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AIMS AND SCOPE

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.

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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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INSTRUCTIONS TO AUTHORS

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

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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/herlegal representative should be enclosed.

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1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of the data for the work;
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 other specific parts of the work. In addition, authors should have confidence in the integrity of the contributions of their co-authors.

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

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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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MANUSCRIPT PREPARATION

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

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

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

Authors are required to submit the following:

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

INSTRUCTIONS TO AUTHORS

during the initial submission. These forms are available for download at www.turkjsurg.com.

Preparation of the Manuscript

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

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

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

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

Manuscript Types

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

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

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

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

Review Articles: Reviews with high citation potential prepared by authors with extensive knowledge on a particular field and whose scientific background has already been proven by a high number of publications in the related field are welcomed. These authors may even be invited by the journal. Reviews should describe, discuss, and evaluate the current level of knowledge of a topic in clinical practice and should guide future studies. The main text should contain Introduction, Clinical and Research Consequences, and Conclusion sections. Please check Table 1 for the limitations for Review Articles.

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

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

The details of the review process are below.

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

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

The following items must be provided:

- The file of the video written in Word format.
- A completed copy of the online broadcast consent form (form will be prepared and linked), together with completed copies of patient consent forms, if appropriate.
- All videos must contain an English narration.
- All videos should also be in the highest resolution possible, more details on accepted file types and resolution are available at this link (authors' video article submission guidelines; https://turkjsurg.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

INSTRUCTIONS TO AUTHORS

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 × 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: Bengisson 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 Ilişkiler. 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/ncidodlElD/cid.htm.

REVISIONS

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

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

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FROM THE EDITOR'S DESK
Turk J Surg 2022; 38 (3): IX
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The Growing Role of Video Materials in Medical Publishing

Dear Readers of Turkish Journal of Surgery,

Physicians are now surrounded with novel tools of the digital age. However, colleagues from my generation grew up and trained in an environment, where they had neither internet nor digital recording devices. Transformation into the new digital age has been much faster than our mental adaptation. Undoubtedly, young colleagues have a better compliance to every novel modern tool in the practice of medicine, but it is still a growing field.

Institutions -such as medical journals- must also adapt themselves to the changes and stay up to date. A relatively new sort of medical publication is "video article". Videos are practical, educative and entertaining. As you may also observe during medical congresses, video sessions always attract a great interest. Scientific videos are now inseparable tools of scientific sharing and surgical education.

Many scientific journals are accepting submissions for video articles, few of them pay special attention to these digital scientific products. TJS has welcomed submissions of video articles for a long time. Nevertheless, there are very few video articles in our archives. To be honest, I do consider this fact as our deficiency in adapting to the digital age. To this purpose, we have worked over the Journal's policy and technical requirements for video submissions during the last two months intensively. Our aim is to welcome more submissions of high-quality and scientifically important videos. Since the current technology of video recording (robotic or laparoscopic surgery, high-definition cameras for open surgery etc.) is very convenient and accessible, we do expect a considerable number of video submissions now.

We have revised the instructions for videos according to current requirements. You may find them on our Journal's web site. Video articles will have on the forthcoming issues a special place and our aim will be to adapt TJS quickly into the digital age. Please submit to TJS not only your best study but also your best video!

On behalf of the editorial team, I wish you a pleasant reading!

Kindest regards,

Kaya SARIBEYOĞLU
Editor-in-Chief
Turkish Journal of Surgery

ORIGINAL ARTICLE
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Liver hanging maneuver is suitable in major hepatectomy for liver malignancies over 5 cm

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ABSTRACT

Objective: Hepatic transection through an anterior approach is required to successfully complete anatomical hepatectomy for large liver malignancies. The liver hanging maneuver (LHM) is an alternative procedure for transection on an adequate cut plane and may reduce intraoperative bleeding and transection times.

Material and Methods: We examined the medical records of 24 patients with large liver malignancies (>5 cm) who had undergone anatomical hepatic resection with LHM (n= 9) or without LHM (n= 15) between 2015 and 2020. Patient demographics, preoperative hepatic function, surgical records, and post-hepatectomy outcomes were retrospectively compared between the LHM and non-LHM groups.

Results: The prevalence of tumors >10 cm was significantly higher in the LHM group than in the non-LHM group ($p< 0.05$). Furthermore, LHM was significantly performed to right and extended right hepatectomies in the background normal liver ($p< 0.05$). Although transection times did not significantly differ between the two groups, the amount of intraoperative blood loss was slightly lower in the LHM group than in the non-LHM group (1.566 mL vs. 2.017 mL), and blood transfusion was not needed for patients in the LHM group. Post-hepatectomy liver failure and bile leakage were not observed in LHM. However, the length of hospitalization was slightly shorter in the LHM group than in the non-LHM group.

Conclusion: LHM is useful for transecting an adequately cut plane in hepatectomy for liver tumors over 5 cm-in-size located on the right side and achieves better outcomes.

Keywords: Large intrahepatic malignancies, anterior hepatectomy, liver hanging maneuver, blood loss

INTRODUCTION

In major hepatectomy, reducing intraoperative blood loss and the need for transfusions may minimize postoperative tumor relapse and prolong the survival of patients with primary liver cancer (1,2). In cases in which large liver tumors occupy and compress the main intrahepatic vasculature, transection of the liver parenchyma through an anterior approach without mobilization of the remnant liver is preferable because the avoidance of liver rotation has the advantages of circumventing tumor dissemination and/or injury produced by compression of the remnant liver (3). Furthermore, a longer transection time due to the loss of the transection plane may increase blood loss.

Belghiti et al. (4) have proposed the liver hanging maneuver (LHM) for right hepatectomy without liver mobilization using a nasogastric tube inserted into the free space between the avascular vena cava surface and the backside of the caudate liver. The lifting of this tube or tape allows parenchymal transection in a deeper site and transection that avoids short hepatic veins (5). LHM has been attracting increasing interest worldwide for major anatomical hepatectomy, particularly that for large liver tumors or tumors compressing the surrounding vascular architecture (6-8). This technique has recently been applied for less invasive anatomical resection (9). Moreover, the transected and remnant liver are both rotated to the counter side by lifting the hepatic back side during transection (8), which is useful for successfully transecting the deeper parenchyma in the final step. Although the primary author had already published a pilot study article on LHM over 10 cm at another institute in the 2000s, in comparisons with the conventional rotated procedure, it currently remains unclear whether LHM minimizes blood loss or reduces transection

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times. Since various transection procedures and materials have recently been developed, LHM alone is not as useful in most cases (10,11). At the time of recent stable time since the 2010s in comparison with a decade ago, further studies are warranted to clarify the significance of LHM in the current era.

To clarify our hypothesis on the minimization of blood loss and reductions in transection times, we retrospectively and historically examined surgical data on liver malignancies large over 5 cm in patients who underwent major hepatectomy and compared these parameters with those of patients who underwent liver resection with or without LHM at a different academic institute.

MATERIAL and METHODS

Study Design and Patients

The study protocol for database access and review, ethics and non-conflict of interests were approved by the Institutional Medical Board of University of Miyazaki Hospital between April 2015 and December 2020 (reference number O-0898, on February 18th, 2021). Patient consent was obtained by the opt-out procedure for one month on the hospital's website in march, but with no disclaimer. We performed liver resection (including more than three segmentectomies) on 24 patients with liver malignancies >5 cm; nine patients (38%) underwent LHM (the LHM group) according to the policy of the first author while the remaining 15 patients underwent resection without LHM (the non-LHM group) by another experienced surgeon's choice and were compared as the control.

Clinical and Surgical Parameters

The following data were collected for analysis: age, sex, background liver disease, liver disease, preoperative liver functions (indocyanine green retention rate at 15 minutes), liver uptake ratio by technetium-^{99}m-galactosyl, human serum albumin, liver scintigraphy, surgical procedure or records (extent of hepatectomy, surgical device, vena cava clamping, operation time, time for liver parenchymal transection, blood loss, and blood transfusion), post-hepatectomy-related complications (uncontrolled ascites, intraabdominal abscess, bile leakage, and hepatic failure), and duration of hospitalization. Uncontrolled ascites or pleural effusion was defined by the use of diuretics for more than two weeks.

The surgical procedure included J-shaped incision laparotomy (upper median plus right-sided transverse incision to the ninth intercostal space) (11). The falciform ligament was cut to expose the confluences of the right, middle, and left hepatic veins and the anterior surface of the vena cava. Mobilization of the remnant liver was not performed on patients who underwent LHM. LHM was conducted according to the method described by Belghiti et al (4). The space between the right and middle hepatic veins was dissected using a right-angled clamp. Loose connective tissue between the anterior surface of the vena cava and the paracaval caudate lobe was dissected from this space using a long Kelly clamp at the space without short hepatic veins (12). A 10-Fr nasogastric tube was inserted and passed easily through the dissecting space. We completed tube insertion within approximately 10 minutes. The tube was then lifted up for LHM. The cut plane along the middle or umbilical fissure hepatic vein was hung up by the tube as previously reported (8). Various anatomical resections are possible using the tube re-positioning technique, as described by Kokudo et al. (13). Hemostatic devices, such as LigaSure®, and ultrasonic coagulation instruments were consistently used in the present series. Hepatic transection was mainly performed in combination with the crush clamping method, while an ultrasonic dissector was used for dissection around the main vessels at the hepatic hilum or inferior vena cava (IVC) (14). Hepatic inflow was intermittently occluded during transection using the Pringle maneuver (15 minutes of occlusion and five minutes of de-clamping) (15). In cases in which bleeding from the compressed hepatic vein was not controlled during hepatectomy, the infrahepatic vena cava was taped and semi-clamping was performed by maintaining central venous pressure (16,17).

Statistical Analysis

The primary endpoints were blood loss and transection times under Pringle's maneuver during hepatectomy, and secondary endpoints were post-hepatectomy morbidity and mortality and length of hospitalization. Continuous data were expressed as means ± SD. Data for different groups were compared using a one-way analysis of variance (ANOVA). Chi-squared test was used for comparisons of categorical variables. Differences between the groups were analyzed by Fisher's exact test or Scheffé's multiple comparison test. A two-tailed p-value of less than 0.05 was considered to be significant. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software, version 22.0 (IBM, Chicago, IL, USA).

RESULTS

Table 1 summarizes demographic and surgical data and comparisons of the LHM and non-LHM hemihepatectomy groups. No significant differences were observed in age or sex between the two groups. Comparisons of background liver diseases and liver tumors showed no significant differences between the non-LHM and LHM groups. Furthermore, the results of preoperative liver function tests did not significantly differ between the two groups. However, the prevalence of tumors >10 cm was significantly higher in the LHM group than in the non-LHM group ($p< 0.05$).

