital stay with age >50 years group in the in-house institutional study (Figure 2C).

We found a higher male to female ratio in patients with secondary peritonitis (Figure 2D). Provided sex to be an adverse factor, we checked for mortality. Among the available datasets, with an exception for Pune and Kerala (South Western India), there was increase mortality (9-56%) in female patients which is also reflected in the in-house study (Figure 2E).

Source of perforation is an important parameter which dictates the outcome of secondary peritonitis. We interrogated the data from seven studies for site of perforations which is directly related to the severity of peritonitis. We found that maximum incidents of peritonitis occurred at the sites of gastroduodenal (34-80%), ileal (6-53%) and appendicular (4-47%) region while lesser incident occur at jejunal (4-7%), colonic (2-10%) and other non-alimentary sites (1-10%) (Figure 2F). Among the available datasets, we were able to check the mortality of patients with respect to perforation site. We found that gastroduodenal perforations had lesser incident of deaths (~10%) while ileal (13-28%) and colonic (16-50%) perforations had higher incidence of death (Figure 2G). Albeit, we observed a significant correlation of death associated with ileal and gastroduodenal perforations. We checked the extension of peritonitis and character of exudate parameters and found higher mortality with diffused form (13-36%) of peritonitis (Figure 2H). Both purulent (4-60%) and feculent (36-100%) natured exudates showed higher death compared to clear exudates (0-12%) in the patients (Figure 2I). Presence of malignancy could not be considered as an independent parameter. Given the lower number of patients with malignancy, we observed variability in death rates (0-100%) of the patients with malignancy and also higher deaths in patients without malignancy (Figure 2J). The parameters for presence of organ failure and high evolution time (>24 hr) contributed significantly towards higher mortality rates. Mortality rate for organ failure was 22-75% and evolution time was 18-32% respectively among the available study locations (Figure 2K and 2L).

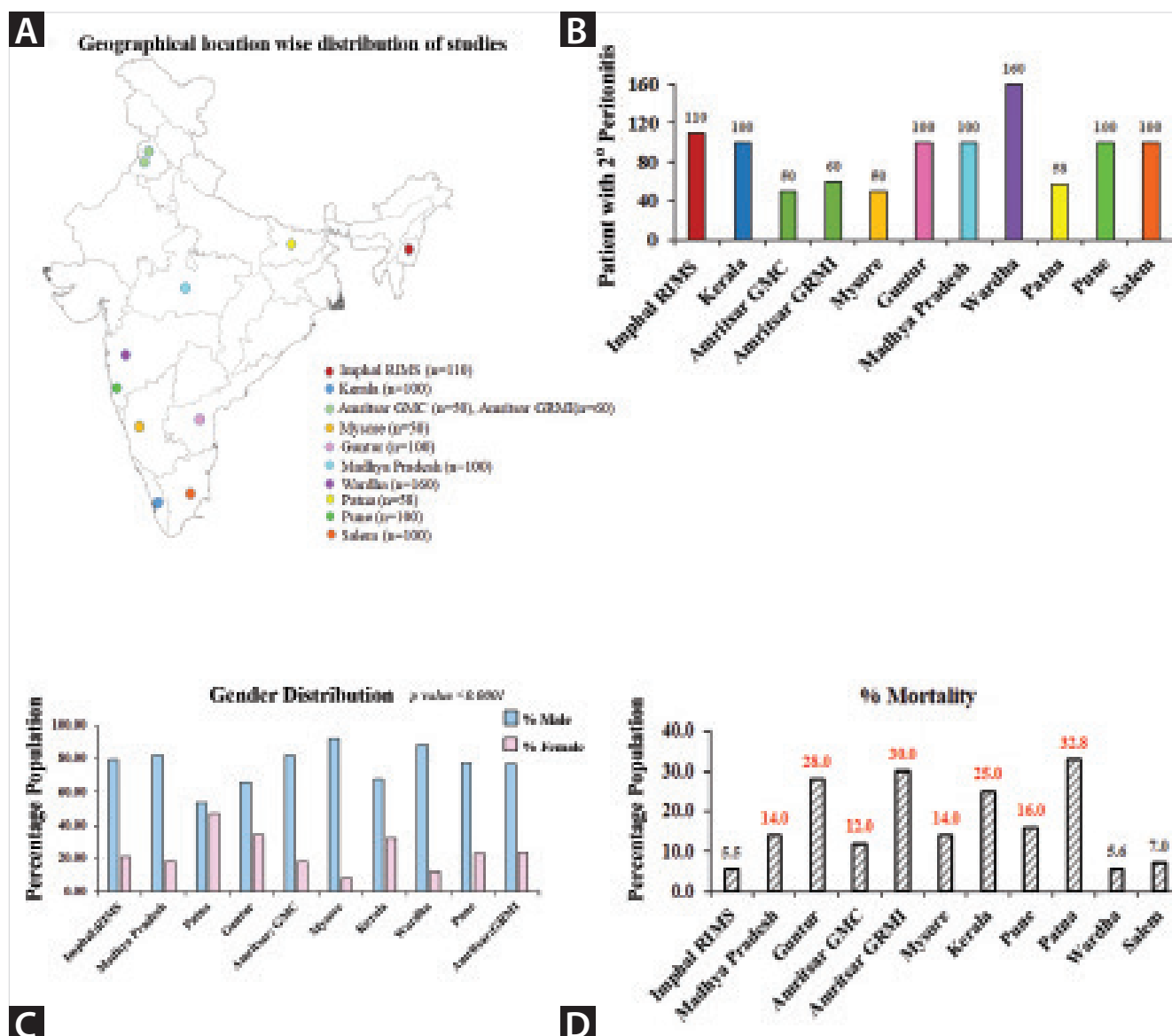


Figure 1. A. Geographical, location wise distribution of the studies on secondary peritonitis from India used in the study. B. Graphical representation of the number of patients in case studies of secondary peritonitis used in the study. C. Study wise distribution of the percentage population of male and female subjects. Mann-Whitney test was performed for statistical significance where ****p< 0.0001. D. Percentage mortality was calculated for all available data sets.

Identifying Key Factors Affecting MPI Scores, Treatment Procedures and Outcomes of In-House Study from North-East India

For surgical procedures, Graham's patch repair, primary repair of perforations, appendectomy, resection and anastomosis, gastrojejunostomy and right hemi-colectomy were performed (Figure 3A). This is relatable with the site of perforation statistics reported earlier in the study. Appropriate MPI scoring system of <21 (mild risk), 21-29 (moderate risk) and >29 (high risk) was adapted for in-house study patients (30,31) (Figure 3B). In the in-house study, the mean MPI value was 22.07, minimum being 10 and maximum being 43. We observed significant correlation

for each study variables except the source of perforation (Figure 3C). Interestingly, we observed a significant positive correlation between the severity of complications and higher MPI scores for patients (Figure 3D). We found an increased mortality rate (21-29 MPI score 5.5%, >29 MPI score 25%) with higher MPI score associated with major complications like faecal fistula, chest infections etc. (Figure 3E). In order to gauge the sensitivity, specificity and best cut-off for MPI score, we used receiver operating characteristic (ROC) curves against mortality and morbidity (complications) (Figures 2F, 2G). The area under the curve (AUC) with respect to mortality and morbidity were 0.911 and 0.749 respectively; indicating MPI an effective scoring system.

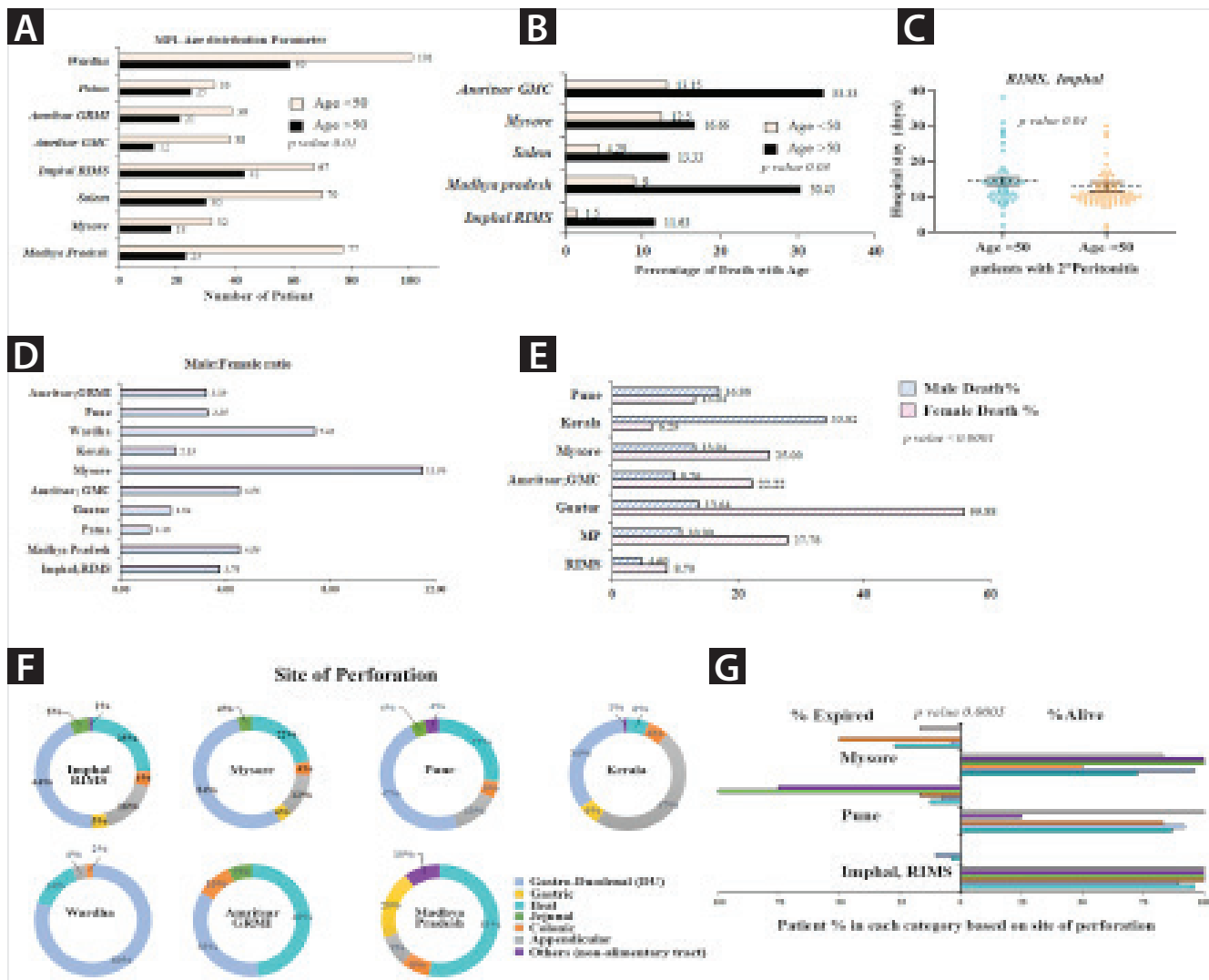


Figure 2. A. Graphical representation of age distribution under various studies. Mann-Whitney test was performed for statistical significance where $p=0.01$. B. Percentage mortality was plotted for indicated groups (>50 years and <50 years). Mann-Whitney test was performed for statistical significance, where $p=0.03$. C. Hospital stay for patients in the number of days were plotted for indicated groups from the in-house study. Mann-Whitney test was performed for statistical significance where $p=0.04$. D. Male and female percentage population was plotted as a ratio (male:female) for indicated studies. E. Death percentage was plotted for indicated groups male and female). Chi-square test for trend was performed for statistical significance, where $p<0.0001$. F. Representation of the indicated perforation sites due to the incidence of secondary peritonitis from indicated studies. G. Patient population mortality based on sites of perforation were plotted as indicated for multiple groups. Kruskal-Wallis test was performed for statistical significance, where $***p=0.0005$.

DISCUSSION

Although MPI scoring system was deemed better or similar to other scoring systems like qSOFA (quick sequential organ failure assessment), APACHE II (acute physiological assessment and chronic health evaluation), and etc. while predicting mortality and morbidity in secondary peritonitis, subsequent sepsis related complications do not reflect well to these scoring systems (26,29,32-35). Since the APACHE II and SAPS scoring system measures permanent biochemical changes and organ

insufficiency for predicting mortality and morbidity, it becomes unreliable to patients developing septic shock post operatively within 24 hours (36). Biochemical parameters like IL-6, C-reactive protein and caspase three levels can often provide leverage for surgical decisions and should be considered alongside the scoring systems (37). We followed the meta data analysis study of Billing et al. for our comparative analysis (30). In our assessment of MPI based studies of secondary peritonitis in Indian population we found some interesting trends and outcomes.

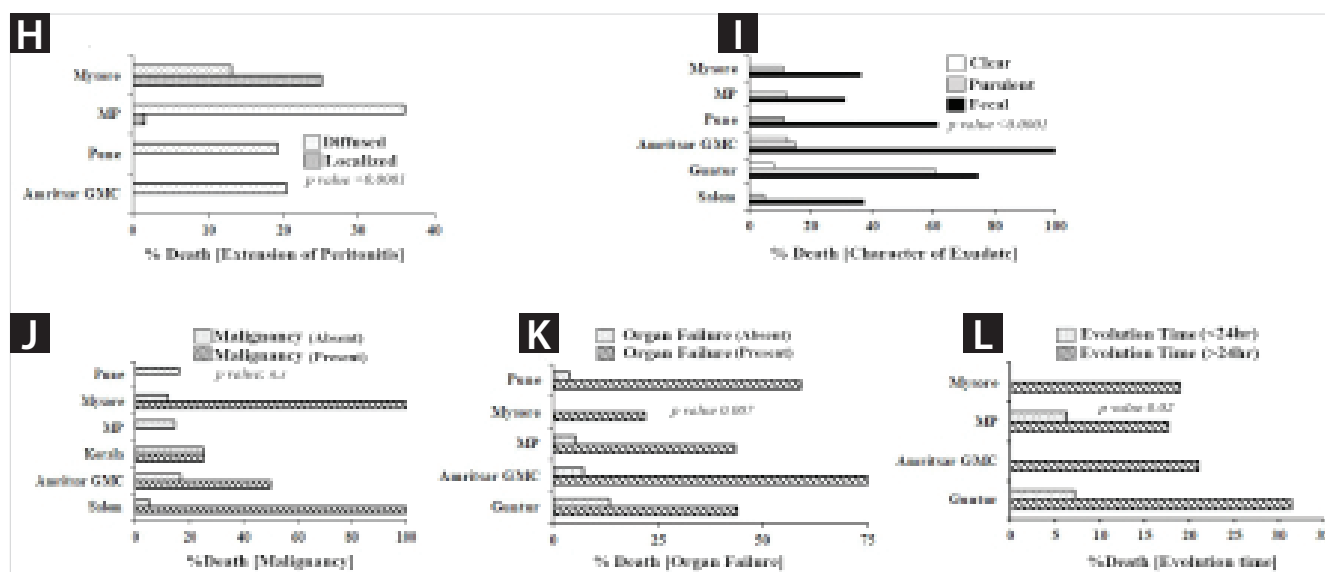


Figure 2 (continue). H. Mortality due to extension of peritonitis as per indicated groups. Chi-square test for trend was performed for statistical significance, where $*p < 0.0001$. I. Mortality in patient based on character of exudates were plotted as indicated for multiple groups. Kruskal-Wallis test was performed for statistical significance, where $****p < 0.0001$. J. Mortality in patients based on malignancy (present or absent) were plotted for indicated studies. Mann-Whitney test was performed for statistical significance, where n.s stands for non-significant. K. Patient mortality based on organ failure (present or absent) were plotted as indicated. Mann-Whitney test was performed for statistical significance, where $*p = 0.007$. L. Patient mortality based on evolution time (>24 hours or <24 hours) was plotted as indicated. Mann-Whitney test was performed for statistical significance, where $*p = 0.02$.

For example, we observed a higher hospital admission for peritonitis patients (~1.5-2 folds) with age <50 years for all the studies. However, the trend in mortality showed an increased death rate (~11-33%) among various studies for patients with age >50 years as observed by others (28,29). Similarly, we observed a biased sex ratio with >~2-fold higher admission for male patients. Opposing, the death rates were higher for females (~2 to 5 folds) as compared to males. The results indicates that MPI scoring system is superior in predicting outcomes even under a biased inclusion of patients and showed similar trends worldwide.

For the site of perforations within the alimentary canal, we found most of the perforations to be of gastroduodenal (40-80%) and ileal (6-48%) origin. We anticipate that infection with helicobacter, acid peptic disorder in the gastroduodenal region while typhoid infections, tuberculosis and trauma in the small bowel (ileal) results in the initiation of the disease (38-40). Given intestinal tuberculosis and typhoid enteritis are common in India, we anticipated a high number of perforations in the upper parts of the alimentary canal as opposed to distal parts in European and North American population (40-42). Appendicular perforations were also common in all studies (5-40%). Interestingly, in the in-house data, we observed more female patients (11 out of 18) with appendicular perforations in comparison to males. Considering the site of the upper alimentary tract, death rates varied from ~10-28%.

Factors like diffused peritonitis and faecal nature of exudates correlated significantly with increased death rates. However, we did not find association of malignancy with death in many studies. We found an obvious association of increased mortality with organ failure and evolution time of the disease. Delayed admission of patients results in sepsis and eventual organ failures in cases of peritonitis (3,5). Unfortunately, even post-surgery, lethality occurs due to septicaemia, disease acuity and organ failure (43).

For the in-house study data, we categorized the patient MPI score as <21 (low), 21-29 (moderate) and >29 (high). We observed a similarity in patient density under MPI categories in various states indicating a trend of low number of patient (<30%) in the category >29. This is relevant as mostly younger generations suffer from secondary peritonitis in India. We observed significant correlation of MPI categories with adverse factors that affect the MPI scores except the site of perforation indicating its effectiveness over our study. Owing to more prevalent non-colonic perforation and lower colonic perforations, it was difficult to conclude any association for the site of perforation. We found more complications like wound infections, faecal fistula and pulmonary complications in patients having >29 MPI score which correlated with increasing mortality in the same group. Finally, to estimate the performance regarding true predictability of MPI scoring system on our in-house data, ROC curves regarding mortality and morbidity were used.

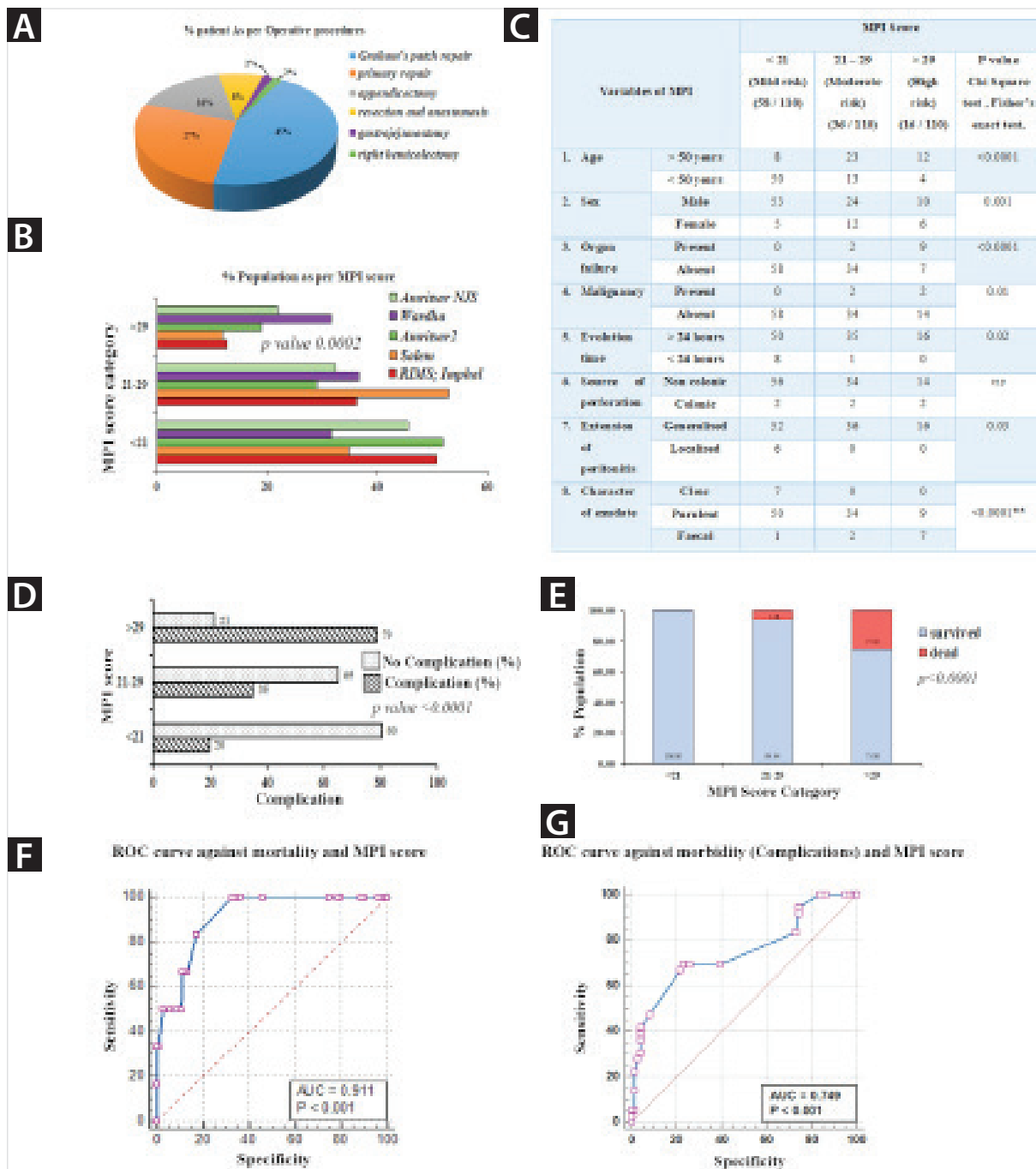


Figure 3. **A.** Patient percentage under various operative procedure on patients with secondary peritonitis from in-house study. **B.** Patient percentage under various MPI score categories were plotted. Chi-square test for trend was performed for statistical significance between categories; where *** $p = 0.0002$. **C.** Table showing patient numbers belonging to indicated categories under MPI score for in-house study. Chi-square test for trend was performed for statistical significance between categories. **Fisher's exact test was performed by combining two groups where Chi-square assumptions for minimal expected value failed. n.s is non-significant. **D.** Percentage patient with complication was plotted against MPI score categories. Chi-square test was performed for statistical significance, where **** $p < 0.0001$. **E.** Percentage mortality (dead and survived) was plotted against MPI categories. Chi-square test was performed for statistical significance, where **** $p < 0.0001$. **F.** ROC curve was plotted for MPI score categories against the number of mortality using Medcalc statistical software. DeLong et al method and binomial exact with 95% confidence interval regarding AUC was performed for statistical significance, where $p < 0.001$. **G.** ROC curve was plotted for MPI score categories against morbidity (complications) using Medcalc statistical software. DeLong et al. method and binomial exact with 95% confidence interval regarding AUC was performed for statistical significance, where $p < 0.001$.

We found significant AUC providing distinction and specificity of prediction between various MPI scores. Surprisingly, mortality rates of in-house study was low (5.5%) as compared to other states of India. Given the overall mortality for secondary peritonitis and associated complications in the Asian population, studies range from ~9-20% in comparison to Western population (~25-40%) which might indicate a genetic and environmental influence (28,29,31). Other groups had reported higher mortality in Indian patients with secondary peritonitis (44). However, the burden of infectious diseases like typhoid, tuberculosis alongside poor patient management should be taken into account while estimating mortality and morbidity in Indian patients. Overall, our study suggests MPI based scoring system is efficient in predicting outcomes and categorizing patients for better management and care.

CONCLUSION

In spite of improved diagnostic modalities and treatment regime, secondary peritonitis and subsequent sepsis-related mortality accounts for ~16 to 34% death in patients worldwide (2,28,29). Our study results indicate MPI parameters like age and sex follow similar trends with the western population regarding mortality. Whereas other parameters like source/site of perforation in most cases were restricted to the upper alimentary canal owing to higher enteric infections as compared to the distal intestinal parts in western population. Mortality rates were significantly higher (>20%) in studies due to high evolution time (>24 hours), diffused nature of peritonitis with associated infection in exudate cultures and comorbidity parameters like sepsis and organ failure. One of the major reasons for such association might be due to delayed presentation, under-developed health care system, unavailability of critical care and delay in early intervention resulting in development of sepsis, SIRS (systemic inflammatory response syndrome) and MODS (multi organ dysfunction syndrome) (29,32-35). From our MPI based studies, we speculate the risk category of peritonitis patients with MPI score as <21 (low risk), 21-29 (moderate risk) and >29 (high risk) as a better assessment parameter to predict treatment modalities and outcomes. We found that age and sex dependent increment in MPI score is often guided by the inclusion of the patients in the studies. Perforation site has a strong association with the severity of secondary peritonitis and development of complications. Gastroduodenal, ileal, appendicular perforations are the most common among all studies. Complications including sepsis, septicaemia and organ failure are always associated with the evolution time of the disease.

Ethics Committee Approval: Ethics approval [No: A/206/REB-Comm (SP)/RIMS/2015/472/90/2018] was obtained from Research Ethics Board Regional Institute of Medical Sciences Imphal before the commencement of the study. Signed informed consents were taken from all participants. Privacy of the participants was maintained. No organ/sample were procured from any prisoners. Apart from the in-house study data, data for all studies were curated from a published work so requirement of ethics approval for published studies was revoked.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - AH, NS; Design - AG, AD, SG, KSS, NS, AH; Supervision - NS, AH; Fundings; AG, KSS, Materials - AG; Data Collection and/or Processing - AG, KSS, AH, NS; Analysis and/or Interpretation - AG, AD, SG, KSS, NS, AH; Literature Search - NS, AH, AD, SG; Writing Manuscript - AG, NS, AH; Critical Reviews - NS, AH, AD.

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

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ORJİNAL ÇALIŞMA-ÖZET

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Coğrafi olarak farklı Hintli hastalarda Mannheim peritonit indeksi kullanılarak sekonder peritonit sonuçları üzerine karşılaştırmalı analitik bir çalışma

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ÖZET

Giriş ve Amaç: Sekonder peritonit, sindirim kanalının delinmesine bağlı olarak periton boşluğunun enfekte olmasıdır. Mannheim peritonit indeksi (MPI), bir cerrahın peritonitli hastanın sağkalım sonucunu tahmin etmesini sağlayan prognostik bir skorlama sistemidir. Artan MPI skorları kötü prognoz ve mortaliteyle ilişkilidir. Bu çalışmanın amacı Mannheim peritonit indeksinin prognozu tahmin etmede bir araç olarak rolünü ve Hindistan alt popülasyonlarında sekonder peritonitli hastaların yaşamları üzerindeki etkisini değerlendirmektir.

Gereç ve Yöntem: Hindistan'ın kuzeydoğusundaki bölgesel bir hastanede sekonder peritonit tanısıyla hastane verilerine dayanan bir çalışma yürütülmüştür. Karşılaştırmalı analiz için Hindistan'ın coğrafi olarak farklı 10 bölgesinden veriler kullanılmıştır.

Bulgular: Hastaların çoğunda genç (<50 yaş) erkeklerin baskın olduğunu gözlemledik. Perforasyon bölgeleri, çoğunluğu gastroduodenal olmak üzere üst sindirim kanalında sık görülmekteydi. Çalışma merkezindeki ölüm oranı birçok Hint çalışmasına kıyasla düşüktü (%5,5), bu da Kuzeydoğu Hint alt popülasyonunda hastalığın sonucunu belirleyebilecek genetik ve çevresel faktörlere bağlı bir olası farka işaret etmektedir.

Sonuç: Mortalite ve morbiditeyi azaltmak için MPI > 29 olan hastalarda agresif resüsitasyon ve hastaların izlenmesi, geniş spektrumlu antibiyotiklerin başlanması ve yoğun bakım desteği düşünülmelidir.

Anahtar Kelimeler: Sekonder peritonit, Mannheim peritonit indeksi, enfeksiyon, mortalite

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Histopathological evaluation after pancreatic surgery: Comparison of the results of HPB-specific pathologists and non-specific pathologists

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ABSTRACT

Objective: The aim of this study was to compare the results of the evaluation of HPB-specific pathologists and general pathologists on the specimens of patients who underwent pancreaticoduodenectomy by the same surgical team.

Material and Methods: The pathological results of 159 patients who underwent pancreaticoduodenectomy (PD) in the periampullary region was retrospectively examined. Histopathological evaluation results of HPB-specific pathologist (S group) and other pathologists (NS group) were compared. Tumor size (mm), total lymph nodes, metastatic lymph nodes, surgical margin positive/negative (RO/R1/R2 resection) and data of patients who underwent vascular resection were evaluated.

Results: The specimens of 91 patients were examined by a HPB-specific pathologist (S group), and the specimens of 68 patients were examined by non-specific pathologists (NS group). When compared in terms of the average total number of lymph nodes and metastatic lymph nodes dissected, a statistically significant result was observed ($p=0.04$, $p<0.01$ respectively). Additionally, surgical margin positivity (R1) was found to be statistically higher in the S group ($p=0.02$).

Conclusion: In order for the success of HPB surgery to be reflected in the clinic, it is of great importance that the specimens are examined by HPB-specific pathologists.

Keywords: Pathology, pancreaticoduodenectomy, lymph nodes, surgical margin

INTRODUCTION

The periampullary region includes the head of the pancreas, the distal part of the common bile duct, papilla of Vater, and the duodenum. Pancreatoduodenectomy (PD) is the procedure for tumors originating from this region. Surgical resection is the only curative therapy for these tumors. Fewer than 30% of pancreatic cancers are resectable at the time of diagnosis (1). Advances in diagnostic methods, standardization in surgical techniques and development of neoadjuvant/adjuvant therapy have enabled the perioperative mortality rate in pancreatic cancers decrease to 2% and increase five-year survival rates to 27% (2-4). Even patients who receive adjuvant therapy after PD develop recurrence in up to 80% (5).

The difficulty to identify pancreatic cancer at an early stage and the tumor's poor response to chemotherapy and radiation therapy are the main causes of the disease's poor prognosis. One of the most frequently mentioned prognostic markers linked to long-term survival after pancreatic cancer resection is undoubtedly achieving negative surgical margins (R0). Median survival after R0 resection in patients with pancreatic adenocarcinoma is 22 months, decreasing to 6 to 11 months for patients with locally advanced disease and 3 to 6 months for patients with metastatic disease (6,7). In addition to negative surgical margins, survival has been observed to be higher in the patient group with well-differentiation histology, lymph node negativity and tumor size <3 cm (8).

Both HPB-specific and non-specific pathologists can gather and assess the histopathological specimens of malignant pancreatic tissues. The aim of this study was to compare the results of the evaluation of HPB-specific pathologists and general pathologists on the specimens of patients who underwent pancreaticoduodenectomy by the same surgical team.

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MATERIAL and METHODS

Pathological results of 203 patients who underwent pancreaticoduodenectomy (PD) due to a mass in the periampullary region between 2020 and 2023 by the same surgeon (M.K.) were retrospectively examined. Patients with metastatic disease (M1), extra-organ invasion, pathological specimens other than adenocarcinoma, and those who underwent distal pancreatectomy or total pancreatectomy were excluded from the study. A total of 159 patients who underwent PD due to periampullary adenocarcinoma (including subtypes) were included in the study. In all surgeries, frozen sections of the pancreatic neck and distal part of the common bile duct surgical margins were routinely performed. R0 resection is defined as complete resection with microscopically negative margins. R1 resection is defined as a macroscopically complete resection with microscopically positive margins (1 mm or more cancer cells at any surface or margin). R2 resection is defined as macroscopically incomplete resection.

Specimens' margins were assessed:

- Anterior surface
- Medial
- Posterior surface
- Pancreatic neck
- Bile duct
- Duodenal/gastric margin

The circumferential resection margin (CRM) in PD specimens consists of the anterior surface, the medial surface facing the superior mesenteric vein (SMV), the surface flanking the superior mesenteric artery (SMA) and the posterior surface (9).

Tumor size (mm), total lymph nodes, metastatic lymph nodes, surgical margin positive/negative (R0/R1/R2 resection) and data of patients who underwent vascular resection were evaluated. Histopathological evaluation results of HPB-specific pathologist (S group) and other pathologists (NS group) were compared.

Statistical Analysis

All data were transferred to a computer environment, and SPSS 20.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical

analysis. In all statistical analyses, $p < 0.05$ value was accepted statistically significant. Independent-samples t-test was used to compare the means of one variable for two groups of cases, and the paired-samples t-test was used to compare the means of two variables for a single group.

This study was approved by Atılım University Medica International Ankara Hospital Ethics Committee (Decision no: 26 Date: 26.10.2023).

RESULTS

The specimens of 91 patients were examined by an HPB-specific pathologist (S group), and the specimens of 68 patients were examined by non-specific pathologists (NS group). There was no statistically significant difference between both groups in terms of tumor size and location. Information on tumor locations and sizes is shown in Table 1.

When compared in terms of the average total number of lymph nodes dissected, it was reported that an average of 23.8 LNs were dissected in the S group and 16.3 LNs were dissected in the NS group, and a statistically significant result was observed ($p = 0.04$). An average of 3.2 metastatic LNs were observed in the S group and 1.1 metastatic LNs in the NS group, and the result was statistically significant ($p < 0.01$).

No patient underwent R2 resection. R1 resection was observed in 14 patients in the S group and three patients in the NS group. Surgical margin positivity (R1) was found to be statistically significantly higher in the S group ($p = 0.02$). Information on the average total number of lymph nodes, average metastatic lymph nodes and surgical margins of the patients is given in Table 2.

Vascular resection was observed in 17 patients in the S group and 14 patients in the NS group. In the S group, 11 patients underwent portal vein resection, and six patients underwent SMV resection. In the NS group, nine patients underwent portal vein resection, and five patients underwent SMV resection. R1 resection was observed at the vascular resection margin in five patients in the S group and in two patients in the NS group. In the S group, after vascular resection, primary repair was performed in 11 patients, peritoneal patch was performed in four patients, and graft repair was performed in two patients. In the NS group, primary repair was performed in 10 patients

Table 1. Tumor size and location of the patients

	S group (%)	NS group (%)	p
Head of pancreas, uncinata process	58 (63.7%)	44 (64.7%)	>0.05
Distal part of the common bile duct	15 (16.5%)	11 (16.2%)	>0.05
Ampullary	18 (19.8%)	13 (19.1)	>0.05
Average tumor size (mm)	30.7 ± 14.8	26.5 ± 11.4	>0.05
Total number of patients	91	68	

Table 2. Average total number of lymph nodes, average metastatic lymph nodes and surgical margins of the patients

	S group (%)	NS group (%)	p
Average total number of lymph nodes	23.8 ± 7.6	16.3 ± 5.3	p= 0.04
Average metastatic lymph nodes	3.2 ± 3.3	1.1 ± 1.8	p< 0.01
Surgical margins			
R0	77 (84.6%)	65 (95.6%)	p= 0.02
R1	14 (15.4%)	3 (4.4%)	
R2	0 (0%)	0	
Patient number	91	68	

Table 3. Vascular (vein) resection of the patients

	S group	NS group	p
R0	12	8	>0.05
R1	5	2	
Unspecified	0	4	
Patient number	17	14	

after vascular resection, and peritoneal patch repair was performed in four patients. In the S group, four of the five patients with R1 margin as a result of vascular resection underwent primary repair and one patient underwent repair with a peritoneal patch. In the NS group, among the patients with R1 margin as a result of vascular resection, one patient underwent peritoneal patching, and one patient underwent primary repair. Although the patients' specimens were marked postoperatively, no information was given regarding the vascular invasion of four patients in the NS group. When the groups were compared, no statistically significant results were found in patients with R1 margin in terms of vascular resection. Information on patients who underwent vascular resection is given in Table 3.