Operative procedure, thoracotomy, extent of hepatectomy, and use of vena cava clamping and surgical devices did not significantly differ between the two groups. Furthermore, no significant differences were observed in the transection time (similar

Table 1. Comparison of patient demographics, surgical records, and postoperative outcomes

	LHM group, n= 9	Non-LHM group, n= 15	p
Age	65 ± 12	62 ± 21	0.907
Sex (male/female)	9 (100)/0	12 (80)/3 (20)	0.225
Background liver			
Normal/chronic hepatitis/cirrhosis/NAFLD/CASH/ jaundice	1 (11)/2 (22)/0/2 (22)/3 (34)/1 (11)	7(47)/2 (13)/2 (13)/1 (7)/1 (7)/2 (13)	0.295
Diseases			
HCC/CCC/CLM/others	4 (44)/1 (11)/2 (22)/1 (11)	6 (40)/3 (20)/6 (40)/0	0.485
Tumor size			
5-10 cm/>10 cm	2 (22)/7 (78)	10 (67)/5 (33)	**0.049**
Preoperative liver functions			
Liver damage grade A/B*	9 (100)/0	15 (100)/0	1.0
Indocyanine green retention rate at 15 minutes (%)	13.1 ± 4.7	9.7 ± 5.4	0.069
Preoperative hyaluronic acid level (ng/mL)	68 ± 44	90 ± 55	0.492
Liver uptake ratio by GSA liver scintigraphy	0.93 ± 0.03	0.94 ± 0.02	0.702
Surgical records			
Thoracotomy (No/Yes)	7 (78)/2 (22)	9 (60)/6 (40)	0.455
Liver stiffness (Soft/Hard)	9 (100)/0	11 (73)/4 (27)	0.259
Blood loss (mL)	1566 ± 1243	2117 ± 1934	0.558
Red cell transfusion (No/Yes)	3 (34)/6 (66) (938 mL)[#]	6 (40)/9 (60) (1.056 mL)	0.999
Total operation time (minutes)	488 ± 152	544 ± 139	0.385
Transection time under inflow occlusion (minutes)	56.4 ± 13.5	68.1 ± 64.4	0.999
Procedures			
(hemi-/extended hemi-/trisectionectomy)	5 (56)/3 (33)/1 (11)	11 (73)/3 (20)/1 (7)	0.205
Right-side/Left-side hepatectomy	8 (89)/1 (11)	7 (47)/8 (53)	**0.018**
Postoperative liver function			
Maximum total bilirubin (mg/dL)	0.68 ± 0.20	0.83 ± 0.46	0.744
Maximum ALT (IU/L)	425 ± 444	547 ± 345	0.209
Minimum prothrombin activity (%)	54 ± 10	49 ± 14	0.503
Patient outcome			
Morbidity (No/Yes)	8 (89)/1 (11)	14 (93)/1 (7)	0.999
Hepatic failure (No/Yes)	9 (100)/0	13 (87)/2 (13)	0.551
Uncontrolled ascites (No/Yes)	7 (78)/2 (22)	12 (80)/3 (20)	0.999
Bile leakage (No/Yes)	9 (100)/0	12 (80)/3 (20)	0.999
Hospital stay (days)	24.2 ± 10.4	30.0 ± 8.9	0.135

Parenthesis shows the ratios (percentage).
Liver Damage grade guided by the General Rules for the Clinical and Pathological Study of Primary Liver Cancer in Japan (16).
GSA: Galactosyl serum albumin, NAFLD: Non-alcoholic fatty liver disease, CASH: Chemotherapy-associated fatty liver disease in colorectal cancer patients, HCC: Hepatocellular carcinoma, CCC: Cholangiocellular carcinoma, CLM: Colorectal liver metastasis, GSA: Galactosyl serum albumin, ALT: Alanine transaminase.
[#]Mean value in patients who received blood transfusions.

to the time of the clamping of hepatic blood inflow), amount of intraoperative blood loss, blood transfusion, or total operation time between the two groups. However, the prevalence of right hepatectomy was significantly higher in the LHM group than in the non-LHM group ($p< 0.05$).

Results on postoperative complications and outcomes were compared. Regarding postoperative complications, no significant differences were observed in the total complication rate between the non-LHM and LHM groups. Furthermore, the prevalence of hepatectomy-related complications and the length of hospitalization did not significantly differ between the two groups. No in-hospital deaths were recorded in the present study.

DISCUSSION

We previously reported another population, limited to large hepatocellular carcinoma (HCC) (>10 cm), between 2000 and 2007, which included initial hepatectomy during a technical learning curve for the first author at a different institute as a pilot

study (18). The findings obtained showed significantly less intraoperative blood loss (1.269 ± 1.407 mL) and shorter transection times (39.7 ± 10.5 minutes) than those by another operator (19). In patients with a large tumor or tumor that invaded adjacent organs, anterior liver transection was preferably performed through the LHM procedure, and hepatic vein transection or the combined resection of invasive parts was conducted in the final step after complete transection to the front of the vena cava. In 2003, Kokudo et al. (13) proposed the gradual tape-repositioning technique for cases of living liver donation, in which the tape is inserted by passing it between Glisson's pedicle and the liver parenchyma. When such reports were published on LHM, LHM had already been performed for various types of anatomical hepatectomies (6,7,20). However, Shindoh et al. reported that LHM for HCC was rarely performed in hepatectomy in a larger series, this procedure did not appear to be the standard, and a conventional anterior approach without LHM was applied in laparoscopic right hepatectomy developed after the 2010s (10). Since the first author performed LHM or hepatectomy when he moved to the present institute, reconfirming the significance of LHM for large liver tumors was attempted in the present study because other experienced operators routinely performed conventionally mobilized hepatectomy without LHM, even for large tumors at this institute.

We compared clinical parameters and outcomes of a small number of patients between the LHM and non-LHM groups in a non-random manner, which is a limitation of the present study. As shown in Table 1, the background and preoperative liver functional reserve in patients in both groups did not significantly differ; however, liver tumors >10 cm were more likely to be treated by the first author and LHM was preferably applied for cases in which mobilization of the resected liver was difficult. However, although tumor characteristics, type of surgical intervention and surgical teams were compared in the two groups, tumor diameter exceeding 10 cm and right hepatectomy rates were significantly higher in the LHM group. Thus, the small number of patients and the retrospective nature of the study reduce the power of the study and make it difficult to interpret precisely. In the next step, a prospective study must be planned by setting these background. Surgical records showed that LHM did not reduce blood loss or transection times from those in the non-LHM group, and this may have been influenced by the selection bias of liver tumors as described above. Furthermore, the present results on blood loss (1566 ± 1243 mL) and transection times (56.4 ± 13.5 minutes) were consistent with previous findings (18). The lead author did not improve the procedures of LHM although the subjects were different between the previous and present LHM studies. Autologous blood transfusion was performed for most cases in the present series, whereas those in the previous series received allogenic transfusion. Blood transfusion, which affects the prognosis of cancer patients, does not appear to be involved in the present case (21).

The application of LHM in right hemi-hepatectomy was significantly more frequent in this cohort. In the case of left hepatectomy, LHM did not appear to be useful because the conventional technique was generally not difficult in many cases. In the LHM group, left-side hepatectomy was trisectionectomy because the operative field around the retrohepatic space was not clearly visualized due to the volume of the liver. Postoperative liver function and patient outcomes were similar and no mortalities occurred, which was consistent with our previous findings (18). In summary, potential reasons for the application of LHM include:

1) Dissection of the liver parenchyma along the main intrahepatic vasculature, particularly hepatic veins compressed by a large liver tumor;

2) Transection in a deeper part near the vena cava may be rapidly performed without injury to the vena cava or short hepatic veins due to shielding with covering tape;

3) Confirming the root of hepatic veins in the case of right hepatectomy and right or left trisectionectomy accompanied identification of the roots of the hepatic veins in right hepatectomy and left or right trisectionectomy in patients with a larger liver volume.

Since half-clamping of the infrahepatic vena cava (16,17) may prevent bleeding from hepatic veins because of a decrease in central venous pressure, we sometimes applied this procedure. However, surgical records did not significantly differ between the present and previous studies (18). According to the vascular anatomy or physique of patients, the application of IVC clamping is needed for large liver tumors compressing the IVC or hepatic veins (17). Regarding parenchymal transection, transecting or hemostatic devices were useful for reducing transection times (14); however, their utility for the control of hepatic venous bleeding remains unclear. Therefore, the development of novel hemostatic compound substances during transection is required (22); however, the use of fibrin glue did not appear to control parenchymal bleeding in hepatectomy (23). This study compares the results of two surgeons who did and did not perform LHM and the two groups were not similar in terms of the removed liver side and tumor sizes. Due to these disadvantages, the two groups might not be able to be precisely compared with each other. Although there is no statistical difference in comparisons, it is suggested that some parameters are advantageous over the other one. Under the light of these results, it seemed that there is no significantly difference between the two groups.

We previously reported that limited liver mobilization LHM may prevent prolonged ascites by limiting the detachment of ligament tissue around the liver (4,20). However, in the present

study, ascites was controlled well, and this result was attributed to the use of novel diuretics as vasopressin receptor inhibitors (Tolvaptan, Otsuka Pharmaceutical Co., Tokyo, Japan). Recent advances in not only surgical techniques, but also perioperative management have also improved patient outcomes.

CONCLUSION

We herein examined the suitability of LHM in major hepatectomy for large liver malignancies using a retrospective cohort study at a single academic institute. The use of LHM was useful in right hepatectomy or trisectionectomy for large liver tumors because it may be useful in identifying the target site of parenchymal resection and an adequate transected plane along compressed hepatic veins for large malignancies.

Ethics Committee Approval: The study protocol was approved by the Institutional Review Board of University of Miyazaki (Decision no: C-0898, Date: 18.02.2021). Written and informed consent was obtained from the opt-out method on our website. All study protocols followed guidelines stated in the Declaration of Helsinki.

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

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ORİJİNAL ÇALIŞMA-ÖZET
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Karaciğer asma manevrası, 5 cm üzerindeki karaciğerin malign tümörlerinde majör hepatektomi için uygundur: Retrospektif kohort çalışması

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ÖZET

Giriş ve Amaç: Karaciğerin büyük malign tümörlerinde anatomik hepatektomiyi başarıyla tamamlamak için önden yaklaşımla hepatik transeksiyon gereklidir. Karaciğer asma manevrası [*liver hanging maneuver* (LHM)] yeterli bir kesme düzleminde transeksiyon için alternatif bir prosedürdür ve intraoperatif kanama ve transeksiyon sürelerini azaltabilir.

Gereç ve Yöntem: 2015-2020 yılları arasında LHM (n= 9) ile veya LHM (n= 15) olmadan anatomik hepatik rezeksiyon yapılan ve karaciğerin büyük malign tümörleri (>5 cm) olan 24 hastanın tıbbi kayıtlarını inceledik. Hasta demografisi, preoperatif hepatik fonksiyon, cerrahi kayıtlar ve post-hepatektomi sonuçları LHM ve LHM dışı gruplar arasında retrospektif olarak karşılaştırıldı.

Bulgular: LHM grubunda 10 cm> tümör prevalansı LHM olmayan gruba göre anlamlı olarak daha yüksekti (s< 0,05). Ayrıca, LHM arka plan normal karaciğerinde sağ ve genişletilmiş sağ hepatektomilere anlamlı olarak daha sık yapıldı (s< 0,05). Transeksiyon süreleri iki grup arasında anlamlı olarak farklılık göstermese de LHM grubunda intraoperatif kan kaybı miktarı LHM dışı gruba göre daha düşüktü (1,566 mL ile 2,017 mL) ve LHM grubundaki hastalar için kan nakline gerek duyulmadı. LHM'de hepatektomi sonrası karaciğer yetersizliği ve safra kaçağı gözlenmedi. Ancak LHM grubunda hastaneye yatış süresi LHM olmayan gruba göre biraz daha kısaydı.

Sonuç: LHM, sağ tarafta bulunan büyük karaciğer tümörleri için uygulanan hepatektomide transeksiyon planını uygun şekilde bölmek için yararlıdır ve daha iyi sonuçlar elde edilmektedir.

Anahtar Kelimeler: Büyük intrahepatik maligniteler, anterior hepatektomi, karaciğer asma manevrası, kan kaybı

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Iatrogenic colon perforation during colonoscopy, diagnosis/treatment, and follow-up processes: A single-center experience

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ABSTRACT

Objective: Iatrogenic colon perforation (ICP) is one of the most feared complications of colonoscopy and causes unwanted morbidity and mortality. In this study, we aimed to discuss the characteristics of the cases of ICP we encountered in our endoscopy clinic, its etiology, our treatment approaches, and results in the light of the current literature.

Material and Methods: We retrospectively evaluated the cases of ICP among 9.709 lower gastrointestinal system endoscopy procedures (colonoscopy + rectosigmoidoscopy) performed for diagnostic purposes in our endoscopy clinic during 2002-2020.

Results: A total of seven cases of ICP were detected. The diagnosis was made during the procedure in six patients and after eight hours in one patient, and their treatment was performed urgently. Whereas surgical procedures were performed in all patients, the type of the procedure varied; laparoscopic primary repair was performed in two patients and laparotomy in five patients. In the patients who underwent laparotomy, primary repair was performed in three patients, partial colon resection and end-to-end anastomosis in one patient, and loop colostomy in one patient. The patients were hospitalized for an average of 7.14 days. The patients who did not develop complications in the postoperative follow-up were discharged with full recovery.

Conclusion: Prompt diagnosis and appropriate treatment of ICP is crucial to prevent morbidity and mortality.

Keywords: Colon perforation, colonoscopy, complication

INTRODUCTION

Colonoscopy is the most effective diagnostic/treatment method in the detection and treatment of colon and distal ileum pathologies. During this procedure, bleeding and perforation that occur independently or iatrogenic are the most feared and common complications (1). Perforation frequency is reported to range from 0.03% to 0.8% in diagnostic colonoscopy (2). Mortality due to colon perforation has been reported in the range of 0%-0.05% (3). Major cause of mortality is generalized peritonitis and sepsis as a consequence of late detection of perforation and delayed treatment (4,5). Formation of iatrogenic colon perforation (ICP) is reported to be related with the age of the patient, insufficient bowel cleansing, presence of dolichocolon, previous abdominal surgeries, procedure type, use of analgesics during the procedure, procedure speed and insufficiency of the time allocated, experience of the endoscopist performing the procedure, and quality of the endoscopy system (6-8).

Detection and treatment of colon perforation during the procedure is critical in preventing mortality and morbidity (9). The experience of and attention given to such complications by the endoscopist are crucial. According to the characteristics of the perforation, endoscopic or surgical therapy must be chosen (10-12).

In this study, we aimed to discuss the characteristics of the cases of ICP, the underlying reasons for its occurrence, our treatment approaches, and results in the light of the current literature.

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MATERIAL and METHODS

Cases of ICP in patients who had undergone lower gastrointestinal system endoscopy (rectosigmoidoscopy and colonoscopy) in the endoscopy unit of our hospital between January 2002 and December 2020 were evaluated retrospectively. Demographic characteristics of the patients, features of the colonoscopy procedure (diagnostic or therapeutic), diagnosis of perforation and characteristics of perforation, treatment modalities, and results were assessed. The colonoscopy technique followed by the endoscopists, adequacy of colon cleansing procedure, and how the perforation was detected were recorded.

All procedures were performed with sedoanalgesia (midazolam, propofol -/+ pethidine) under the supervision of an anesthesiologist. The procedures were performed by ten general surgeons and five gastroenterologists. The endoscopy experience of the specialists ranged from 2 to 25 years. Each endoscopist applied his own protocol for colon cleansing of the patients. Pre-anesthetic examinations were performed before the procedure. Fujinon series colonoscopes (EC-250 WL5, 530, 600 EC, 600 WL, 700 series) were used.

Written informed consent for endoscopy procedure and data sharing of the patients was obtained before the procedure. The study was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee (50-2290).

RESULTS

A total of 9108 colonoscopy and 601 rectosigmoidoscopy procedures were evaluated. Of the patients who underwent colonoscopy, 4325 were males and 4783 were females. Of those who underwent rectosigmoidoscopy, 240 were males, and 361 were females. Perforation occurred in seven patients (0.072%) who underwent colonoscopy due to complaints of iron deficiency anemia, occult blood positivity in stool, change in defecation/constipation, abdominal pain, and rectal bleeding. Among these patients, five were females, and two were males. Mean age of the patients was 72.28 years, and their average body mass index (BMI) was 25.14 kg/m^2.

The perforation area was in the sigmoid colon in five patients, descending colon–sigmoid colon junction in one case, and rectosigmoid corner in one case. Only in one case, the perforation developed on the mesenteric side, in the others (n= 6) the perforation was observed on the antimesenteric side of the colonic lumen. A total of ten perforations were detected in the colon, their diameters were 0.5-6 cm involving 10%-75% of the lumen. The average diameter of the perforations was 2.85 cm. Whereas multiple perforations were detected in the same area during surgery in two patients, serosal tears were observed in one patient. Diagnosis was made during the procedure in six patients and after eight hours in one patient. In the patients in whom ICP was detected during the procedure, surgery was performed under emergency conditions. While three patients underwent laparotomy-primary repair, laparotomy-partial colon resection and end-to-end anastomosis, and laparoscopic primary repair were performed in one and two patients, respectively. Laparotomy and loop colostomy were performed for the patient who was diagnosed late. Laparotomy had to be preferred instead of laparoscopy in these patients. When we looked at the causes of laparotomy in our patients, two patients had advanced chronic heart disease. Laparotomy was performed because an increase in intra-abdominal pressure was not desired. One patient had a large perforation area. One patient was diagnosed late and laparotomy was preferred in the other patient due to peritonitis carcinomatosis. Abdominal drainage was performed in all patients after surgery, and the patients were followed up with broad spectrum antibiotic therapy. The patients were hospitalized for an average of 7.14 (3-13) days. The longest duration of hospitalization (13 days) was required for the patient diagnosed late. All patients were discharged after complete recovery (Table 1).

The colonoscopy technique followed by the endoscopists, adequacy of colon cleansing, and how perforation was detected were questioned. Difficulty reaching the terminal ileum was detected in three patients with perforation, and in two patients, there was difficulty in the passage of the sigmoid colon. In two patients, a sudden abdominal distension was observed when trying to reach the terminal ileum, whereas a suspicion of perforation was noted in one patient, and there was difficulty in passing the rectosigmoid corner in one patient. Perforation was suspected on observing fresh blood on return in two patients, whereas a sudden discharge and relief were observed in the colonoscope in three patients, leading to suspicion of perforation. Perforation was confirmed using standing plain abdominal radiography and abdominal computed tomography (CT) (Figures 1,2). Direct visualization of the perforation sites occurred in three patients, and the diagnosis was made by observing intra-abdominal organs in three patients (Table 2) (Figures 3,4). In one patient, diagnosis could not be made early, and the patient was discharged; however, the patient applied to the emergency clinic with severe abdominal pain eight hours later.

The clinical signs of perforation were defined as pronounced distension in the abdomen, increased and prominent tympanism, fresh blood in unexpected areas, a sudden feeling of relief and emptiness while pushing the colonoscope forward, mucosal tears, appearance of perforation, and appearance of intraperitoneal organs. Despite the lack of statistical analysis, some obvious risk factors for perforation were noted, such as advanced age (mean age 72.3 years), female sex (71.5%), dolichocolon, previous abdominal surgery, peritoneal carcinomatosis, rapidly performed procedure, loop formation, difficulty in accessing the ileocecal valve, and quality of the instrument used.

Table 1. Characteristics of the patients with perforation

Patient	Age (years)	Sex	BMI	Colonoscopy Indication	Location of Perforation	Localization of Perforation in the Lumen	Size (cm, its Ratio to Lumen)	Treatment	Duration of Hospitalization (days)	Accompanying Diseases
1	71	F	26.7	Iron deficiency	Descending-sigmoid colon junction	Antimesenteric wall	5 (70%)	EL + primary repair + drainage	6	HT
2	81	F	22.5	Constipation, abdominal pain	Sigmoid colon	Injury on the mesenteric side and serosal injury	2 (25%)	EL + primary repair + drainage	6	CHD
3	87	F	31.2	Anemia	Sigmoid colon	Antimesenteric wall + serosal injury at two points	2.5, 0.5 (30%, 5%)	EL + primary repair + biopsy from metastases + drainage	5	Stomach tumor Carcinomatosis
4	59	F	26	Rectal bleeding	Sigmoid colon	Antimesenteric wall	0.5 (10%)	Laparoscopic primary repair + drainage	3	Hysterectomy
5	63	M	22	Constipation	Sigmoid colon	Antimesenteric and mesenteric wall	6 (75%)	EL + loop colostomy + drainage	10	(–)
6	76	M	17.4	Anemia, OBS (+)	Sigmoid colon	Antimesenteric and mesenteric wall	2, 3, 4 (25%, 35%, 50%)	EL + partial resection + end-to-end anastomosis	13	CHD + COPD + HT
7	69	F	30.2	Anemia	Rectosigmoid corner	Antimesenteric wall	3 (35%)	Laparoscopic primary repair +drainage	3	(–)

BMI: Body mass index, CHD: Chronic heart disease, COPD: Chronic obstructive pulmonary disease, EL: Explorative laparotomy, HT: Hypertension, OBS: Occult blood in the stool.