DISCUSSION

When evaluating periampullary region cancers, the location of the cancer's origin is important in terms of patient management, prognosis, survival, tumor staging and accurate evaluation of cancer data records (10,11). In tumors of the periampullary region, histopathological evaluation is difficult in terms of tumor origin due to large tumor size and anatomical proximity of the structures to each other (11). When tumor size and location were compared, it was seen that there was no statistically significant difference between the two groups. This is because the evaluation of tumor size and tumor localization (in line with the clinical information given to the pathologist) can be easily performed by all pathologists.

There is no evidence that extended lymph node resection in pancreatic cancer surgery influences survival, thus in patients undergoing extended lymphadenectomy, morbidity and

mortality rates have appeared to be higher (1,12). However regional lymphadenectomy and removal of at least 16 lymph nodes are necessary for optimal long-term outcomes (13). In our surgical practice, we do not perform extended lymphadenectomy, but we routinely perform regional lymph node dissection. In our study, it was observed that a sufficient number of lymph node dissections were performed on average in both groups. However, it was observed that more lymph node dissections were counted on average in the S group than in the NS group (S group= 23.8 vs NS group= 16.3, p= 0.04). In addition, in terms of metastatic lymph nodes, it was observed that on average more metastatic lymph nodes were counted in the S group than in the NS group (S group= 3.2 vs NS group= 1.1, p< 0.01). The presence of metastatic lymph nodes is important for pancreatic cancer staging and prognosis. A study by Benassai et al. has revealed that the survival of patients with negative lymph nodes was significantly higher than those with lymph node positivity (8). However, studies have shown that metastatic lymph nodes have a negative effect on survival (14,15). Considering that the patients were operated on by the same surgeon and with the same standard surgical technique, it can be seen that the number of total and metastatic lymph nodes dissected was higher in the S group. These findings suggest that HPB specific pathologists perform a more detailed evaluation of lymph nodes compared to general pathologists.

Numerous factors affect survival in pancreatic cancer patients who undergo pancreatoduodenectomy as part of their treatment course. Achieving negative surgical margins (R0) is one of the most consistently reported prognostic factors associated with long-term survival following resection of pancreatic adenocarcinoma. Resection margin (RM)

involvement is an independent prognostic factor in pancreatic cancer. R1 rates are reported between 16% and 75% in the literature (1,9,16). Although R2 resection is not seen in any patient in our study, the number of patients who underwent R1 resection is statistically significantly higher in the S group than in the NS group (S group= 14 vs NS group= 3, $p= 0.02$). Additionally, 15.4% of R1 resections were performed in the S group and 4.4% in the NS group. Although frozen sections of the pancreatic neck and the distal part of the common bile duct surgical margins are routinely performed in our surgical practice, it was observed that very few R1 resections were performed in the NS group, incompatible with the literature. Pathological evaluation is limited to the SMA or 'uncinate' margin, resulting in low R1 rates at some high-volume pancreatic cancer centers (17). In our study, we found that all surgical margins were examined in all patients in the S group, but no information was given about the medial and posterior parts of the CRM in the NS group. We think that the reason why R1 resection was very low in the NS group was because the CRM was not evaluated well.

In the literature, the risk of positive surgical margins appears to be increased in cases of large tumor size and periampullary region cancers that undergo vascular resection (17,18). When the groups were compared, it was observed that there was no statistically significant difference in terms of surgical margin positivity in patients who underwent vascular resection. It appears that the likelihood of a positive surgical margin in patients who underwent vascular resection is higher than in those who did not undergo vascular resection. From this perspective, it is necessary to prevent positive surgical margins by using patches or grafts, if necessary, in patients with vascular invasion. It should not be forgotten that the important thing is to ensure negativity of surgical margins.

CONCLUSION

The information pathologists provide about the specimen is of vital importance in terms of treatment for postoperative disease and survival. Just as hepatobiliary surgery requires specialization, pancreatic pathology also requires specialization. In order for the success of HPB surgery to be reflected in the clinic, it is of great importance that the specimens are examined by HPB-specific pathologists.

Ethics Committee Approval: This study was approved by Atılım University Medicana International Ankara Hospital Ethics Committee (Decision no: 26 Date: 26.10.2023).

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ORJİNAL ÇALIŞMA-ÖZET

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Pankreas cerrahisi sonrası histopatolojik değerlendirme: HPB'ye özgü patolojiler ile spesifik olmayan patolojilerin sonuçlarının karşılaştırılması

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ÖZET

Giriş ve Amaç: Bu çalışmanın amacı, aynı cerrahi ekip tarafından pankreatikoduodenektomi yapılan hastaların spesmenlerinin HPB-spesifik patolojiler ve genel patolojilerin değerlendirme sonuçlarını karşılaştırmaktır.

Gereç ve Yöntem: Periapüller bölgede pankreatikoduodenektomi (PD) uygulanan 159 hastanın patoloji sonuçları retrospektif olarak incelendi. HPB-spesifik patolojiler (S grubu) ve diğer patolojilerin (NS grubu) histopatolojik değerlendirme sonuçları karşılaştırıldı. Patoloji spesmenleri değerlendirilerek, tümör boyutu (mm), total lenf nodu, metastatik lenf nodu, cerrahi sınır pozitif/negatifliği (RO/R1/R2 rezeksiyonu) ve vasküler rezeksiyon yapılan hastaların verileri gruplar karşılaştırılarak değerlendirildi.

Bulgular: HPB-spesifik patolojiler (S grubu) tarafından 91 hastanın, non-spesifik grupta (NS grubu) ise 68 hastanın spesmen sonuçları incelendi. Ortalama toplam lenf nodu sayısı ve diseke edilen metastatik lenf nodu sayısı açısından karşılaştırıldığında istatistiksel olarak anlamlı sonuç gözlemlendi (sırasıyla p= 0,04, p< 0,01). Ayrıca cerrahi sınır pozitifliği (R1) S grubunda istatistiksel olarak daha yüksek bulundu (p= 0,02).

Sonuç: HPB ameliyatlarının başarısının kliniğe yansiyabilmesi için patoloji spesmenlerinin HPB-spesifik patolojiler tarafından incelenmesi önem taşımaktadır.

Anahtar Kelimeler: Patoloji, pankreatikoduodenektomi, lenf nodları, cerrahi sınır

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Biliary cysts in adults: Cerrahpaşa experience

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ABSTRACT

Objective: Biliary cysts are biliary duct dilatations, with 20% of the cysts being diagnosed in adulthood. Abdominal pain, jaundice and palpable abdominal mass are defined as the classical triad. However, nausea, vomiting, fever, itching and weight loss are frequent complaints. There are several treatment options depending on the type of the cyst. This study aimed to share our experience with biliary cysts and contribute to the literature on this subject.

Material and Methods: Thirty patients, who received treatment for biliary cyst from January 1981 to December 2018 at our clinic, were studied retrospectively. The patients were analyzed based on age, sex, type of the cyst, diagnosis and treatment methods, post-op follow up and complications.

Results: Twenty-seven of the patients were females, and three were males. The patients were aged between 16 and 76 years, and the median age was 41.9 years. All patients presented with abdominal pain, which was accompanied by cholangitis in nine patients, nausea and vomiting in four patients, dyspepsia in three patients and palpable mass in one patient. According to the Todani classification, biliary cyst findings were consistent with Type I in 23 patients, Type V in three patients, Type IV in two patients, Type II in one patient and Type III in one patient.

Conclusion: Diagnosis and treatment are complex in biliary cysts due to anatomical proximity and variations. Therefore, it would be beneficial to refer them to referral centers. Choice of treatment should be based on the type of the cyst.

Keywords: Biliary cysts, choledochal cysts, Todani, surgical treatment

INTRODUCTION

Biliary tract cysts are surgical issues typically encountered in newborns and children; however, approximately 20% of the cases are diagnosed as late as adulthood. These lesions are usually referred to as choledochal cysts; however, biliary tract cyst is a more suitable term as the cystic dilatation can develop at any part of the biliary tree and it is not specific to the main bile duct (1,2).

Classification system for extrahepatic biliary tract cysts was first proposed by Alonso-Lej, F. in 1959. This classification was revised by Todani in 1977 to include intrahepatic cysts, and the same author updated the system in 2003 based on an anomalous pancreaticobiliary junction (APBJ) case (1,2).

Todani identified five essential biliary cysts, and cystic dilatation of the cystic duct was added in recent years as Type VI classification (3,4).

The incidence rate of biliary cysts is reported to be between 1/100.000 and 1/150.000. The rates are higher at the south and east of the continental Asia (1/1000), and 1/2-2/3 of the reported cases are from Japan. There are around 4000 patients reported up to date. Biliary cysts are more common in females (80%), and they can be seen in women three to eight times more compared to men. Past cases were seen predominantly in children; however, in new cases, the rates in children and adults are remarkably close (1,5,6).

There are different theories on the formation of biliary cysts. The most widely accepted theory is anomalous pancreaticobiliary junction (APBJ). Anomalous pancreaticobiliary junction (Babbitt theory) is seen in 50-80% of the patients with biliary cysts. This is usually seen together with a long common duct facilitating reflux of the pancreatic juice into the biliary tract (5,7). As the ductal junction is outside the duodenum wall and therefore it is devoid of the sphincter of Oddi, it causes reflux of the pancreatic juice into the biliary tree (7).

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Most biliary cyst cases show symptoms and are identified before the age of 10. In 20% of the cases, the complaints do not emerge until adulthood (>16 years). Classical presentation includes the triad of abdominal pain, jaundice and palpable abdominal mass, and it is more frequent in children compared to adults, and most of the patients present only with one or two findings of the triad. Recurrent pain in the epigastric or right hypochondrium region, abdominal tenderness and mild jaundice are the most common onset symptoms (1,5,8).

Cysts are usually suspected during transabdominal US (ultrasound) or CT (computed tomography) imaging of a patient with abdominal pain, jaundice or an abdominal mass. Imaging methods to be utilized for the assessment of biliary cysts are transabdominal US, CT, MRCP (magnetic resonance cholangiopancreatography), ERCP (endoscopic retrograde cholangiopancreatography), EUS (endoscopic ultrasound) and hepatobiliary scintigraphy (HIDA). MRCP has been more commonly preferred in recent years as it is non-invasive (5,8).

The purpose of our study was to draw attention to biliary cysts due to their rare frequency and contribute to the literature on this issue.

MATERIAL and METHODS

Thirty patients who underwent surgery due to biliary tract cysts between January 1981 and December 2018 were included in the study. The data was retrospectively studied using medical records of the patients. The patients were analyzed based on age, sex, type of the cyst, diagnosis and treatment methods, post-op follow up and complications, and the topic was studied in line with the relevant literature.

All quantitative data were expressed as mean \pm standard deviation. Qualitative variables were defined by frequencies (%). This study was approved by the Ethics Committee of İstanbul University Cerrahpaşa, Cerrahpaşa Medical Faculty in 17.06.2020 with number 83045809-60401.02.

RESULTS

Twenty-seven of the patients were females, and three were males. The patients were aged between 16 and 76 years, and median age was 41.9 years. Twenty-one patients were diagnosed with biliary cysts before surgery. The remaining nine patients were hospitalized with different diagnoses including jaundice, choledocholithiasis, hydatid cyst and were diagnosed during the surgery. All patients presented with abdominal pain accompanied by cholangitis in nine patients, nausea and vomiting in four patients, dyspepsia (fever, pain, jaundice) in three patients and painful palpable mass in one patient.

According to the Todani classification, choledochal cysts findings were consistent with Type I in 23 patients, Type V in three patients, Type IV in two patients, Type II in one patient and Type III in one patient. Roux-en-Y hepaticojejunostomy

reconstruction was performed in 16 patients who underwent cholecystectomy + cystectomy due to Type I choledochal cysts, and continuity was ensured in five patients with hepaticoduodenostomy. One patient with Caroli syndrome limited to the left lobe of the liver received left hepatectomy + cholecystectomy + choledochal T-tube drainage. Of the two patients with Type V solitary liver cyst, one received partial cystectomy + cystoraphy + T-tube drainage, and the other patient with localized cyst in segment III ductus and choledoch stones received segment III resection + choledochotomy + T-tube drainage. One of the patients who previously underwent drainage received cystojejunostomy, and four patients received cystoduodenostomy procedures.

US and CT were more commonly used for diagnosis in early patients (11 patients) and recent patients received US followed by a MRCP (20 patients). Pre-op ERCPs were performed for 12 patients for diagnosis and treatment purposes; however, one of the procedures failed. No other preoperative concomitant anatomical anomalies were noted. Two patients who developed post-operative intra-abdominal abscess and collection underwent percutaneous drainage, and two patients with wound site infection were treated with wound dressing.

One patient, who had undergone cholecystectomy + choledocoduodenostomy and developed recurrent cholangitis due to anastomosis stricture in the long-term follow-up, and underwent Roux-en-Y hepaticojejunostomy. One patient who underwent cholecystectomy + cystectomy + Roux-en-Y hepaticojejunostomy in 2004 developed afferent loop syndrome in 2006 and underwent segmental jejunal resection + reanastomosis procedures. One patient who had been operated with cholecystectomy + cystectomy + Roux-en-Y hepaticojejunostomy developed incisional hernia after one year.

Mean hospitalization period was 10.5 days, and mean follow-up period was 8.1 years. No malignancies were observed in the pathological specimens.

Choledochal cyst was discovered in one patient who was taken into surgery for cholelithiasis at another center; the surgery was terminated without any intervention. The second operation was performed in our clinic, and the patient's Type I choledochal cyst was resected successfully.

In another case, a 40-year-old male patient had biliary cyst accompanying gallbladder cancer. Gallbladder cancer (T1-stage according to the TNM classification) was incidentally identified in the cholecystectomy piece; gallbladder bed excision and lymphadenectomy were planned for the patient. A type 1 biliary cyst was diagnosed during the preoperative imaging, and it was resected concurrently. No other malignancies were observed in the pathological examination.

One patient, who was diagnosed with Caroli disease based on the imaging studies due to abdominal pain and cholangitis, had stone of the left intrahepatic biliary tracts and mechanical jaundice. Percutaneous transhepatic catheter (PTC) and biliary drainage was performed pre-operatively, and then the patient received left hepatectomy + cholecystectomy + T-tube drainage. The patient later received percutaneous drainage for post-operative intra-abdominal abscess and was discharged on day 17.

After the introduction of hepatopancreatobiliary surgery in 2000, our clinic abandoned drainage procedures, and performed the resection procedures for all cases, and usually preferred Roux-en-Y hepaticojejunostomy for the reconstruction. Since this study included a large group of patients going back to 1981, some surgical operations that we do not prefer today were also included in the series.

DISCUSSION

The classical presentation of biliary cysts includes the triad of abdominal pain, jaundice and palpable abdominal mass, and it is more frequent in children compared to adults. Most patients usually present with one or two findings of this triad; but nausea, vomiting, fever, itching and weight loss are also among the common complaints (9,10).

The patients may present to the hospital with signs and symptoms of biliary cyst complications such as pancreatitis, cholangitis and obstructive jaundice. Although rare, another presentation is acute rupture of the cyst with subsequent bile peritonitis (5). Nine of our patients presented with cholangitis during diagnosis, seven of which were treated with medical therapy, and the remaining two were operated after biliary drainage with ERCP and PTC for concomitant mechanical icterus.

Advances in the imaging methods have contributed greatly to biliary cyst diagnosis and classification. Cystic lesions are mostly identified by US or CT first. Ultrasound sensitivity differs between 70% and 97%. The best non-invasive imaging method for biliary tract cysts is MRCP. ERCP and PTC give us detailed anatomical information. ERCP can effectively show the relationship between the pancreatic duct and biliary duct. PTC can be preferred when ERCP is inconclusive in intrahepatic and proximal biliary ducts. MRCP was performed for all 20 patients, the records of whom we could access (Figure 1, 2).

Biliary cysts should be differentiated from pancreatic, mesenteric and hepatic cysts (simple cyst, hydatid cyst) which are not connected to the biliary tract. If there is still suspicion after CT and MRCP, hepatobiliary scintigraphy (HIDA) or ERCP can be performed to establish the connection with the biliary tract (5,8).

Biliary cysts can be mistaken for hydatid cyst in endemic regions. This was the issue of our previous study (11). We focused on this issue after we found a solitary intrahepatic cyst



Figure 1. MRCP demonstrating extrahepatic biliary duct dilatation in a Type I cyst.

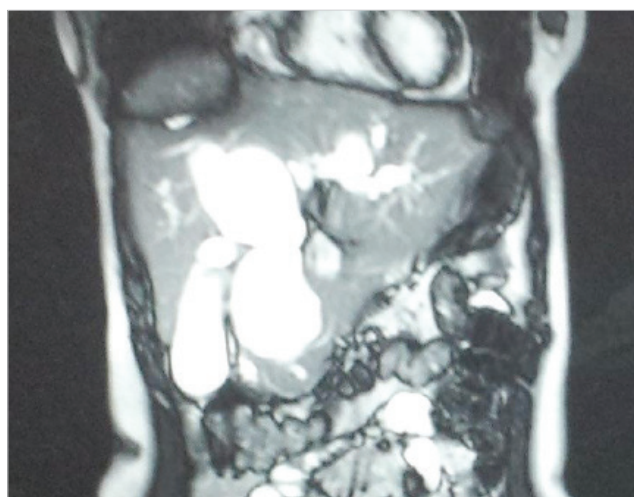


Figure 2. MRCP appearance of extrahepatic and intrahepatic biliary duct dilatation in a Type IVA cyst.

extending outside the surface of the liver in a patient who was taken into operation with hydatid liver cyst diagnosis.

The treatment approach in biliary cysts depends on the type of the cyst. Type I, II or IV cysts are generally eligible for surgical resection. Type I and IV cysts are treated with total excision and Roux-en-Y hepaticojejunostomy or hepaticoduodenostomy (1,8).

Type II cysts are eligible for simple excision. Cholecystectomy may also be used. T-tube is placed if there is a defect on the common bile duct after the excision. Type III cysts are treated with sphincterotomy or endoscopic resection if they are symptomatic. Type V cysts are harder to treat; they require prevention against recurring cholangitis and sepsis. The cysts which are limited to one lobe are treated with right or left hepatectomy, and patients with widespread cysts are transplantation candidates (5,8).

Cases with ascending cholangitis should be treated with antibiotics and bile drainage regardless of the type of the cysts (ERCP or PTC). Of the 21 patients who underwent cystectomy for type I or IV choledochal cysts; 16 received Roux-en-Y hepaticojejunostomy, and hepaticoduodenostomy was preferred for five patients (Figure 3).

Type V cysts may be solitary or multiple. They are referred to as Caroli cysts in most resources (1). This is true for multiple intrahepatic cysts; however, existence of solitary intrahepatic cysts should also be taken into consideration. There were two



Figure 3. Resection of the Type I biliary cyst.

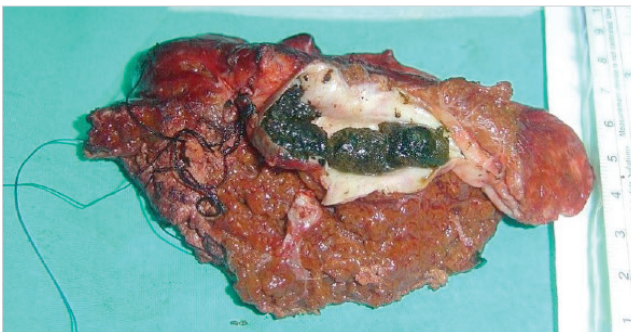


Figure 4. Segment 3 resection of the Type V solitary cyst.

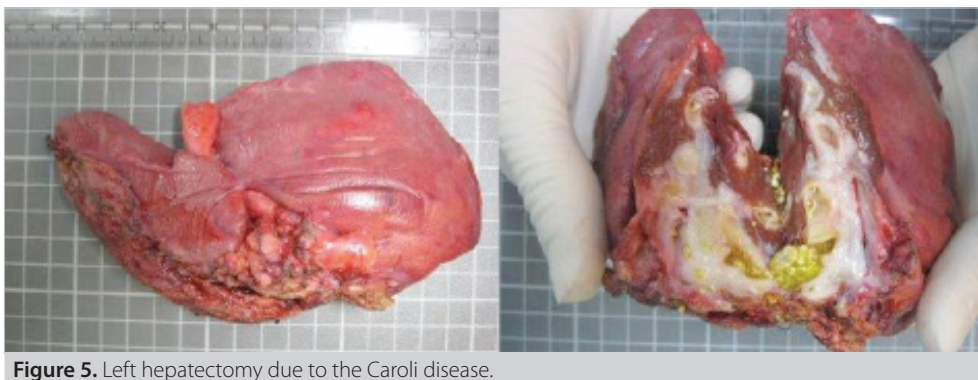


Figure 5. Left hepatectomy due to the Caroli disease.

cases that met this definition in our case series. The treatment method for solitary cysts can be determined based on localization. Of the two cases that met this definition, one received left lateral segmentectomy due to the cystic dilatation of segment III duct and the stones in it (Figure 4). The other case with exophytic growth from the liver surface received partial cystectomy and choledochal T-tube drainage.

In the current literature, it was recommended that in multiple intrahepatic cysts (Caroli), lobectomy should be performed if the disease is limited to one lobe, and if it is widespread, the recommendation is to treat the cholangitis episodes (antibiotics, PTC) first, and then perform liver transplantation (1,5). There was one patient with multiple intrahepatic biliary cysts (Caroli) in our case series. The patient received left hepatectomy as the disease was localized in the left lobe (Figure 5).

In biliary cysts, the whole bile tree is under the risk of cholangiocarcinoma due to APBJ and pancreaticobiliary reflux. Removal of the cyst does not eliminate future risk of cholangiocarcinoma development (7,12,13).

We did not encounter any cholangiocarcinoma cases in our series.

As for the classical knowledge that biliary cysts carry a risk of cholangiocarcinoma development, we would like to underline that biliary cysts are most common in the Far East and Southeast Asia. Sastry et al. have demonstrated that cancer developed in 7.5% of patients with biliary cysts (70.4% cholangiocarcinoma, 23.5% gallbladder cancer and 6.1% other cancers) (12,14).

Tyson and El-Serag have reported that the rate of malignancy transformation in biliary cysts is higher in Asians (18%) versus Americans (6%). It is also known that biliary tract parasites (*Clonorchis sinensis*, *Opisthorchis viverrini*) are commonly seen in those areas (12,13). In these cases, the risk of cholangiocarcinoma development is certainly associated with concurrent parasites (chronic irritation) rather than biliary cysts.

By their nature, biliary cysts may include some anomalies that could be considered as a complexity for surgeons. Concurrent ductal and vascular anomalies increase the difficulty of surgery. They can be more troublesome when they are detected during surgery rather than preoperative tests (15,16).

An interesting revelation of our series was that some of the cases were not diagnosed with choledochal cysts before surgery. If surgeons with limited experience in this area unexpectedly detect choledochal cysts during surgery, they may choose outdated options for treatment of choledochal cysts. Procedures such as choledocoduodenostomy, cystojejunostomy and T-tube drainage that we came across in our series should be considered within that context.

Hepaticoduodenostomy has been associated with higher gastric and biliary cancer due to bile reflux. Furthermore, meta-analyses comparing RHYJ and hepaticoduodenostomy have found more reflux and gastritis in hepaticoduodenostomy. A wide anastomosis facilitating bile flow to the intestine and reducing anastomotic stricture and bile reflux after cyst excision may prevent complications and development of carcinoma in intrahepatic ducts (8,17).

As long as there are no contraindications, choledochal cysts are resected in order to prevent development of malignancies and complications in the future.

CONCLUSION

In conclusion, biliary cyst diagnosis and treatment should be referred to specialized, advanced facilities as complications are frequent in this area due to anatomical proximity and variations. In Type I cysts, which is the most common subgroup, surgical methods of choice are total cyst resection and RY hepaticojunostomy.

Ethics Committee Approval: This study was approved by Cerrahpaşa Faculty of Medicine Deanery Clinical Researches Ethics Committee (Decision no: 83045809-60401.02., Date: 07.07.2020).

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**ORİJİNAL ÇALIŞMA-ÖZET**

Turk J Surg 2023; 39 (4): 315-320

Erişkinde biliyer kistler: Cerrahpaşa deneyimiAli Vedat Durgun¹, Sefa Ergün¹, Başar Can Turgut¹, Osman Şimşek¹, Mehmet Velidedeoglu¹, Kaya Sarıbeyoğlu², Salih Pekmezci¹¹ İstanbul Üniversitesi-Cerrahpaşa Cerrahpaşa Tıp Fakültesi, Genel Cerrahi Anabilim Dalı, İstanbul, Türkiye² Charite Üniversitesi, Genel Cerrahi Anabilim Dalı, Berlin, Almanya**ÖZET**

Giriş ve Amaç: Biliyer kistler, safra kanallarında oluşan genişlemeler olup %20 kadarı erişkin yaşta tanı almaktadır. Biliyer kist olgularında karın ağrısı, sarılık ve palpabl abdominal kütle, klasik triyad olarak tanımlansa da hastaların büyük kısmında, bu triyadın sadece bir ya da iki ögesi saptanır. Bulantı, kusma, ateş, kaşıntı ve kilo kaybı sık görülen şikayetlerdir. Tedavide kistin tipine bağlı olarak farklı seçenekler bulunmaktadır. Çalışmamızda biliyer kist olgularındaki deneyimimizi okuyucuyla paylaşmak ve bu konudaki literatüre katkı sunmak amaçlanmıştır.

Gereç ve Yöntem: Kliniğimizde Ocak 1981 ve Aralık 2018 yılları arasında biliyer kist nedeniyle tedavi uygulanan 30 hasta retrospektif olarak incelendi. Hastalar, yaş, cinsiyet, kist tipi, tanı ve tedavi yöntemlerine, ameliyat sonrası takip ve komplikasyonlarına göre analiz edildi.

Bulgular: Hastaların 27'si kadın, üçü erkekti. Yaş aralığı 16-76 olup median yaş 41,9 idi. Yirmi bir hastaya biliyer kist tanısı ameliyat öncesinde konulmuş olup, diğer dokuz hasta mekanik ikter, koledokolithiyazis, hidatik kist vb. tanılarla yatırılmış ve ameliyat sırasında tanı almışlardır. Hastaların hepsinde karın ağrısı şikayeti mevcut idi, dokuz hastada kolanjit bulguları, dört hastada bulantı, kusma, üç hastada dispepsi, (ateş, ağrı, sarılık) bir hastada ağırlı palpabl kütle eşlik ediyordu. Todani sınıflamasına göre 23 hasta Tip I, üç hasta Tip V, iki hasta Tip IV, bir hasta Tip II, bir hasta Tip III biliyer kist ile uyumlu idi.

Sonuç: Biliyer kistler, tanısı ve tedavisi komplike olgulardır. Anatomik komşuluklar ve varyasyonlar nedeniyle ameliyatlarda zorluk derecesi yüksektir. Bu nedenle referans merkezlerine yönlendirilmelerinde yarar vardır. Tedavi şeklinin seçiminde kistin tipine göre davranmak esastır.

Anahtar Kelimeler: Biliyer kistler, koledokal kistler, Todani, cerrahi tedavi

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Safe postoperative outcomes following early cholecystectomy for acute calculus cholecystitis regardless of symptom onset

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ABSTRACT

Objective: There is growing evidence for reduced post-operative complications, and lower hospital costs associated with early cholecystectomy for acute calculus cholecystitis (AC) compared to delayed surgery. Limited high-quality evidence exists for how early, if at all, should surgeons be operating emergently for AC based on symptom onset.

Material and Methods: Seven hundred seventy-four patients who had cholecystectomy performed by a single surgeon between January 2015-October 2022 were retrospectively reviewed. Five hundred forty-one patients were analysed. Patients were divided into three groups based on symptom onset: Group 1: 0-72 hours (n= 305), Group 2: 72 hrs-1 week (n= 154) and Group 3: >1 week (n= 82).

Results: Median operative time was most prolonged in Group 2 (96.5 minutes), and had the greatest proportion of reconstituting 95% cholecystectomies (n= 22/154, 14.29%) compared to Group 1 (p> 0.05). The conversion to open was between 0.65-1.64% in all groups. The greatest proportion of bile leak occurred in Group 1 (n= 7/305, 2.3%) followed by Group 3 (n= 1/82, 1.22%) (p> 0.05). All were successfully managed with ERCP and biliary stent. Median hospital stay was significantly prolonged in Group 2 (2.3 days) compared to Group 1 (2 days) (p= 0.03). The proportion of 95% cholecystectomies in Group 2 and 3 were not significant compared to Group 1.

Conclusion: Early cholecystectomy for calculus cholecystitis, irrespective of the timing of symptoms appears to have safe postoperative outcomes. Surgeons do not necessarily need to limit early cholecystectomy for within 72 hours of symptom onset.

Keywords: Cholecystitis, early cholecystectomy, timing, postoperative outcomes

INTRODUCTION

Cholelithiasis is a condition affecting up to 6.5-15% of the Western population (1,2). Approximately 1-4% of these patients develop complications, of which 70% are related to acute cholecystitis (3-5). Acute calculus cholecystitis (AC) accounts for a significant proportion of patients admitted to the emergency department in general surgery. Due to the high risk of developing recurrent cholecystitis and other complications such as gallstone pancreatitis and cholangitis, laparoscopic cholecystectomy (LC) is recommended. Current evidence suggests clinical benefits following early LC during the index admission. Compared to delayed LC, early LC is related to reduced long term biliary complications (bile duct injury/bile leaks), wound infections, conversion to open rates, shorter total admission length of stay, and overall lower hospital costs (6-10). In 2013, the Tokyo Guidelines for the management of acute cholecystitis (TG13) recommended that cholecystectomy should be performed within 72 hours after symptom onset (11). LC performed for AC 72 hours after onset of symptoms is believed to increase the risk of perioperative complications due to the distorted anatomy of the Calot's triangle from inflammatory adhesions secondary to prolonged inflammation. However, in drafting the Tokyo Guidelines (TG18), it was noted that it is often difficult to precisely determine the duration since symptom onset (12,13). There is heterogeneity in the literature with regards to the definition of early surgery including cholecystectomy within 24 hours of hospital admission or symptom onset, within 72 hours since patient admission or symptom onset, or within one week since onset of symptoms (12). Thus, it remains difficult to ascertain the optimum timing that will reduce postoperative complications, and the length of stay.

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The TG18 recommends early LC for AC in those patients capable of withstanding surgery, regardless of the onset of symptoms (recommendation 2, level B) (13). Thus, the aim of this study was to evaluate the safety and to compare the postoperative outcomes of early LC for AC based on the duration of symptom onset. The authors hypothesized that early LC is safe, regardless of the duration of symptoms of AC.

MATERIAL and METHODS

Patient Population and Data Collection

This was a retrospective, cohort study on consecutive patients who had early cholecystectomy for acute calculous cholecystitis, between January 2015 to October 2022. All cholecystectomies were performed by the principal investigator, a senior consultant general surgeon. All procedures were initially attempted laparoscopically, then converted to open if deemed necessary. Hospital data was extracted from the Local Health District Medical Records Department. The authors initially collected 775 patients who had LC, of which 234 patients were excluded. Excluded patients were those that had:

- 1) Gallstone pancreatitis (n= 82),
- 2) Elective/delayed cholecystectomy (n= 82),
- 3) Acalculous cholecystitis (including gallbladder polyps) (n= 3),
- 4) Cholangitis (n= 7),
- 5) Absence of cholecystitis on final histopathology (biliary colic) (n= 2),
- 6) Cholecystectomy for gallbladder dyskinesia (n= 1),
- 7) Concurrent cholecystectomy as part of another procedure (n= 5), and
- 8) Those who had incomplete data (n= 52).

After exclusion, 541 patients were included in the study. They were divided into three groups: Group 1 305 patients <72 hours of symptom onset to LC; Group 2 154 patients 72 hours-7 days of symptom onset to LC; Group 3 82 patients >7 days of symptom onset to cholecystectomy.

The decision to operate was made by the principal investigator based on the presence of AC (suspected and definitive diagnosis) defined according to TG18 (13). A suspected diagnosis of AC was considered when local signs of inflammation were present, as well as at least one systemic sign of inflammation. Local signs of inflammation included right upper quadrant pain/tenderness, mass, or positive Murphy's sign. Systemic signs included fever ≥ 38 degrees celsius, elevated white cell count (WCC) $> 11.1 \times 10^9/L$, and/or elevated c reactive protein (CRP) > 3 mg/L. A definitive diagnosis of AC included the above, and imaging findings of calculus AC. Imaging findings of inflammation were not necessarily required for LC if

cholelithiasis had been confirmed previously. AC was confirmed intraoperatively, as well as on final histopathology.

Patient demographics, preoperative, intraoperative, and postoperative variables were reviewed, in detail. Preoperative temperature (normal range= 36-38°C), WCC (normal range= $3.9-11.1 \times 10^9/L$), CRP (normal range= ≤ 3 mg/L), AST (normal range= 10-35 U/L), ALT (normal range= 10-35 U/L), ALP (normal range= 30-110 U/L), GGT (normal range= ≤ 35 U/L), bilirubin (BR) (normal range= ≤ 19 $\mu\text{mol/L}$) were taken at its highest recorded value between admission and LC. Gallbladder wall thickness was tabulated using ultrasound and/or histopathology measurements. Operation time was taken from knife to skin to completion of wound closure. LC (10 mm umbilical Hasson port, 3 x 5 mm right upper quadrant ports) and open cholecystectomy (OC) (right subcostal incision) were performed in a standard fashion, with an attempt at intraoperative cholangiogram (IOC) in all cases. If a filling defect was found during IOC, all patients underwent postoperative endoscopic retrograde cholangio-pancreatography (ERCP). A reconstituting 95% cholecystectomy was consistently performed as the transection of the gallbladder at the gallbladder neck after control of the cystic artery. This technique was chosen when there was dense inflammation, and the risk of bile duct injury was perceived to be high. This involved gentle, careful dissection around the full circumference of the neck, commonly using hydrodissection to improve safety while separating the gallbladder neck from the cystic plate. Following transection, any gallstones in the proximal cystic duct and neck of the gallbladder were extracted. Next, the distal gallbladder neck was further mobilized off the cystic plate using hydrodissection and limited diathermy. This allowed for IOC via the neck of the gallbladder using a ureteric catheter secured using a large ratcheted grasper across the gallbladder neck. Next, a polydioxanone (PDS) endoloop was used to close the distal gallbladder neck, and the excess neck tissue was sent for histopathology as a separate specimen. This achieved an approximately 95% cholecystectomy. If the IOC was unsuccessful, a postoperative magnetic resonance cholangiopancreatography (MRCP) was performed, with subsequent ERCP if there was choledocholithiasis. Bile duct injury was defined as suspected or confirmed injury to the hepatic or common bile duct. Bile leak was defined as any observable bile in the abdominal drain. Clavien-Dindo classification grade ≥ 2 related ≤ 30 -day readmission only included patients who were readmitted within 30 days requiring pharmacological treatment with drugs other than those allowed for Clavien-Dindo classification grade 1, requiring surgical, endoscopic, radiological intervention, intensive care management, or death of patient (14).