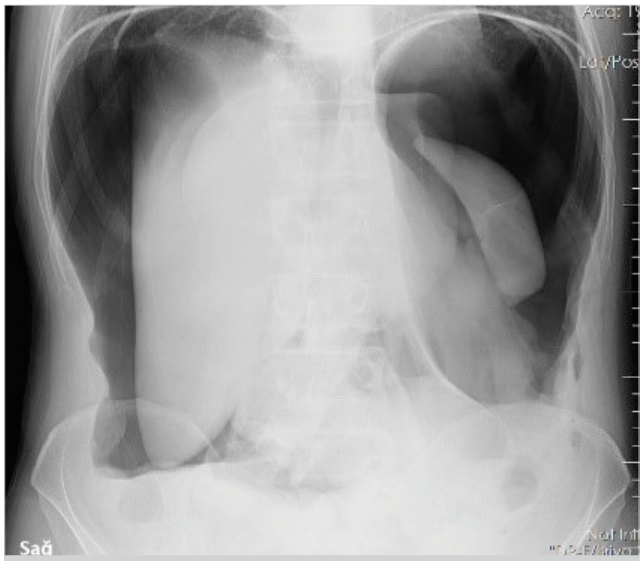

Figure 1. Diffused free air in standing plain abdominal radiography.

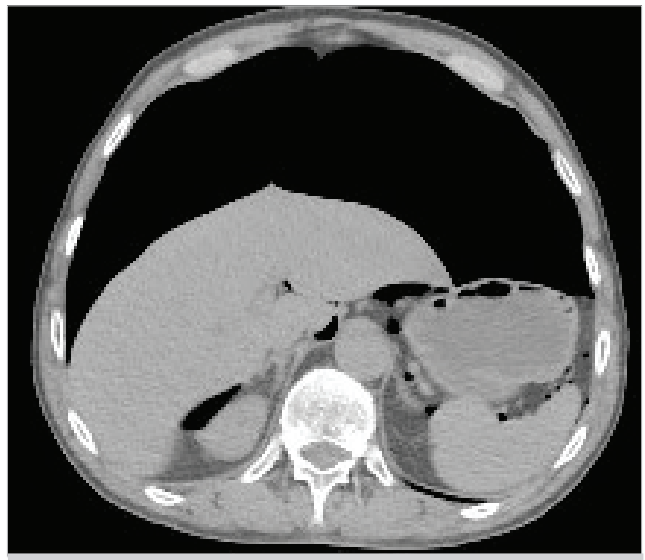

Figure 2. Free air visualized in computed tomography image.

Table 2. Endoscopic diagnostic features in iatrogenic colon perforation (Statements by the endoscopist who performed the procedure)

Cases	Endoscopy Support	Process Features	Indirect Signs of Perforation	Direct Signs of Perforation	Time of Diagnosis
1	Nurse-assisted	Perforation development in the sigmoid colon on the way	Loop formation in the sigmoid colon and sudden relaxation of the colonoscope	Direct visualization of the perforation area	During the process
2	Self	Total colonoscopy	Difficulty crossing the recto-sigmoid field	Direct visualization of the perforation area	During the process
3	Nurse-assisted	Difficulty reaching terminal ileum	Significant distension development in the abdomen and fresh blood at the perforation site	Direct visualization of the perforation area	During the process
4	Self	Perforation development in the sigmoid colon on the way	Sudden relief in the colonoscope	Visualization of intra-peritoneal organs	During the process
5	Self	Total colonoscopy procedure and spastic colon	Not noticed	Not noticed	8 hours after the procedure (with standing abdominal radiography + abdominal computed tomography)
6	Nurse-assisted	Difficulty reaching the terminal ileum	Development of significant distension in the abdomen sudden relief from the colonoscope	Visualization of intraperitoneal organs	During the process
7	Self	A difficult total colonoscopy procedure	Fresh blood at the perforation site and mucosal tears	Visualization of intra-peritoneal organs	During the process

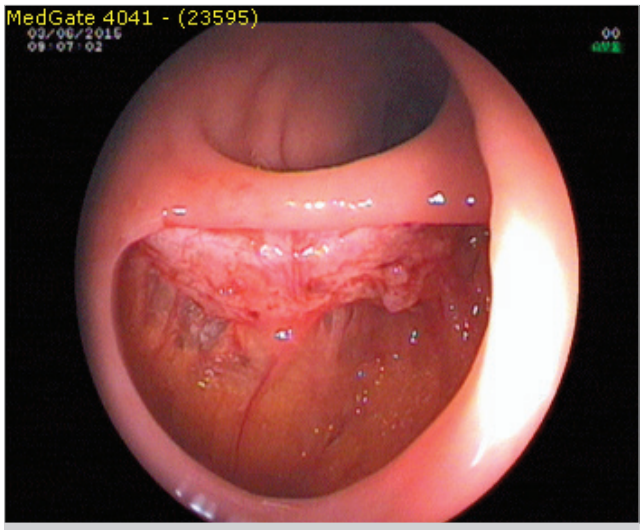

Figure 3. Direct view of colon perforation.

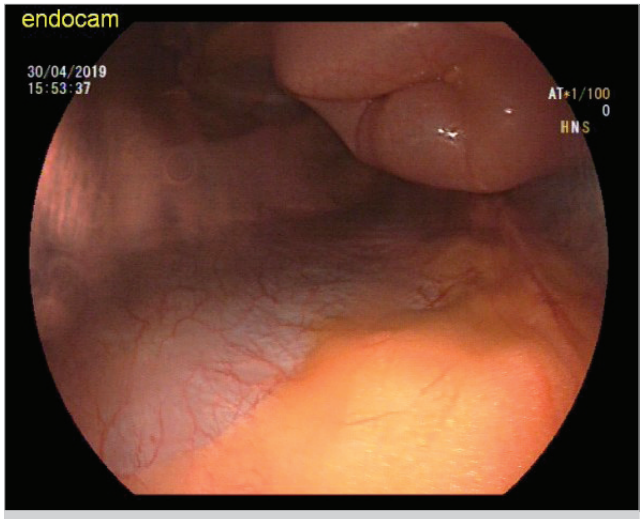

Figure 4. Peritoneal cavity and small intestines.

Table 3. Perforation markers we identified during colonoscopy
Significant distension in the abdomen
Increased pronounced tympanism
Fresh bleeding in unexpected areas
In the situation where the colonoscope is stretched (hardened), the colonoscope suddenly relaxes while trying to move proximally
Tear or perforation in the mucosa
Visualization of intraperitoneal organs

DISCUSSION

Bleeding and perforation due to diagnostic and therapeutic procedures performed during colonoscopy and rectosigmoidoscopy are the most common complications associated with colonoscopy (1,4,13-15). The frequency of perforations in diagnostic colonoscopy is between 0.03% and 0.8% in different studies, whereas it is between 0.15% and 3% in therapeutic procedures (3). Mortality due to colon perforation has been reported in the literature at rates of 0%-0.05% (3). It is reported that 6% of colon perforations are asymptomatic; 75% of the patients with perforations can be diagnosed in ≤24 hours, approximately 98% in ≤96 hours, whereas in some cases, ≥2 weeks are required (4,16). In all of our patients, ICP occurred during diagnostic procedures, and most of them (six out of seven) were diagnosed during the procedure; only one patient was diagnosed eight hours after the procedure. The rate of occurrence of perforations reported in this study was found to be compatible with the literature.

Table 4. Risk factors for iatrogenic colon perforation in the patients
Female sex
Advanced age
History of previous surgery
Peritoneal carcinomatosis
Dolichocolon
Loop formation
Procedure performed in a fast manner

Major reason for the occurrence of mortality and morbidity is generalized peritonitis and sepsis, which occur as a result of the delay in the detection of perforations (4,5). Formation of perforation is affected by the following factors: age> 70 years; female sex; low BMI; insufficient bowel cleansing; structural colon pathologies (dolichocolon, diverticulosis, megacolon); diverticulitis; previous abdominal surgeries (especially in the pelvic area); inflammatory bowel diseases (Crohn's and ulcerative colitis); peritoneal carcinomatosis; abdominal wall hernias with intestinal content; use of steroids; hypoalbuminemia; history of radiotherapy in the pelvic area; pain during the procedure; procedures performed with analgesia; speed of the procedure and insufficient time; procedure followed by and the experience of the endoscopist; and quality of the colonoscope and endoscopy system (6-8,17-22). Among our patients, advanced age, female sex, dolichocolon, previous abdominal surgery, peritoneal carcinomatosis etc. were identified as risk factors for perforation. Contrary to previous reports, the average BMI in the patients with perforations was 25.14 kg/m^2, which was within normal limits.

There are three major mechanisms for the development of perforation, which are difficulty in passing through the bends in the colon mechanically with the loop or endoscope tip, barotrauma due to excessive air insufflation and electrocautery in therapeutic procedures, and ischemia occurring as a result of laser and argon plasma coagulation procedures (3,9,23-25). Further, serosal tears are known to occur without mucosal damage

due to mechanical stress (26). In our study, when the causes of perforation were investigated by consulting with the specialists who performed the procedure, it was understood that there was a loop formation in four patients, difficulty in turning the rectosigmoid corner in one patient, whereas no such difficulties were observed in one patient. In an interrogation about perforation, endoscopists stated that the colonoscope suddenly relaxed in two patients due to the occurrence of strain, significant distension occurred in the abdomen in two patients, fresh blood in the perforation area was observed in two patients, and mucosal tears were observed in one patient.