Statistical Analysis

Statistical analysis was performed using SPSS 23.0 (SPSS Inc., Chicago, IL, USA) and Microsoft Excel 2019 (Microsoft Corporation, USA). Categorical measurements were summarized as number and percentages. Continuous non-homogeneous parameters were measured using medians and continuous homogenous parameters were calculated using mean and standard deviations. Chi-square test was used for comparing categorical variables. Independent Student's t-test was used to compare patient groups where appropriate, with $p < 0.05$ considered statistically significant.

RESULTS

Median age of the cohort was 44 years. Those who were operated between 3-7 days (Group 2) since symptom onset tended to be older (46 years) than those operated within 72 hours of symptom onset (44 years) (Group 1) ($p = 0.04$). There were more females (66.9%-73.2%) than males (26.8%-33.1%) in all three groups (Table 1).

In terms of preoperative data, those that were operated after one week of symptom onset (Group 3) had a significantly thicker gallbladder wall thickness (5.63 mm) compared to Group 1 (4.96 mm), likely owing to the prolonged inflammation ($p = 0.05$). White cell count (WCC) and c reactive protein (CRP) tended to be similar between all groups. Liver enzymes were all statistically greater in Group 2 than in Group 1. There was a small variance in the mean bilirubin level between all groups (Table 1).

Intraoperatively, Group 2 had the most prolonged median operative time (96.5 minutes) and had the greatest proportion of 95% cholecystectomies ($n = 22/154$, 14.29%). However, these were not statistically significant to Group 1. Interestingly, Group 3 had the shortest operative time of 84.5 minutes, possibly related to reduced inflammation. The conversion rate from LC to OC was 1.3% among all groups. A greater proportion of patients in Group 2 ($n = 15/154$, 9.74%) and 3 (7/82, 8.54%) had suppurative/necrotizing/gangrenous cholecystitis in comparison to Group 1 (14/305, 4.59%) although this was not statistically significant ($p = 0.16$, $p = 0.054$). Bile duct injury occurred only once in Group 1 and Group 3. All were successfully managed with ERCP with biliary stent without complications (Table 1).

Postoperatively, proportion of bile leak was greatest in Group 1 ($n = 7/305$, 2.3%) followed by Group 3 ($n = 1/82$, 1.22%), of which all were successfully managed without complications with ERCP and biliary stent. There were two returns to theatre. The first patient was otherwise well, who returned to theatre within a few hours after an uncomplicated LC. There was bleeding from possibly the cystic artery after dislodged clips. The second patient was elderly with heart failure, atrial fibrillation, on

warfarin who returned to theatre on postoperative day six. There was bleeding from the edge of liver adjacent to the gallbladder stump. Postoperative median length of stay was significantly prolonged in Group 2 (2.3 days) compared to Group 1 (2 days), $p = 0.03$. There were small number ($n = 4$, 0.74%) of Clavien-Dindo classification grade ≥ 2 related ≤ 30 -day readmissions due to gallbladder fossa collection and postoperative pain ($n = 1$), *Clostridium difficile* colitis ($n = 1$), nonspecific colitis ($n = 1$) and choledocholithiasis ($n = 1$). There was unfortunately one death following a laparoscopic 95% cholecystectomy for necrotizing cholecystitis, where a 69-year-old patient had a suspected aspiration pneumonia on postoperative day 14. The patient had seizures and catatonia, and after prolonged admission of reduced responsiveness and hypoxia, was palliated six weeks post operation (Table 1).

Table 2 tabulates all patients who had a 95% cholecystectomy. Compared to all patients analyzed, they were significantly older, a greater proportion was males (47.3% vs 31.2%, $p = 0.006$), had higher preoperative temperature (37.35°C vs 37.1°C, $p = 0.003$), higher preoperative bilirubin (16 $\mu\text{mol/L}$ vs 11 $\mu\text{mol/L}$, $p = 0.003$), prolonged operation time (118 minutes vs 91 minutes, $p < 0.001$), higher conversion to open (8.1% vs 1.3%, $p = 0.0001$), greater proportion of bile leak postoperatively (5.4% vs 1.48%, $p = 0.02$), and prolonged median hospital stay (3 days vs 2 days, $p < 0.001$). There were no deaths, or recurrent biliary colic/cholecystitis in the 95% cholecystectomy patients to date (from seven years ago).

DISCUSSION

There is growing evidence to suggest that early cholecystectomy for AC has statistically significant lower morbidity, shorter hospital stay, and lower hospital costs compared to delayed cholecystectomy (6-10,15). However, there remains ongoing debate with regards to the timing of early LC, partly due to the variability in the definition of early LC, and the perceived increased risk of postoperative complications and conversion rates if early LC is performed beyond 72 hours of symptom onset.

A recent meta-analysis of randomized trials has suggested that early cholecystectomy for AC ≤ 72 hours from symptoms reduces open conversion rates in comparison to cholecystectomy ≤ 7 days from symptoms ($p = 0.044$). In addition, cholecystectomy ≤ 24 hours from admission is the best strategy to reduce total in-hospital stay (12). An ACS-NSQIP review of early cholecystectomy for AC has concluded that cholecystectomy should be performed within two days of hospital admission, which is based on 1.4 times increase in major complications, and 2-times increase in mortality when surgery was delayed to within 3-7 days of hospital admission (16).

Table 1. Patient demographics and perioperative variables between groups 1-3

Characteristic	Total (n= 541)	Group 1: <72 hours of symptom onset (n= 305)	Group 2: 72 hours-7 days since symptom onset (n= 154)	Group 3: >7 days of symptom onset (n= 82)	p-value: Group 2 vs. Group 1; Group 3 vs Group 1
Sex, n (%)					
Male	169 (31.2)	96 (31.5)	51 (33.1)	22 (26.8)	0.72; 0.42
Female	372 (68.8)	209 (68.5)	103 (66.9)	60 (73.2)	
Age, median (range)	44 (14-97)	44 (15-88)	46 (14-97)	43 (17-95)	0.04 ; 0.39
Time of symptom onset to cholecystectomy hours, median (range)	86 (9-672)	46 (9-72)	120 (75-168)	196 (170-672)	<0.01, <0.01
Highest preoperative temperature °C, median (range)	37.1 (35.3-40.2)	37.2 (36-40.2)	37.1 (35.3-39.8)	36.9 (35.4-39)	0.04; 0.003
Gallbladder wall thickness, mean (SD)	5.10 (2.94)	4.96 (2.82)	5.05 (2.76)	5.63 (3.57)	0.38; 0.05
CRP mg/L, median (range)	11 (1-664)	9.5 (1-453)	11.5 (1-357)	12 (1-664)	0.46; 0.14
WCC x10 ⁹ /L, median (range)	10.1 (2.2-66)	10.1 (2.2-27.6)	10.5 (3.8-66)	9.3 (2.6-23.6)	0.61; 0.09
AST U/L, median (range)	28 (7-1097)	25 (6-980)	38.5 (8-827)	29 (9-1097)	0.003 ; 0.09
ALT U/L, median (range)	40 (9-1571)	37 (9-996)	52.5 (12-1571)	39 (12-1020)	0.01; 0.05
ALP U/L, median (range)	94 (13-829)	89 (13-829)	101 (32-750)	96.5 (41-572)	0.01 ; 0.14
GGT U/L, median (range)	53 (5-1600)	42 (7-1600)	75.5 (12-1217)	53 (5-781)	0.01 ; 0.15
Bilirubin µmol/L, median (range)	11 (2-415)	10 (2-415)	13 (2-152)	9 (2-165)	0.07; 0.07
Operation time minutes, median (range)	91 (26-235)	93 (47-235)	96.5 (26-192)	84.5 (36-156)	0.15; 0.004
95% cholecystectomy, n (%)	74 (13.7)	42 (13.77)	22 (14.29)	10 (12.2)	0.88; 0.71
Conversion to open, n (%)	7 (1.3)	5 (1.64)	1 (0.65)	1 (1.21)	0.38; 0.78
Histopathology, n (%)					
Cholecystitis only	495 (91.5)	285 (93.44)	137 (88.96)	73 (89.02)	0.2; 0.3
Cholecystitis with suppurative/necrotizing/gangrenous changes	36 (6.66)	14 (4.59)	15 (9.74)	7 (8.54)	0.054; 0.16
Cholecystitis with incidental low-grade dysplasia	4 (0.74)	3 (0.98)	1 (0.65)	0 (0)	0.71
Cholecystitis with incidental adenocarcinoma	3 (0.55)	1 (0.33)	1 (0.65)	1 (1.22)	0.32; 0.32
Cholecystitis with other pathology	3 (0.55)	2 (0.66)	0 (0)	1 (1.22)	0.001
Bile duct injury, n (%)	2 (0.37)	1 (0.33)	0 (0)	1 (1.2)	0.32
Bile leak post operatively	8 (1.48)	7 (2.3)	0 (0)	1 (1.22)	0.54
Takeback to theatre, n (%)	2 (0.37)	0 (0)	2 (1.3)	0 (0)	
Postoperative stay days, median (range)	2 (0-47)	2 (0-11)	2.3 (0-47)	1 (0-14)	0.03 ; 0.33
Clavien-Dindo classification Grade ≥2 related ≤30-day readmission, n (%)	4 (0.74)	0 (0)	1 (0.65)	3 (3.66)	
Death, n (%)	1 (0.37)	0 (0)	1 (0.65)	0 (0)	

SD: Standard deviation, CRP: C-reactive protein, WCC: White cell count, AST: Aspartate aminotransferase, ALT: Alanine transaminase, ALP: Alkaline phosphatase, GGT: Gamma-glutamyl transferase.

Table 2. Patient characteristics of the 95% cholecystectomy group

Characteristic	95% cholecystectomy (n= 74)	p (vs. total)
Sex, n (%)		
Male	35 (47.3)	0.006
Female	39 (52.7)	
Age, median (range)	57 (21-84)	0.0001
Highest preoperative temperature °C, median (range)	37.35 (35.9-39.7)	0.003
Gallbladder wall thickness mm, mean (SD)	5.53 (2.67)	0.13
Bilirubin µmol/L, median (range)	16 (5-415)	0.003
Operation time, minutes, median (range)	118 (51-235)	<0.001
Conversion to open, n (%)	6 (8.1)	0.0001
Bile duct injury, n (%)	1 (1.35)	0.26
Bile leak post operatively, n (%)	4 (5.4)	0.02
Postoperative stay days; median (range)	3 (1-41)	<0.001
Death, n (%)	0 (0)	
Recurrent biliary colic/cholecystitis, n (%)	0 (0)	

The principal findings of the study were that there was no significant difference in postoperative outcomes in Groups 2 and 3 compared to Group 1 in terms of 95% cholecystectomy rates, conversion to open, bile duct injury, and bile leak postoperatively. In regard to patients who had bile duct injury, or postoperative bile leak, they were all definitively managed with ERCP and stent. In keeping with other studies, there was a statistically significant greater length of stay in Group 2 compared to Group 1 (12,17). However, this greater length of stay in absolute terms did not appear to be significantly increased (0.3 days greater than Group 1). An interesting finding was that in those who had LC for symptom onset >7 days, there was a statistically significant shorter operative time (84.5 minutes) compared to those who had LC for symptom onset <72 hours (93 minutes) ($p= 0.004$), a comparable postoperative length of stay despite recording the highest mean gallbladder wall thickness, and the perceived operative challenges of dense inflammation. These patients were delayed due to underlying multiple comorbidities that required preoperative anesthetics assessment and medical optimization (e.g. withholding of anticoagulants/antiplatelets), delayed presentation of symptoms, and unexpected delays in operating theatre availability. The reason for this may be that these patients received prolonged periods of antibiotics to settle the inflammation, and/or that there was a selection bias towards those patients who had severe biliary colic, with changes of AC at hospital presentation, but reporting symptoms for more than seven days.

In the subgroup analysis of 95% cholecystectomy patients, there were statistically significant increases in operation time, conversion to open cholecystectomy, bile leak, and

postoperative stay. It appears that this group of patients had more severe cholecystitis, owing to significantly older age, greater ratio of males, higher preoperative temperature, and higher preoperative bilirubin. A study by Ambe et al. have concluded that the male sex is a risk factor for gangrenous and necrotizing cholecystitis (18). Despite this, there were no statistical difference in 95% cholecystectomy rates between the subgroups, no reported recurrent biliary colic/cholecystitis, and no recorded mortality. This is in contrast to studies that quote a 1.8% reoperation rate following 95% cholecystectomy (19-20).

The study suggests that early cholecystectomy is safe for acute calculus cholecystitis, regardless of timing of the onset of symptoms. This correlates with previous findings in a study of 222 patients, where it demonstrated that early LC beyond five days of symptoms was safe, and not associated with increased complications (16). The duration of symptoms in AC was not an independent risk factor and should not influence the surgeon's decision to perform early LC (16). The authors suspect that this finding is attributed to increasing experience and technical skill over time, and the increasing utilization of laparoscopic subtotal cholecystectomy in the treatment of early AC (20).

The strengths of this study are that this was a single consultant surgeon, single institution analysis involving a large number of patients. Some limitations to this study include the retrospective nature of this study, heterogeneity of the patients, inherent inaccuracies in the symptom onset provided by the patients, inherent variable delays in access to theatre, inability to ascertain whether patients represented for postoperative complication outside of the facility, and no prolonged longitudinal follow-up of patients, particularly the 95% cholecystectomy patients. Further studies to prospectively

investigate the outcomes (including hospital costs) of early LC for AC, as well as comparing early subtotal cholecystectomy with delayed cholecystectomy for AC would be beneficial.

CONCLUSION

The present study suggests that early LC for AC is safe, regardless of the timing of symptom onset. Surgeons do not necessarily need to limit early LC for within 72 hours of symptom onset. In difficult AC, laparoscopic reconstituting 95% cholecystectomy can be utilized with acceptable postoperative outcomes.

Ethics Committee Approval: This study was approved by Human Research Ethics Committee (HREC), Research Office, Western Sydney Local Health District. The study reference number is 2019/ETH02056.

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ORİJİNAL ÇALIŞMA-ÖZET

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Semptom başlangıcından bağımsız olarak akut taşlı kolesistit için erken kolesistektomi sonrası iyi postoperatif sonuçlar

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ÖZET

Giriş ve Amaç: Akut taşlı kolesistit (AK) için erken kolesistektomi ile ilişkili postoperatif komplikasyonların ve hastane maliyetlerinin gecikmiş operasyona kıyasla daha düşük olduğuna dair kanıtlar giderek artmaktadır. Cerrahların semptom başlangıcına bağlı olarak AK için ne kadar erken operasyon yapmaları gerektiğine dair sınırlı sayıda yüksek kaliteli kanıt mevcuttur.

Gereç ve Yöntem: Ocak 2015-Ekim 2022 tarihleri arasında tek bir cerrah tarafından kolesistektomi yapılan 774 hasta retrospektif olarak incelendi. Beş yüz kırk bir hasta analiz edildi. Hastalar semptom başlangıcına göre üç gruba ayrıldı: Grup 1: 0-72 saat (n= 305), Grup 2: 72 saat-1 hafta (n= 154) ve Grup 3: >1 hafta (n= 82).

Bulgular: Medyan operasyon süresi en uzun Grup 2'deydi (96,5 dakika) ve Grup 1'e kıyasla en yüksek oranda %95 kolesistektomi (n= 22/154, %14,29) uygulanmıştı (p> 0,05). Açık ameliyata dönüşüm tüm gruplarda %0,65-1,64 arasındaydı. En yüksek safra kaçağı oranı Grup 1'de (n= 7/305, %2,3) görülürken, bunu Grup 3 (n= 1/82, %1,22) izledi (p> 0,05). Tüm hastalar ERCP ve biliyer stent ile başarılı bir şekilde tedavi edilmiştir. Medyan hastanede kalış süresi Grup 2'de (2,3 gün) Grup 1'e (2 gün) kıyasla anlamlı derecede uzundu (p= 0,03). Grup 2 ve 3'teki %95 kolesistektomi oranı Grup 1'e kıyasla anlamlı değildi.

Sonuç: Taşlı kolesistit için erken kolesistektomi, semptomların zamanlamasına bakılmaksızın, iyi postoperatif sonuçlara sahip gibi görünmektedir. Cerrahların erken kolesistektomiye semptomların başlamasından sonraki 72 saatle sınırlandırması gerekmemektedir.

Anahtar Kelimeler: Kolesistit, erken kolesistektomi, zamanlama, postoperatif sonuçlar

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Questionnaire survey of virtual reality experiences of digestive surgery at a rural academic institute: A pilot study for pre-surgical education

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ABSTRACT

We developed a prototype VR platform, VECTORS L&M (VLM), aiming to enhance the understanding of digestive surgery for students, interns, and young surgeons by limiting costs. Its efficacy was assessed via questionnaires before implementation in surgical education. The VLM provides nine-minute VR views of surgeries, from both 180- and 360-degree angles. It was created with L.A.B. Co., Ltd. and incorporates surgery videos from biliary malignancy patients. Following VLM development, a survey was conducted among surgeons who had experienced it. Twenty-eight participants (32% of observers) responded to the survey. A majority (81%) reported positive experiences with the VR content and showed interest in VR video production, though some reported sickness. Most respondents were experienced surgeons, and nearly all believed VR was important for medical education with a mean score of 4.14 on a scale of up to 5. VR was preferred over 3D printed models due to its application versatility. Participants expressed the desire for future VR improvements, such as increased mobility, cloud connectivity, cost reduction, and better resolution. The VLM platform, coupled with this innovative teaching approach, offers experiential learning in intraabdominal surgery, effectively enriching the knowledge of students and surgeons ahead of surgical education and training.

Keywords: Surgical education, medical staff, internship doctors, digestive surgery, virtual reality

Video links: <https://turkjsurg.com/video/UCD-6202-v1.mp4>

<https://turkjsurg.com/video/UCD-6202-v2.mp4>



INTRODUCTION

The field of operative simulation systems using the latest computerized technology has witnessed significant advancements in the past two decades (1-5). Notably, the use of three-dimensional (3D) angiographic images from contrast-enhanced computed tomography (CT) has revolutionized surgical simulation and navigation, greatly enhancing the safety of surgical procedures such as the SYNAPSE VINCENT (Fujifilm Medical Co., Ltd., Tokyo, Japan), which enables surgeons to simulate the anatomy before surgery, proving invaluable for both training and experienced surgeons in preoperative simulation (5,6). These systems have gained widespread commercial popularity and convenience, leveraging high-resolution radiological images and advanced workstations.

Recently, extended or cross-reality (XR) technology, such as virtual reality (VR) and augmented reality, has found applications in the field of surgery. For instance, the Holoeyes MD system (Holoeyes Inc., Tokyo, Japan) uses 3D holograms to enhance the surgeon's understanding of surgical anatomy before and during operations (7,8). Recently, there has been a growing application of XR technology during the peri-Coronavirus disease 2019 era (9,10). While various VR systems have been adopted in the field of cardiovascular or orthopedic surgery worldwide, the development of VR for digestive surgery or operating nursing has been limited. Furthermore, the existing VR systems and contents in Japan still require high costs. Nonetheless, we

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still believe that XR, including VR, can significantly enhance the understanding of operative procedures for medical students and young trainees entering the surgical field. Evidence of educational or training usefulness for digestive organ surgery has not been fully elucidated. Therefore, it is essential to examine the significance of this technological advancement in the field of general surgery, from medical students to experienced surgeons. To develop a VR platform for digestive surgery education with reasonable costs, we collaborated with a rural company to produce the VR prototype content depicting the operating atmosphere and procedures. As a preliminary step, we conducted a surgical evaluation using a questionnaire among 28 surgeons at a rural academic institute, aiming to establish a practical and affordable VR educational platform in digestive surgery.

MATERIALS and METHODS

Participants

The VR contents presented in this study were experienced by surgeons who attended the 59th Kyushu Associations of Surgery, Pediatric Surgery, and Endocrine Surgery held in Miyazaki City, Miyazaki on March 10 and 11, 2023. The VR system used in this study, called the Virtual Educational Communication Tool for Operating Room in Surgery by L.A.B. Co., Ltd. (<https://livecity.co.jp/LAB/index.php>) and Miyazaki University (VECTORS L&M), was exhibited, and a total of 87 participants had the opportunity to try the prototype contents of VECTORS L&M. Eventually, 28 (32%) of 87 participants responded to our questionnaire. We followed the guidelines in the Declaration of Helsinki, which provides ethical principles for research involving human participants, including studies that use identifiable human material and information. The institutional ethics committee has approved our study protocol (C-0149, Date: 14.03.2023 and O-1116-2, Date: 08.05.2023). Informed consent was obtained from each participant using the opt-out method, where a declaration was presented on the website of the Clinical Research Support Center, University of Miyazaki Hospital, allowing participants to decline participation within one month.

VR Tool and Production of Surgical Contents

1. List of equipment used for photographing the operating field

The cameras used were the LUMIX GH5S (Panasonic, Osaka, Japan) and Insta360Pro2 (Insta360, Shenzhen, Guangdong, China). The storage medium was Blackmagic Video Assist 7" 12G HDR (Blackmagic Design, Melbourne, Australia). The crane for fixing the camera was SWIFT JIB 50 (Heiwa Seiki Industry Co., Ltd., Saitama, Japan).

2. Flow of setting imaging conditions at the operating field

The means for installing cameras were described as follows: During the process of installing the camera, ensuring safety

(without contamination) and non-interference were considered absolute conditions. Based on these conditions, it was judged that the installation of a tripod was not adequate, and installation with a crane was proposed, and a test was conducted several times. As a result, we preliminarily confirmed that the system was safe and that the equipment did not obstruct the practitioner, and then we decided to introduce the final setting.

During the test shooting of the video, it was found that the luminosity of the operative field became a significant issue. The surgical shadow-less light used in the surgical field was positioned at a higher altitude than anticipated, and the video image was overexposed. Attempts were made to address this by adjusting the sensitivity of the International Organization for Standardization (ISO) and the shutter speed. However, when the luminous intensity was adjusted to match the operating field, the surrounding areas became excessively dark, posing a potential issue for future tests. The test footage was examined, and efforts were made to correct the video, but the overexposed and excessively dark portions of the footage could not be adequately adjusted. As a result, since it is difficult to respond with conventional MP4 file recording, we proposed to save it as a raw file and then edit it to selectively adjust the luminosity. Eventually, through further adjustments and additional fixes, it was determined that the basic problem was resolved, and the shooting conditions were established based on the results of the test shooting under the aforementioned conditions.

3. Production shooting: Equipment used and condition setting

The camera settings of the LUMIX GH5S were ISO 320, shutter speed 4000, anamorphic 3.3K, and 59.94 fps. In the first half, high-definition multimedia interface raw data was obtained by an output to video assist and shoot. The raw data settings showed the best quality settings, which were recorded on a 2TB solid-state drive. In the second half, we switched to vlog settings inside the camera, which was a secure digital memory card. By using Insta360 Pro2, the entire 360-degree inside operating room video with 8K and 29.97 fps was photographed from the wall. The quality level was determined to be high and was recorded on a 2TB solid-state drive.

4. Editing work regarding equipment and processes used for editing

The data captured using the Insta360 Pro2 camera was processed and converted into a 360-degree video using the Insta360 Stitcher software. Subsequently, at the Da Vinci Solve Studio at L.A.B. Co., Ltd. (Miyazaki, Japan), the raw and log data obtained from the LUMIX camera were subjected to color correction. Additionally, the video footage shot at the operating field using the Insta360 Pro2 camera underwent color correction as well. Eventually, Adobe Premiere Pro was used to



Figure 1. Wearing a VR headset by the author.

VR: Virtual reality.

convert the LUMIX footage into VR video format and edit it to include only the relevant parts for the evaluation by the main researcher's panel.

5. Watching VR videos

For the viewing of VR video, the DPVR® Pro (Shanghai, China), a 4K compatible headset licensed by L.A.B. Co., Ltd., was applied (Figure 1).

Patient selection

During an actual surgical procedure, a patient diagnosed with extrahepatic cholangiocarcinoma and scheduled for a pancreaticoduodenectomy was selected. A written informed consent with signature was obtained by this patient to record VR videos and for the secondary use of those videos in educational study. The operative video was captured from the skin incision to the intraabdominal procedures for one hour. To capture the perspective of the main operator, a 180-degree-angled video camera was positioned near the right shoulder, replicating the visual angle of a typical third assistant. Video of the delivery of operative forceps between the scrub nurse and the doctors was focused. The other side of the view from the first assistant operator was taken by the 180-degree camera as well (Figure 2, Supplement Video 1). The 360-degree camera was set at the entrance of the operating room, and the video of zoom-in and zoom-out focusing operators was arranged (Figure 3, Supplement Video 2). The time of the edited video from the 180- and 360-degree cameras was 15 and four minutes, respectively. Participants watched both videos and answered questions.

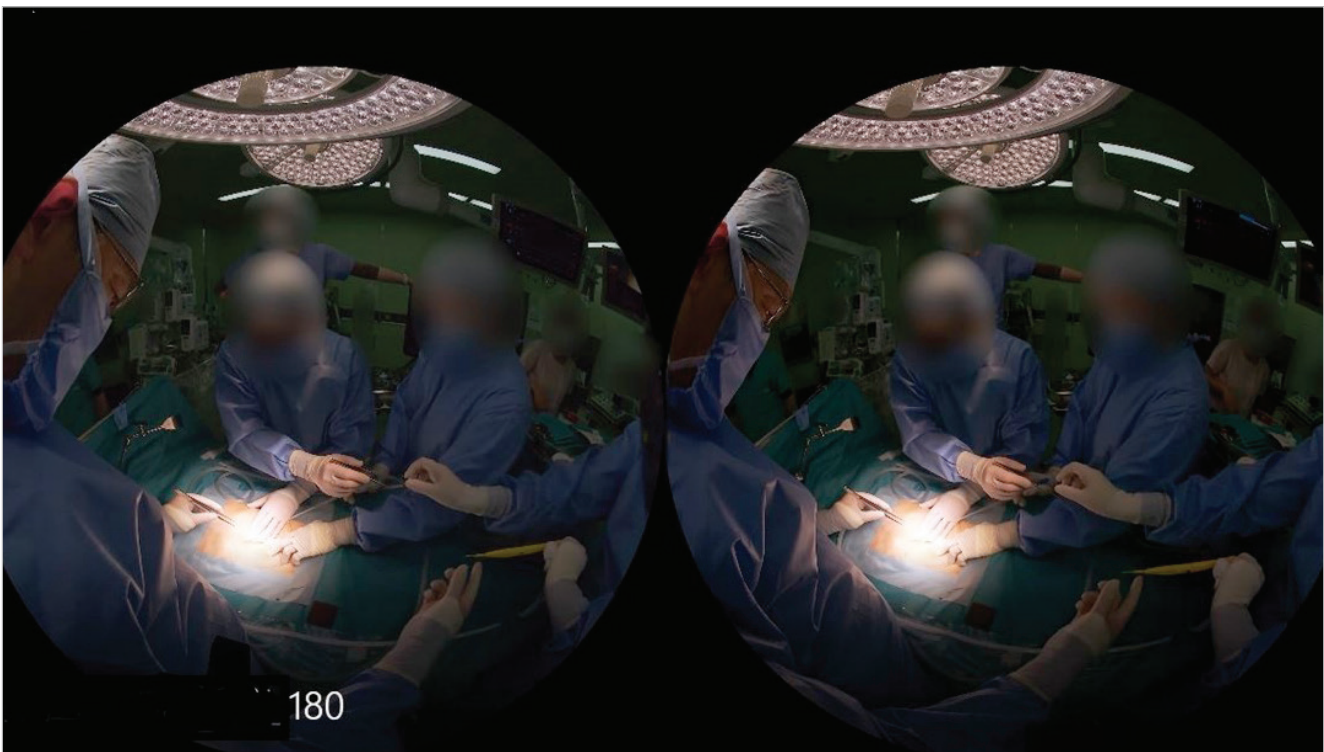
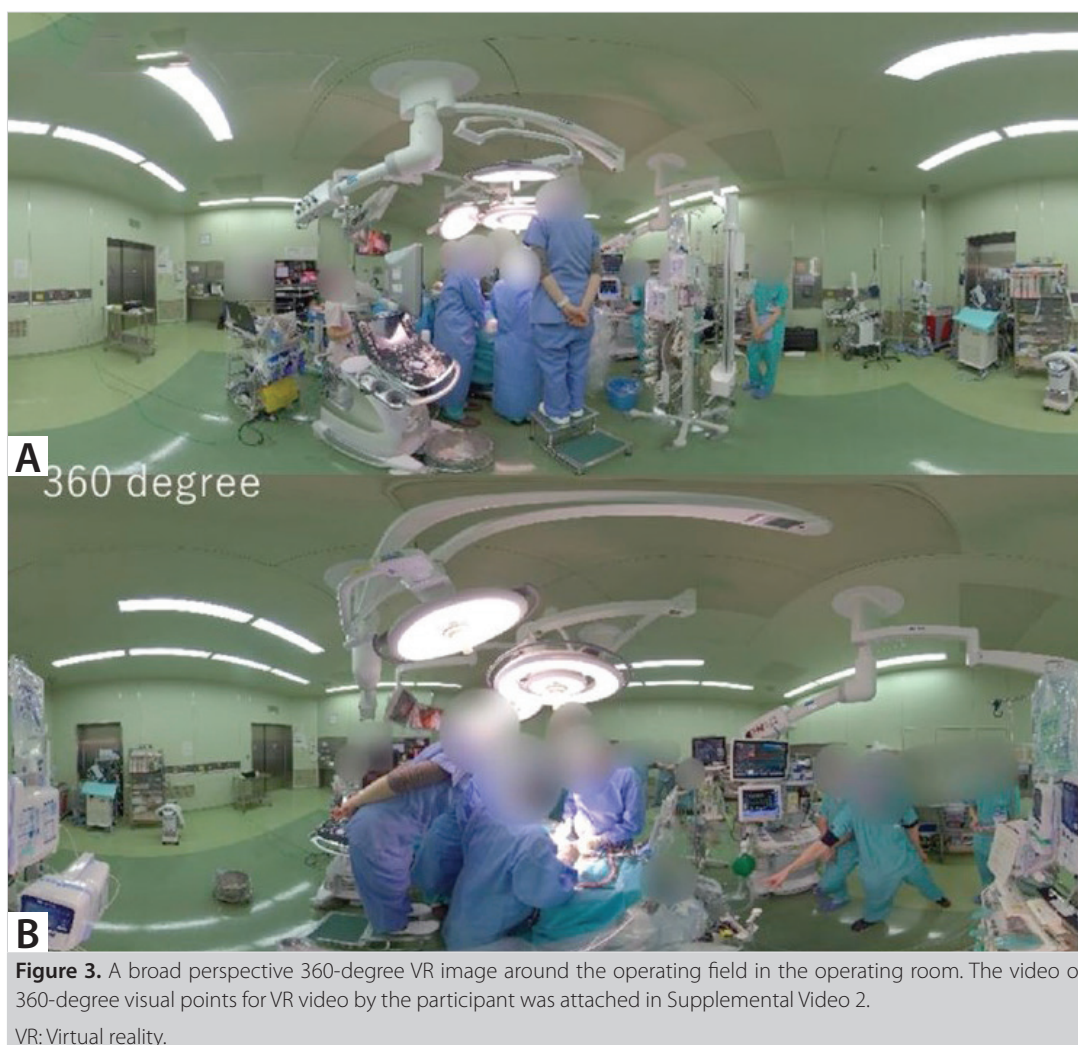


Figure 2. A broad perspective 180-degree VR image from the third assistant surgeon between the first operator and instrument nurse. The video of 180-degree visual points for VR video by the participant was attached in Supplement Video 1.

VR: Virtual reality.



Questionnaire

The survey questionnaire consisted of three questions regarding VR imaging by the production company L.A.B. Co., Ltd., and seven questions regarding surgical issues using VR imaging by the Department of Surgery, University of Miyazaki Faculty of Medicine. The first three queries were about the production company, and questions four to 10 corresponded to surgical researchers, which included the following:

- 1) Please watch this operative video and tell us your honest impressions;
- 2) Are you interested in VR video production? [Scored with a scale ranging between 1 (not at all) and 5 (very interested)];
- 3) Please let us know if you have any ideas on the use of VR images;
- 4) Occupation;
- 5) Have you tried other or original surgical simulation systems or educational contents that utilize VR?
- 6) Which of the following types of VR content are you most interested in? (Multiple choices: simulation of the doctor, surgical anatomy visualization, patient education, student education, trainee or major medical education, virtual medical training, etc.);
- 7) How important do you think VR content is for medical education and training? [Scored with a scale ranging between 1 (not important at all) and 5 (very important)];
- 8) Which is more useful, a 3D printing product or VR content?
- 9) What kind of improvements do you expect for future VR content and information technology (IT) innovations to make in surgical education and skills?
- 10) and were there any technical issues or challenges encountered while using VR content? For statistics, continuous variables were expressed as mean \pm standard deviation (SD). The results of 28 people participating in the study may not give a statistically significance due to the small size of the target audience.

RESULTS

Questionnaire About the Production company

1. Honest impressions on the operative video: The description rate was 21 (75%), and the blank answer was seven out of 28 participants. A good reputation was found in 17 of 21 (81%) participants. Virtual realism seemed to be evaluated by nine participants, including their opinion of VR sickness. Three participants reported no satisfaction with the quality of VR.
2. Interest in VR video production: About 82% of the participants felt interested in the present VR imaging quality. The median and mean scores were 4 and 4.14, respectively.
3. Ideas on the use of VR images: Answers for the recent surgical application were observed in three participants at the present level of VR images. A combined visual and hand simulation was expected in two.

Questionnaire About the Surgical Researchers

4. Occupation: Eighteen participants (64%) were expert surgeons, comprising three with expertise in thoracic surgery, one in vascular surgery, four in hepatobiliary and pancreatic surgery, and ten in digestive tract surgery. The number of intern doctors or resident surgeons was eight (29%), and the number of surgical educational instructors (surgeons) was two (7%).
5. Exposure to other or original surgical simulation systems or educational contents that utilize VR: Five surgeons used commercial-based 3D imaging analysis system for computed tomography.
6. Most interesting VR content: Twenty-five answers were expectations for the usual operating simulation using VR, XR, or augmented reality like holograms or projection mapping procedures. Except for the present VR system, several educational VR contents were required.
7. Opinion on VR content in medical education and training: Twenty-six participants (93%) thought that VR content was important for medical education or training. The median and mean scores were 4 and 4.32, respectively.
8. More useful between a 3D printing product and VR content: By comparing questions, the usefulness of VR content was required for some reasons, mainly variously applicable.
9. Expected improvements in future VR content and IT innovations to be made in surgical education and skills: Various opinions or expectations for future development regarding IT solutions were required. Among them, more usefulness or light mobility during operation or internet cloud connection and lower cost (mainly contents or system fees) were predominant.
10. Technical issues or challenges while using VR content: Five steps of zoom-in functions or light modulation were controlled by using a headset apparatus with VECTORS L&M contents.

However, some participants required more development of resolution or light adjustment by the zoom-in function.

DISCUSSION

Current understanding suggests that VR technology is increasingly being integrated into surgical practice for various applications, such as surgical planning, training, and intraoperative guidance, as described above (2,7-13). However, a thorough exploration of the potential advantages, disadvantages, and limitations of VR in surgery is necessary. One presumed advantage is improved training. VR provides a safe and repeatable platform for surgical training, which helps reduce the learning curve associated with complex surgical procedures (13,14). It can simulate a wide array of scenarios a surgeon may encounter, thereby providing invaluable experience. Currently, preoperative planning is essential, and surgeons often use 3D imaging to visualize the anatomy of patients before surgery (1-5).

VR can enhance comprehension of the unique anatomy and pathology of the patient and aid in decision-making. XR technology may be useful for patient orientation or education (9,10). Among these technologies, VR can be primarily used to educate patients about their conditions and the surgical procedures they will undergo, potentially reducing their anxiety and improving their understanding (11-14). XR technology could possibly decrease operative time because practicing on a virtual model of the anatomy of the patient can potentially reduce the duration of the actual surgical procedure, leading to better outcomes and less time under anesthesia for the patient. Nevertheless, these emerging technologies require validation with the latest resources to keep pace with advancements (11-15).

Regarding VR content creation, the production of high-quality videos is crucial, and therefore, technical support from specialized VR companies is often sought. It is important to note that commercial IT or DX medical solutions can be costly, which could pose a barrier to widespread use (15). For example, a renowned company in Japan charges 20 million yen (1.54.000 USD) for basic VR cloud costs, along with an annual contract fee (not publicly disclosed but required in practice). Additional fees apply if custom content is created. However, some institutes have implemented low-cost VR systems (11). Despite these costs, companies with a strong concept can create high-resolution VR content, similar to what is used in tourism, which is not solely limited by technical costs.

We initially conducted market research in Japan, and our product required several meetings and sessions in the operating room to finalize the video-taking scenario, which cost us 8.00.000 yen, or approximately 6.200 USD. This cost was significantly lower than that of commercial products. We have produced two types of content: 1) a 180-degree wide video showing the perspective of an assistant operator, and 2) a 360-degree

wide video inside the operating room. Additionally, we are currently working on creating content for a robotic surgical workshop and primary damage control surgery at the emergency room (not published yet). The current image resolution of our content is state-of-the-art 8K (8000 pixels) full-high vision. The first author of the study served as the primary operator and provided voice-over explanations for the content. Importantly, no adverse events occurred during the operation. It took us seven days of editing to complete this prototype VR content, which was then used in a questionnaire-based prospective trial at a surgical congress.

In response to a query from the product company, approximately 61% of the participants responded positively to the VR content. However, some participants experienced technical issues, which can be attributed to their familiarity with the latest generation of VR games. Previous reports have indicated that hologram or computer graphics-based operative simulations have been well received (5-14). These simulations can be altered or synthesized using the latest graphics software. However, it is important to note that real images used for virtual experiences might be influenced by background lighting or movement. Interestingly, from the perspective of surgeons, only 18% of the participants reported using surgical simulation systems, suggesting a potential interest in VR or computerized images. Around 64% of the participants expressed interest in using VR for confirming surgical anatomy or simulating operations, while the remaining participants were interested in training or education. Most participants recognized VR content as a valuable surgical tool, aligning with the acceptance of 3D operation simulation systems in the last decade. Previously, 3D printing materials created from Digital Imaging and Communication in Medicine data have been used for surgical simulation or donor organ preparation in liver transplantation (16). However, these materials have not been widely adopted or developed due to high individual costs despite our attempt to create a hepatectomy sample (17). Additionally, producing these materials required a specialized technician, a ventilated room to eliminate organic matter produced during the printing process, and access to suitable materials for each organ. The disposal of these materials also posed challenges. Contrastingly, digital imaging could potentially resolve these issues, with the exception of the lack of tactile sensation. Consequently, only a small number of participants still required 3D-printed samples. The ideal solution may lie in combining the latest technology to replace traditional anatomical models (18).

Disadvantages and limitations of VR in surgical practice include high cost associated with individual contracts and the significant initial investment required for VR equipment and software. Regular updates and maintenance can further increase the

overall cost, as described above. Additionally, while VR provides a learning platform, there is a learning curve associated with becoming proficient in using VR technology. Currently, there are no widely accepted standards or certification processes for VR surgical training programs, which could lead to inconsistencies in training quality. This lack of standardization might suggest instability in such systems. Therefore, the utility of VR and other XR systems will be progressively demonstrated as IT develops.

At our institution, we have plans to incorporate this VR system into the clinical practice of medical students and gather evidence on its efficacy as a VR platform. However, some users may experience physical discomfort or symptoms such as nausea, dizziness, or eyestrain, commonly referred to as VR sickness (19,20). In our current study, one participant reported experiencing such symptoms. Since personal characteristics were not obtained through this questionnaire, this issue will be further evaluated in the next phase involving medical students. For experienced surgeons, despite the rapid advancement of VR technology, it still cannot fully replicate the tactile feedback experienced during actual surgery. This technological limitation could potentially reduce the effectiveness of VR as a training tool for experienced surgeons. For patients scheduled for surgery, the issues to be resolved are more complex compared to medical or co-medical staff. Data privacy is a significant concern due to ethical considerations in VR simulations (21).

CONCLUSION

Our original VR platform, VECTORS L&M, which provides the perspective of surgeons and medical practitioners, has generated high expectations as a clinical and educational tool, even in its prototype stage. We have the vision to continue the development of this unique surgical education platform, making it more affordable and integrating its tools into practical training, research, and internships in surgical medicine. We also plan to advance the assessment of understanding before and after the VR experience for the participants and utilize this tool for the improvement of clinical skills and the recruitment of surgeons.

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

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**ORJİNAL ÇALIŞMA-ÖZET**

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Bölgesel bir akademik enstitüde sindirim cerrahisinin sanal gerçeklik deneyimlerinin anket çalışması: Cerrahi öncesi eğitim için bir pilot çalışma

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ÖZET

Maliyetleri sınırlandırarak öğrenciler, stajyerler ve genç cerrahlar için sindirim cerrahisi anlayışını geliştirmeyi amaçlayan bir prototip VR platformu olan VECTORS L&M'yi (VLM) geliştirdik. Cerrahi eğitimde uygulanmadan önce etkinliği anketlerle değerlendirildi. VLM, ameliyatların hem 180 hem de 360 derecelik açılardan dokuz dakikalık VR görünümünü sağlamaktadır. L.A.B Co., Ltd ile oluşturulmuştur ve biliyer malignite hastalarının ameliyat videolarını içermektedir. VLM gelişimini takiben, bunu deneyimleyen cerrahlar arasında bir anket yapıldı. Yirmi sekiz katılımcı (gözlemcilerin %32'si) ankete yanıt vermiştir. Çoğunluk (%81) VR içeriğiyle ilgili olumlu deneyimler bildirdi ve VR video prodüksiyonuna ilgi gösterse de bazıları rahatsızlık hislerini bildirdi. Katılımcıların çoğu deneyimli cerrahlardı ve neredeyse hepsi VR'nin tıp eğitimi için önemli olduğuna inanıyordu ve ortalama 4,14 puan 5'e kadar çıktı. VR, uygulama çok yönlülüğü nedeniyle 3D baskılı modellere göre tercih edildi. Katılımcılar, artan mobilite, bulut bağlantısı, maliyet azaltma ve daha iyi çözünürlük gibi gelecekteki VR iyileştirmeleri için arzularını dile getirdiler. VLM platformu, bu yenilikçi öğretim yaklaşımı ile birleştiğinde karın içi cerrahide deneyimsel öğrenme sunarak cerrahi eğitim ve öğretimden önce öğrencilerin ve cerrahların bilgilerini etkili bir şekilde zenginleştirmektedir.

Anahtar Kelimeler: Cerrahi eğitim, sağlık personeli, stajyer doktorlar, sindirim cerrahisi, sanal gerçeklik

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Translation and validation of Indonesian hemorrhoidal disease symptom score (HDSS) and short health scale hemorrhoidal disease (SHSHD)

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ABSTRACT

Objective: Hemorrhoidal disease, which affects nearly 40% of people, is characterized by pathological alterations and distal displacement of hemorrhoidal tissue. The short health scale (SHSHD) and the hemorrhoidal disease symptom score (HDSS) are two tools that can be utilized to assess the quality of life of hemorrhoidal patients. The present study aims to translate, modify, and validate the HDSS and SHSHD questionnaires in Indonesian.

Material and Methods: This cross-sectional study assessed the validity and reliability of the HDSS and SHSHD Indonesian adaptation instrument in hemorrhoidal patients from April 15, 2022, and April 1, 2023.

Results: There were 91 study subjects, 55 males and 36 females. The study showed that the subscale interpretations of the R-values and the full scale scored above 0.25, indicating weak to very strong correlations. These results mean that the HDSS and SHSHD questionnaires are valid for use. Based on the study's results, the R-value of each item, domain, and total score ≥ 0.8 ($p < 0.05$) indicates that the HDSS and SHSHD instruments are reliable.

Conclusion: The Indonesian adaptation of the HDSS and SHSHD demonstrates validity and reliability as an assessment tool for measuring the health-related quality of life in Indonesian patients diagnosed with hemorrhoidal disease.

Keywords: Disease, hemorrhoid, quality of life, questionnaires

INTRODUCTION

Hemorrhoidal disease, which affects nearly 40% of people, is characterized by distal hemorrhoidal tissue displacement and pathological alterations (1,2). Symptoms of hemorrhoidal disease can be severe discomfort, physical limitations, and decreased quality of life (3). Hemorrhoids are typically categorized as internal or external based on where they are discovered. The columnar epithelium is the layer that covers internal hemorrhoids that are visible above the dentate line. In contrast, squamous epithelium covers external hemorrhoids (4-6).

Every year, many people are diagnosed with hemorrhoids. The degree of their pathology will determine available treatments. Non-operative treatment is an option for first, second, and third-degree hemorrhoids (7,8). Non-operative treatment cannot reverse structural abnormalities in the hemorrhoidal tissue. At the same time, invasive procedures frequently result in problems and recurrence. In addition, if hemorrhoidal disease is not appropriately controlled, the severity and symptoms can worsen with time. Hemorrhoid disease is supposed to be avoided by focusing on dietary behaviors and reducing risk factors (3).

There are questionnaires developed to measure the severity of hemorrhoid disease. The hemorrhoid severity score (HSS), initially suggested by Nystrom, has been created with a multi-symptom approach based on five primary symptoms of hemorrhoidal disease (pain, itching, bleeding, soiling, and prolapse) (9-12). The SHS is divided into four categories: symptoms, functional status, specific problems that arise, and overall well-being. Each category is comprised of one question. A simplified hemorrhoidal-related quality-of-life tool is the SHS (12-14). Then Khan et al. have created the "PNR-Bleed" classification system based on four primary

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aspects to more precisely describe hemorrhoidal disease: the degree of prolapse (P), the number (N) of primary columns affected, the relationship (R) of hemorrhoidal tissue to the dentate line, and the amount of bleeding (B) (15).

The hemorrhoidal disease symptom score (HDSS) and short health scale hemorrhoidal disease (SHSHD) have yet to be translated into Indonesian, which is the primary consideration in translating and verifying them. In the present study, HDSS and the SHSHD are translated, modified, and validated for Indonesian.

MATERIAL and METHODS

Patient

This study was longitudinal. Surgical departments in several hospitals selected patients with hemorrhoidal disease symptoms for this study. Between April 15, 2022, and April 1, 2023, all patients diagnosed with hemorrhoidal disease and treated surgically or conservatively were included in the validity and reliability analysis. The surgeons used the patient's medical history, physical examination, and medication to diagnose and evaluate hemorrhoidal disease. The process of the patient's treatment was unaffected by this study. The patients conducted the informed consent form supplied with the questionnaire. Patients who were cognitively or linguistically impaired were not included in the study. The survey was distributed to patients using Google Forms. Patients had to complete the informed consent forms before completing the questionnaire. In this study, incomplete responses were not assessed.

Measurements

This study started with adapting the original HDSS and SHSHD questionnaires into the Indonesian language. The HDSS and SHSHD questionnaires were translated into Indonesian using World Health Organization (WHO) guidelines that have been altered for cross-cultural adaptation. These steps include forward translation, back translation, pre-testing including expert committee, and documentation. For forward translation, the questionnaire was translated into Indonesian by two qualified translators who were also fluent in English and familiar with the terms used in the HDSS and SHSHD questionnaires. To confirm the accuracy of the translation, it is necessary to independently back-translate to the initial translation, meaning to translate it back from the target language into the original language. For backward translation, it is recommended to have at least two translators proficient in their native language (the original language) execute the translation. To prevent bias, it is preferable that back-translators are not informed about the particular subjects that the questionnaire aims to measure. The results of the backward translation of the two translators were discussed with one of the reviewers, who had a medical

background and English language skills. Then, a backward translation synthesis was produced. The expert committee evaluated all translations and assessed if they accomplished semantic, idiomatic, experiential, and conceptual equivalence with the original versions. To create a prefinal version of the translated questionnaire, any inconsistencies would need to be resolved, and the expert committee members would need to agree on all aspects. The final phase involved conducting pre-testing, cognitive interviews, and face validity testing using the face-to-face approach. Before finalizing the translated questionnaire, conducting a pilot test on a small group of the expected respondents is essential. This methodology enables the researchers to verify that the translated items have preserved the identical meaning to the original items, eliminating any potential ambiguity in the translated questionnaire. This step may be iterated several times to achieve the ultimate translated version of the questionnaire. Following the pre-testing phase, the researchers found several instances of ambiguity and reached a consensus on the definitive form of the questionnaire. The researchers engaged in extensive deliberation on the initial questionnaire and the outcomes of the pre-testing phase, ultimately arriving at a consensus. As part of the translation process, certain components were modified to better align with the Indonesian context. Nevertheless, there were no substantial alterations; hence, the translated version remained consistent with the original questionnaire. The frequency of patient-reported symptoms, such as discomfort, itching, bleeding, and prolapse, examined patient problems. Patients were asked about their recent three-month symptoms. Then each symptom was scored between 0 and 20 based on the following criteria: 0= never, 1= Less than once a month, 2= Less than once a week, 3= 1-6 days per week, 4= Every day (always) (Figure 1).

Data Analysis

Data analysis for this study used descriptive presentation employing frequency distribution, proportion, and average calculations for each variable. SPSS software was used to process the research data that had been gathered. The validity test of the Indonesian translation of the HDSS and SHSHD questionnaires was used in data analysis. The validity test was carried out using the Pearson correlation test, which evaluates the relationship between the possible answers and the final score on the question. The test items are valid when the significance level is $p < 0.05$.

RESULTS

The present study included 91 respondents, with a higher number of 55 (60.4%) male subjects and 36 female subjects (39.6%) (Table 1). Respondents in the age range of 18-34 years

Hemorrhoidal Disease Symptom Score
The following questions deal with symptoms caused by hemorrhoids. Your answers should reflect your symptoms during the last 3 months (1 answer per question).

1. How often do you feel pain from your hemorrhoids?
☐ Never ☐ Less than once a month ☐ Less than once a week ☐ 1–6 days per week ☐ Every day (always)
2. How often do you feel itching or discomfort of the anus?
☐ Never ☐ Less than once a month ☐ Less than once a week ☐ 1–6 days per week ☐ Every day (always)
3. How often do you bleed when passing stool?
☐ Never ☐ Less than once a month ☐ Less than once a week ☐ 1–6 days per week ☐ Every day (always)
4. How often do you soil your underwear (soiling from the anus)?
☐ Never ☐ Less than once a month ☐ Less than once a week ☐ 1–6 days per week ☐ Every day (always)
5. How often do you feel a swelling or a prolapsing hemorrhoid?
☐ Never ☐ Less than once a month ☐ Less than once a week ☐ 1–6 days per week ☐ Every day (always)

Short Health Scale₁₀₀
The following questions deal with how your symptoms caused by hemorrhoids affect your daily life (one answer per question).

1. In your view, how severe are your symptoms caused by hemorrhoids? Please grade your symptoms on a 7-point scale, where 1 is "no symptoms" and 7 is "severe symptoms."

No symptoms Severe symptoms

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐

2. Do your symptoms interfere with your daily activities? Please grade your answer on a 7-point scale, where 1 is "not at all" and 7 is "interfere to a very high degree."

Not at all Interfere to a very high degree

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐

3. Do your symptoms cause much concern? Please grade your answer on a 7-point scale, where 1 is "no concerns" and 7 is "constant concerns."

No concerns Constant concerns

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐

4. How is your general feeling of well-being? Please grade your answer on a 7-point scale, where 1 is "very good" and 7 is "very bad."

Very good Very bad

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐

Figure 1. HDSS and SHSHD.

HDSS: Hemorrhoidal disease symptom score, SHSHD: Short health scale adapted for hemorrhoidal disease.

were most prevalent, namely 33 (36.3%). Thirty-nine respondents (39.6%) were high school graduates, and most (31.9%) were self-employed. Furthermore, 34 (37.3%) had difficulty straining, and 57 (62.6%) said they typically have bowel movements more than four times per week. Based on the reported information, 51 (56%) respondents did not have a family history of hemorrhoids, and 49 (53.8%) had medical treatment. Additionally, the lump could be entered with the help of the respondents' fingers in 39 (42.9%). Fifty-nine (64.8%) of the respondents reported internal-type hemorrhoids.

This study conducted a validity test on 91 respondents. The results showed that all questions on the HDSS and SHSHD questionnaires had an R-value greater than the R table. This indicates that the HDSS and SHSHD questionnaires are valid for use. The reliability test performed in this study aimed to determine whether or not the questionnaire was consistent. The reliability test was carried out, and the findings revealed that the reliability test value on this questionnaire was 0.822 (Table 2). These results indicated that this questionnaire was reliable since they proved it passed the reliability test. It is determined to be reliable because the reliability test value is greater than the Cronbach alpha value, which is set at 0.7.

As an obvious result, a comparative approach was selected for the analysis. A plot and a Bland-Altman analysis (mean difference or limits of agreement), as shown in Figure 2, were utilized to compare two different values for the same variable. Both the HDSS and SHSHD instruments had a bias of -0.5, while the standard deviation was 5.78, the lower LOA was -16, and the upper LOA was 6.

DISCUSSION

One of the most common diseases in Indonesian society is hemorrhoids, characterized by swelling of the veins (return vessels) around the anus due to inflammation. Bleeding and prolapse, which are most frequently related to internal hemorrhoids, are the most common symptoms of hemorrhoids. External hemorrhoids that have thrombosis expand in painful conditions. Most people with piles symptoms improve with changes in diet and bowel habits. Patients who have internal hemorrhoids will not experience itching or pain. Still, symptoms can be detected when blood is seen during bowel movements. The hemorrhoid lump may emerge and feel severely obstructed in cases of severe swelling.

Table 1. Demographics and clinical characteristics of the patients

Characteristic	Value (n)	Percentage (%)
Sex		
Male	55	60.4
Female	36	39.6
Age (years)		
18-34	33	36.3
35-44	22	24.2
45-59	30	33.0
>60	6	6.6
Family history of hemorrhoids		
Yes	40	44.0
No	51	56.0
Treatment		
Medical	49	53.8
Traditional	42	46.2
Type of hemorrhoids		
Internal	59	64.8
External	13	14.3
Do not know	19	20.9
Bowel movement (per week)		
<1	4	4.4
1	3	3.3
2	7	7.7
3	16	17.6
4	4	4.4
>4	57	62.6
Straining (per week)		
<1	34	37.4
1	11	12.1
2	9	9.9
3	18	19.8
4	2	2.2
>4	17	18.7

Table 2. Results of reliability tests

Reliability statistics	
Cronbach's alpha	n of items
.822	9

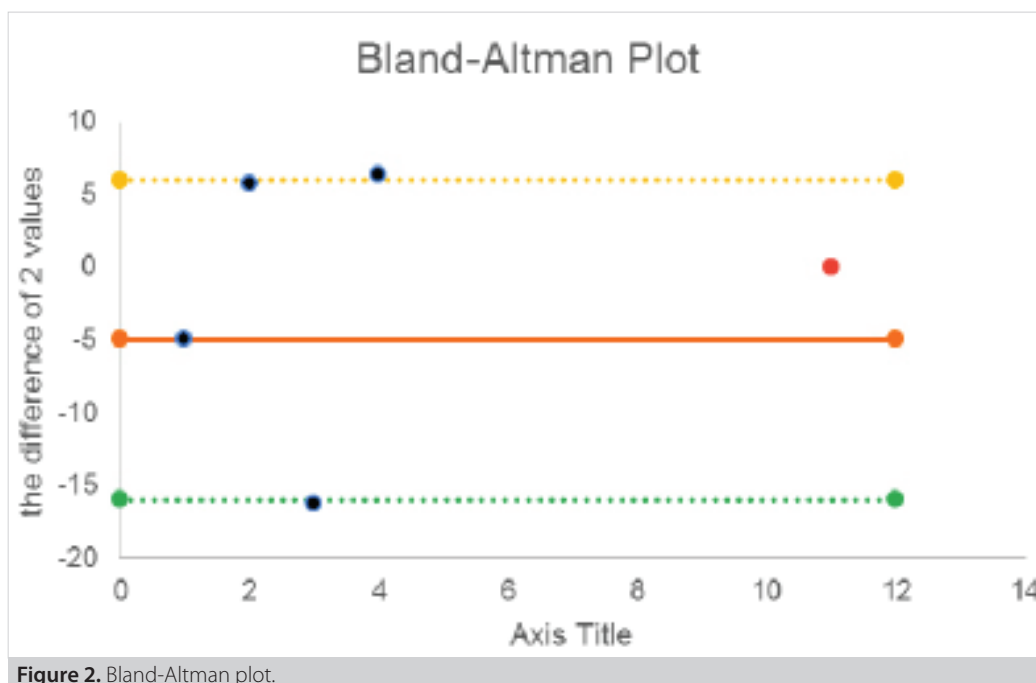


Figure 2. Bland-Altman plot.

Many factors might lead to hemorrhoids, including defecating too forcefully or spending too much time on the toilet, which may also affect the blood vessels surrounding the anus. As a result, hemorrhoids may develop. According to this study, 62.6% of respondents with hemorrhoids had bowel movements more than four times each week due to the possibility of swollen veins around the anus from frequent defecation; a higher frequency of bowel movements might result in hemorrhoids. Hemorrhoids are also associated with a high frequency of straining. However, only 18.7% of responders to this survey strained more than four times every week.

The Goligher classification system, which is frequently used, bases the severity of hemorrhoid disease on the amount of rectal prolapse. Hemorrhoids come into four categories: Grade 1 hemorrhoids bleed but do not prolapse; Grade 2 hemorrhoids may prolapse after straining but heal naturally; Grade 3 hemorrhoids may prolapse after exertion but can be cured, and Grade 4 hemorrhoids prolapse permanently and cannot be treated (16). The prolapse degree must be known to select an efficient hemorrhoid treatment plan. Unfortunately, due to the omission of symptoms associated with quality of life, disease etiopathogenesis, and particular clinical circumstances, Goligher's classification has limitations (17).

Several grading systems have been created to get around these limitations. The existence and frequency of various symptoms are the primary objectives of all grading systems based on patient self-reported scores. The frequency of pain, irritation, itching, soiling, and prolapse hemorrhoid reduction were all examined by Nystrom in 2009 using a five-point scale

(9). The system passed good validation and is straightforward to use and replicate. However, it disregards the prevalence and occurrence of prolapses that may be reduced manually (18).

A comparable method was demonstrated in 2011 by Giordano et al. The severity of hemorrhoidal symptoms was evaluated using a specially designed questionnaire. Five criteria were each rated on a range of 0 to 4, with 0 representing no symptoms and 4 representing recurrent symptoms (19). The Nystrom score was recently modified by Roervik et al. to take the frequency of prolapse experienced by the patient into account rather than the requirement for manual reduction (12). In addition, they modified the SHS, which had previously been used to evaluate individuals who suffered from inflammatory bowel illness, so that it could be applied to hemorrhoidal disease. Even when considering SHS standards for quality of life, this technique preserves an exceptionally high degree of accuracy to the Goligher classification (14).

A remarkable score was produced by combining the SHSHD with the HDSS. The HDSS scores each item based on one of five different hemorrhoidal disease categories. The scores range from 0 to 4. A score of 0 meant that the symptom was gone entirely. In contrast, a score of 20 indicated that the clinical condition was in its worst possible condition. The overall score for each of the five parameters was added to arrive at an overall score for the patient's condition. The SHS is a quality of life-based score that considers patients' concerns, their general sense of well-being, the intensity of their illnesses, and how these things impact their daily lives. The scale is depicted in Figure 1, extending from 1 (representing the best

clinical situation) to 28 (representing the worst clinical situation) (9,12,20).

The study's results demonstrated that the whole scale and the subscale interpretations of the R-values scored above 0.25, indicating weak to very strong correlations. The HDSS and SHSHD questionnaires can be used because of these findings. Item Var0002 on the questionnaire has the lowest R-value, which is 0.390. However, it suggests a weak correlation between the two factors. Var00007 and Var00001, which have R-values of 0.2061 ($p=0.001$) on the questionnaire, show a significant correlation between the two variables.

This study used mean rank ($k=2$), absolute consistency, and a two-way mixed effects model to evaluate results. For the total score outcome, the HDSS and SHSHD questionnaires demonstrated excellent reliability (0.822, 95% CI= 0.818-0.776). Additionally, the domains of the individual and physical scores displayed excellent reliability. The letter r ($-1 \leq r \leq 1$), which indicates Pearson's coefficient correlation, is a method to measure the correlation between two tests. A score of $r \geq 0.7$ is regarded as acceptable for questionnaire reliability. According to study findings, the HDSS and SHSHD instruments are reliable, which shows that the r value of each item, domain, and overall score is ≥ 0.8 ($p < 0.05$). On Plot and Bland-Altman analysis, the HDSS and SHSHD instruments showed a bias score of -0.5 with a cut-off score of 0 (95% CI= -0.16-0.6) to 12 (95% CI= -0.16-0.6). The HDSS and SHSHD measurement results will be at least 0.6 points, according to this assessment's 95% confidence level, if additional population testing is carried out.

This study demonstrates that the Goligher hemorrhoid classification system relies on the rectal prolapse degree, which is in line with the research of Dekker et al. (2022), where a systematic review and meta-analysis has been carried out to compare various scoring systems used in evaluating hemorrhoidal disease (16). The results show that some of these scoring systems have good validity and reliability in measuring the severity of hemorrhoidal disease.

The results emphasized the importance of choosing the most effective treatment strategy based on the appropriate classification of hemorrhoidal disease. Gallo et al. (2020) have also highlighted the need for common standards for trials and guidelines in treating hemorrhoids (17). Thus, this study suggests that developing a comprehensive classification that considers factors such as associated symptoms, quality of life, and specific clinical situations will help choose the right treatment strategy and improve the care of patients with hemorrhoids.

The findings show the importance of Goligher's classification and quality of life assessment using SHS in hemorrhoidal

disease. Additionally, as Rørvik et al. (2019) have demonstrated that using SHS as an evaluation method may provide detailed data regarding how hemorrhoidal symptoms affect patients' daily lives (12). The findings of this study further support the significance of considering psychosocial factors and patients' well-being when managing hemorrhoids. As a result, combining the SHS with the Goligher classification may offer a more comprehensive approach to diagnosing and treating hemorrhoidal disease. Following research by Jin et al in 2020, the study findings noted that the SHSHD and the HDSS were combined to produce a remarkable score. Jin et al. also stated that combining these two scores can assist doctors in determining the most efficient treatment strategy for patients with hemorrhoids (21).

CONCLUSION

After translation, modification, and validation, the HDSS and SHSHD questionnaires were verified for the Indonesian language. The qualities and objectivity of the concept, such as validity and reliability, must be emphasized when developing the questionnaire. These Indonesian HDSS and SHSHD questionnaires demonstrate validity and reliability as an assessment tool for measuring the health-related quality of life in patients diagnosed with hemorrhoidal disease.

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The study was published with the written consent of the patient.

Ethics Committee Approval: This study was approved by Muhammadiyah University of Yogyakarta Faculty of Medicine Health Research Ethics Committee (Decision no: 130/EC-KEPK FKIK UMY/V/2022, Date: 17.05.2022).

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

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**ORİJİNAL ÇALIŞMA-ÖZET**

Türk J Surg 2023; 39 (4): 336-343

Endonezya hemoroidal hastalık semptom skoru (HDSS) ve kısa hemoroidal hastalık sağlık ölçeğinin (SHSHD) çevirisi ve geçerliliğiFadli Robby Amsriza¹, Rizka Fakhriani², Asmaya Aji Pangki³¹ Muhammadiyah Yogyakarta Üniversitesi Tıp ve Sağlık Bilimleri Fakültesi, Cerrahi Anabilim Dalı, Bantul, Endonezya² Muhammadiyah Yogyakarta Üniversitesi Tıp ve Sağlık Bilimleri Fakültesi, Kulak Burun Boğaz Anabilim Dalı, Baş Boyun Cerrahisi Bilim Dalı, Bantul, Endonezya³ Endonezya İslam Üniversitesi Tıp Fakültesi, Cerrahi Anabilim Dalı, Sleman, Endonezya**ÖZET**

Giriş ve Amaç: İnsanların yaklaşık %40'ını etkileyen hemoroidal hastalık, hemoroidal dokunun patolojik değişiklikleri ve distal yer değiştirmesi ile karakterizedir. Kısa sağlık ölçeği (SHSHD) ve hemoroidal hastalık semptom skoru (HDSS) hemoroidal hastaların yaşam kalitesini değerlendirmek için kullanılabilecek iki araçtır. Bu çalışmanın amacı HDSS ve SHSHD anketlerini Endonezceye çevirmek, modifiye etmek ve doğrulamaktır.

Gereç ve Yöntem: Bu kesitsel çalışmada, 15 Nisan 2022 ve 1 Nisan 2023 tarihleri arasında hemoroid hastalarında HDSS ve SHSHD Endonezce uyarlama aracının geçerliliği ve güvenilirliği değerlendirilmiştir.

Bulgular: Çalışmaya 55 erkek ve 36 kadın olmak üzere 91 kişi katıldı. Çalışma, R-değerlerinin alt ölçek yorumlarının ve tam ölçeğin 0,25'in üzerinde puan aldığını ve zayıf ile çok güçlü korelasyonlara işaret ettiğini gösterdi. Bu sonuçlar, HDSS ve SHSHD anketlerinin kullanım için geçerli olduğu anlamına gelmektedir. Çalışmanın sonuçlarına göre, her bir maddenin, alanın ve toplam puanın R-değerinin $\geq 0,8$ ($p < 0,05$) olması, HDSS ve SHSHD araçlarının güvenilir olduğunu göstermektedir.

Sonuç: HDSS ve SHSHD'nin Endonezya uyarlaması, hemoroidal hastalık tanısı almış Endonezyalı hastalarda sağlıkla ilgili yaşam kalitesini ölçmek için bir değerlendirme aracı olarak geçerlilik ve güvenilirlik göstermektedir.

Anahtar Kelimeler: Hastalık, hemoroid, yaşam kalitesi, anket

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Zinc supports liver regeneration after partial resection

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ABSTRACT

Objective: Safe removal of extensive liver tumor burdens depends on regeneration of the remnant liver, which requires a large amount of zinc over a short period of time. We studied how zinc influences regeneration.

Material and Methods: We measured perioperative serum zinc concentrations after liver cancer diagnosis in 77 patients undergoing hepatectomy to determine how serum zinc affected short-term outcomes and remnant liver regeneration.

Results: Serum zinc concentration at diagnosis showed no correlation with inflammatory or nutritional parameters except for a weak correlation with the lymphocyte-to-monocyte ratio. When patients were divided into a high pre-hepatectomy zinc group ($\geq 75 \mu\text{g/dL}$, $n = 39$, H group) and a low zinc group ($< 75 \mu\text{g/dL}$, $n = 38$, L group), short-term results such as mortality ($p > 0.999$), morbidity ($p = 0.490$), and hospital stay ($p = 0.591$) did not differ between groups. However, hypertrophy in the future liver remnant after hepatectomy in the H group ($127.7 \pm 24.7\%$ of original volume) was greater than in the L group ($115.9 \pm 16.7\%$, $p = 0.024$). In a subgroup of patients with extended hepatectomy, hypertrophy was $130.9 \pm 26.8\%$ in the H group vs. $116.4 \pm 16.5\%$ in the L group ($p = 0.037$).

Conclusion: Greater serum zinc at diagnosis was associated with greater hypertrophy in the future liver remnant.

Keywords: Zinc, hepatectomy, liver regeneration, nutritional parameters, short-term outcome

INTRODUCTION

Safe removal of an extensive liver tumor burden, a principal goal of hepatobiliary surgeons, largely depends on regeneration of the remnant liver after resection. Strong stimulation of hypertrophy in the remnant is indispensable. Multiple variables including the extent of liver resection (1-4), liver function (1,4-7), age (5), and hepatotrophic factors in portal blood (8,9) have been shown to influence liver regeneration after hepatectomy.

After partial hepatectomy, hepatocytes undergo a synchronized sequence of priming/initiation, proliferation, and growth termination. These steps are essential for the restoration of hepatic structure and function. Zinc, the second most prevalent trace element in the body, is essential for normal cell growth, development, and differentiation. A clinical role for zinc in wound healing was initially postulated in treating pilonidal sinuses (10). After investigators then reported depressed wound healing in zinc-deficient compared to zinc-sufficient experimental animals, zinc has taken on an important role in clinical wound healing (11,12). Hepatocyte regeneration after liver resection represents a form of wound healing that requires a large amount of zinc over a short period of time. This demand is partly met by the induction of a zinc and copper binding protein, metallothionein, during a priming phase soon after resection (13). Metallothionein can transfer zinc to various metalloenzymes and transcription factors, while metallothionein knockout mice show impaired liver regeneration (14). Thus, zinc is essential for liver regeneration.

We hypothesized that liver regeneration after partial hepatectomy for an extensive tumor burden could be enhanced by zinc supplementation. As a preliminary step, the present retrospective study examined the effect of pre-hepatectomy serum zinc concentrations on short-term clinical outcomes after hepatectomy and also the possibility of a relationship between serum zinc concentration and postoperative changes in remnant liver volume.

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MATERIAL and METHODS

Patients

We measured perioperative serum zinc concentration in 77 patients who underwent hepatectomy between April 2021 and December 2022 at the Department of General and Gastroenterological Surgery, Showa University Fujigaoka Hospital.

These patients included 47 males and 30 females; their median age was 69 years (range, 49 to 87). Histologic diagnoses in these patients were metastatic carcinoma, typically from a colorectal primary, in 38 (49.4%); hepatocellular carcinoma in 22 (28.6%); cholangiocarcinoma in four (5.2%); and biliary cancer in 10 (13.0%). Three patients had other histologic types of cancer (3.9%). Hepatectomy procedures were partial resection of a segment in 38 patients and resection of one segment or more in 39. Ten of the patients in the latter group were undergoing repeat hepatectomy for remnant liver disease.

In a manner described in a previous report, patients with low to intermediate serum zinc concentrations at time of liver tumor diagnosis were given an opportunity to receive an oral zinc supplement preoperatively (Novelzin, Novel Pharma, Tokyo, Japan) if they and their attending physicians chose (15). Patients' freedom to choose was particularly important because the supplement represented a significant out-of-pocket expense. Daily doses were 50 or 100 mg, based upon serum zinc concentrations at diagnosis.