Perforations caused by direct mechanical effects are the most common type in the sigmoid colon and rectosigmoid region, whereas those occurring due to barotrauma are the most common in the cecum. The most important causes of perforation are the loop formation in the sigmoid colon and angulation at the rectosigmoid junction and excessive insufflation (3,4). In a study by Iqbal et al., the frequency of ICP has been reported as 52% in the sigmoid colon, 17% in the cecum, 14% in the ascending colon, 8% in the descending colon, 7% in the transverse colon, and 1% in the rectum. In addition, they have reported perforation sizes of 0.1-6 cm (average 1.7 cm) and found that the defects in perforations developed with electrocautery are smaller than those developed due to mechanical injuries (27). In our study, all of the perforations occurred in the sigmoid colon or its proximity, and all of the perforations were caused by mechanical effects.

The factors that increase postperforation morbidity and mortality are diagnosis time, degree of peritoneal contamination, accompanying diseases, and perforation size (28). Detecting and treating colon perforation during the procedure is of critical importance in avoiding mortality and morbidity. Early diagnosis and treatment and surgical intervention when necessary are the best strategic approaches to prevent mortality and morbidity (29-31). The experience of the endoscopist and attention paid to these factors are important. In patients who are suspected of perforation but cannot be diagnosed directly, direct radiographs should be taken first. If direct radiographs are normal and suspicion of perforations remains, abdominal CT with oral contrast should be performed (27,32). In this study, the diagnosis was made on the basis of directly observing perforation site in three patients and by visualizing the intraperitoneal organs in three patients. In one patient whose diagnosis was delayed, significant distension, defense, and rebound were observed in the abdomen on standing direct abdominal radiography and abdominal CT. The diagnosis was made by visualizing widespread free air.

There are three basic treatment modalities for ICP: conservative, endoscopic, and surgical therapies. When choosing the modality, it is necessary to consider the location and characteristics of the perforation, time of occurrence, colonic pathologies, level of peritoneal contamination, and the peritonitis status of the patient (9). Conservative treatment requires broad-spectrum antibiotherapy, adequate hydration and parenteral nutrition, cessation of oral intake, and nasogastric decompression. Conservative treatments are reported by some authors to be selectively applied to some patients; however, this is not a risk-free choice (33-35). In cases where conservative treatment is unsuccessful, surgical procedures have to be applied, and severe peritonitis, peritoneal contamination, and sepsis may be encountered. In these cases, major surgical procedures and developing septic scenarios cause significant increases in mortality (33,36,37).

In recent years, endoscopic treatments have played a key role in the treatment of perforations, and consequently, the need for surgery for small perforations has considerably decreased (38). With through-the-scope and over-the-scope clips developed in recent years, 93% and 89% success rates were reported in ICP closures of <2 cm, respectively. Endoscopic treatment is recommended for ICPs of <2 cm in treatment-follow-up algorithms (11,39). Perforation can be closed with band ligation technique, end-loop clip, and self-expendable metal stent as alternative techniques other than clip closure (40-44). These patients should additionally receive conservative treatments and their clinical and laboratory and radiological findings should be closely monitored. It is very important that patients who do not improve in the follow-up undergo surgical treatment without delay (11).

Early diagnosis and emergency surgical intervention make it possible to avoid peritoneal contamination and primary colon repair (9). The treatment to be applied in surgery should be selected according to the degree of peritoneal contamination, severity of peritonitis, and size and number of injuries. Open surgery should be preferred in cases where laparoscopy is difficult. Laparoscopic approach in ICPs is a strategically safer treatment option with minimal morbidity and mortality compared to the open surgical method and conservative methods (33,34). The most important thing determining the prognosis after diagnosis is the treatment method to be chosen. However, the treatment to be chosen is mostly limited by the hospital facilities and practical experience of the specialists (10).

Although there was no mortality in our patients, the patient who was diagnosed late had to undergo a staged surgical procedure that involved a loop colostomy due to the common peritonitis scenario. The duration of hospitalization of this patient was long. Primary repair was performed by open surgical method or laparoscopically in all of our patients diagnosed during the procedure. Only one patient required resection anastomosis. Duration of hospitalization and morbidity of these patients were significantly less.

Limitations

The limitation of the study is that our patients were treated only with surgical method. However, we would like to point out that the main goal of the study was not treatment comparison. It was to determine the frequency of perforation and perforation risk factors. Therefore, we believe that this limitation does not have a major impact on the value of our study.

CONCLUSION

In our case series, main indications for surgical treatment in all patients can be listed as inadequate experience of the endoscopy team in closing perforations, large perforation areas (6, 5, and 4 cm, respectively in three cases), and the endoscopy team's predisposition to surgery. In conclusion, ICPs are a rare complication of colonoscopy; however, they have high mortality and morbidity, which may be avoided by early diagnosis and endoscopic treatment in appropriate cases.

Main Points:

ICPs are a rare complication of colonoscopy, our frequency was 0.072%.

Early diagnosis and treatment of ICP is the most important point.

Inadequate experience of the endoscopy team in closing perforations is the main indication for surgical treatment.

Ethics Committee Approval: This study was approved by S.B.Ü. İstanbul Training and Research Hospital Clinical Research Ethics Committee (Decision number: 2896 Date: 30.07.2021).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – N.G.; Design – N.G.; Supervision – N.G., R.İ.; Data Collection and/ or Processing – N.G., A.H.G., H.Ü.; Analysis and/or Interpretation – N.G., R.İ., A.Ö.; Literature Search – N.G., B.Ö.; Writing Manuscript – N.G.; Critical Reviews – R.İ., A.A.

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

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ORİJİNAL ÇALIŞMA-ÖZET
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Kolonoskopi sırasında iyatrojenik kolon perforasyonu vakalarımız, tanı/tedavi ve takip süreçleri

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ÖZET

Giriş ve Amaç: İyatrojenik kolon perforasyonu (İKP) kolonoskopi işleminin en korkulan komplikasyonu olup, morbidite ve mortaliteye sebep olmaktadır. Bu çalışmada endoskopi ünitemizde İKP sıklığını, vakaların özelliklerini, oluşumunun altında yatan sebepleri, tedavi yaklaşımlarını ve sonuçları güncel literatür ışığında tartışmayı amaçladık.

Gereç ve Yöntem: 2002-2020 yıllarında endoskopi ünitesinde diagnostik amaçlı gerçekleştirilen 9,709 alt GİS endoskopisi (kolonoskopi + rektosigmoidoskopi) sırasında iyatrojenik olarak gelişen kolon perforasyonu vakalarını retrospektif olarak değerlendirdik.

Bulgular: Toplam yedi vaka tespit edildi. İCP sıklığı %0,072 olarak saptandı. Tanı, hastaların altısında işlem sırasında, birinde sekiz saat sonra kondu ve tedavileri gerçekleştirildi. Tüm hastalara cerrahi uygulandı. İki hastaya laparoskopik primer tamir işlemi, beş hastaya laparotomi yapıldı. Laparotomi yapılanlarda üç hastaya primer tamir, bir hastaya parsiyel kolon rezeksiyonu ve uç uca anastomoz, bir hastaya lup kolostomi yapıldı. Ortalama 7,14 gün hastane yatışı oldu. Postop takiplerinde komplikasyon gelişmeyen hastalar şifa ile taburcu edildi.

Sonuç: İKP'nin erken teşhisi ve uygun tedavisi, morbidite ve mortalitenin önlenmesinde en önemli faktörlerdir.

Anahtar Kelimeler: Kolon perforasyonu, kolonoskopi, komplikasyon

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ORIGINAL ARTICLE
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Evaluation of knowledge and practice regarding mammography among a group of Turkish women attending a tertiary hospital

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ABSTRACT

Objective: Early detection is the most important cornerstone of breast cancer in determining treatment outcome and survival. In this study, it was aimed to investigate the level of knowledge, attitude, and practice of mammography in the early diagnosis of breast cancer in a group of women.

Material and Methods: Data of this descriptive study were collected under observation with the help of a questionnaire. Female patients over 40 years of age or over 30 years of age with a family history of breast cancer admitted to our general surgery outpatient clinic for a health problem other than breast were included.

Results: A total of 300 female patients with a mean age of 48.7 ± 10.9 years (min-max, 33-83 years) were included. Median frequency of correct answers among the women participating in the study was 83.7% (76.0-92.0). Mean score obtained by the participants from the questionnaire was 75.7 ± 15.8 (the median score 80; 25^{th}-75^{th} centiles, 73.3-86.7). Slightly more than half of the patients (159 patients, 53%) had at least one mammography scan before. The level of mammography knowledge was negatively correlated with age and the number of previous mammographies, and positively correlated with education level ($r= -0.700$, $p< 0.001$; $r= -0.419$, $p< 0.001$ and $r= 0.643$, $p< 0.001$, respectively).

Conclusion: Although the level of knowledge about breast cancer and early diagnosis methods in women was at a satisfactory level, it is obvious that mammography screening practice of women without any breast symptoms is very low. Therefore, it should be aimed to increase women's awareness of cancer prevention and compliance with early diagnosis methods and to promote participation in mammography screening.

Keywords: Breast cancer, mamography, screening, the level of knowledge

INTRODUCTION

Breast cancer is the most common type of cancer in women worldwide and is the second cause of cancer-related death after lung cancer (1). It has been reported that the incidence of breast cancer has increased in studies conducted since 1990 in all developing countries, including Türkiye (1,2). According to the cancer registry unit of the cancer control department's cancer report 2015 data, it is reported that 17.183 women were diagnosed with breast cancer in 2015, and the incidence of breast cancer increased nearly twice (3). In a recent study evaluating 44 populations around the world between 1998 and 2012, it was reported that breast cancer increased in premenopausal women in high-income countries, whereas the increasing postmenopausal breast cancer burden was most notable in countries undergoing socioeconomic transitions (4). In addition, breast cancer death rates are reported to decrease over time in most high-income countries but continue to increase in many low-middle income and low-income countries (5).

It is known that the probability of a woman developing breast cancer in her lifetime is remarkable. In order to reduce cancer deaths in the community, cancer must be detected at an early stage. Therefore, early diagnosis is extremely important in facilitating the treatment of breast cancer and reducing mortality (6). Early diagnosis of breast cancer can be achieved by educating women well and applying screening programs. The aim of screening programs is to detect breast-related pathologies at an early stage in women with no complaints by various methods (clinical breast examination, mammography, and breast self-examination). According to the breast

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cancer early diagnosis guideline, after the age of 40, women should have annual or biennial mammography, clinical breast examination and regular monthly breast self-examination. Although breast self-examination is a very effective method for early detection of breast cancer by patients themselves, it is not used enough among women (7). Apart from this, mammography, which is an inexpensive, easily applicable and safe imaging method, is a very useful test in the screening of breast cancer. Many international studies have shown that mammography screening reduces breast cancer mortality by 15-20% (8,9).