Relationships Between Serum Zinc and Other Nutritional Parameters

Serum zinc concentrations at the time of diagnosis were examined for association with other inflammatory and nutritional parameters, specifically body mass index (BMI), Onodera prognostic nutritional index (PNI), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), C-reactive protein-to-albumin ratio (CAR), Glasgow prognostic score (GPS), modified GPS, and controlling nutritional status (CONUT) score (16-19). Parameters were calculated using the following formulas: BMI = body weight (kg)/[height (m)]²; PNI = 10 × serum albumin (g/dL) + 0.005 × lymphocyte count (/mm³); NLR = neutrophil count (/mm³)/lymphocyte count (/mm³); PLR = platelet count (/mm³)/lymphocyte count (/mm³); LMR = lymphocyte count (/mm³)/monocyte count (/mm³), and CAR = serum C-reactive protein (mg/dL)/serum albumin (g/dL). GPS, modified GPS, and CONUT scores were obtained according to previous reports (17-19).

Hepatectomy Procedures

The guiding principle of hepatectomy was assurance of tumor-free margins. Acceptability of a hepatectomy procedure for a

given patient was determined by a prediction score (PS) system introduced by Yamanaka and the predicted remnant liver indocyanine green (ICG) disappearance rate from plasma (KICG) (20-22). PS was calculated using the formula $-84.6 + 0.933 a + 1.11 b + 0.999 c$, where *a* was the resection fraction (%) calculated from computed tomographic (CT) volumetry; *b*, the ICG retention rate at 15 min; and *c*, the age of the patient. Remnant KICG (rem KICG) was calculated using the formula, $KICG \times [\text{estimated future liver remnant (FLR) volume} / \text{total estimated liver volume (TELTV)}]$. Both FLR volume and TELV were calculated based on CT volumetry as described in the next paragraph. A PS less than 50 and/or a rem KICG more than 0.05 indicated that a given hepatectomy would be acceptable.

Parenchymal dissection was performed using ultrasonic dissectors during either open or laparoscopic approaches. When necessary, the liver pedicle was clamped intermittently in cycles including 15 min of clamping and five min of reperfusion. The Brisbane 2000 terminology of the International Hepato-Pancreato-Biliary Association was used to designate operative procedures (23).

CT Volumetry

CT was performed with a scanner possessing 64 rows of detectors (Revolution Maxima or Discovery CT 750HD; GE, Fairfield, CT, US). After administering a contrast agent (Iopromide 370; Fujifilm Toyama Chemical, Tokyo, Japan), serial transverse scans were obtained from the dome of the liver to its most inferior extent using the following settings: 100 KV; Max 560 mA-sec (AutomA Noise Index, 10.5); section thickness/collimation, 5/0.625 mm; feed/rotation, 20.62 mm; rotation time, 0.4 sec; and reconstruction increment, 2.5 mm. Areas of interest in each slice of the liver were traced with a cursor, and the corresponding area was calculated by computer. The estimated FLR volume was calculated from data obtained prior to hepatectomy, and TELV was calculated from the data obtained before hepatectomy and one week after hepatectomy. Estimated FLR volume was calculated using the following formula: $\text{TELV before hepatectomy (mL)} - \text{estimated volume planned to be resected (mL)}$. When a hepatectomy procedure was altered intraoperatively because of newly detected tumor, technical difficulty in carrying out the planned procedure, or other reasons, estimated FLR volume was calculated as follows: $\text{TELV before hepatectomy (mL)} - \text{actual resected liver volume (mL)}$. The hypertrophy ratio in terms of liver volume corresponding to FLR after hepatectomy was calculated using the formula, $[\text{TELV one week after the procedure (mL)} / \text{volume of FLR before the procedure (mL)}] \times 100 (\%)$.

Short-Term Outcome

Postoperative patient outcomes were assessed using hepatectomy-related morbidities, mortality, and duration of

hospital stay. Grades of post-hepatectomy liver failure (PHLF) and bile leakage (BL) were based on the criteria of the International Study Group of Liver Surgery (ISGLS) (24,25). Morbidities were assessed according to the Dindo-Clavien classification (26).

Data Analysis

Statistical comparisons of baseline data were performed by the Mann-Whitney U test, the χ^2 test, or Fisher's exact test as appropriate. Correlations between two continuous variables was calculated by Spearman's rank correlation coefficient. A difference was considered significant when p had a value below 0.05.

Ethical Approval and Consent to Participation

The study protocol was approved by the Institutional Ethics Committee of Showa University, Japan (notice of IRB approval of protocol number, 2023-002-A). All patients included in this study provided informed consent for use of anonymous data through an opt-out methodology.

RESULTS

Serial Changes of Serum Zinc

At diagnosis, serum zinc concentration considering all patients (median with range) was 66 $\mu\text{g/dL}$ (24-142). Among the 77 participants, zinc was administered preoperatively to 50. Before

hepatectomy, median serum zinc concentration in those 50 patients increased to 75 $\mu\text{g/dL}$ (47-167); $p=0.002$ vs. the zinc concentration at diagnosis (Figure 1A). In 27 patients without preoperative administration of zinc, the concentration decreased from 66 $\mu\text{g/dL}$ (44-134) at diagnosis to 60 $\mu\text{g/dL}$ (4-134) before the operation ($p=0.056$) (Figure 1B). In the 50 patients with preoperative administration of zinc, serum zinc increased from 65 $\mu\text{g/dL}$ (24-142) to 75 $\mu\text{g/dL}$ (47-167, $p<0.001$) (Figure 1C).

Relationships Between Serum Zinc and Other Inflammatory/Nutritional Parameters

Possible relationships between serum zinc at diagnosis and other inflammatory and/or nutritional parameters were analyzed. No relationships were evident between serum zinc at diagnosis and other parameters such as BMI ($R=-0.005$, $p=0.963$), Onodera PNI ($R=0.014$, $p=0.902$), NLR ($R=-0.096$, $p=0.407$), PLR ($R=-0.028$, $p=0.809$), and CAR ($R=-0.022$, $p=0.853$). Only LMR showed a weak correlation with serum zinc concentration ($R=0.213$, $p=0.063$) (Figure 2).

Serum zinc concentration (median with range) of patients with a GPS of 0 ($n=65$) was 66.0 $\mu\text{g/dL}$ (42-142), while that of patients with GPS of 1 or 2 ($n=12$) was 66.5 $\mu\text{g/dL}$ (24-120, $p=0.911$). Serum zinc concentration of patients with modified GPS of 0 was 65.0 $\mu\text{g/dL}$ (42-134), while that of patients with modified

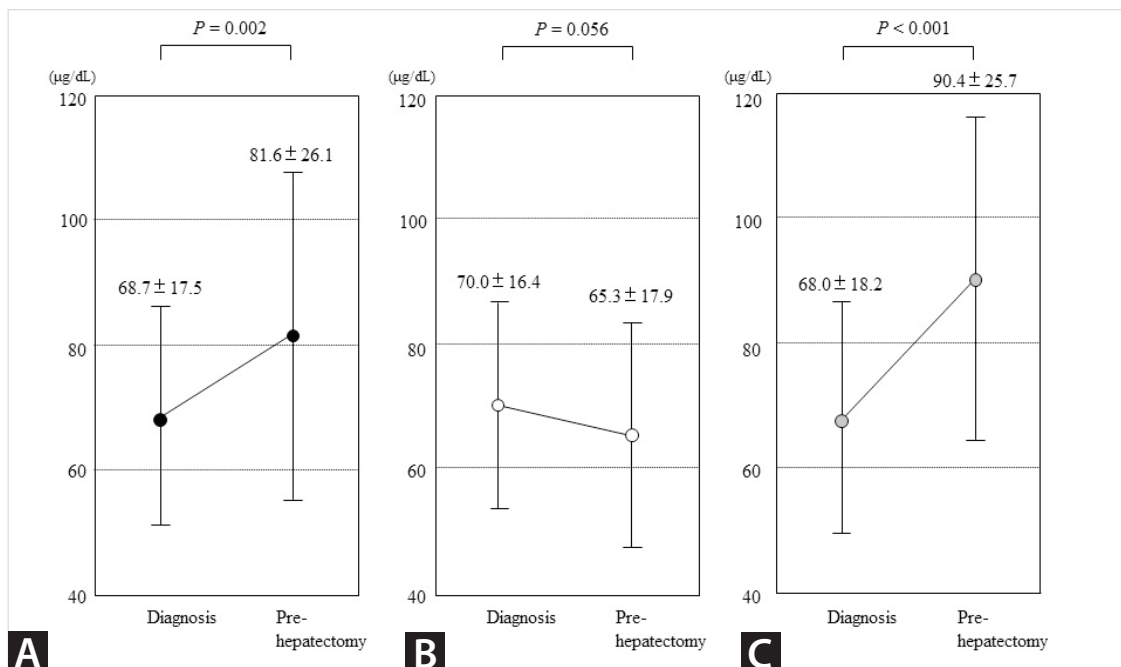


Figure 1. Changes in serum zinc concentration between serum samples taken at the time of liver cancer diagnosis and those taken shortly before hepatectomy. **A.** Considering all 77 patients in the study, serum zinc concentrations increased on average between these two time points ($p=0.002$). **B.** In the 27 patients without administration of zinc, serum zinc concentrations decreased during this period ($p=0.056$). **C.** In the 50 patients with administration of zinc, serum zinc concentrations increased ($p<0.001$).

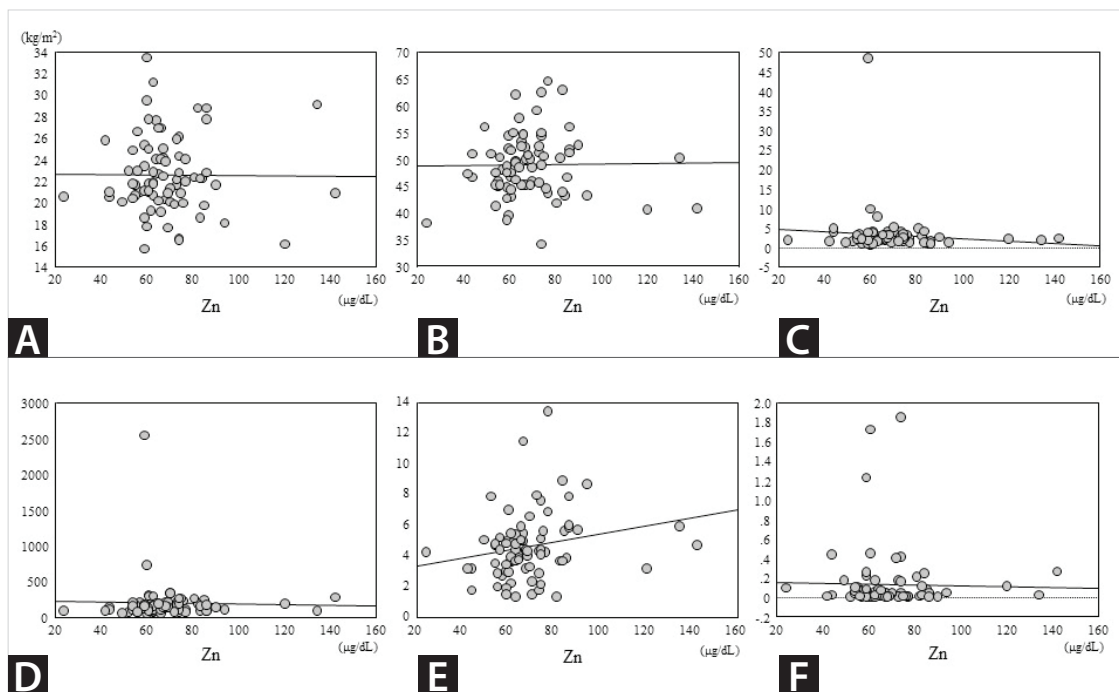


Figure 2. Scatter plots showed no relationships between zinc concentration at diagnosis and most other inflammatory or nutritional parameters. **A.** Body mass index (BMI), $R = -0.005$, $p = 0.963$. **B.** Onodera prognostic nutritional index (PNI), $R = 0.014$, $p = 0.902$. **C.** Neutrophil-to-lymphocyte ratio (NLR), $R = -0.096$, $p = 0.407$. **D.** PLR ($R = -0.028$, $p = 0.809$). **F.** CAR ($R = -0.022$, $p = 0.853$). **E.** Only LMR showed some correlation, though weak, with serum zinc at diagnosis ($R = 0.213$, $p = 0.063$).

GPS of 1 or 2 ($n = 20$) was $72.5 \mu\text{g/dL}$ (24-142, $p = 0.546$). Serum zinc concentrations (median with range) according to CONUT score were $64.5 \mu\text{g/dL}$ (44-134) in patients with a score of 0 ($n = 18$), $64.0 \mu\text{g/dL}$ (42-86) in those with a score of 1 ($n = 21$), $69.0 \mu\text{g/dL}$ (44-142) in those with a score of 2 ($n = 21$), $60.0 \mu\text{g/dL}$ (24-86) in those with a score of 3 ($n = 11$), and $73.0 \mu\text{g/dL}$ (59-120) in those with a score of 4 ($n = 5$). No relationship was evident between serum zinc and CONUT score.

When patients were divided into two groups defined by median serum zinc concentration at diagnosis, no difference was evident between the high-zinc group ($66 \mu\text{g/dL}$ or more) and the low-zinc group (less than $66 \mu\text{g/dL}$) in terms of Onodera PNI (median, 50.14; range, 34.11-64.5) vs. median, 47.54; range, 38.19-62.15; $p = 0.282$); NLR (median, 2.444; range, 1.018-5.206 vs. median, 2.229; range, 0.818-48.5; $p = 0.855$); PLR (median, 152.1; range, 63.6-345.8 vs. 147.45; range, 57.11-2542; $p = 0.457$); or CAR (median, 0.028; range, 0.002-1.852 vs. median, 0.03; range, 0.002-1.72; $p = 0.8625$).

Only for LMR was a difference evident between the high-zinc group (median, 4.464; range, 1.349-13.5) and the low-zinc group (median, 3.979; range, 1.389-7.956; $p = 0.045$).

Impact of Serum Zn Concentration on Short-Term Outcome

Patients were divided into two groups relative to the median pre-hepatectomy zinc concentration for all patients: a high-zinc group ($\geq 75 \mu\text{g/dL}$, $n = 39$; H group) and a low-zinc group

(<75 $\mu\text{g/dL}$, $n = 38$, L group). Demographic and clinical characteristics were comparable between groups (Table 1). The H group included more patients who received zinc supplementation before hepatectomy (36/39 or 92%) than did the L group (14/38 or 37%; $p < 0.001$). Although segmentectomy or more extensive liver resection tended to be performed more frequently in the H group (23/39 or 59%) than in the L group (16/38 or 42%; $p = 0.174$), no other differences concerning surgical details were observed between these groups.

Mortality occurred in one patient in the H group (2.6%; $p > 0.999$) from aspiration pneumonia. Considering both groups together, 43 nonfatal complications occurred in 36 patients, including grade A liver failure in 11, pulmonary embolism and/or deep vein thrombosis in seven, biliary complications in six, delirium in four, pneumonia in two, and others in 13. No difference in postoperative morbidity was evident between the groups ($p = 0.173$). In the L group, Clavien-Dindo grade 1 postoperative complications occurred in seven patients, grade 2 in 11, and grade 3a in three. In the H group, grade 1 complications occurred in three patients, grade 2, in eight, grade 3a in two, grade 3b in one, and grade 5 in one. Overall, the two groups showed no difference in grade of postoperative complications ($p = 0.498$). Hospital stay was comparable between the L group (13 days, 8-55) and the H group (12 days, 4-49; $p = 0.591$; (Table 2).

Table 1. Patient characteristics in low- and high-zinc groups

	Low zinc (n= 38)	High zinc (n= 39)	p
Patient-related			
Age in years	71.5 (49-87)	69 (50-86)	0.968
Sex			
Male	24	23	0.816
Female	14	16	
Disease			
Metastasis	18	20	0.909
HCC	10	12	
CCC	2	2	
Biliary cancers	6	4	
Others	2	1	
ICGR15, %	10.7 (3.1-41.24)	8.97 (3.21-35.85)	0.369
Pathologic F number			
0	1	5	0.390
1	26	23	
2	1	2	
3	1	1	
4	2	5	
(NA)	(7)	(3)	
Serum Zn, µg/dL			
At diagnosis of tumor	63 (24-86)	69 (42-142)	0.055
Preoperative	62.5 (47-74)	99 (75-167)	<0.001
Treatment-related			
Zn administration	14	36	<0.001
Extent of hepatectomy			
Partial	22	16	0.224
Segment	3	1	
Two segments	0	3	
Section	9	11	
Hemiliver	4	7	
Trisection	0	1	
Surgical approach			
Open	23	26	0.640
Laparoscopic	15	13	
Duration of operation, min	415 (176-653)	440 (168-727)	0.935
Blood loss, mL	255 (0-740)	200 (0-1086)	0.192

Zn: Zinc, HCC: Hepatocellular carcinoma, CCC: Cholangiocarcinoma, Ca: Cancer, ICGR15: Indocyanine green retention rate at 15 minutes, NA: Not available.

Table 2. Short-term outcome

	Low zinc (n= 38)	High zinc (n= 39)	p
Morbidity	21 (55.3%)	15 (38.5%)	0.173
Clavien-Dindo class			
1	7	3	0.498
2	11	8	
3a	3	2	
3b	0	1	
5	0	1	
Details of complications			
Liver failure, grade A	8	3	0.072
PE/DVT	5	2	
Biliary-related complications	5	1	
Delirium	3	1	
Pneumonia	1	1	
Others	3	10	
Mortality	0	1 (2.6%)	>0.999
Hospital stay, days	13 (8-55)	12 (4-49)	0.591

PE: Pulmonary embolism, DVT: Deep vein thrombosis.

Impact of Preoperative Serum Zinc Concentration on Volumetrically Measured Hypertrophy of the Future Liver Remnant

Hypertrophy ratio in terms of liver volume corresponding to FLR after hepatectomy (TELV at postoperative week 1/FLR volume before resection $\times 100$) was $127.7 \pm 24.7\%$ in the H group (median 122.5%, range 88.9 to 200.7%) and $115.9 \pm 16.7\%$ in the L group (115.2%, 91.0-157.4). Hypertrophy ratio in the H group was greater than in the L group ($p = 0.024$) (Figure 3A). When hypertrophy ratios were compared within subgroups defined by extent of resection, hypertrophy ratios were similar between H and L groups among patients who underwent partial resection: (L group, mean \pm SD, $115.6 \pm 17.2\%$; median with range, 110.2%, 9-152.4%; H group, $122.2 \pm 20.5\%$ and 122.2% , 88.9% to 152.3%; $p = 0.450$) (Figure 3B). Among the patients who underwent extended resections with segmentectomy or resections of greater extent, hypertrophy ratio was greater in the H group ($130.9 \pm 26.8\%$; 122.5% , 96.2 to 200.7) than in the L group ($116.4 \pm 16.5\%$; 115.6% , 91.4 to 157.4; $p = 0.037$) (Figure 3C).

According to CT volumetry-based calculations of actual liver volume in all patients, FLR volume before hepatectomy in the H group was smaller than in the L group (H group, 784.9 ± 240.3 vs. 935.5 ± 225.8 in the L group, $p = 0.016$) (Figure 4A). However, liver resection rate calculated as (resected liver volume/TELV before hepatectomy) $\times 100$ (%) did not differ between the L group ($19.7 \pm 15.3\%$) and the H group ($26.5 \pm 20.1\%$; $p = 0.17$). In

the subgroup of patients who underwent extended resection, a similar tendency was observed (699.3 ± 241.7 in the H group vs. 878.6 ± 189.4 in the L group, $p = 0.019$) (Figure 4C), while TELV one week after resection did not differ between H and L groups (Figure 4).

DISCUSSION

Time intervals between serum sampling for zinc measurement at diagnosis and at sampling at time of hepatectomy did not differ between patients who received zinc supplementation (22.5 ± 12.5 days) and those who did not (39.4 ± 38.7 , $p = 0.172$). However, serum zinc gradually decreased during the preoperative period in patients without zinc supplementation, possibly reflecting tumor burden, stress related to preoperative examinations, and treatments preceding hepatectomy such as chemotherapy. This suggests that zinc supplementation during the preoperative period would be desirable.

Zinc deficiency has several possible clinical manifestations including skin lesions, poor wound healing, altered mental status, and altered immune function (27). Zinc also is essential for cell differentiation and protein synthesis, which involve various metalloenzymes such as DNA polymerase and RNA polymerase. We therefore considered whether serum zinc concentration could affect such inflammatory and nutritional parameters as blood cell counts and determinations of serum proteins such as albumin and C-reactive protein. However, serum zinc concentrations showed no relation with these variables. Serum zinc also showed no influence on GPS or CONUT scores.

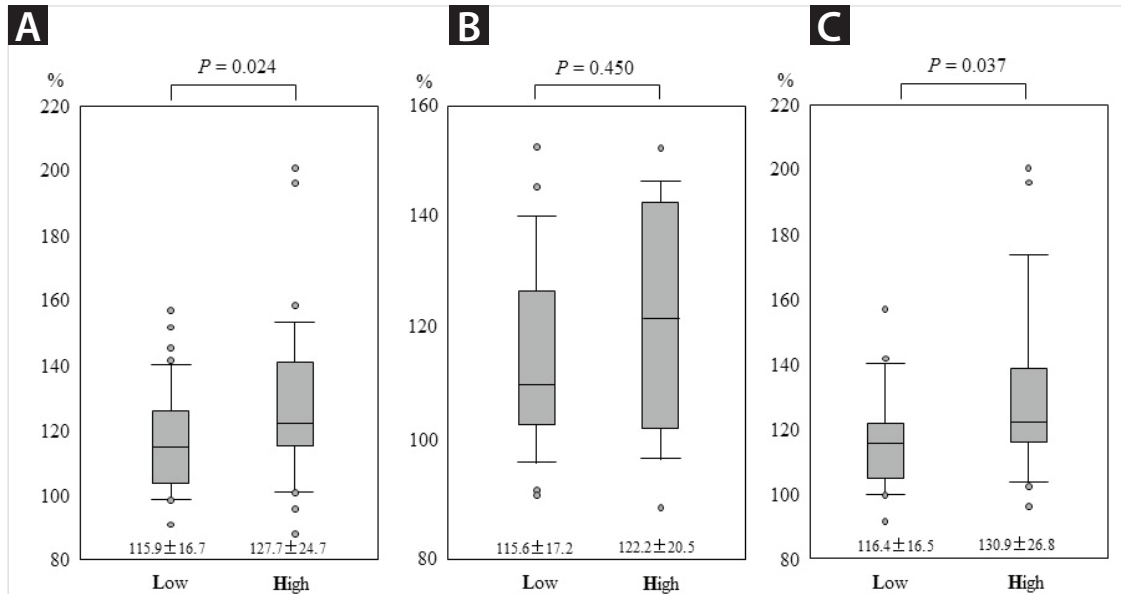


Figure 3. Hypertrophy ratio of future liver remnant volume after hepatectomy. **A.** Considering all patients, the hypertrophy ratio in patients with high serum zinc (H group) was greater than in those with a low zinc concentration (L group, $p=0.024$). **B.** Among patients with partial resection, hypertrophy ratios were similar between groups ($p=0.450$). **C.** Among extended resections including segmentectomy or more, the hypertrophy ratio was greater in the H group than in the L group ($p=0.037$).

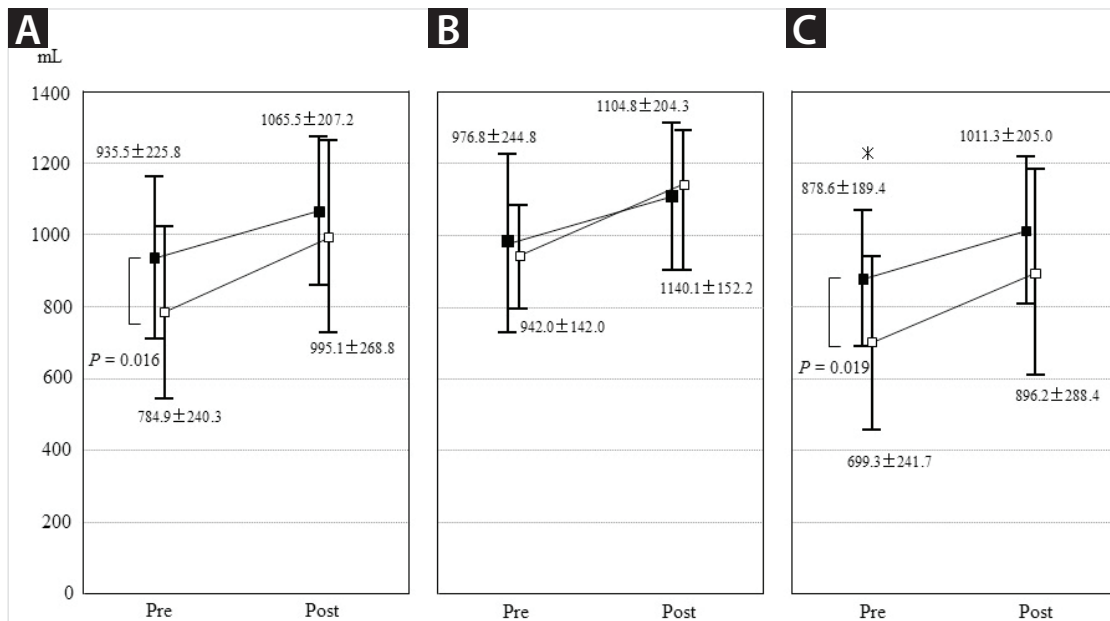


Figure 4. Future liver remnant volume at time of surgery (Pre) and one week later (Post). **A.** Considering all patients, future liver remnant (FLR) volume in patients with high serum zinc concentrations (H group, unfilled squares) was smaller preoperatively than in patients with low zinc (L group, black squares; $p=0.016$), with no significant difference in volume one week later. **B.** Considering patients with partial resection, no difference in FLR volume was evident between zinc-defined groups at either time point. **C.** Among patients with extended resection, preoperative FLR volume in the H group was smaller than in the L group ($p=0.019$). Total estimated liver volume one week after resection was not different between H and L groups, regardless of the extent of resection.

Further, when patients were divided into two groups according to serum zinc concentration at diagnosis, no differences in inflammatory/nutritional parameters between the groups were apparent except for LMR. Short-term results included no differences of morbidity, mortality, or hospital stay related to patients' pre-hepatectomy serum zinc concentrations.

LMR is a proposed systemic inflammatory marker that has been investigated as a prognosticator in patients with solid tumors; a low lymphocyte count might suggest a diminished immunologic reaction against the tumor, while tumor-associated macrophages, which are derived from circulating monocyte populations, have been reported to favor tumor progression (28,29). Accordingly, a low LMR generally suggests a poor prognosis. Metallothionein mRNA has been reported to rapidly increase in mononuclear cells upon consumption of a zinc supplement, and metallothionein expression appears related to zinc accumulation in various organs (30,31). Although relationships between serum zinc concentration and LMR remain unclear, changes in serum zinc may affect inflammatory/nutritional status, especially in patients with a substantial tumor burden.

Liver hypertrophy ratio in terms of liver volume corresponding to the FLR after hepatectomy was greater in patients with high preoperative serum zinc concentrations than in those with low serum zinc, which suggests that in some way zinc contributes to liver regeneration after hepatectomy. Shortly after injury, regenerating cells require large amounts of zinc; to meet this requirement, metallothionein is induced. Mocchegiani et al. have reported that plasma zinc concentrations are reduced at 24 h and 48 h after a surgical procedure (32). Partial hepatectomy reduces plasma zinc concentrations during the early postoperative period (24 to 48 hours), when it is needed for compensatory liver growth. Later in the period of compensatory liver growth (7th to 15th days), zinc balance is restored to positivity, accompanied by normalization of serum zinc concentration. Further, liver concentrations of metallothionein, which correlate with zinc accumulation, are increased at 24 and 48 hours after hepatectomy (31). In normal human liver, zinc is the predominant metal bound to metallothionein (33). Several reports present details of zinc transfer of metallothioneins to various metalloenzymes and transcription factors. Cellular metallothionein turnover and accumulation are directly linked to zinc availability (31). To summarize, adequate serum zinc concentrations are highly important during the early stages of remnant liver regeneration (34).

Various reports have estimated the time needed for complete restoration of liver volume after hepatectomy as two to six months (35-38). Differences in time requirement between reports may reflect methods of observation, extent of resection, and presence and nature of coexisting liver disease. After an intermediate or large resection, 90% or more of initial volume

was found to be regained within one to three months in livers without additional coexisting disease, while livers with coexisting pathology attained only 70% to 80% of initial volume after two to five months (1). In our present study, background liver fibrosis graded according to Japanese general rules for clinical and pathologic study of primary liver cancer represented only F0 or F1 in at least 70% of patients in both zinc-defined groups, showing no intergroup difference (39). A functional parameter, the ICGR15 value, also was comparable between our H and L groups. We evaluated regenerative liver volume soon after surgery because zinc should influence regeneration most conspicuously during the early period, while background liver status might have more confounding effect at a later time. According to our results, more hypertrophy was observed in patients with high preoperative serum zinc concentrations than in those with lower concentrations, especially when a hepatic segment or more was resected, which suggests that high serum zinc had a positive effect on liver regeneration. Liver regeneration after hepatectomy has been found to be influenced by extent of resection. Residual liver volume immediately following hepatectomy was smaller in the H group than in the L group, while TELV one week after resection was similar between these groups. The difference in liver hypertrophy in terms of liver volume corresponding to FLR after hepatectomy therefore could have been influenced by differences in extent of liver resection between groups. However, while liver resection ratio relative to whole-liver volume was similar between the L and H groups, the actual residual liver volume after hepatectomy was smaller in the H than the L group. Therefore, the stimulus for postoperative liver hypertrophy might have been equally intense in both groups. Comparisons involving larger numbers of patients might resolve the uncertainty.

CONCLUSION

Serum zinc influenced remnant liver hypertrophy independently of previously reported nutritional and inflammatory markers. Although preoperative serum zinc concentration had no impact on short-term outcome, it appeared to affect liver regeneration in the period immediately following liver resection, including in patients with extended resections.

Ethics Committee Approval: This study was approved by Showa University Ethics Committee (Approval no: 2023-002-A, Date: 13.04.2023).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - KT; Design - KT; Supervision - KT; Data Collection and/or Processing - YT, HO, AN, YM; Analysis and/or Interpretation - YT, HO, YM; Literature Review - KT; Writer - YT, KT; Critical Review - KT.

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

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ORJİNAL ÇALIŞMA-ÖZET

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Çinko kısmi rezeksiyon sonrası karaciğer rejenerasyonunu destekler

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ÖZET

Giriş ve Amaç: Kapsamlı karaciğer tümörü yükünün güvenli bir şekilde ortadan kaldırılması, kısa bir süre içinde büyük miktarda çinko gerektiren kalan karaciğerin yenilenmesine bağlıdır. Çinkonun yenilenmeyi nasıl etkilediğini inceledik.

Gereç ve Yöntem: Serum çinkonun kısa vadeli sonuçları ve kalan karaciğer rejenerasyonunu nasıl etkilediğini belirlemek için hepatektomi geçiren 77 hastada karaciğer kanseri tanısı sonrasında perioperatif serum çinko konsantrasyonlarını ölçtük.

Bulgular: Teşhis anındaki serum çinko konsantrasyonu, lenfosit/monosit oranı ile zayıf bir korelasyon dışında enflamatuvar veya beslenme parametreleriyle hiçbir korelasyon göstermedi. Hastalar hepatektomi öncesi yüksek çinko grubuna ($\geq 75 \mu\text{g/dL}$, $n=39$, H grubu) ve düşük çinko grubuna ($< 75 \mu\text{g/dL}$, $n=38$, L grubu) ayrıldığında, kısa dönem sonuçlar mortalite ($p>0,999$), morbidite ($p=0,490$) ve hastanede kalış ($p=0,591$) gibi değerler gruplar arasında farklılık göstermedi. Bununla birlikte, H grubunda hepatektomi sonrası gelecekte oluşacak karaciğer kalıntısındaki hipertrofi (orijinal hacmin $127,7 \pm 24,7\%$ 'si), L grubuna göre daha fazlaydı ($115,9 \pm 16,7\%$, $p=0,024$). Genişletilmiş hepatektomili hasta alt grubunda hipertrofi H grubunda $130,9 \pm 6,8\%$ iken L grubunda $116,4 \pm 16,5\%$ idi ($p=0,037$).

Sonuç: Tanı anında daha yüksek serum çinkosu, gelecekteki karaciğer kalıntısında daha fazla hipertrofi ile ilişkiliydi.

Anahtar Kelimeler: Çinko, hepatektomi, karaciğer rejenerasyonu, beslenme parametreleri, kısa vadeli sonuç

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Laparoscopic gastrectomy for gastric cancer: A single cancer center experience

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ABSTRACT

Objective: Laparoscopic gastrectomy (LG) was challenging to most surgeons due to the two-dimensional view, difficult manipulations of the instruments, ergonomic discomfort, and the associated muscular spasm and effort. Technological advances with improved surgical experience, have made LG a more feasible and favorable approach for gastric cancer (GC) patients.

Material and Methods: LG was performed in 44 patients with GC between July 2015 to June 2022, in the Department of Surgical Oncology, Oncology Center, Mansoura University, Egypt, and we assessed the surgical outcomes of this approach as an initial experience of a single cancer center.

Results: Twenty-seven patients underwent laparoscopic distal gastrectomy, and seventeen underwent laparoscopic total gastrectomy. Two cases had combined resection. Operative time was 339.2 ± 76.73 min, while blood loss was 153.86 ± 57.51 mL. The patients were ambulant on postoperative day 0, oral intake was started within three days (range 1-5 days) and the hospital stay was six days (range 3-9 days).

Conclusion: LG for GC is a feasible approach for both early and advanced GC patients as it allows for adequate diagnosis of the peritoneal disease, meticulous dissection, and identification of the lymph nodes with minimal blood loss and decrease surgery-related problems and encourage the early patients' discharge from hospital and return to daily life activities.

Keywords: Laparoscopic gastrectomy, gastric cancer, minimally invasive surgery

INTRODUCTION

Gastric cancer (GC) incidence is considered the sixth most common cancer worldwide and the third one regarding cancer mortality (1). Gastrectomy and D2 lymphadenectomy remain the main line of treatment of GC patients despite the progress in the investigations of the molecular nature of GC and the development of many targeted treatments (2). Laparoscopic gastrectomy (LG) for GC was first performed by Kitano et al. in 1994, and since then, this approach has been used worldwide due to its unique features (3). LG has numerous advantages including minimal blood loss, decrease in postoperative pain, early return of bowel function, and daily activity that leads to short hospital stay (4,5).

LG was challenging to most surgeons due to the two-dimensional view, difficult instrumental manipulations, ergonomic discomfort, and the associated muscular effort (6). The advances in the instruments and improved surgical experience have encouraged surgeons to practice LG in early GC patients (7). Many studies from Asia have reported LG with favorable surgical outcomes as there is a high incidence of early GC due to the well-established nationwide screening program (8). GC frequency in Western countries is less than in Asian countries, and it is diagnosed mostly at a locally advanced stage. Therefore, the reports on LG for GC in Western countries are very few (9,10).

There are randomized controlled trials from multiple Eastern centers that have reported the feasibility and efficacy of LG in early GC patients (11,12). Moreover, few Western randomized controlled trials compared laparoscopic and open gastrectomy (13). These clinical trials have reported the same long-term outcomes of both laparoscopic and open gastrectomy, which made LG a popular approach in the surgical treatment of GC patients (14). The present study aimed to demonstrate the surgical feasibility and the safety of LG as a minimally invasive technique for GC patients in a single cancer center.