It is well-known that sufficient levels of knowledge of breast cancer have a positive effective factor on having mammography screening. Studies conducted in recent years have reported that the level of knowledge of women about breast cancer and mammography screening has increased significantly compared to previous years, but it has not reached a satisfactory level (3,7). In addition, the knowledge level of breast cancer and mammography screening practice have been shown to be associated with age, education level, family history of breast cancer, and economic status (10-12).

Despite the nationwide organized screening programs carried out in our country in recent years to raise awareness, it has been reported that the frequency of mammography screening is not sufficient, and the delay in the diagnosis of breast cancer continues to be a problem (3,7,10). In this study, we aimed to investigate the level of knowledge, attitude, and practice of mammography in the early diagnosis of breast cancer in women who applied to the our general surgery outpatient clinic for a health problem other than the breast.

MATERIAL and METHODS

This study was conducted between November 2020 and September 2021. Informed consent was obtained from all participants included in the study. This study was approved by the local ethics committee. Data of this descriptive study were collected under observation with the help of a questionnaire between November 2020 and September 2021. The questionnaire form consisted of 15 questions compiled by the researchers after the literature review on the subject and was applied to women over 40 years of age or over 30 years of age with a family history of breast cancer who admitted to our general surgery outpatient clinic for a health problem other than the breast. Before the questionnaire, sociodemographic characteristics of the women, such as age, family history and education level, were noted. In addition, it was recorded whether the women had mammography screening before and if they did, how many times they underwent mammography. The questionnaire consisted of 15 questions measuring the level of knowledge of the participants about the mammography method used in the early diagnosis of breast cancer and are answered as true or false (dichotomous scale). A total of 100 points is obtained as a result of correctly answering all 15 questions related to mammography. The participant was scored 6.7 points for each correct answer (100/15) and zero points for each incorrect answer.

SPSS 27.0 (IBM Corporation, Armonk, New York, United States) program was used in the analysis of the variables. Distribution of the data was evaluated with Shapiro-Wilk francia test. Mann-Whitney U with Monte Carlo tests were used together in comparing quantitative data of two independent groups. While Jonckheere-Terpstra test and Monte Carlo test were used together to compare more than two groups with each other according to quantitative data, Dunn's test was used for post-hoc analysis. Spearman's rho test was used to evaluate the correlations of the variables. Quantitative variables were expressed as mean (standard deviation), median (minimum/maximum or 25^{th} percentile/75^{th} percentile), while categorical variables were shown as number (n) and frequency (%). The variables were analyzed at 95% confidence level, and a p value less than 0.05 was considered as significant.

RESULTS

A total of 300 women with a mean age of 48.7 ± 10.9 years (median age 44 years; min-max, 33-83 years) were included in the study. Of these women, 4.7% were illiterate, 16.0% were primary school graduates, 17.7% were secondary school graduates, 34.0% were high school graduates, and 27.7% were university graduates. Only 13.7% of the cases had a family history of breast cancer. One hundred and forty-one (47%) patients did not have mammography before. Slightly more than half of the patients (159 patients, 53%) had at least one mammography scan before (Table 1).

More than 90% of the participants knew very well that mammography should be done in the week after the end of the menstruation, the breasts should be gently compressed between two plates during mammography, mammography reduces breast cancer deaths, and that a person with a breast mass should undergo mammography and/or ultrasonography after the examination. On the other hand, the questions with the lowest level of knowledge were as follows: Q1. Mammography screening is a life-saving method, Q7. Cosmetic materials such as deodorant, talcum powder and lotion should not be used before mammography, Q14. It is possible to detect all types of breast cancer with mammography. Median frequency of correct answers among women participating in the study was 83.7% (76.0-92.0) (Table 2). Mean score obtained by the participants from the questionnaire was 75.7 ± 15.8 (median score 80; 25^{th}-75^{th} centiles, 73.3-86.7).

Table 1. Educational level, family history of breast cancer, mammography practice and age distribution characteristics of the women included in the study

Educational level		Number	%	Age (years) Median (25^{th}-75^{th} centiles)
	Illiterate	14	4.7%	74 (67-80)
	Primary school	48	16.0%	57 (52-67)
	Secondary (middle) school	53	17.7%	46 (40-56)
	High school	102	34.0%	42 (40-46)
	University	83	27.7%	40 (40-45)
Family history of breast cancer				
	No	259	86.3%	44 (40-55)
	Yes	41	13.7%	42 (37-56)
Number of previous mammographies				
	None	141	47.0%	40 (40-41)
	1	64	21.3%	45 (43-50)
	2	37	12.3%	52 (48-61)
	3	39	13.0%	55 (52-66)
	4≤	19	6.3%	60 (57-65)

Table 2. The questionnaire applied to the participants in the study and the frequency of correct/incorrect answers

	Incorrect Answer n (%)	Correct Answer n (%)
1. Mammography screening is a life-saving method	98 (32.7)	**202 (67.3)**
2. Mammography is taken using X-rays at a slightly higher dose than a chest X-ray, but within non-hazardous limits	67 (22.3)	**233 (77.7)**
3. It is preferred to perform mammography in the week following the end of the menstrual period, when the breasts are least sensitive	4 (1.3)	**296 (98.7)**
4. Mammography is performed by gentle compression of the breasts between two plates	3 (1.0)	**297 (99.0)**
5. In the examinations performed by the physician, only 1.5-2 cm and large-sized masses can be detected, while masses below 0.5 cm in the breast can also be detected with mammography	48 (16.0)	**252 (84.0)**
6. Mammography is the best choice for breast cancer screening	55 (18.3)	**245 (81.7)**
7. Cosmetic materials such as deodorant, talcum powder and lotion should not be used before mammography	228 (76.0)	**72 (24.0)**
8. Mammography screening is a reliable method for early detection of breast cancer	49 (16.3)	**251 (83.7)**
9. Every woman should have a mammogram screening annually or biennially after the age of 40	72 (24.0)	**228 (76.0)**
10. Mammography is the diagnostic method that best shows irregular micro-calcification, which is the earliest sign of breast cancer	33 (11.0)	**267 (89.0)**
11. Previously taken mammograms (evaluation report, if any) should also be taken while going to perform mammography	7 (2.3)	**293 (97.7)**
12. Mammography screening can also be performed in 20s	58 (19.3)	**242 (80.7)**
13. Breast cancer death rates decreased with mammography screening	25 (8.3)	**275 (91.7)**
14. It is possible to detect all types of breast cancer with mammography	165 (55.0)	**135 (45.0)**
15. A patient presenting with a breast mass should first be examined by a physician and, if necessary, mammography and/or breast ultrasound should be performed	26 (8.7)	**274 (91.3)**
Overall (%)	**16.3 (8.3-24.0)**	**83.7 (76.0-92.0)**

Table 3. Evaluation of the factors affecting the knowledge level of the participants in mammography screening

		n	Overall Score Median (q1/q3)	p	
Educational level					
	Illiterate	14	41.1 (26.7/46.7)	Illiterate vs Primary school p= 0.001[b] Illiterate vs Secondary school p <0.001[b] Illiterate vs High school p< 0.001[b] Illiterate vs University p< 0.001[b] Primary school vs Secondary school p< 0.001[b] Primary school vs High school p< 0.001[b] Primary school vs university p< 0.001[b] Secondary school vs High school p= 0.001[b] Secondary school vs University p< 0.001[b] High school vs Secondary school p< 0.001[b]	<0.001[a]
	Primary school	48	63.3 (46.7/73.3)		
	Secondary (middle) school	53	76.8 (66.7/80.0)		
	High school	102	81.1 (80.0/86.7)		
	University	83	86.7 (80.0/93.3)		
Family history of breast cancer					
	No	259	80.0 (66.7/86.7)	0.001[c]	
	Yes	41	86.7 (73.3/100.0)		
Number of previous mammographies					
	None	141	80.0 (80.0/86.7)	None vs 1 p= 0.999[b] None vs 2 p= 0.999[b] None vs 3 p< 0.001[b] None vs 4≤ p< 0.001[b] 1 vs 2 p< 0.001[b] 1 vs 3 p= 0.001[b] 1 vs 4≤ p< 0.001[b] 2 vs 3 p< 0.001[b] 2 vs 4≤ p= 0.099[b] 3 vs 4≤ p= 0.999[b]	<0.001[a]
	1	64	86.7 (73.3/86.7)		
	2	37	73.3 (60.0/80.0)		
	3	39	66.7 (53.3/73.3)		
	4≤	19	73.3 (60.0/73.3)		
			r		

[a]Jonckheere-Terpstra test (Monte Carlo), [b]Post Hoc test: Dunn's Test, [c]Mann-Whitney U Test (Monte Carlo), q1: 25[th] centile, q3: 75[th] centile.

Table 4. Characteristics of the participants (n= 141) who did not have a mammogram before

Educational level		Number	%	Overall Score, Median (q1-q3)	p
	Illiterate	7	5.0%	40 (26.7-46.6)	<0.001[a]
	Primary school	10	7.1%	80 (51.6-81.6)	
	Secondary (middle) school	23	16.3%	80 (80-86.7)	
	High school	51	36.2%	80 (80-80)	
	University	50	35.4%	86.7 (80-93.3)	
Family history of breast cancer					
	No	120	85.1%	80 (80-83.3)	<0.001[b]
	Yes	21	14.9%	96.5 (93.3-100)	

[a]Jonckheere-Terpstra test (Monte Carlo), bMann-Whitney U test (Monte carlo), q1: 25[th] centile, q3: 75[th] centile.

It was determined that the level of knowledge about mammography was significantly higher in those with a high education level and a family history of breast cancer (p< 0.05) (Table 3). The level of mammography knowledge was negatively correlated with age and the number of previous mammographies, and positively correlated with education level (r= -0.700, p< 0.001; r= -0.419, p< 0.001 and r= 0.643, p< 0.001, respectively).

Mean age of the women who did not undergo a mammography before was 43.1 ± 9.7 years (median 40 years), and mean

knowledge score was 80.4 ± 13.6 (median 80; 25th-75th centiles, 80-86.7). While the level of knowledge of women who did not undergo a mammography before was the lowest in the uneducated group, it was highest in women who were university graduates. In addition, women with a family history of breast cancer had a significantly higher level of knowledge about mammography ($p< 0.05$) (Table 4).

DISCUSSION

Screening women for breast cancer with various methods and at regular intervals after a certain age is vital for early diagnosis and treatment. Determining the knowledge, attitudes and behaviors of women on this issue is indispensable for the success of the screening programs. In the current study, we evaluated the knowledge levels and attitudes about mammography screening in women over 40 years of age or over 30 years of age with a family history of breast cancer. In addition, the relationship of the knowledge level of the participants with age, education level, and numbers of previous mammographies were investigated. In studies conducted in our country 15-20 years ago, it was reported that women had insufficient or incorrect information about the importance of breast cancer screening and early diagnosis (11,12). However, in recent years, as a result of educational activities regarding breast cancer screening and early diagnosis (informative meetings, TV programs, brochure, and social media sharing, etc.) carried out by both the ministry of health and non-governmental organizations, a significant increase in the knowledge level of women about breast cancer and mammography screening has been reported in various studies (7,13-15) but still has not reached a satisfactory level. In our study, mean score of the participants in the questionnaire prepared about mammography, a method used in the early diagnosis of breast cancer, was 75.7 ± 15.8 and median score was 80 (25th-75th centiles, 73.3-86.7). Although this score seems far above the level of knowledge 15-20 years ago, it is clear that it is not sufficient and must be increased further. The women included in the study were well aware that mammography reduces breast cancer mortality rates, mammography is performed by gently compression of the breasts between two plates, and that it is more appropriate to apply mammography one week after menarche. However, the knowledge that some cosmetic products, which complicates the assessment of mammography, should not be used before the screening, was insufficient among the participants. Therefore, it is necessary to provide more effective educational program on early diagnosis and screening of breast cancer with various audio-visual tools, and in this way, the level of knowledge of women about mammography should be increased.

Mammography is an effective and reliable method that can show the masses that are too small to be detected on physical examination or ductal carcinoma in situ, which is a noninvasive form. Detection of breast cancers at an early stage positively affects the clinical course of the disease and has been shown to reduce mortality in various studies (16). In general, in our country and worldwide, women are recommended to have a mammography screening every one or two years after the age of 40. In addition, there is a prevailing opinion that this screening should be started at an earlier age in those with a family history of breast cancer. Most of the participants in our study had a good level of knowledge that mammography screening is reliable in the diagnosis of breast cancer and that it has a life-saving aspect by providing early diagnosis. In addition, most of the participants in our study were aware that mammography screening should be done after the age of 40. However, despite the high level of awareness, 53% of the participants in our study underwent a mammography at least once before, while the remaining 47% did not perform mammography. Mean age of the women who had no previous mammography practice was 43.1 ± 9.7 years (range, 35-82 years). The wide age range shows that although the women included in the study were aware of the importance of breast cancer screening such as mammography, they could not reflect it on their behavior and frequently ignored it. Similarly, in many studies conducted in different countries around the world, including our country, it has been reported that the frequency of regular mammography screening is very low (11,14,15,17-21). Interestingly, even in health care professionals, who are in the best position to provide health education, the rate of having a regular mammography screening is low (39.4%) as shown in the study of Akpınar et al. (22). Although it is known that early diagnosis of breast cancer is of vital importance, the rate of mammography screening remains low due to lack of time, ignoring, forgetting, economic reasons (cost), no complaints about the breast, fear of being diagnosed with cancer, and being young (7,23). In order to be successful in mammography screening program, it is necessary to promote knowledge and behavior change in both women and health professionals.

Knowledge about mammography is known to be affected by various factors. In many studies, it has been reported that the level of knowledge about breast cancer and mammography screening is associated with age, the level of education and economic status (14,19,23,24). In our study, in line, the level of knowledge of women regarding mammography was found to be associated with the level of education and age. As expected, the level of knowledge was positively associated with the level of education and family history of breast cancer, but, interestingly, it was negatively associated with age and the number of previous mammographies. This can be explained by the fact that women with lower education levels had higher age (or vice versa) in our study. On the other hand, in the study of Koçyiğit et al. (24), unlike our study, it has been reported that mean knowledge score of women about breast cancer and mammography

increases with age. The authors tried to explain this by the fact that younger women thought that breast cancer occurred in older women and that they were not at risk for breast cancer. Moreover, in many studies, similar to our study, it has been reported that women with a family or friend's history of breast cancer have a higher knowledge score than those without (24,25).

This study has some limitations that must be acknowledged. Since there is no internationally standardized questionnaire about breast cancer and mammography screening, we created a questionnaire measuring the level of knowledge about mammography in women as a result of the literature review, which is one of the most important limitations of our study. In this study, the knowledge level of women about mammography screening was questioned, but no evaluation was made in terms of the factors that caused the participants not to have regular mammography screening. In addition, this study was performed in the general surgery outpatient clinic of our tertiary hospital, so the findings of this study cannot be generalized to a particular region or to the whole of our country.

In conclusion, in this study, it was concluded that the majority of women had a fairly good level of knowledge about mammography screening; however, some topics need to be improved with various tools. In addition, it was shown that the level of knowledge related to mammography screening was positively correlated with education level and family history of breast cancer. As shown in our study and many studies conducted in different countries around the world, although the level of knowledge about breast cancer and early diagnosis methods in women is at a satisfactory level, it is obvious that the mammography screening practice of women is very low. For this reason, it should be aimed to increase women's awareness of cancer prevention and compliance with early diagnosis methods and to promote participation in mammography screening.

Ethics Committee Approval: This study was approved by İstanbul Medipol University Non-invasive Clinical Research Ethics Committee (Decision number: 852, Date: 12.11.2020).

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ORİJİNAL ÇALIŞMA-ÖZET
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Üçüncü basamak bir hastaneye başvuran bir grup Türk kadınının mamografi ile ilgili bilgi ve uygulamalarının değerlendirilmesi

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ÖZET

Giriş ve Amaç: Erken teşhis, meme kanserinin tedavi sonucunu ve sağkalımı belirlemede en önemli köşe taşıdır. Bir grup kadında meme kanserinin erken tanısında mamografi bilgi, tutum ve uygulama düzeylerini araştırmayı amaçladık.

Gereç ve Yöntem: Tanımlayıcı nitelikte olan bu çalışmanın verileri bir anket yardımıyla toplanmıştır. Genel cerrahi polikliniğimize meme dışı bir sağlık sorunu ile başvuran, ailesinde meme kanseri öyküsü olan 40 yaş üstü ve 30 yaş üstü kadınlar dahil edildi.

Bulgular: Yaş ortalaması 48,7 ± 10,9 (min-maks, 33-83) yıl olan toplam 300 kadın dahil edildi. Araştırmaya katılan kadınların ortanca doğru cevap verme sıklığı %83,7 (76,0-92,0) idi. Katılımcıların anketten aldıkları ortalama puan 75,7 ± 15,8'dir (ortanca puan 80; 25.-75. yüzdelik, 73,3-86,7). Hastaların yarısından biraz fazlası (159 hasta, %53) daha önce en az bir mamografi çektirdi. Mamografi bilgi düzeyi yaş ve önceki mamografi sayısı ile negatif, eğitim düzeyi ile pozitif korelasyon gösterdi (sırasıyla; r= -0.700, p< 0,001; r= -0.419, p< 0,001 ve r= 0,643, p< 0,001).

Sonuç: Kadınların meme kanseri ve erken tanı yöntemleri hakkında bilgi düzeyi tatmin edici düzeyde olmasına rağmen, meme semptomu olmayan kadınların mamografi tarama uygulamasının çok düşük olduğu aşikardır. Bu nedenle kadınların kanserden korunma ve erken tanı yöntemlerine uyum konusunda farkındalıklarının artırılması ve mamografi taramasına katılımın teşvik edilmesi hedeflenmelidir.

Anahtar Kelimeler: Meme kanseri, mamografi, tarama, bilgi düzeyi

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ORIGINAL ARTICLE
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Elderly trauma patients and the effect of trauma scores on hospitalization decision

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ABSTRACT

Objective: Hospitalization, mortality and trauma scores are important in trauma patients aged ≥65 years. The present study aimed to investigate the use of trauma scores in the prediction of hospitalisation and mortality in trauma patients aged ≥65 years.

Material and Methods: Patients aged ≥65 years who presented to the emergency department with trauma over a one-year period were included in the study. Baseline data of the patients together with their Glasgow Coma Scale (GCS), Revised Trauma Score (RTS), Injury Severity Score (ISS), hospitalisation and mortality were analysed.

Results: A total of 2264 patients were included in the study, of whom 1434 (63.3%) were women. The most common mechanism of trauma was simple falls. Mean GCS scores, RTSs and ISSs of the inpatients were 14.87 ± 0.99, 6.97 ± 0.343 and 7.22 ± 5.826, respectively. Furthermore, a significant negative correlation was found between the duration of hospitalisation and GCS scores ($r= -0.158$, $p< 0.001$) and RTSs ($r= -0.133$, $p< 0.001$), whereas a positive significant correlation with ISSs ($r= 0.306$, $p< 0.001$) was observed. The ISSs ($p< 0.001$) of the deceased individuals were significantly elevated, whereas their GCS scores ($p< 0.001$) and RTSs ($p< 0.001$) were significantly decreased.

Conclusion: All trauma scoring systems can be used to predict hospitalisation, but the results of the present study suggest that the use of ISS and GCS in making the decision regarding mortality is more appropriate.

Keywords: Emergencies, geriatrics, trauma, trauma scores

INTRODUCTION

The risk of exposure to trauma in elderly individuals increases as the elderly population in contemporary societies increases, and the opportunities for the elderly to have a healthy and active life improves (1). Mortality rate due to trauma is high, hospitalisation period is longer and complications are higher and more severe in the elderly although the likelihood of serious injuries is lower compared to that in younger individuals (2).

The mechanism of trauma in the elderly is different from that in younger individuals. Accidents and falls are common in the elderly, resulting in more frequent fractures, complications, hospitalisation and death. Falls among the elderly may be associated with increased mortality, limitation of functions, loss of independence and reduced quality of life (3). Older age is also a factor that increases the risk of road accidents. Decreased peripheral vision or hearing contributes to an increased risk of pedestrian and road accidents among the elderly. Violent assaults constitute 6% of trauma admissions in the elderly, whereas the same rate is 25% in younger individuals (3,4). Recently observed notable injuries involve non-accident-related injuries, including those that are caused by the family or caregiver.

Scoring systems are used to evaluate triage, mortality and morbidity as well as for predicting prognosis. The present study aimed to assess trauma patients aged ≥65 years who presented to the emergency department and to investigate the usefulness of the most commonly used trauma scoring systems, i.e. Glasgow Coma Scale (GCS), Revised Trauma Score (RTS) and Injury Severity Score (ISS), in the decision regarding hospitalisation and prediction of mortality.