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MATERIAL and METHODS

Study Design

Between July 2015 and June 2022, 44 patients with GC underwent LG in the Department of Surgical Oncology, Oncology Center, Mansoura University. This study was approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Mansoura University with a code number (R.22.02.1613). The procedure and its possible complications were explained and instructed to all patients in this study, and written informed consent was obtained from them before surgery. We included, in this study, any patients with operable GC without preoperative evidence of abdominal or distant metastasis. At the same time, we excluded stage IV GC patients, those with previous gastric surgery, need emergent gastrectomy for bleeding or perforation, and unfit patients for general anesthesia or laparoscopic surgery. All patients had upper gastrointestinal endoscopy for tumor localization and pathological confirmation, a computed tomography scan for accurate tumor staging, and endoscopic ultrasound for primary tumor invasion and regional lymph node assessment. Neoadjuvant and adjuvant chemotherapy was offered to the patients according to National Comprehensive Cancer Network (NCCN) guidelines. The 8th edition of the American Joint Committee on Cancer TNM Staging System for GC was used for tumor staging (15). The patients' baseline criteria were reported including age, sex, body mass index, and the American Society of Anesthesiologists (ASA) score.

Surgical Procedures

All patients were operated on in a supine position with slight head elevation (reverse Trendelenburg position) and legs

separated where the main operator stood. The assistant position was on the left side of the patient while the endoscopist position was on the right side of the patient. After pneumoperitoneum, a 30° rigid electro-laparoscope was inserted through a (10 mm) trocar in the supra or infra-umbilical region. Additional four trocars were inserted; a (10 mm) trocar was placed in the left side of the patient in the midclavicular line about 3 cm above the umbilicus level and a (5 mm) trocar was placed in the same location on the patient's right side. Two (5 mm) trocars were placed in the pre-axillary line on both sides below the costal margin by about 2 cm. An additional epigastric (10 mm) trocar for the liver retractor was applied (Figure 1).

Preoperative staging laparoscopy was done with peritoneal lavage for the assessment of presence of any tumor cells (CYT + was considered M1 disease). LG with D2 lymphadenectomy was done using the harmonic scalpel (by Ethicon™) or Ligasure (by Covidien™) as recommended by the Japanese Gastric Cancer Association (Figure 2) (16). Reconstruction was done in the form of Billroth type II gastrojejunostomy and entero-enterostomy or Roux-en-Y gastrojejunostomy in cases of laparoscopic distal gastrectomy (LDG) and functional side-to-side esophagojejunostomy in cases of laparoscopic total gastrectomy (LTG) using articulating laparoscopic linear stapler (Echelon® flex 60 mm).

Study Outcomes

Operative data including operative time, type of gastrectomy, methods of reconstruction, and estimated blood loss were collected. Short-term outcomes such as ambulation, oral intake, ICU, hospital stay, and associated postoperative complications were reported. Long-term outcomes were evaluated along with overall survival (OS) and disease-free survival (DFS).



Figure 1. Trocars placement with epigastric liver retractor.

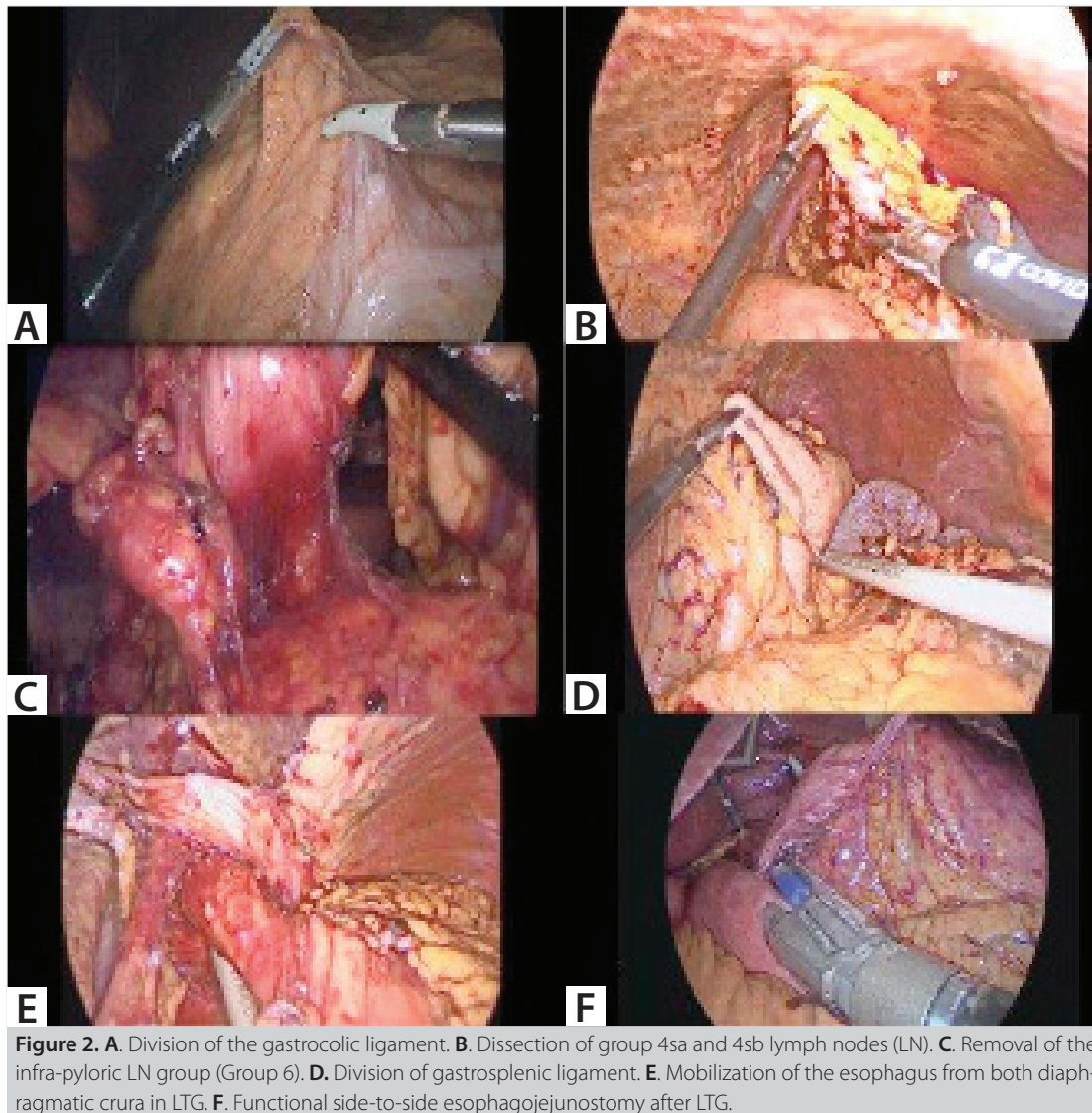


Figure 2. A. Division of the gastrocolic ligament. B. Dissection of group 4sa and 4sb lymph nodes (LN). C. Removal of the infra-pyloric LN group (Group 6). D. Division of gastrosplenic ligament. E. Mobilization of the esophagus from both diaphragmatic crura in LTG. F. Functional side-to-side esophagojejunostomy after LTG.

Statistical Analysis

The Statistical Package for Scientific Studies (SPSS) v26.0 (IBM Corp., Chicago, IL, USA) on MacOS v11.9 was used for data analysis. Qualitative data were described using numbers and percentages. Quantitative data were described using medians for non-parametric data and means and standard deviation (SD) for parametric data, after testing normality using the Kolmogorov-Smirnov test. Kaplan-Meier method was used for OS and DFS.

RESULTS

Clinicopathological Characteristics

The patients' mean age in the current study was 52.82 ± 12.59 years (Table 1), and the BMI had a mean of 32.82 ± 3.81 kg/m².

Female was the common sex (59.1%) and (79.5%) had an ASA score of I. Nine patients had comorbidities while 21 patients had previous abdominal surgeries. The lower part of the stomach was the most common tumor location in 28 patients, and it was of diffuse type in 34 patients. The gross appearance of the tumor was mostly type II according to Borrmann classification in (38.6%) of the patients and type III in (31.8%) of the patients, cT2, cT3, and cT4a were found in (22.7%, 27.3%, and 29.5%, respectively) and (47.7%) of the patients had a node-positive tumor. Neoadjuvant chemotherapy was given to 26 patients according to NCCN guidelines.

Table 1. Patients' demographics who underwent laparoscopic gastrectomy for gastric cancer

	Patients, n= 44 (%)
Age, years (mean \pm SD)	52.82 \pm 12.592
BMI, kg/m ² (mean \pm SD)	32.82 \pm 3.817
ASA score	
I	35 (79.5%)
II	9 (20.5%)
Sex	
Male	18 (40.9%)
Female	26 (59.1%)
Comorbidities	
None	35 (79.5%)
Hypertension	3 (6.8%)
Diabetes	1 (2.3%)
Hepatic	4 (9.1%)
Combined	1 (2.3%)
Complaint	
Dyspepsia	26 (59.1%)
Vomiting	10 (22.7%)
Bleeding	8 (18.2 %)
Previous abdominal surgeries	
No	23 (52.3%)
Appendectomy	4 (9.1%)
Umbilical hernioplasty	3 (6.8)
Caesarean section	8 (18.2)
Cholecystectomy	2 (4.6)
Incisional hernia	1 (2.3%)
Exploration for perforated DU	1 (2.3%)
Ureteric stone extraction	2 (4.6%)
Tumor location	
Upper	8 (18.2%)
Middle	8 (18.2%)
Lower	28 (63.6%)
Tumor differentiation	
Moderate differentiated	24 (54.5%)
Poor differentiated	19 (43.2%)
Undifferentiated	1 (2.3%)
Lauren classification	
Diffuse	34 (77.3%)
Intestinal	10 (22.7%)
Borrmann classification	
I	5 (11.4%)
II	17 (38.6%)
III	14 (31.8%)
IV	8 (18.2%)

Table 1. Patients' demographics who underwent laparoscopic gastrectomy for gastric cancer (continue)

	Patients, n= 44 (%)
cT stage	
T1a	4 (9.1%)
T1b	4 (9.1%)
T2	10 (22.7%)
T3	12 (27.3%)
T4a	13 (29.5%)
T4b	1 (2.3%)
cN stage	
Negative	23 (52.3%)
Positive	21 (47.7%)
Neoadjuvant chemotherapy	
No	18 (40.9%)
Yes	26 (59.1%)
The regimens of neoadjuvant chemotherapy	
ECF	18 (69.2%)
FLOT	6 (23.1%)
Fluorouracil/Cisplatin	2 (7.7%)
Tumor size at diagnosis (cm; mean \pm SD)	3.08 \pm 1.460

BMI: Body mass index, ASA: American Society of Anesthesiology, ECF: Epirubicin/Cisplatin/Fluorouracil, FLOT: Fluorouracil/Leucovorin/Oxaliplatin/Docetaxel.

Surgical and Short-Term Outcomes

Twenty-seven patients had LDG with Billroth type II gastroduenostomy and entero-enterostomy or Roux-en-Y gastroduenostomy, and 17 patients had LTG with functional side-to-side esophagojejunostomy (Table 2). There was combined resection in two cases (one patient had a splenectomy and one patient had a splenectomy and distal pancreatectomy). Mean operative time was 339.2 ± 76.73 min, estimated blood loss was 153.86 ± 57.51 mL, and 12 patients needed intraoperative blood transfusion. We had three cases with intraoperative complications (two cases with intraoperative bleeding and one case with colonic injury). Conversion to laparotomy was done in the two cases of intraoperative bleeding. The patients were ambulant on postoperative (POD) zero, ICU stay had a median duration of 1.5 days (range 1-5 days), oral intake was started in a median duration of three days (range 1-5 days), and hospital stay was six days (range 3-9 days). In this study, 18 patients had grade II postoperative complications according to Clavien and Dindo (CD) classification (seven cases with total parenteral nutrition, six cases with blood transfusion, two cases with postoperative antibiotics, two cases with pneumonia, and one case with hypertension). Four cases had postoperative complication grade III (two cases with abdominal collection, one case with pleural effusion, and one case with the biliary leak which was treated conservatively). Regarding 30-day mortality, we had only one case due to atrial fibrillation on POD 5.

Histopathological Characteristics

Postoperative pathological tumor size was 4.59 ± 2.14 cm while the mean number of lymph nodes (LN) dissected was 21.55 ± 4.33 and the number of positive lymph nodes was 4.89 ± 5.3 . Most of the tumors in this study were poorly differentiated adenocarcinoma (56.8%) (Table 3). Lymphovascular and perineural invasion were found in 31.8% and 36.4%, respectively. Pathological T3 and T4a stages were the commonest and found in 43.2% vs 34.1% while the pathological N1, N2, and N3 stages were found in 31.8%, 20.5%, and 29.5% respectively. Omental infiltration was found in four cases, infiltrated proximal margin was in one case, and infiltrated distal margin was in two cases.

Long Term Outcomes

Median duration of follow-up in this study was 42 months (range 9-86 months). Thirty-two patients in the current study received adjuvant chemotherapy and five patients received adjuvant radiotherapy (Table 4). Mean duration of DFS was 59.62 ± 5.44 months (Figure 3), and tumor recurrence developed in 13 patients in the form of (four cases with a peritoneal disease, seven cases with hematogenous metastasis, one case with local recurrence and one case with port-site recurrence). Treatment of recurrent cases included (chemotherapy in 11 cases, radiotherapy in one case, and surgical resection in one case). Mean OS of the patients was 62.41 ± 5.19 months (Figure 4).

Table 2. Surgical characteristics of the patients who underwent laparoscopic gastrectomy for gastric cancer

	Patients, n= 44 (%)
Type of gastrectomy	
Distal	27 (61.4%)
Total	17 (38.6%)
Combined resection	
No	42 (95.5%)
Yes	2 (4.5%)
Reconstruction	
Billroth type II and entero-enterostomy	9 (20.5%)
Roux-en-Y gastrojejunostomy	18 (40.9%)
Functional side-to-side esophagojejunostomy	17 (38.6%)
Conversion rate	
No	42 (95.5%)
Yes	2 (4.5%)
Operation time (min; mean \pm SD)	339.20 \pm 76.735
EBL (mL; mean \pm SD)	153.86 \pm 57.515
Blood transfusion	
No	32 (72.7%)
Yes	12 (27.3%)
Operative complications	
No	41 (93.2%)
Yes	3 (6.8%)
POP complications (CD classification)	
CD I	21 (47.7%)
CD II	18 (40.9%)
CD III	4 (9.1%)
30-day mortality	
No	43 (97.7%)
Yes	1 (2.3%)
Ambulation (days; median, range)	0 (0-3)
Oral intake (days; median, range)	3 (1-5)
ICU stay (days; median, range)	1.5 (1-5)
Hospital stay (days; median, range)	6 (3-9)
EBL: Estimated blood loss, POP: Postoperative, CD: Clavien-Dindo.	

DISCUSSION

LG for GC is considered a widely accepted therapeutic option due to its superiority in decreasing intraoperative blood loss, reducing postoperative pain, and complications that lead to short hospital stay (17,18). There is a meta-analysis that has demonstrated the advantages of LG compared to open gastrectomy regarding surgical and oncological outcomes (19,20). LG for GC has been recently used in multiple centers worldwide due to the improvement in surgical experience, innovation of the equipments, and promotion of laparoscopic surgeries by many academic organizations (21). We conducted

this approach in our center to evaluate the surgical and oncological outcomes of this minimally invasive approach to our patients with GC.

In the current study, the patients had a mean age of 52.82 years, and 59.1% were female, which was a statistical finding, not a selection criterion, while another study reported patients with a mean age of 61 years and were male in 62.6 % (22). The mean BMI of our patients was high 32.82 kg/m² and the patients had large and thick greater omentum that made infracolic omentectomy and the associated lymphadenectomy difficult, the BMI of patients in Inokuchi et al was 21.9 kg/m² (23).

Table 3. Histopathological characteristics of the gastric cancer resected

	Patients, n= 44 (%)
Tumor size (cm; mean \pm SD)	4.59 \pm 2.141
The mean number of LN dissected \pm SD	21.55 \pm 4.332
The mean number of positive LN \pm SD	4.89 \pm 5.306
Tumor Differentiation	
Well-differentiated	2 (4.5%)
Moderate differentiated	17 (38.6%)
Poorly differentiated	25 (56.8%)
Lymphovascular invasion	
Absence	30 (68.2%)
Present	14 (31.8%)
Perineural invasion	
Absence	28 (63.6%)
Present	16 (36.4%)
Omental infiltration	
Negative	40 (90.9%)
Positive	4 (9.1%)
Proximal margin	
Free	43 (97.7%)
Infiltrated	1 (2.3%)
Distal margin	
Free	42 (95.45%)
Infiltrated	2 (4.55%)
Pathological T stage	
pT2	9 (20.5%)
pT3	19 (43.2%)
pT4a	15 (34.1%)
pT4b	1 (2.3%)
Pathological N stage	
pN0	8 (18.2%)
pN1	14 (31.8%)
pN2	9 (20.5%)
pN3	13 (29.5%)

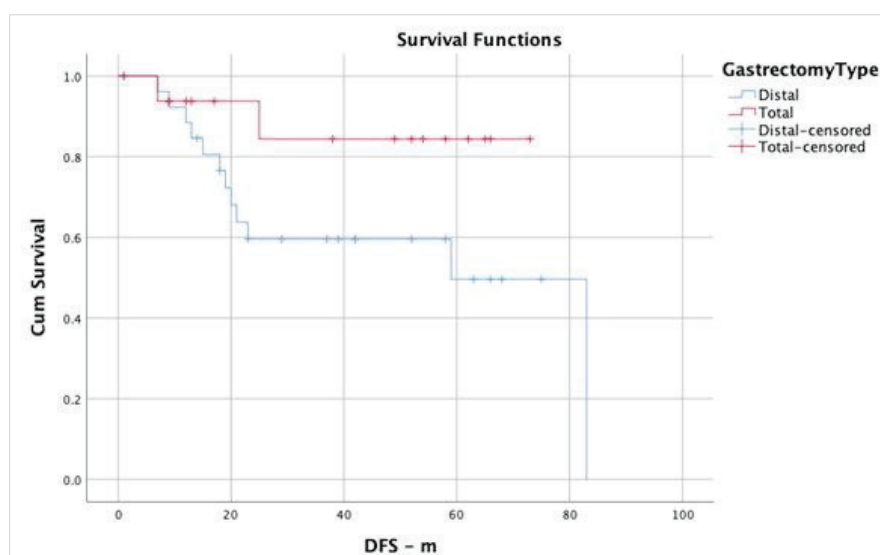
LN: Lymph node.

Tumor location in our study was commonly in the distal part of the stomach and that was comparable to another study (63.6% vs. 62.7%), so most of the patients underwent distal gastrectomy (24). Approximately 81.8% of the patients in this study had cT staging $>cT1$, and 47.7% of the patients had node-positive tumors. Therefore, 59.1% of the patients received neoadjuvant chemotherapy according to NCCN guidelines for improving surgical and oncological outcomes. Another study reported cT staging $>cT1$ in 93.1%, and 43.5% had node-positive tumors, so preoperative treatment was delivered in 67% of their patients (25). Of the 44 patients; 27 patients had distal gastrectomy with

Billroth type II gastrojejunostomy and entero-enterostomy or Roux-en-Y gastrojejunostomy, and 17 patients had total gastrectomy with functional side-to-side esophagojejunostomy as it was a more familiar method for reconstruction in our center. Combined organ resection in the form of splenectomy in one case and splenectomy with distal pancreatectomy in another case were due to the associated lymphadenectomy in the former case and tumor infiltration in the latter one. Another literature has reported associated splenectomy in nine cases (23).

Table 4. The patients' follow-up data

	Patients, n= 44 (%)
Adjuvant chemotherapy	
No	12 (27.3%)
Yes	32 (72.7%)
Adjuvant radiotherapy	
No	39 (88.63%)
Yes	5 (11.36%)
Overall survival (months; mean \pm SD)	62.41 \pm 5.194
Disease-free survival (months; mean \pm SD)	59.62 \pm 5.449
Tumor recurrence	
No	31 (70.5%)
Yes	13 (31.8%)
Type of recurrence	
No	31 (70.5%)
Peritoneal	4 (9.1%)
Hematogenous	7 (15.9%)
Local	1 (2.3%)
Port-site	1 (2.3%)
Treatment of recurrence	
Chemotherapy	11 (25%)
Radiotherapy	1 (2.3%)
Surgical resection	1 (2.3%)

**Figure 3.** Kaplan-Meier curve of DFS of patients who underwent LG for GC.

Operative duration in this study was 339.2 min, with about 153.86 mL as EBL, another study had a shorter operative time of about 237 min with an EBL of 36.9 mL (26). This was because they had only four cases of LTG while we had 17 cases who underwent total gastrectomy besides the BMI of our patients was high with prolonged duration of the omentectomy and lymphadenectomy, and 21 patients in this study had previous

abdominal surgeries with extensive adhesions. At the beginning of this case series, we tried to improve the learning curve of this approach, therefore the operative time was decreased in the subsequent cases. We experienced a conversion to open gastrectomy due to uncontrolled bleeding in two cases with hepatic diseases with large omental varices. Similarly, Obama et al. had reported conversion to open gastrectomy in one case

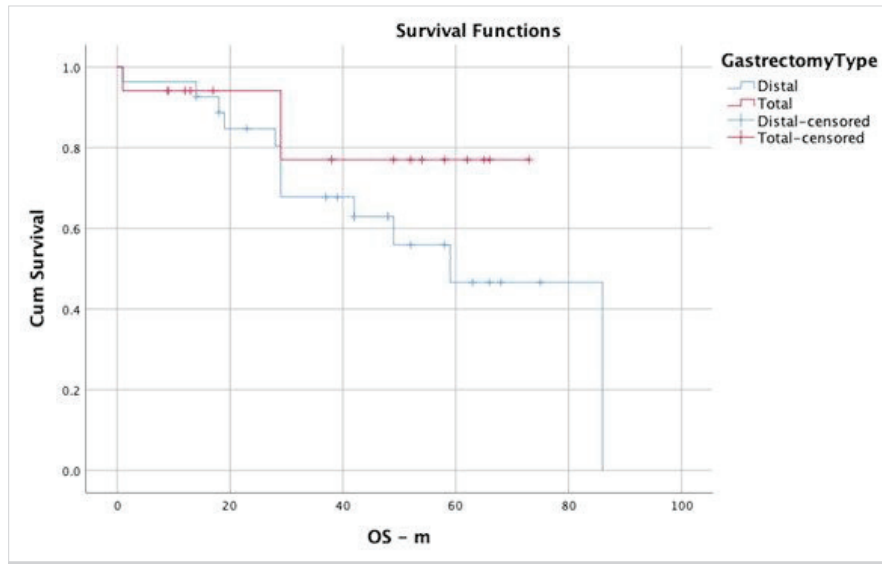


Figure 4. Kaplan-Meier curve of OS of patients who underwent LG for GC.

due to intraoperative bleeding (24). The patients in the current study were ambulant in POD zero, and we started oral intake early with a median duration of three days as an enhanced recovery after surgery (ERAS) protocol. Eighteen patients had CD grade II morbidities, four patients had CD grade III morbidities; two cases with an abdominal collection that was radiologically drained, one case with pleural effusion that needed chest tube insertion, and one case with biliary leakage treated conservatively for nine days, so the hospital stay had a median duration of six days. There was one case with in-hospital 30-day mortality due to atrial fibrillation and was admitted to ICU for five days. Omori et al. reported the oral intake in POD 2 and they had minor complications (seven cases with wound infection, two cases with delayed gastric emptying, and one case with intraperitoneal fluid collection), and the hospital stay in their study was seven days with no in-hospital mortality (27). A meta-analysis has demonstrated both approaches of laparoscopic and open gastrectomy and concluded that postoperative complications were significantly less by LG especially wound-related problems and pneumonia (28).

The pathological tumor size in this study was 4.59 cm and we harvested about 21 lymph nodes, which was more than recommended by the American Joint Committee on Cancer and the NCCN guidelines which recommend retrieving and examining at least 15 nodes. The mean number of positive lymph nodes in this study was 4.89. Wu et al. had a comparable tumor size of 4.19 cm and they had more harvested lymph nodes by 30.9 but the positive lymph node number was 2.9. Regarding, pathological staging; pT3 staging in our study was found in 43.2% and pT4a in 34.1%, while pN1 staging was in 31.8%, pN2 was in 20.5%, and pN3 in 29.5%. These stages were more advanced than that reported by Wu et al. as they had pT1

in 36.5% of the patients and pN0 in 57.1% of them due to their well-established screening programs for GC and tumors were presented in early stages (29). LG for advanced GC has been practiced by several centers in Asia with a high volume of GC patients, and they have reported favorable surgical outcomes (30). Moreover, oncologic outcome was superior when performed by experienced laparoscopic surgeons.

Median duration of follow-up in the current study was 42 months. Short postoperative recovery period has an impact on oncological outcomes as the patients with LG alleviate wound complications and other systemic morbidities that may delay their adjuvant therapy. A recent randomized controlled trial on patients who received neoadjuvant chemotherapy for advanced GC and then had LG reported less surgical trauma and the patients completed their adjuvant chemotherapy with minimal adverse effects (31). The mean duration of DFS was 59.62 months, and hematogenous metastasis was the most common in seven patients followed by peritoneal disease in four patients and local recurrence and port-site recurrence occurred in two cases. The peritoneal recurrence may be attributed to that we had 16 patients with pT4 tumors since there is no evidence that correlates between LG and the high risk of peritoneal and port-site metastasis. Moreover, these results are consistent with studies that were applied to advanced GC patients (32). Treatment options for these recurrent cases were variables and included chemotherapy in 11 cases with visceral and peritoneal recurrence, radiotherapy in one case with bony metastasis, and surgical resection in the case with port site recurrence as the patient did not have any local disease or distant metastasis. Long et al. reported the recurrence rate in 49.1% of cases; peritoneal recurrence in 21.9%, port site recurrence in 0.3%, hematogenous in 5.7%,

locoregional in 4.5%, distant lymph node in 4.8% and mixed type in 12% (33). This study has limitations in that it was a single-center experience designed in a retrospective pattern. The number of patients was relatively small as the study was conducted in a low-volume center for GC patients. Another limitation was the inclusion of both early and advanced GC patients with different tumor locations, that underwent distal and total gastrectomy.

CONCLUSION

LG for GC is a feasible approach for both early and advanced GC patients as it allows adequate diagnosis of the peritoneal disease without laparotomy, meticulous dissection, and identification of the lymph nodes with minimal blood loss and decreases surgery-related problems that may delay the adjuvant therapy and encourage the early patient discharge from hospital and return to daily life activities.

Ethics Committee Approval: This study was approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Mansoura University with a code number (R.22.02.1613). A written informed consent was signed by all the patients before inclusion in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - AA, AS, AA; Design - AA, AS; Supervision - AA, AS, MS; Data Collection and/ or Processing - AA, IAE, MS, MAE, AA; Analysis and/or Interpretation - AA, AS, MS, AA; Literature Search - AA; Writing Manuscript - AA; Critical Reviews - All of authors.

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ORIJİNAL ÇALIŞMA-ÖZET

Turk J Surg 2023; 39 (4): 354-364

Gastrik kanser için laparoskopik gastrektomi: Tek bir kanser merkezi deneyimi

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Onkoloji Merkezi, Mansoura Üniversitesi, Cerrahi Onkoloji Anabilim Dalı, Mansoura, Mısır

ÖZET

Giriş ve Amaç: Laparoskopik gastrektomi (LG), iki boyutlu görünüm, aletlerin zor manipülasyonu, ergonomik rahatsızlık ve buna bağlı kas spazmı ve efor nedeniyle çoğu cerrah için zorlayıcıydı. Gelişen cerrahi deneyimle birlikte teknolojik ilerlemeler, LG mide kanseri hastaları için daha uygulanabilir ve uygun bir yaklaşım haline getirmiştir.

Gereç ve Yöntem: Mısır Mansoura Üniversitesi, Onkoloji Merkezi, Cerrahi Onkoloji Bölümünde Temmuz 2015-Haziran 2022 tarihleri arasında 44 gastrik kanserli hastaya LG uygulandı ve bu yaklaşımın cerrahi sonuçları tek bir kanser merkezinin ilk deneyimi olarak değerlendirildi.

Bulgular: Yirmi yedi hastaya laparoskopik distal gastrektomi ve on yedi hastaya laparoskopik total gastrektomi uygulandı. İki olguda kombine rezeksiyon uygulandı. Ameliyat süresi $339,2 \pm 76,73$ dakika, kan kaybı ise $153,86 \pm 57,51$ mL idi. Hastalar ameliyat sonrası 0. günde ayakta idi, oral alım üç gün içinde başladı (aralık 1-5 gün) ve hastanede kalış süresi altı gündü (aralık 3-9 gün).

Sonuç: Gastrik kanser için laparoskopik gastrektomi (LG), peritoneal hastalığın yeterli tanısına, titiz diseksiyona ve lenf nodlarının minimal kan kaybı ile tanımlanmasına izin verdiği ve cerrahiye bağlı sorunları azalttığı ve hastaların hastaneden erken taburcu edilmesini ve günlük yaşam aktivitelerine dönmesini teşvik ettiği için hem erken hem de ileri gastrik kanser hastaları için uygulanabilir bir yaklaşımdır.

Anahtar Kelimeler: Laparoskopik gastrektomi, gastrik kanser, minimal invaziv cerrahi

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The silent threat: A retrospective study of right-sided traumatic diaphragmatic hernias in a university hospital

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ABSTRACT

Objective: In hospital attendance, 75% of diaphragmatic hernias occur on left as opposed to 25% on the right side. Right side hernias are associated with abdominal injuries, mainly the liver. However, right-side injuries are frequently underdiagnosed due to the complexity of associated injuries and high mortality rates. The aim of this study was to perform a retrospective analysis of records from our clinical experience to investigate demographics, TM, diagnosis, morbidity, and mortality associated with right sided TDH. These findings may provide insights into improving the clinical management of patients with this serious injury, potentially reducing morbidity and mortality rates.

Material and Methods: Retrospective analysis of the medical records of patients from the trauma database of the Division of Trauma Surgery at University of Campinas in 32-year period was performed. Only records of patients with right sided TDH were included in the analysis.

Results: Blunt trauma was the most common mechanism. Diagnoses were made by laparotomy in eight cases, all these cases were hemodynamically unstable. TDH grade III injury occurred in most cases followed by grade IV. Liver injuries were present in almost all cases, most of them high grade, followed by colon and small bowel. Extra-abdominal associated injuries with a predominance of femur fractures, pelvic fractures and hemothorax. Post-operative complications were associated with length of stay in intensive care unit. Pneumonia was the most frequent complication. The overall mortality rate was 16%.

Conclusion: Most diagnoses were performed through laparotomy and not by radiologic exams, due to hemodynamic instability on admission. There is underdiagnosis of right-side TDH due to the high-energy trauma mechanism with high grade associated injuries and mortality on pre-hospital.

Keywords: Trauma, abdominal injuries, diaphragm, diaphragmatic hernia

INTRODUCTION

Traumatic diaphragmatic hernia (TDH) is defined as the protrusion of abdominal structures through an injured diaphragm into the thoracic cavity. TDH is most often caused by blunt trauma (BT) because it involves a more severe trauma mechanism (TM). However, its actual incidence may be slightly higher than expected due to underdiagnosis (1). The diagnosis of diaphragmatic injury is challenging for the surgeon and depends on a high index of suspicion, TM and interpretation of radiological images. In hospital care, 75% of TDH occur on the left versus 25% on the right (2-4). Explanation for this fact involves three mechanisms. First, the existence of an area of muscle weakness at the embryonic fusion area on the left posterolateral diaphragm. Next, the liver attributes a protective effect to the diaphragm on the right during sudden increases in intra-abdominal pressure, and finally, the underdiagnosis of patients with right diaphragmatic rupture due to the severity of associated injuries, mainly liver damage. On the other hand, in the literature, there is a higher incidence of TDH on the right side in the autopsies, demonstrating severity of the associated injuries (5,6). For the diagnosis of the initial phase, the awareness of these factors is mandatory for the surgeon, when these go unnoticed in trauma patients, this serious injury remains unidentified leading to significant mortality and morbidity. Trauma care is a global challenge for public health authorities. The aim of this study was to perform a retrospective analysis of records from our clinical experience to investigate demographics, TM, diagnosis, morbidity, and mortality associated with right sided TDH. These findings may provide insights into improving the clinical management of patients with this serious injury, potentially reducing morbidity and mortality rates.

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MATERIAL and METHODS

This is a retrospective study based on a retrospectively collected database from the medical records of patients of the Division of Trauma Surgery (DCT) at University of Campinas between January 1990 and July 2022. The metropolitan area of Campinas has a population of 3.5 million, encompassing 21 cities. Clinics Hospital of Campinas is a referral hospital for the population using the public health system in this region. It is a like a level 1 trauma center with 420 beds, specific trauma floor with 16 beds dedicated to low complexity injuries, and intensive care unit (ICU) only for polytrauma with 10 beds for patients with high complexity injuries.

The records of 425 patients with diaphragmatic injury by blunt or penetrating trauma (PT) were evaluated. Fifty-five patients with herniation were evaluated and 12 patients with exclusive right sided TDH were analyzed for demographic data, mechanism (BT or PT), hemodynamic status at admission [unstable patients are those with a systolic blood pressure (SBP) <90 mmHg], grade of the injury, herniated organs, diagnostic methods (preoperative and intraoperatively), the interval between diagnosis and surgery (less than 24 h), length of stay (LES) in the ICU and trauma floor, associated injuries, morbidity, and mortality. Trauma scores were calculated using the injury severity score (ISS).

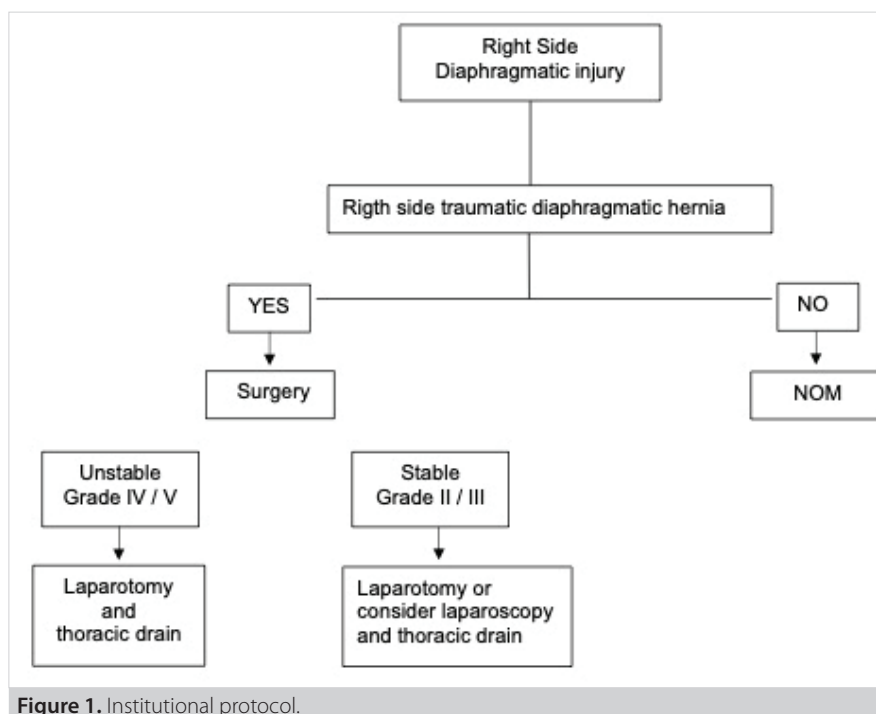
Diaphragm injury was graded according to the American Association for the Surgery of Trauma (AAST) injury scale (7) as follows: grade I, diaphragm contusion; grade II, laceration less than or equal to 2 cm; grade III, laceration greater than 2 cm

and less than 10 cm; grade IV, laceration greater than 10 cm, with tissue loss less than or equal to 25 cm²; and grade V, laceration with tissue loss greater than 25 cm². Patients with left side hernias, grade I injuries, congenital defects, hiatal hernias, chronic and delayed traumatic hernias for more than 14 days were excluded.

Trauma surgery institutional protocol for the treatment of TDH, after the diagnosis, entails surgical exploration, which uses laparotomy, preferable in unstable or high-grade injuries, or laparoscopy (Figure 1). After recognizing TDH, the injury is treated by repairing defects with an interrupted nonabsorbable suture, such as polypropylene, in open surgery. In laparoscopy, injury is treated with polyglactin uninterrupted suture. Further, an ipsilateral chest tube or a nasogastric tube may be placed at the site of the injury for drainage (Figure 2). Descriptive statistics were used to analyze the data, with continuous variables expressed as means and categorical data expressed as frequencies and percentages. The results are presented in tables, which provide a clear and concise overview of the key findings of the study. Approval for the study was obtained from the University of Campinas and Institutional Review Board without restriction (Protocol No: 2.692.996, Date: 06.05.2018 and 5.892.808, Date: 02.14.2023).

RESULTS

Right-sided TDH were predominant in young males (75%). The most common mechanism of trauma was BT, accounting eight (67%) cases. Of these, motor vehicle collisions were the most common, accounting for seven (87%) cases, followed by



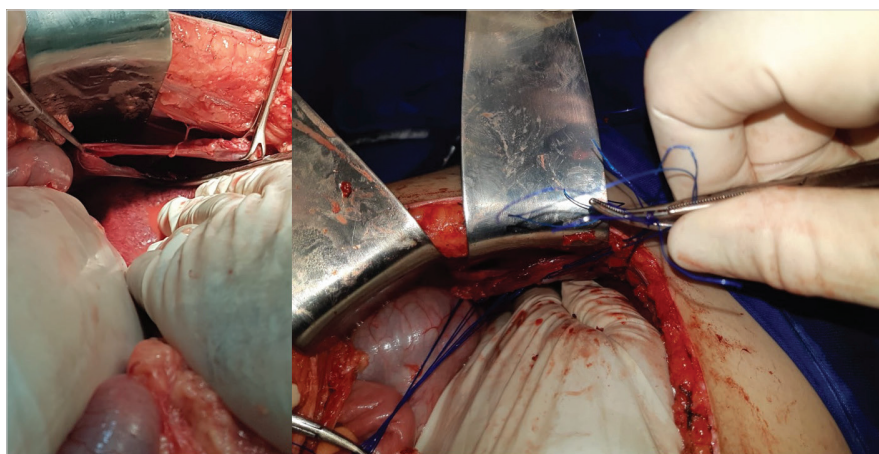


Figure 2. Grade III right side diaphragmatic injury on trauma laparotomy.

pedestrians hit by car in one (13%). All vehicle occupants were drivers, and in 80% of cases, the collision occurred on the right side of the vehicle compartment. In PT, three (75%) suffered a gunshot wound (GSW) and one (25%) from a stab wound (SW). Diaphragmatic grade III injury occurred in six cases (50%), grade IV in four (33%) and grade V in two (17%). Liver in eight patients (67%) was the most herniated organ, followed by the stomach with three (25%) and small bowel with one case (8%). Description between BT vs. PT analyses is shown in Table 1.

Eleven cases underwent laparotomy, one case with BT and stable clinical condition, was started with laparoscopy and had to be converted to laparotomy during the procedure due to technical difficulties (Figure 3). Two cases underwent laparotomy with thoracotomy.

Associated injuries were present in 11 out of 12 cases (92%). Liver injuries were the most common, occurring in 11 cases (92%), with a predominance of grade III and IV injuries. Colon injuries were present in four cases (36%) and small bowel injuries in two cases (18%), both predominantly grade II injuries. Extra-abdominal associated injuries were also observed in 10 cases (83%), with a predominance of femur fractures (40%). Hemothorax and open book pelvic fracture was observed in three cases each (30%). Associated injuries are summarized in.

In eight cases (67%), the diagnosis was made intraoperatively during laparotomy due to hemodynamic instability. Only four cases (33%) were able to undergo imaging exams prior to surgery due to their stable condition. Preoperative diagnosis was made in four cases (33%), with two based on chest radiography (CXR) (50%) and the other two with multi-slice computed tomography (CT). CXR showed common abnormal findings such as elevation of the right diaphragm, intrathoracic abdominal structures, and pulmonary contusion with rib fractures in all cases (Figure 4). CT showed herniation of abdominal contents and hump sign, as well as indirect findings

such as pulmonary contusion with rib fractures and mediastinal shift (Figures 5).

Postoperative complications occurred in six patients (50%). Pneumonia was the most frequent complication in BT (four cases, 50%) while, in PT, abdominal cavity abscess was present in two (50%). Mean LES in ICU was 13 and trauma floor were 18 days. ICU patients are commonly associated with prolonged mechanical ventilation and are three times more likely to undergo tracheostomy. An ISS greater than 15 was found in nine cases (75%) and greater than 25 in three, mostly observed associated with BT, as well as the cases with hemodynamic instability, which for the most part (six cases, 75%) were BT with liver injury. Overall mortality was two cases (17%), one BT and the other PT, both with hemorrhagic shock. Both were unstable during primary survey, high grade liver injury with hemothorax and ISS greater than 25, requiring massive transfusion during admission.

DISCUSSION

Comprehending the distinctions between blunt and penetrating trauma in relation to diaphragmatic injury is imperative. There is limited literature available on right sided TDH. Most of the right-side diaphragmatic injuries in our survey were caused by BT. Penetrating wounds often result in small defects, with occult injuries remaining silent before symptoms appear. On the other hand, BT commonly leads to large linear ruptures with immediate herniation. In our survey, BT with right side TDH grade III injury occurred in most cases followed by grade IV, with immediate herniation. Our study demonstrated that 67% of right-side TDH resulted from BT, which is strongly correlated with the high incidence of traffic injuries in the metropolitan region of Campinas. Specifically, 87% those hernias were caused by motor vehicle collisions, whereas 13% resulted from pedestrian hit by car.

Table 1. Description between BT vs PT analyses

	Penetrating	Blunt
Deaths	4 (33%)	8 (67%)
Male	4 (33%)	5 (42%)
Female	0	3 (25%)
Age		
<18 y	0	0
18-29 y	2 (16.6%)	2 (16.6%)
30-59 y	2 (16.6%)	6 (50%)
>60 y	0	0
SBP on admission		
< 90 mmHg	1 (25%)	6 (75%)
> 90 mmHg	3 (75%)	2 (25%)
Diagnosis		
CXR	1 (25%)	1 (12.5%)
CT	0	2 (25%)
Laparotomy	3 (75%)	4 (50%)
Laparoscopy	0	1 (12.5%)
Herniated organ		
Liver	2 (50%)	6 (75%)
Stomach	2 (50%)	1 (12.5%)
Small bowel	0	1 (12.5%)
Grade of injury		
III	3 (75%)	3 (37.5%)
IV	1 (25%)	3 (37.5%)
V	0	2 (25%)
ISS		
<25	4 (100%)	5 (62.5%)
>25	0	3 (37.5%)
Complications		
Infection	0	4 (50%)
Thrombosis	0	2 (25%)
Abscess	2 (50%)	0

According to Rodriguez-Morales et al., the diagnosis of TDH should be based on trauma kinematics and clinical assessment (3). Kearney et al. have demonstrated that lateral collisions can increase the risk of ipsilateral diaphragmatic hernia up to threefold (8). Despite the challenges in data collection, our study found that all vehicle occupants were drivers and in 80% of cases, the collision occurred on the right side of the vehicle passenger compartment, consistent with Kearney's proposed pattern. These findings underscore the importance of early recognition of diaphragmatic injuries in trauma patients, particularly in lateral collisions. Our findings are like Brown and Richardson's, regarding the organ that is typically herniated, it is

not surprising that the liver is the most affected in the majority of cases, given its proximity (4).

Intrahospital studies have shown that left-sided TDH account for 75% of cases, whereas right-sided account for 25% (6,9,10). This disparity involves three mechanisms. Firstly, Lucido and Wall demonstrated in 1963 the existence of a muscular weakness area in the embryonic fusion point in the postero-lateral left diaphragm (11). Secondly, the liver provides a protective effect to the right diaphragm during sudden increases in intra-abdominal pressure. Finally, there is an underdiagnosis of patients with right diaphragmatic rupture (1,5,6,9,10,12).

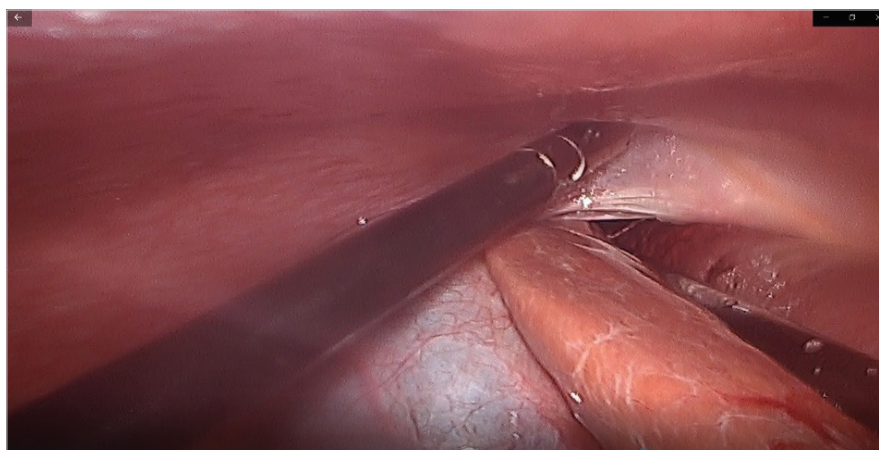


Figure 3. Diaphragmatic injury site on the laparoscopy.

Currently, intrahospital diagnosis of right-sided post-traumatic diaphragmatic hernias in severe blunt trauma patients is possible due to improvements in trauma systems. Including the efficient pre-hospital teams that stabilize and scoop to run patients to trauma center, trained trauma teams consisting of surgeons or emergency physicians in the trauma bay, 24/7 blood bank availability, and equipment such as CT, improved the accuracy of images facilitating their accurate interpretation by experienced radiologists. These advancements have led to an increase in the diagnosis of right-sided diaphragmatic hernias, which were previously underdiagnosed.

A study by Aun et al. compared two groups, one of which consisted of 97 cases of diaphragmatic hernias treated surgically and the other included 146 cases evaluated in 12,276 consecutive autopsies of patients without medical care (5). Autopsy group showed a higher incidence of right-sided diaphragmatic ruptures (49.6%) compared to the hospitalized group (14.4%). Additionally, the autopsied group had a greater number of associated injuries and more severe injuries,

including orthopedic and pelvic trauma, traumatic brain injury, and high-grade liver injuries. Shock was the main cause of death in over 80% of the autopsy group in contrast to the 15% in the hospitalized. The study concluded that patients with right-sided diaphragmatic hernias have severe injuries are quickly deadly.

Similarly, to Aun, Desforges have stated that there is a higher pre-hospital mortality rate in patients with right sided hemidiaphragm rupture, which is attributed to higher kinetics needed to produce an injury, typically associated with significant vascular tears in the inferior vena cava or hepatic veins (13). Boulanger et al. have observed that right-sided post-traumatic diaphragmatic hernias are more severe due to the greater number of associated injuries and found that all cases of right-side diaphragmatic hernia has associated abdominal injuries (6). Our findings demonstrate that associated injuries were present in almost all cases (92%), with high-grade liver injuries being the most common. Extra-abdominal associated injuries were observed, with a predominance of femur fractures and "open book" pelvic fractures. These results support the existing literature that emphasizes the severity of injuries resulting from high-energy mechanisms (6). Additionally, 67% of patients underwent intraoperative diagnoses by laparotomy, mainly due to hemodynamic instability. Only 33% were stable enough to undergo for imaging exam. These findings underscore the need for prompt surgical intervention in cases of right-sided diaphragmatic hernias. Moreover, like Boulanger we also observed higher injury severity scores ($ISS > 25$) in blunt trauma (6). Therefore, the presence of TDH following BT should alert the surgeon to the likelihood of associated solid-organ and pelvic injuries.

Awareness for the diagnosis of diaphragmatic injuries is crucial. Aronoff et al. have reported that physical examination is disappointing for diagnosing these injuries after blunt trauma, as it can only identify 44% of cases (10). We attribute the low

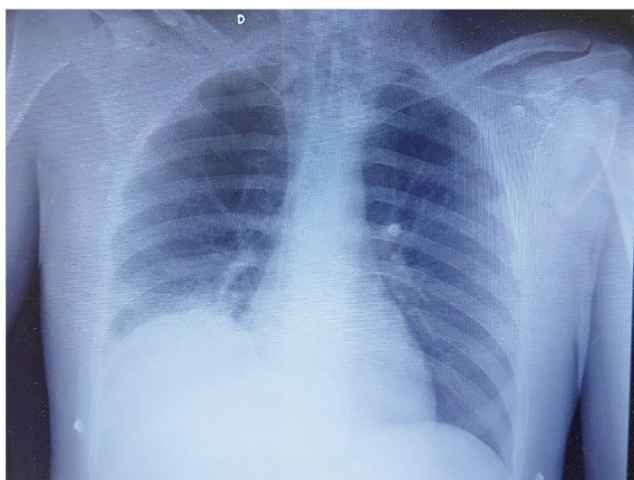


Figure 4. CXR abnormal findings (elevated diaphragm).

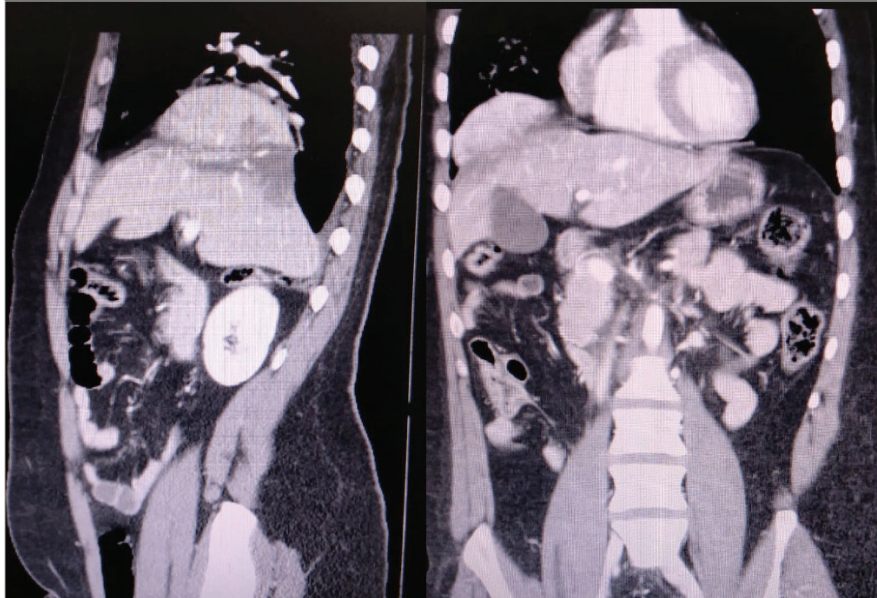


Figure 5. CT Hump sign.

sensitivity to three factors: first, lack of familiarity of surgeons with the disease; second, the low specificity of physical examination, which is often performed in a noisy trauma bay, making it difficult to perform assessment; and third, as patients with diaphragmatic hernias usually have associated injuries, hemodynamic shock or ventilatory compromise may divert the attention of the examiner.

CXR has limited diagnostic value. Gelman et al. have reported that the most sensitive radiographic finding for diagnosis is a 5 cm elevation of the diaphragmatic dome, seen in 61% of cases, followed by intrathoracic abdominal viscera in 45% although most radiographs are normal (14). CT has enhanced diagnostic accuracy and allowed for nonoperative management of hemodynamically stable polytrauma patients. The sensitivity of CT for blunt traumatic diaphragmatic injury ranges from 71 to 82%, with specificity ranging from 75 to 100%, while in penetrating trauma, sensitivity is 86 to 94% and specificity is 79 to 96% (15-18). Coronal and sagittal reformations contribute to the diagnostic accuracy, improving sensitivity and specificity. Our survey assessed the preoperative imaging methods for patients with some hemodynamic stability. CXR and CT were used to diagnose half of the patients each. The most frequent findings on CXR were right-sided diaphragm elevation of 5 cm and rib fractures. On the other hand, CT revealed abdominal viscera into the thorax, the "hump sign" and indirect findings such as pulmonary contusion, mediastinal shift, and rib fractures. However, it should be highlighted that due to most trauma patients arriving at the trauma bay unstable, the diagnosis by laparotomy remains the most performed method. Early diagnosis and surgical repair are mandatory to avoid catastrophic sequelae (19).

Despite the advantages of imaging modalities such as CT, the decision to perform a laparotomy was based on the associated abdominal injuries and hemodynamic status. In the context of blunt trauma and the possibility of associated injuries, hemodynamic and ventilatory instability may occur, questioning the role of laparoscopy. However, since the first report of the use of laparoscopy as a diagnostic and therapeutic tool, there has been a significant advancement in the technique. The experience of surgeons in elective procedures on the diaphragm, such as hiatal hernias, has made laparoscopy feasible in well-selected cases with appropriate devices that facilitate suturing. Our series involved one case in which diagnostic laparoscopy was used to diagnosis, this can be explained by inexperienced laparoscopic surgeons, but this, there was no differences observed in outcomes despite the treatment method.

Complications after surgery are not the same for penetrating and blunt injuries (20). In our study, many complications were associated with respiratory causes and not necessarily attributed to the diaphragmatic hernia. All survivors with BT had a significant length of stay in the trauma floor and intensive care unit, with a longer duration of mechanical ventilation, reflecting the severity and multiplicity of injuries, this observation can be explained by the fact that pneumonia was the most common complication, especially due to its association with mechanical ventilation.

Zazour et al. have reported a mortality rate of 21%, with higher mortality in patients with right-sided diaphragmatic injuries (21). Boulanger et al. have found a mortality rate of 41%, while our study had an overall mortality of 17%, with one PT and one BT resulting in death (6). All deaths had high grade liver and

lung laceration, evolved with the lethal triad. Early mortality is mainly related to the associated injuries rather than the diaphragmatic hernia and post operation complications. Therefore, post-traumatic diaphragmatic hernia serves as a marker for serious and lethal injuries.

The retrospective design of this study introduces some limitations. There is a possibility of biases due to changes in perspectives and tendencies in patient assessment when analyzing existing data. Additionally, data collection was relied on reviewing charts at the participating institution, which may have resulted in errors or omissions.

CONCLUSION

Diagnosis is often made via laparotomy due to hemodynamic instability. Most cases presented associated injuries indicating high-energy trauma, with the liver being the most herniated and injured in right-sided diaphragmatic hernias. The lethal triad was the main cause of death.

Ethics Committee Approval: This study was approved by University of Campinas and Institutional Review Board (Protocol No: 2.692.996, Date: 06.05.2018 and 5.892.808, Date: 02.14.2023).

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**ORİJİNAL ÇALIŞMA-ÖZET**

Türk J Surg 2023; 39 (4): 365-372

Sessiz tehdit: Bir üniversite hastanesinde sağ taraflı travmatik diyafram hernileri üzerine retrospektif bir çalışma

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ÖZET

Giriş ve Amaç: Hastaneye başvuruda diyafragma fıtıklarının %75'i solda, %25'i ise sağ tarafta meydana gelir. Sağ taraftaki fıtıklar, başta karaciğer olmak üzere karın yaralanmalarıyla ilişkilidir. Bununla birlikte, sağ taraftaki yaralanmalar, ilgili yaralanmaların karmaşıklığı ve yüksek ölüm oranları nedeniyle sıklıkla eksik teşhis edilmektedir. Bu çalışmanın amacı, sağ taraflı TDH ile ilişkili demografik özellikler, TM, tanı, morbidite ve mortaliteyi araştırmak için klinik deneyimlerimizden elde edilen kayıtların retrospektif bir analizini yapmaktır. Bu bulgular, bu ciddi yaralanmaya sahip hastaların klinik yönetiminin iyileştirilmesi ve potansiyel olarak morbidite ve mortalite oranlarının azaltılması konusunda fikir verebilir.

Gereç ve Yöntem: Campinas Üniversitesi Travma Cerrahisi Anabilim Dalı travma veri tabanından 32 yıllık dönemdeki hastaların tıbbi kayıtlarının retrospektif analizi yapıldı. Analize sadece sağ taraflı TDH'li hastaların kayıtları dahil edildi.

Bulgular: Künt travma en sık görülen mekanizmaydı. Sekiz olguda tanı laparotomi ile konuldu, bu olguların tümünün hemodinamikleri stabil değildi. Çoğu vakada TDH derece III yaralanma meydana geldi ve bunu derece IV izledi. Çoğu yüksek dereceli olmak üzere hemen hemen tüm vakalarda karaciğer yaralanmaları mevcuttu ve bunu kolon ve ince bağırsak takip ediyordu. Femur kırıkları, pelvik kırıklar ve hemotoraksın ağırlıklı olduğu karın dışı ilişkili yaralanmalar. Ameliyat sonrası komplikasyonlar yoğun bakım ünitesinde kalış süresiyle ilişkiliydi. Pnömoni en sık görülen komplikasyondur. Genel ölüm oranı yüzde 16 oldu.

Sonuç: Başvuru anında hemodinamik dengesizlik nedeniyle tanıların çoğu radyolojik incelemelerle değil laparotomi yoluyla konuldu. Yüksek enerjili travma mekanizması nedeniyle, hastane öncesi yüksek dereceli yaralanma ve mortalite nedeniyle sağ taraf TDH tanısı yetersiz konulmaktadır.

Anahtar Kelimeler: Travma, karın yaralanmaları, diyafram, diyafram hernisi

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Repair of stoma prolapse with the “peristomal cerclage” method using vessel tape

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ABSTRACT

Stoma prolapse is one of the most common late complications following stoma construction. Although prolapses can be managed conservatively, they often require surgical revision. This study aimed to describe a revision method called *peristomal cerclage* applied with local anesthesia to treat stoma prolapse. A 66-year-old male patient with advanced rectal cancer underwent sigmoid loop colostomy one year ago due to a distal occlusive tumor. A revision of the colostomy prolapse that developed postoperatively was planned. After the reduction of the 12 cm prolapse into the abdomen under local anesthesia, a repair was performed in the form of peristomal wrapping of a vessel tape; except for short-term abdominal distension, no complications developed in the patient. He is currently in the postoperative 26th month and terminal period, and his colostomy is working normally. The present report aimed to describe the *peristomal cerclage* method, a minimally invasive revision procedure applied to patients with stoma prolapse, and to deliver its long-term results. It is important to report the results obtained with the more widespread use of this method.

Keywords: Stoma, colostomy, prolapse, cerclage

INTRODUCTION

Stoma prolapse is one of the late complications of stoma construction and is defined as the invagination of the proximal intestine through the mouth of the stoma. It is more common, especially in transverse loop colostomies. It is relatively less common in the extraperitoneal colostomy technique (1,2). Although it does not pose a vital risk for the patient, apart from cosmetic negativities and stoma care difficulties, ischemia, ulceration and necrosis are seen as a result of incarceration developing in prolapse, though uncommon. In these cases, urgent surgical intervention is required with a high probability of morbidity (3). In addition to resection operations performed by laparotomy or laparoscopy to repair prolapsed stoma, local revision and resection techniques have been described (4,5). Conservative interventions such as placing prolapsed bowel loops in the abdomen and fixing them to the colostomy opening in the abdominal wall have also been described in elderly patients or temporary colostomies (1,2,6). The report presented here aimed to describe a conservative local revision procedure performed by placing a silicone vessel tape around the colostomy after pushing the prolapsed loop into the abdomen under local anesthesia.

CASE EXAMPLE and TECHNICAL DETAILS

A 66-year-old patient with an obstructive mass in the rectum was evaluated as inoperable in an external center due to lung and liver metastases and bladder invasion, and chemotherapy was started. Our clinic re-evaluated the patient, and it was decided to open a colostomy due to the tendency of the intestinal passage to be obstructed, and a loop colostomy was performed on the sigmoid colon under general anesthesia. The patient developed colostomy prolapse, which started to develop six months after the operation and reached approximately 12 cm in size (Figure 1). It was decided to perform a revision with local anesthesia for the prolapse. The patient was operated on with cefazolin (2 gr/IV) prophylaxis without bowel preparation after eight hours of fasting. Ten mL of prilocaine/lidocaine local

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Figure 1. Stoma prolapse observed in sigmoid loop colostomy.

anesthesia was applied around the colostomy. The pressure was applied on the colostomy section protruding from the stoma, and it was sent into the abdomen, and the lumen was checked with a touch. Four 1 cm radial incisions were made around the colostomy, and a circumferential tunnel was created on the fascia around the stoma using these incisions (Figure 2). A silicone vessel tape with a diameter of 5 mm was placed in the tunnel in a double layer surrounding the stoma. In order to prevent the recurrence of the prolapse and not have difficulty in defecation, the vascular tape was adjusted to cover the index finger (new stoma diameter, approximately 1.7 cm) and tied with a silk suture, the skin incisions were closed, and the operation was terminated. Postoperative pain was minimal, and the patient was discharged on the same day, with continued oral nutrition in the form of watery food. The patient had mild abdominal distension and difficulty defecating on the second postoperative day, oral intake was restricted, and the colostomy started to work 48 hours later. No obstruction, recurrence of prolapse, or other complications developed at the 26-month follow-up (Figure 3). The perineum of the patient, who is currently in the terminal period, is in a necrotic state, and a bladder fistula has developed into the wound. However, the patient's oral feeding continues, and the colostomy works well after the revision procedure called the *peristomal cerclage*.

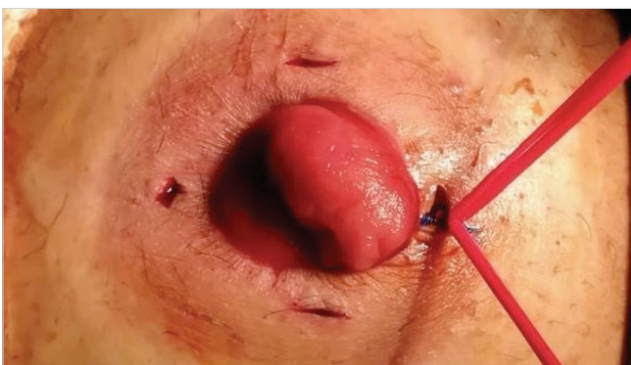


Figure 2. Application of "peristomal cerclage" technique.



Figure 3. Appearance six months after revision of stoma prolapse.

DISCUSSION

The overall complication rate after stoma construction is between 21-70% (2,3,7). Colostomy prolapse is one of the most common late complications. The incidence rates are 2-26% and depend on long-term follow-up (7,8). Stoma prolapse is most common in transverse loop colostomies and relatively less common in end colostomies and extraperitoneal colostomies (2,7,9). Distal obstruction is important among the etiological factors (1). In addition to obesity and increased intra-abdominal pressure, there are factors such as the excessively large opening of the fascial defect and the redundant and tortuous nature of the proximal sigmoid colon (7). Asymptomatic or minimally symptomatic patients are initially approached conservatively; no intervention is required unless complications develop. However, surgical treatment can be planned if the prolapse is severe, accompanied by parastomal hernia, and cosmetic problems or stoma care difficulties are in question. Rarely, intussusception and necrosis may develop in a prolapsed stoma, in which case urgent surgical intervention is required (10).

Surgical treatment can be performed with an abdominal or peristomal approach. In the abdominal approach, resectioning the prolapsed colon and creating a new stoma is the definitive procedure (1). In the peristomal approach, the modified Altemeier procedure to resect the prolapsed bowel segment or the modified Delorme's procedure for mucosal resection/plication can be applied (4,11). Recently, local revision techniques have been defined with linear stapler devices, which shorten the operation time. Although this technique can be applied safely, it brings an additional cost (4,5,12).

Conservative interventions, which are also applied peristomal, such as placing the prolapsed loops in the abdomen and fixing them to the colostomy opening in the abdominal wall, have also been described, but recurrence is common in this technique (1,2,6).

The Thiersch procedure, a treatment method applied in patients who cannot handle general anesthesia and laparotomy in rectal prolapse, may be an alternative to use in colostomy

prolapse (13). This conservative method applied in rectal prolapses constituted a prototype for the *peristomal cerclage* technique we applied in our case. The described technique is a low-cost method that can be applied under local anesthesia, is minimally invasive, does not require a stapler device, and is applied only with vessel tape. During the patient's long-term follow-up of 26 months, it functioned as a satisfactory definitive treatment method. The Sao Paulo study, similar to this method, was applied in 10 male patients, and a polypropylene mesh strip was used peristomal, and no recurrence was observed in the applied cases (14). Since the material they use is not elastic and healing is by fibrosis, this technique may cause colostomy stricture in the long term. The vascular tape we use is a silicone material used in the seton treatment of anal fistulas, and it is an important advantage that it does not cause fibrosis around the stoma. In addition, it is preferable due to its stretching feature during passive defecation from the colostomy. However, this procedure is not suitable for ischemic or ulcerated prolapse cases due to the risk of necrosis and perforation.

CONCLUSION

Peristomal cerclage, which is applied under local anesthesia and with daily hospitalization to repair colostomy prolapse, was defined in this report. This technique can be applied in suitable cases due to its advantages, such as satisfactory postoperative recovery, low cost, and no recurrence and complications in the present case in the long postoperative period of 26 months.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - AHD; Design - SA; Supervision - AHD; Data Collection and/or Processing - İK, SA, RA; Analysis and/or Interpretation - RA; Literature Search - SA, İK; Writing Manuscript - SA, AHD; Critical Reviews - AHD.

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

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**TEKNİK SUNUM-ÖZET**

Türk J Surg 2023; 39 (4): 373-376

Damar teypini kullanarak “peristomal serklaj” yöntemiyle stoma prolapsusunun onarımı

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ÖZET

Stoma prolapsusu, stoma yapımını takiben en sık görülen geç komplikasyonlardan biridir. Prolapsuslar konservatif olarak tedavi edilebilmelerine rağmen, sıklıkla cerrahi revizyon gerektirirler. Bu çalışmada, stoma prolapsusunu tedavi etmek için lokal anestezi ile uygulanan “peristomal serklaj” adı verilen bir revizyon yöntemi tanımlanmıştır. Örnek olguda ileri rektum kanseri olan 66 yaşındaki erkek hastaya bir yıl önce distalde tıkaçıcı tümör nedeniyle sigmoid loop kolostomi açılmıştı. Ameliyat sonrası gelişen kolostomi prolapsusunun revizyonu planlandı. Lokal anestezi altında 12 cm’lik prolapsus batın içine redükte edildikten sonra subkutan yerleştirilen damar teypinin peristomal sarılması şeklinde bir onarım yapıldı; kısa süreli batın distansiyonu dışında hastada herhangi bir komplikasyon gelişmedi. Hasta şu anda postoperatif 26. ay ve terminal dönemdedir ve kolostomisi normal olarak çalışmaktadır. Bu çalışma, stoma prolapsusu olan hastalara uygulanan minimal invaziv bir revizyon prosedürü olan peristomal serklaj yöntemini tanımlamayı ve uzun dönem sonuçlarını bildirmeyi amaçlamaktadır. Bu yöntemin daha yaygın kullanımı ile elde edilen sonuçların bildirilmesi önemlidir.

Anahtar Kelimeler: Stoma, kolostomi, prolapsus, serklaj**DOI:** 10.47717/turkjsurg.2023.6154



Adult idiopathic hypertrophic pyloric stenosis presenting with gastroduodenal intussusception: A rare case report

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ABSTRACT

Adult idiopathic hypertrophic pyloric stenosis (AIHPS) is a rare entity first described by Cruveilhier in 1835. There are only approximately 200 cases reported in the English literature to date. Histologically, it may be mistaken for spindle cell neoplasms such as gastrointestinal stromal tumour (GIST). Patients with AIHPS usually present with early satiety, abdominal fullness, postprandial vomiting, epigastric pain, and eructations. Adult intussusception is rare and only accounts for 5% of all intussusceptions. Gastroduodenal intussusception is one of the rare types of adult intussusception. This is more likely to occur when a benign or malignant stomach lesion acts as a lead point. We report a case of AIHPS in a 70-year-old lady presenting with gastroduodenal intussusception. An oesophagogastroduodenoscopy (OGDS) was performed, and it revealed a diffusely thickened and narrowed pyloric antrum. A contrasted computed tomography (CECT) of the thorax and abdomen showed a distended stomach with circumferential thickening of the pylorus. The pre-pyloric antrum was intussuscepting into the pylorus, and the apex is seen within the first part of duodenum. She underwent distal gastrectomy with a Roux-en-y reconstruction via laparoscopic approach and was discharged well. AIHPS is a rare condition and should be a differential in adults presenting with gastric outlet obstruction. We believe in cases of AIHPS presenting with gastroduodenal intussusception, a distal gastrectomy with reconstruction is a reasonable approach. A multidisciplinary approach is essential to obtain the best outcome.

Keywords: AIHPS, distal gastrectomy, adult intussusception, GIST, primary AIHPS

INTRODUCTION

Adult idiopathic hypertrophic pyloric stenosis (AIHPS) is a rare entity first described by Cruveilhier in 1835 (1). The primary or idiopathic form has no discernable predisposing factor while the more common secondary form is triggered by other diseases of the upper gastrointestinal tract (2,3). It is important to note that while recognizing malignant cells is often uncomplicated, spindle cell neoplasms such as gastrointestinal stromal tumour (GIST) might be challenging to differentiate from AIHPS (2).

Adult intussusception is rare and only accounts for 5% of all intussusceptions (4). Gastroduodenal intussusception is one of the rare types of adult intussusception, accounting for only 10% of cases (4). With this in mind, we report the first case of AIHPS presenting with gastroduodenal intussusception. This case has been reported in line with the SCARE criteria (5).

CASE REPORT

A healthy 70-year-old woman presented to us with reduced effort tolerance and intermittent vomiting for the past three months. It was associated with central abdominal pain, and she has progressive early satiety for the past month. Upon further history, she claims to have intermittent maelenic bowel movements as well for the past one year. She had an unintentional weight loss of three kg in the past year as well. On clinical examination, she was pale but otherwise normotensive. Her abdominal examination was unremarkable and digital rectal examination showed brownish stools. Her blood investigation revealed a haemoglobin level of 49 g/L (microcytic hypochromic picture), and she was admitted for further assessment and blood transfusion.

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Figure 1. Upper endoscopy still images of stomach showing edematous pyloric mucosa intussuscepting into the first part of duodenum.

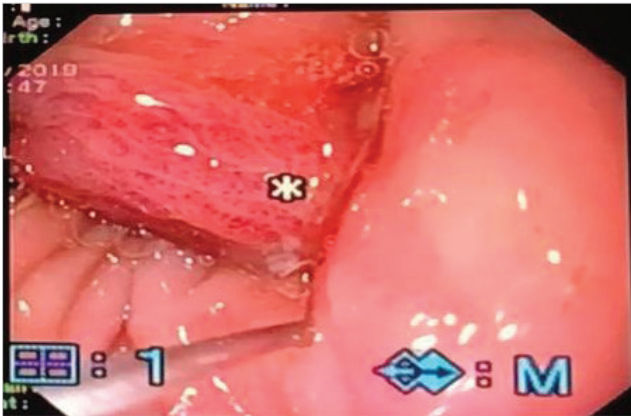


Figure 2. Upper endoscopy still images of stomach showing edematous pyloric mucosa intussuscepting into the first part of duodenum.

An oesophagogastroduodenoscopy (OGDS) was performed, and it revealed a distorted anatomy of the stomach. The pyloric antrum was diffusely thickened and oedematous with its mucosa intussuscepting into the first part of duodenum (Figures 1,2). We were unable to perform duodenal intubation because of that. A presumptive diagnosis of the pre-pyloric gastric tumour was made. Tissue biopsy taken from the pre-pyloric antrum suggested it to be a GIST with the background of chronic active gastritis. A contrasted computed tomography (CECT) of the thorax and abdomen was done, and it showed a distended stomach with circumferential thickening of the pylorus measuring 1.6 cm (Figure 3). The pre-pyloric antrum was intussuscepting into the pylorus, and the apex is seen within the first part of duodenum (Figures 4,5). There were no suspicious features from the soft tissue mass, and there was no distant metastasis seen.

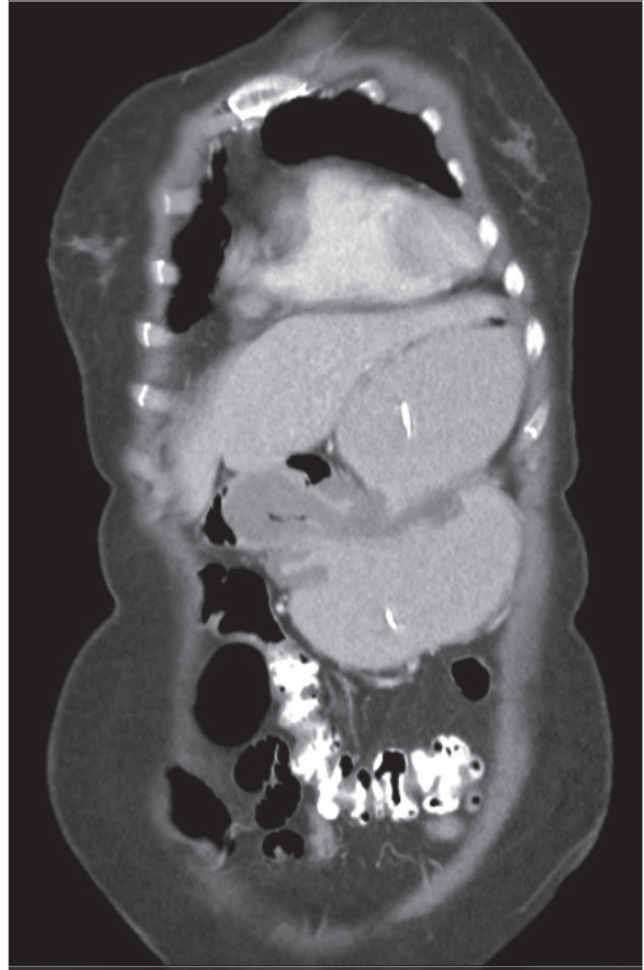


Figure 3. Coronal view of the CECT of the abdomen showing a distended stomach with circumferential thickening of the pylorus measuring 1.6 cm.



Figure 4. Axial and sagittal view of CECT of the abdomen showing pre-pyloric antrum intussuscepting into the pylorus, and the apex is seen within the first part of duodenum.



Figure 5. Axial and sagittal view of CECT of the abdomen showing pre-pyloric antrum intussuscepting into the pylorus, and the apex is seen within the first part of duodenum.

After a multidisciplinary meeting, we performed a distal gastrectomy with a Roux-en-y reconstruction via a laparoscopic approach. Her postoperative recovery was complicated with acute coronary syndrome, which required care in the intensive care unit for two days. She was subsequently discharged well on postoperative day nine. The histopathological report of the resected specimen did not show any GIST cells. The circumferential thickened pylorus showed hypertrophied circular layer of the muscularis propria with evidence of acute and chronic inflammatory cells infiltration. The duodenal mucosa showed eroded mucosa with congested blood vessels. There are no surface ulcerations, neutrophils, crypt abscess or evidence of malignancy (Figure 6,7). With the final pathology report, we came to the diagnosis of AIHPS causing gastroduodenal intussusception. During her last follow up at the outpatient clinic, she remained well and asymptomatic.

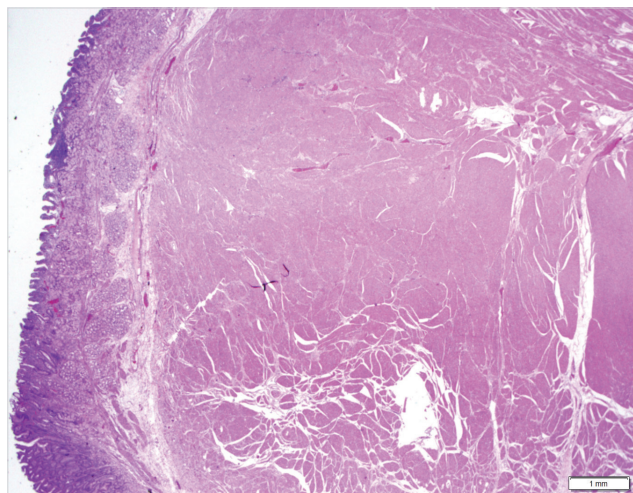


Figure 6. Microscopic examination of the sections from thickened pylorus at 1.25x and 20x magnification show hypertrophied circular layer of the muscularis propria mildly infiltrated with acute and chronic inflammatory cells.

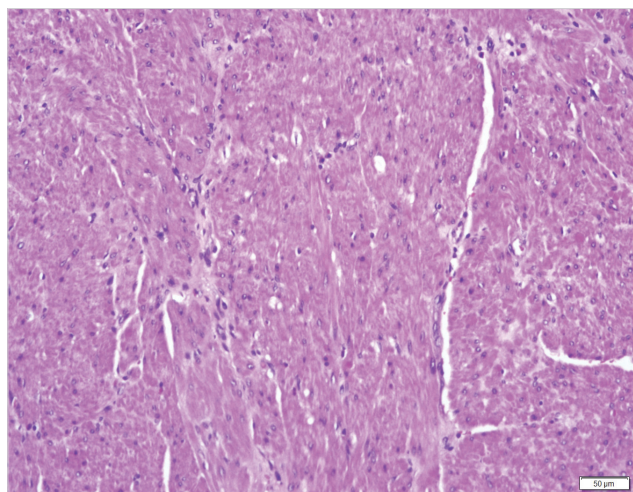


Figure 7. Microscopic examination of the sections from thickened pylorus at 1.25x and 20x magnification show hypertrophied circular layer of the muscularis propria mildly infiltrated with acute and chronic inflammatory cells.

DISCUSSION

AIHPS is a rare entity first described by Cruveilhier in 1835 (1). There are only approximately 200 cases reported in the English literature to date (2). The commonly accepted etiological classification is into a primary and secondary form (2). The primary or idiopathic form has no discernable predisposing factor while the more common secondary form is triggered by other diseases of the upper gastrointestinal tract (2,3). These include excessive healing of previous gastric or proximal duodenal ulcers, GIST, vagal hyperactivity, previous operation causing extrinsic adhesions, carcinoma and bezoars (2).

On microscopic examination, the primary form demonstrates substantial hypertrophy of the pyloric muscles while in the secondary form, there is localized replacement by fibrous tissues, with scanty or no smooth muscle hypertrophy. Differentiation of these two forms is usually the task of the pathologist. It is important to note that while recognizing malignant cells is often uncomplicated, spindle cell neoplasms such as GIST might be challenging to differentiate from AIHPS (2). As in our case, it is possible that the initial tissue biopsy was mistaken for GIST.

Intussusception is defined as an invagination of one part of the gastrointestinal tract into another. Adult intussusception only accounts for 5% of all intussusceptions (4). Unlike intussusception in children, 80-90% of intussusception in adults have an identifiable cause (6). Gastroduodenal intussusception is one of the rare types of adult intussusception, accounting for only 10% of cases (4). It occurs when part of the stomach invaginates through the pylorus into the duodenum (7). Various pathologies such as an inflammatory fibrinoid polyp, hamartoma, adenoma, leiomyoma, lipoma, adenocarcinoma and leiomyosarcoma may serve as a lead point (4,6,7). In a review of gastroduodenal intussusception caused by gastric tumours, it was found that epithelial tumours cause almost 70% (8). To the best of our knowledge, this is the first reported case of AIHPS causing gastroduodenal intussusception.

Patients with AIHPS usually present with early satiety, abdominal fullness, postprandial vomiting, epigastric pain, and eructations (9,10). Associated anorexia and unintentional weight loss are also common (11). An uncommon presenting complaint of our patient is symptomatic iron deficiency anemia, which is a more common complaint seen in GIST (8). We postulated this might have occurred due to three reasons. The first reason is that our patient was malnourished due to inadequate dietary intake, which is caused by the existing AIHPS leading to chronic gastric outlet obstruction. The concomitant gastroduodenal intussusception, which may cause mucosal ulceration due to pressure necrosis, may lead to blood loss as well. Microscopic examination of the resected duodenal mucosa did show erosion suggestive of ischemia. Lastly, iron absorption takes place predominantly at the duodenum and upper jejunum. As our patient has gastroduodenal intussusception, this might have interfered with the dietary iron absorption.

The diagnosis of AIHPS is made based on clinical history, examination, upper endoscopic examination, imaging studies and tissue biopsy (12). Abdominal examination is usually unremarkable unless the stomach is dilated, unlike its juvenile counterpart where an "olive sign" can be elicited (10,11). An OGDS examination is essential for a thorough visual inspection of the upper gastrointestinal tract. A fixed, narrow pylorus with a smooth border has been described as cervix sign may be seen. This sign persists after anticholinergic therapy and can be differentiated from pylorospasm when pressure is applied via

OGDS (13). Often, duodenal intubation can be challenging with a standard gastroscope (10). Endoscopic findings are non-specific for AIHPS as it may be mistaken for GIST or diffusely infiltrating adenocarcinoma due to the normal appearing mucosa (11). Tissue biopsy is therefore essential, but as the gastric mucosa is normal, submucosal malignancy cannot be ruled out (11).

Various imaging modalities have been employed to aid the diagnosis of AIHPS. This includes plain radiographs, upper gastrointestinal contrast studies, CECT of the abdomen, and video capsule endoscopy. Plain radiographs of the abdomen may show a distended stomach, mottled appearance of gastric content, an indentation of gastric air shadow by the peristaltic wave and hypertrophy of the gastric rugae just proximal to the pylorus (14). The findings, however, are not specific to AIHPS and can be seen in any patient with gastric outlet obstruction (15). Kirklin or mushroom sign, a convex indentation at the duodenal bulb base, if present, is highly suggestive of AIHPS (12).

Upper GI contrast studies if performed, frequently show delayed gastric emptying with an elongated pyloric canal and a distended stomach (15). CECT of the abdomen is essential to exclude secondary causes of gastric wall thickening such as malignancy or GIST. In AIHPS, a CECT scan may show thickening of the distal gastric wall, but it is non-specific (9,15). In our case, a CECT helped us diagnose the pyloric wall thickening as well as the resulting gastroduodenal intussusception, although, at that time, a pyloric tumour was our likely diagnosis. Of note, CT enterography, a modern diagnostic tool used for small bowel disorders, may be helpful in the diagnosis of AIHPS (10).

Surgical resection is the mainstay treatment for patients presenting with AIHPS. Various surgical procedures have been employed, and these include distal gastrectomy with Billroth I or II reconstruction, gastroenterostomy, and pyloromyotomy with or without pyloroplasty (3,11,15). A more conservative endoscopic dilatation has also been attempted, but these ultimately result in a recurrence (11,15). If a preoperative diagnosis of AIHPS can be accurately made, laparoscopic pyloroplasty is a safe and effective procedure, with less morbidity than a gastrectomy (3). In our case, however, the patient presents acutely with symptomatic gastroduodenal intussusception, and we are unable to exclude malignancy of the pylorus. Hence, a more extensive surgical resection is undertaken.

CONCLUSION

AIHPS is a rare condition and should be a differential in adults presenting with gastric outlet obstruction. In the treatment of AIHPS, it is suggested that laparoscopic pyloroplasty may be less invasive. We believe in cases of AIHPS presenting with gastroduodenal intussusception, a distal gastrectomy with reconstruction is a more reasonable approach. A multidisciplinary approach is essential in dealing with rare diseases, and tailored management is required to obtain the best outcome.

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**OLGU SUNUMU-ÖZET**

Türk J Surg 2023; 39 (4): 377-382

Gastroduodenal intussusepsiyon ile başvuran bir hastada görülen yetişkin idiyopatik hipertrofik pilor stenozu: Nadir bir olgu sunumuLoo Guo Hou¹, Baharudin Nadia Nafasha¹, Hameed Sultan Mohamed Arif¹, Rajan Reynu¹, Ritza Kosai Nik¹, Rasul Hamidi Lizawati²¹ Ulusal Malezya Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalı, Bandar Tun Razak, Malezya² Ulusal Malezya Üniversitesi Tıp Fakültesi, Patoloji Anabilim Dalı, Bandar Tun Razak, Malezya**ÖZET**

Yetişkin idiyopatik hipertrofik pilor stenozu (AIHPS), ilk olarak 1835 yılında Cruveilhier tarafından tarif edilen nadir bir durumdur. İngilizce yayımlanan literatürlerde bugüne kadar bildirilen yaklaşık 200 vaka vardır. Histolojik olarak, gastrointestinal stromal tümör gibi iğ hücre neoplazmalarıyla karıştırılabilir. AIHPS'li hastalarda genellikle erken doygunluk, karında dolgunluk, postprandiyal kusma, epigastrik ağrı ve geçirme şikayetleri görülür. Yetişkinlerde görülen intussusepsiyon nadirdir ve tüm intussusepsiyonların yalnızca %5'ini oluşturur. Gastroduodenal intussusepsiyon, nadir görülen yetişkin intussusepsiyon tiplerinden biridir. Bu durumun, benign veya malign bir mide lezyonu öncüsü bir odak oluşturduğunda ortaya çıkması daha olasıdır. Bu çalışmada, gastroduodenal intussusepsiyon ile başvuran 70 yaşında bir kadında gözlenen bir AIHPS vakasını sunuyoruz. Hastaya yapılan özofagogastroduodenoskopide yaygın olarak kalınlaşmış ve daralmış bir pilorik antrum saptandı. Kontrastlı bilgisayarlı tomografide, pilorda çevresel kalınlaşma ile birlikte dilate bir mide görüldü. Prepilorik antrum pilorun içine doğru invajine olmuş ve apeksi duodenumun ilk bölümünde görülüyordu. Laparoskopik yaklaşımla Roux-en-Y rekonstrüksiyonu ile distal gastrektomi yapıldı ve hasta iyilik haliyle taburcu edildi. AIHPS nadir görülen bir durumdur ve gastrik çıkış tıkanıklığı görülen erişkinlerde ayırıcı tanıda yer almalıdır. Gastroduodenal intussusepsiyon ile başvuran AIHPS vakalarında, rekonstrüksiyonun eşlik ettiği bir distal gastrektominin makul bir yaklaşım olduğuna inanıyoruz. En iyi sonucu elde etmek için multidisipliner bir yaklaşım esastır.

Anahtar Kelimeler: Yetişkin idiyopatik hipertrofik pilor stenozu, Roux-en-Y rekonstrüksiyonu ile distal gastrektomi, yetişkinlerde görülen intussusepsiyon, gastrointestinal stromal tümör

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Primary pancreatic hydatid disease: A rare presentation of echinococcosis

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ABSTRACT

Hydatid disease is a zoonotic parasitic disease which rarely involves pancreas primarily. Diagnosis of pancreatic hydatid cyst is a challenge and operative skills are important to avoid spillage of cyst's content. A 19-year-old male patient was admitted to hospital with recurrent abdominal pain which was on epigastrium and left upper quadrant of abdomen. Pain was not associated with nausea, vomiting or fever. An abdominal computed tomography (CT) scan was ordered. As a result of abdominal CT scan, there was a cystic area in tail of pancreas with a diameter of 5.6 cm which includes septa and there was calcification on borders of the cyst. Possible diagnosis were either pancreatic hydatid disease, pancreatic cyst adenoma or cystadenocarcinoma or pseudocyst of autoimmune pancreatitis. Whole body positron emission tomography (PET-CT) scan showed no other cyst or lesion other than pancreatic cyst. Hydatid disease indirect hemagglutination test has been studied and it was positive. Imaging studies and laboratory results were suggested hydatid disease and laparoscopic distal pancreatectomy has been applied. Primary pancreatic hydatid disease should be in differential diagnosis when newly appearing pancreatic cyst has been diagnosed, especially in endemic areas. Appropriate surgical technique has to be applied to avoid dissemination of cyst's content.

Keywords: Echinococcosis, hydatid disease, pancreas, pancreatectomy, laparoscopy

INTRODUCTION

Hydatid disease is a zoonotic parasitic disease which is endemic in countries raising farm animals like Middle Eastern countries, India, New Zealand, Australia, Türkiye and South Europe (1,2). Hydatid disease can involve with many organ but effects liver in 70% of patients and lungs in 20% of patients. This disease also effects muscles, bones, brain and spleen (1,3). This disease primarily involves pancreas very rarely and in literature 0.2-2% of all hydatid diseases were reported as primary pancreatic hydatid disease (4,5).

Diagnosis of a pancreatic hydatid cyst is a real diagnostic challenge. Final diagnosis can only be made during or after surgery but imaging and laboratory studies can help making diagnosis before surgery. A suspicion of pancreatic hydatid cyst is important preoperatively and surgical operation without spillage of cyst's contents is a must.

CASE REPORT

Nineteen-years-old male patient was admitted to hospital with recurrent abdominal pain. Pain was located in the epigastrium and left upper quadrant of abdomen and it was not associated with nausea, vomiting or fever. There was no relationship with food and not relieved with antacids. There was a tenderness on left upper quadrant. The patient had no history of previous abdominal operation. His vitals were stable and laboratory tests and abdominal CT scan were ordered.

Laboratory test results were completely in normal limits including white blood cell counts, serum CRP, amylase and lipase counts. In abdominal CT scan, there was a cystic area in tail of pancreas with a diameter of 5.6 cm which includes septa and there were calcifications on borders of the cyst (Figure 1). Pancreatic tail was replaced by the cysts. Pancreas head and body were normal. There was no lesions on liver, spleen and kidneys. There was no involvement of major artery and veins.

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Possible diagnosis were either pancreatic hydatid disease, pancreatic cyst adenoma or cystadenocarcinoma or pseudocyst of autoimmune pancreatitis. To make a differential diagnosis, immunoglobulin G subtypes have been studied and only IgG2 was higher than normal limits. Hydatid disease indirect hemagglutination test has been studied and it was positive. Endoscopic ultrasound imaging has been applied. It showed that a 3.4 cm x 4.1 cm cyst with septa located at the pancreatic body and there was no normal pancreatic tissue at the body localization due to compression. It also showed cysts at the tail portion of the pancreas but it couldn't be measured and pancreatic duct was dilated. PET-CT scan was ordered for metabolic characterization of the cysts and whole body scan. It showed no lesions other than cysts in pancreas. There was no significant FDG up-

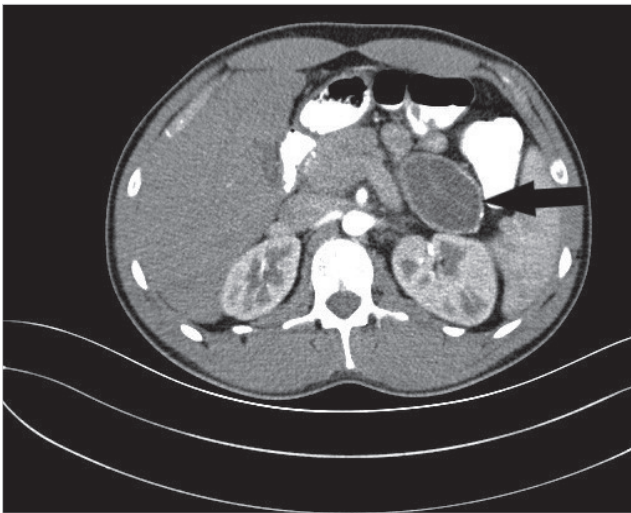


Figure 1. An image from computed tomography scan of patient. Black arrow represents pancreatic hydatid cyst.

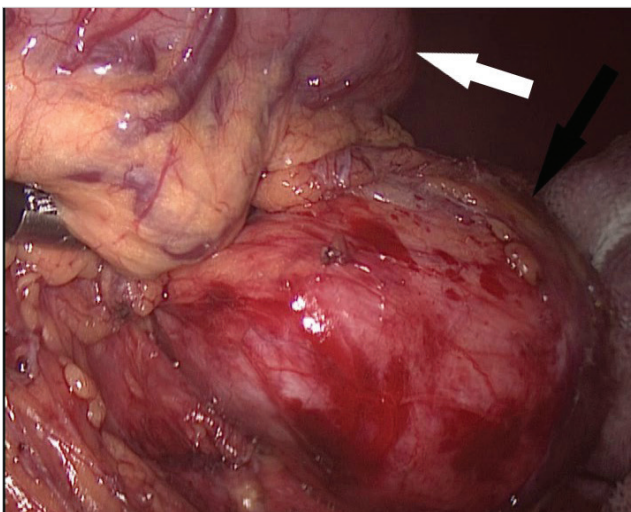


Figure 2. Intraoperative appearance of pancreatic hydatid cyst. Black arrow represents pancreatic hydatid cyst, white arrow represents stomach.

take. At the pancreatic tail, a centrally hypodense cyst which were measured 63 mm x 35 mm and were including septa has been observed.

Imaging studies and laboratory results were suggested hydatid disease and surgical operation was planned for this patient. Spleen preserving laparoscopic distal pancreatectomy has been performed (Figure 2). In total of 4 trocars (1 x 15 mm, 1 x 12 mm, 2 x 5 mm ports) have been used for operation. Twelve mm trocar was placed on umbilicus for the camera and 15 mm trocar was placed from 5 cm left superiolateral site. Right 5 mm trocar was placed from 5 cm right superiolateral to the umbilical port and left 5 mm port placed more left superiolateral to the 15 mm trocar. Fifteen mm trocar was used for entrance of laparoscopic stapling device. Operation time was 185 minutes and estimated blood loss was approximately 120 mL. Excised material has been taken out after widening of 15 mm trocar entrance site. An specimen retrieval bag was used and serious care was taken during this removal process to avoid spillage of cyst content.

There was no complications during admission and patient discharged fifth day postoperatively. Albendazole therapy (800 mg/day) was started after surgery for three months. After analysis of specimen in the pathology department, diagnosis of the patient was concluded with pancreatic hydatid cyst and eosinophil-rich mixed type moderate inflammatory cell infiltration at the cyst wall. At the end of one year of follow-up, patient has no complaint or complications of surgery.

DISCUSSION

Primary pancreatic hydatid disease is a very rare entity constituting only 0.2-2% of all cases of hydatid disease (4,5). Hydatid disease involves liver and lung in 90% of all cases (1,3). Primary involvement of pancreas with hydatid disease is an unexpected diagnosis for most physicians. Primary pancreatic hydatid cysts are mostly seen in the head (57%), body (24%) and tail (19%) (1-3,6). In this case hydatid cyst was located in the tail and it replaced pancreatic tissue.

Echinococcus granulosus is acquired through oral route and it can be spread to the pancreas mainly with hematogenous pathway, and it also uses peripancreatic lymphatic pathway, retroperitoneal and pancreatobiliary pathway (2,7,8).

Clinical presentation can be different from each other based on size and location of hydatid cyst inside of the pancreas in addition to pancreatic canal involvement (1-3,6-8). Cysts that located in the head of pancreas may cause jaundice, cholangitis and pancreatitis but cysts are located in body and tail may be more silent and they can grow slowly until they cause symptoms (fullness, early satiety, abdominal discomfort and pain) or complications (6,7). Complications of pancreatic hydatid disease may be rupture, biliary or intestinal fistula, segmental portal hypertension, vascular thrombosis, acute or chronic pancreatitis (1-3,5-8).

In this case, patient has a cyst in the tail of pancreas and cyst hadn't been noticed unless it started to cause pain.

Pancreatic cysts have a wide range of differential diagnosis. Diagnosis of primary pancreatic hydatid disease is mostly with imaging studies but being suspicious especially in endemic countries can change the surgical approach to the cysts (1,8). Gold standard diagnostic test is histopathologic examination postoperatively (9). Cysts has to be excised or aspirated without spreading protoscolices inside abdomen. Dissemination of hydatid cyst contents inside of body can cause anaphylaxis and recurrences. CT scan, MR imaging, PET-CT or USG can help with diagnosis but none of them satisfactory. CT scan that shows an rounded cystic lesions with curvilinear calcification, indulating membrane, multiple degenerating daughter cyst inside of mother cyst can help with diagnosis of hydatid disease. CT scan also can help with the evaluation of the complications of hydatid disease such as pancreatitis and opening of the hydatid cyst to the pancreatic canal. USG can show multi vesicular cysts, limited by a clean wall, contains daughter cysts and peripheral calcifications (1-3,7). T2 weighted MR images show distinctive low intensity rim of hydatid cyst (10). Various serological test can be used if there is clinical suspicion of hydatid disease. Enzyme linked immuno-absorbent assay gives positive result in 85% of hydatid disease (2,8). Serum immunoelectrophoresis, complement fixation test, immunofluorescence assay and indirect hemagglutination test can be used. In this case, CT scan helped to include hydatid disease as a differential diagnosis. Indirect hemagglutination test was used and it was positive. This result increased our suspicion for primary pancreas hydatid disease.

Surgery is the main choice of treatment of hydatid disease. Complete excision of cyst or distal pancreatectomy can be applied if hydatid cyst is located at the tail of pancreas. In lesions that located at the head of the pancreas partial cystectomy or pericystectomy can be applied. Before excision of the cyst, injection of scolical material is important to decrease the risk of spreading protoscolices to the abdomen. Careful aspiration of the cavity is crucial. Omentoplasty can be applied after cleaning inside of the cavity (2,3). In this case, laparoscopic distal pancreatectomy had been applied. During laparoscopic technique, excision or suction of the cyst must be careful to prevent spillage of the content. Preoperative and postoperative use of albendazole can help prevent recurrences but it is not enough alone (2,8). A good surgical technique is essential.

CONCLUSION

Primary pancreatic hydatid disease is a rarity and differential diagnosis of this disease is a clinical challenge. Especially in

endemic areas, hydatid disease of pancreas should be kept in mind when a pancreatic cyst is seen.

Acknowledgment

Authors declare that they have no competing interests. An informed consent was taken from the patient.

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Author Contributions: Concept - All of authors; Design - All of authors; Supervision - All of authors; Materials - All of authors; Data Collection and/or Processing - All of authors; Analysis and/or Interpretation - All of authors; Literature Search - All of authors; Writing Manuscript - All of authors; Critical Reviews - All of authors.

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**OLGU SUNUMU-ÖZET**

Turk J Surg 2023; 39 (4): 383-386

Pankreasın primer hidatik hastalığı: Ekinokokozun nadir bir türüMehmet Köstek¹, Özgür Bostancı¹, Muharrem Battal¹, Hüseyin Alkım²¹ Sağlık Bilimleri Üniversitesi, Şişli Hamidiye Etfal Eğitim ve Araştırma Hastanesi, Genel Cerrahi Kliniği, İstanbul, Türkiye² Sağlık Bilimleri Üniversitesi, Şişli Hamidiye Etfal Eğitim ve Araştırma Hastanesi, Gastroenteroloji Kliniği, İstanbul, Türkiye**ÖZET**

Hidatik hastalık, nadiren primer olarak pankreası tutan zoonotik parazitik bir hastalıktır. Pankreatik hidatik kistin tanısının konulması klinisyeni zorlamakta ve kist içeriği yayılmadan operasyonun tamamlanması için cerrahi beceri önem taşımaktadır. On dokuz yaşında erkek hasta epigastri-umda ve karın sol üst kadranda olan tekrarlayıcı karın ağrısı ile hastanemize başvurdu. Ağrının bulantı, kusma ve ateşle ilişkisi yoktu. Çekilen tüm batin bilgisayarlı tomografisinde, pankreas kuyruk kesiminde içerisinde septaların ve sınırlarında kalsifikasyonların bulunduğu 5,6 cm çapında kistik bir yapı görüldü. Ayırıcı tanıda, pankreatik hidatik hastalık, pankreas kistadenomu, kistadenosarkomu veya otoimmün pankreatite sekonder oluşmuş olabilecek psödokist mevcuttu. Tüm vücut fluorodeoksiglukoz pozitron emisyon tomografisinde pankreas kisti dışında herhangi başka bir kist ya da lezyon görülmedi. Hidatik hastalık için yapılan indirekt hemaglutinasyon testi pozitif sonuçlandı. Görüntüleme ve laboratuvar sonuçları hidatik hastalık ile uyumluydu ve hastaya laparoskopik distal pankreatektomi uygulandı. Yeni oluşmuş pankreatik kisti bulunan hastalarda, özellikle endemik bölgelerde, primer pankreatik hidatik hastalık ayırıcı tanıda bulunmalıdır. Kistin içeriğinin batına yayılmadan uygun cerrahinin yapılması büyük önem taşımaktadır.

Anahtar Kelimeler: Ekinokokoz, hidatik hastalık, pankreas, pankreatektomi, laparoskopi**DOI:** 10.47717/turkjsurg.2023.4768



How to do it: Splenic flexure mobilisation via medial trans-mesocolic approach

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ABSTRACT

Complete splenic flexure mobilization is a critical step in left-sided colorectal resections. Surgeons use three approaches-anterior, medial, and lateral-to divide peritoneal ligaments connecting the left colon. The decision to perform mobilization varies, with minimal impact on post-operative outcomes but longer surgery times and rare complications. Pancreatic injury risk is low, though other structures, like arteries and the duodenum, may be at risk. Our video outlines the medial trans-mesocolic approach, with the patient positioned in lithotomy. We expose the duodenal-jejunal flexure, ligate the inferior mesenteric vein, and perform medial to lateral dissection, completing splenic flexure mobilization. This video vignette outlines how to perform this technique for left sided colorectal resections.

Keywords: Laparoscopic surgery, colorectal, colorectal cancer, left hemicolectomy, anterior resection

Video link: <https://turkjsurg.com/video/UCD-6258-v1.mp4>



How I do it

Complete splenic flexure mobilization is a technically challenging step in performing left sided colorectal resections including left hemicolectomy and anterior resection. The aim of performing splenic flexure mobilization is to achieve adequate oncological resection margins with complete mesocolic excision and allow a tension free anastomosis for gastrointestinal continuity (1). There are three techniques described in literature to perform splenic flexure mobilization, which can be characterized into anterior approach, medial approach, and lateral approach (2). In each approach, the primary aim is to divide the peritoneal ligaments that connect the left colon to surrounding structures including the gastrocolic ligament, splenocolic ligament, phrenocolic ligament and pancreaticocolic ligament.

Splenic flexure mobilization may be performed routinely, selectively, or not at all by surgeons. A recent meta-analysis regarding post operative outcomes following splenic flexure mobilization in laparoscopic and open left sided resections has revealed no statistically significant difference in anastomotic leak, conversion to open, post-operative bleeding, intra-abdominal collection, ileus, wound infection, length of stay, R0 resection margin and local recurrence rates (3). The meta-analysis has also shown significantly longer operative time and higher incidence of intra-operative complications although overall rare with splenic flexure mobilization (3). Pancreatic injury during splenic flexure mobilization is rare (0.6%); however, it can lead to major complications if they occur (4). Other structures that may be injured during dissection are left branch of middle colic artery, marginal artery, duodenum, spleen, inferior mesenteric vein, and left ureter. When comparing the three approaches to splenic flexure mobilization, the lateral approach had higher rate of intraoperative complication compared to medial and anterior approach (5).

In the video S1, we outline the necessary steps to perform splenic flexure mobilization with a medial trans-mesocolic approach. The patient is positioned in litho-

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tomy with left side tilt and ports placed to triangulate towards the left upper quadrant. The first step involves exposure of the duodenal-jejunal flexure. Adhesions around the duodenal-jejunal flexure are taken down to expose the inferior mesenteric vein. The inferior mesenteric vein is seen just lateral to the duodenal-jejunal flexure and is ligated at the lower border of the pancreas. Medial to lateral dissection begins inferior to the inferior mesenteric vein in the embryological plane above Gerota's fascia. Dissection continues until the left colonic wall is visualized. The lesser sac is then entered inferiorly through the avascular window in the transverse mesocolon, superior to the duodenal-jejunal flexure. The pancreaticocolic ligament is divided which connects the dissection created earlier to the lesser sac. A Raytec is placed in the space once medial dissection is completed. The greater omentum is then divided above the transverse colon to enter the lesser sac. Dissection is continued laterally towards the splenic flexure. Lateral dissection is continued through the left paracolic gutter until the Raytec placed earlier is visualized. This completes splenic flexure mobilization, and the planned surgical resection is continued.

Ethics/patient consent

The patient featured in this video has provided written consent for medical videography and publication. This can be supplied on request by contacting the corresponding author. Providing written consent satisfies the ethical requirements at our institution for the purposes of educational publication.

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Author Contributions: Concept - AA, AB, ANV; Design - ANV, LDW; Supervision - AA, AB, ANV; Materials - BBWL; Literature Search - BBWL; Writing Manuscript - BBWL, LDW; Critical Reviews - ANV, LDW, AA, AB, ANV.

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VIDEO MAKALE-ÖZET

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Medial transmezokolik yaklaşımla splenik fleksür mobilizasyonu: Nasıl yapılır?

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ÖZET

Tam splenik fleksür mobilizasyonu, sol taraflı kolorektal rezeksiyonlarda kritik bir adımdır. Cerrahlar sol kolonu sabitleyen peritoneal ligamentleri bölmek için anterior, medial ve lateral olmak üzere üç yaklaşım kullanmaktadır. Mobilizasyon gerçekleştirme kararı, ameliyat sonrası sonuçlar üzerinde minimal etkiye sahip olmakla birlikte daha uzun ameliyat süreleri ve nadir komplikasyonlarla değişmektedir. Pankreas yaralanması riski düşüktür ancak arterler ve duodenum gibi diğer yapılar risk altında olabilir. Videomuz, hasta litotomi pozisyonundayken medial transmezokolik yaklaşımı özetlemektedir. Bu teknikte, duodenal-jejunal fleksurayı açığa çıkarıyoruz, inferior mezenterik veni bağlıyoruz ve medialden laterale diseksiyon gerçekleştirerek splenik fleksura mobilizasyonunu tamamlıyoruz. Bu video, sol taraflı kolorektal rezeksiyonlar için bu tekniğin nasıl uygulanacağını özetlemektedir.

Anahtar Kelimeler: Laparoskopik cerrahi, kolorektal, kolorektal kanser, sol hemikolektomi, anterior rezeksiyon

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