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MATERIAL and METHODS

Geriatric patients aged ≥65 years who presented to the emergency medical clinic with trauma between January 2012 and December 2012 were included in our study upon approval of the local ethics committee. The patients were classified into groups based on the cause of the trauma as follows: simple fall, road accident (RA), pedestrian accident (PA), exposure to blunt trauma by assault (Battery) and others (falling from height, burn and penetrating injury). Baseline data together with GCS scores, RTSs, ISSs, hospitalisation and mortality of the patients were recorded. Patients ≥65 years of age with non-traumatic complaints and all the patients below 65 years of age, patients that left the hospital without being evaluated in the emergency department, patients who were examined but whose relevant files could not be accessed and patients with missing data were excluded from the study.

Statistical package for the social science (SPSS Version 21.0, IBM Corporation, Armonk, NY, USA) and MedCalc (Version 10.1.6.0, Ostend, Belgium) software package was used for data analysis. Numerical data were expressed in mean ± standard deviation, whereas qualitative data were expressed in percentage. Kolmogorov-Smirnov and Shapiro-Wilk normality tests were used to test the distribution of continuous variables. One-way analysis of variance was used to compare more than two independent groups. The relation between binary groups with continuous variables was investigated using the post hoc test. Categorical data were compared using the Chi-Square test (cross-tab). Pearson correlation test was used to determine the correlation. Binary logistic regression was used due to the two-category dependent variables. The enter method was used for the logistic regression analysis. A p value of <0.05 was considered significant in all the analysis results.

RESULTS

Out of 27.745 individuals aged ≥65 years who were admitted in the emergency medicine clinic throughout a one-year period, 2264 (8.16%) patients who presented to the emergency department with trauma were investigated (Table 1). Of these patients, 1434 (63.3%) were females. Patients' ages varied between 65 and 100 years, and their mean age was 74.89 ± 7.21.

Table 1. Basic data of the patients and pathologies

	Simple Fall	RA	PA	Battery	Other*	Mortality
N (female/male)	**2110 (1359/751)**	**17 (11/6)**	**90 (44/46)**	**30 (13/17)**	**17 (7/10)**	**16 (6/10)**
Age (mean ± SD)	74.98 ± 7.3	76.29 ± 7.1	73.84 ± 5.5	70.97 ± 5.6	73.88 ± 8.1	75.81 ± 5.6
Upper extremity fracture	630-29.8	4-23.5	14-15.5	1-3.3	1-5.9	1-6.3
Fracture of lower extremity	232-10.9	1-5.8	17-18.8	-	1-5.9	1-6.3
Maxillofacial bone fracture	50-2.3	1-5.8	8-8.8	2 (6.6)	2-11.8	5-31.3
Vertebral fracture	37-1.7	-	4-4.4	1 (3.3)	3-17.6	2-12.5
Pelvic fracture	34-1.6	-	5-5.5	-	1-5.9	3-18.8
Costal fracture	21-0.99	1-5.8	2-2.2	1 (3.3)	2-11.8	2-12.5
Subarachnoid haemorrhage	7-0.33	-	4-4.4	1 (3.3)	2-11.8	8 (50)
Contusion cerebri	6-0.28	-	5-5.5	-	2-11.8	6-37.5
Subdural bleeding	5-0.23	-	3-3.3	1 (3.3)	1-5.9	4 (25)
Haemothorax	5-0.23	-	-	-	-	-
Intraparenchymal bleeding	3-0.14	-	1-1.1	-	-	3-18.8
Pneumothorax	3-0.14	-	-	-	-	-
Lung contusion	2-0.09	-	-	-	3-17.6	3-18.8
Epidural bleeding	1-0.04	-	2-2.2	-	-	3-18.3
Hospitalisation period	12.33 ± 37.09	13.88 ± 15.28	31.42 ± 83.76	21.87 ± 48.56	21.88 ± 26.97	85.31 ± 152.45
Mortality	8 (50)	-	4 (25)	-	4 (25)**	
RTS	7.113 ± 0.33	7.14 ± 0.33	7.10 ± 0.34	6.96 ± 0.18	6.64 ± 0.98	5.44 ± 1.32
ISS	7.84 ± 10.35	5.35 ± 2.78	8.07 ± 9.89	5.30 ± 5.77	13.59 ± 18.91	37.44 ± 25.27
GCS	14.97 ± 0.44	14.64 ± 1.68	14.76 ± 1.43	14.80 ± 0.76	13.41 ± 3.55	9.94 ± 4.1

RTSs: Revised trauma scores, ISSs: Injury severity scores, GCS: Glasgow coma scale, RA: Road accident, PA: Pedestrian accident, Battery: Exposure to blunt trauma by assault.
*Other n (female/male): Falling from height= 10 (3/7), Burn= 3(2/1), Injury with Penetrating Tool= 4 (2/2).
**Falling from height

Table 2. Comparison of Glasgow Coma Scale (GCS) scores, Revised Trauma Scores (RTSs), Injury Severity Scores (ISSs) of the hospitalised patients and deceased individuals

	Hospitalisation			Mortality		
	Yes	No	p	Yes	No	p
n	**589 (397/192)**	**1889**		**16 (6/10)**	**2248 (1428/820)**	
RTSs	6.97 ± 0.343	7.14 ± 0.34	**<0.0001**	5.44 ± 1.32	7.11 ± 0.31	<0.0001
ISSs	7.22 ± 5.826	4.04 ± 3.37	**<0.0001**	37.44 ± 25.27	4.64 ± 2.73	<0.0001
GKS	14.87 ± 0.99	14.98 ± 0.40	**<0.0001**	9.94 ± 4.10	14.99 ± 0.30	<0.0001

RTSs: Revised trauma scores, ISSs: Injury severity scores, GCS: Glasgow coma scale.

A review of the trauma mechanisms indicated that there were 2110 simple falls, 90 pedestrian accidents, 17 road accidents, 30 assaults and 17 other injuries (including 10 falls from a height (3/7), 3 burn injuries (2/1) and 4 penetrating injuries (2/2).

Although the number of simple falls was significantly higher in women (p< 0.001), the PA (p= 0.004) and battery (p= 0.022) cases were higher in men, whereas there was no difference in sex in terms of RA and other injuries.

Although the fractures found were mostly in the extremities, those involving multiple organs were also observed. In addition, a total of 16 patients died, including eight deaths associated with simple falls, four with PA and four with falling from a height. Subarachnoid haemorrhage (50%) and cerebral contusion (37.5%) were the most common injuries among the deceased individuals.

A total of 26% of the patients (n= 589) included in the study were hospitalised, whereas 563 (24.9%) patients were referred to the Orthopaedics clinic, 14 (4%) to the intensive care unit (ICU), seven to the neurosurgery clinic, two to the thoracic surgery clinic, two to the general surgery clinic and one (0.26%) to the neurology clinic. The patients' mean duration of hospitalisation across all the groups was 13.30 ± 40.83 hours, whereas patients in the PA group had the longest stay of 31.42 ± 83.76 hours. The duration of hospitalisation of the deceased individuals was 85.31 ± 152.45 hours. Mean GCS scores, RTSs and ISSs of the inpatients were 14.87 ± 0.99, 6.97 ± 0.343 and 7.22 ± 5.826, respectively. There was a significant difference in mean GCS scores, RTSs and ISSs of the patients who were hospitalised and of those who were discharged from the emergency department (Table 2). Furthermore, a significant negative correlation between the duration of hospitalisation and GCS scores (r= –0.158, p< 0.001) as well as RTSs (r= –0.133, p< 0.001) was observed, whereas there was a positive correlation between the duration of hospitalisation and ISS (r= 0.306, p< 0.001). Mean GCS scores, RTSs and ISSs of the 16 deceased individuals at the time of admission to the emergency department were 9.94 ± 4.10, 5.43 ± 1.31 and 37.44 ± 25.27, respectively. A significant difference was observed in mean GCS scores, RTSs and ISSs of the deceased individuals and of the patients who were treated. GCS scores (p< 0.001) and RTSs (p< 0.001) were significantly decreased in the deceased individuals, whereas ISSs (p< 0.001) were significantly elevated (Table 2). The results of binary logistic regression analysis to evaluate which variables were possible predictors for hospitalization and mortality are presented in Table 3.

DISCUSSION

Although the characteristics of ageing vary based on socioeconomic and sociocultural constructs, it is largely associated with a decrease in mental activities; impaired perception; lack of attention; decrease in sensory functions, such as vision and hearing; delay in reflexes; general muscle weakness and movement disorders, all increasing the risk of exposure to trauma among the elderly (5).

The sex with the highest rate of admission for trauma varies. A retrospective study by Mc Gwin G et al. (6) on 401 geriatric trauma patients has emphasised that 76% of the patients re women. However, in another study by Demaria EJ et al., (7) 65.8% of the geriatric trauma cases have consisted of men. In the present study, the majority of geriatric trauma patients (63.3%) were women. Falling, the most common cause of trauma, may have accounted for the foregoing difference on the grounds that women had relatively less muscle tissue and were susceptible to a high incidence of postmenopausal osteoporosis and the fact that women were more exposed to falling and home accidents due to their more active living conditions at home. Falling is one of the most common causes of trauma in the elderly population, followed by road accidents (8). In the present study, simple falls ranked first among the causes of injury. Although the incidence of falling is higher in the elderly population, there are studies reporting that road accidents are traumatic injuries that are leading causes of death among the elderly (9,10). In the present study, 50% of the deaths were caused by falling-related injuries, whereas 25% were due to PA. Consistent with the studies by Day RJ and Hukkelhoven CW et al., head traumas have proven to be major factors leading to mortality (11,12). A review of sites of injury among the cases included in the study indicated that all the deceased individuals had suffered head trauma. Furthermore, complications associated with head trauma, in-

Table 3. Binary logistic regression results

		B	SE	% 95 CI	Exp (B)	p
Hospitalisation	Constant	1.213	3.637		3.364	0.739
	Age	-0.037	.008	0.948-0.980	0.964	<0.001
	Sex	0.472	0.121	1.215-1.952	1.540	<0.001
	GKS	2.262	0.251	5.864-15.709	9.597	<0.001
	RTS	-5.131	0.452	0.002-0.014	0.006	<0.001
	ISS	0.521	0.030	1.589 -1.786	1.684	<0.001
	R^2 (Cox-Snell)= 0.237 R^2 (Nagelkerke)= 0.347 Model: X^2 (2)= 611.177, p< 0.001					
Mortality	Constant	3.192	4.187		24.330	0.446
	Age	0.070	1.059	0.928-1.240	1.073	0.341
	Sex	-1.035	1.059	0.045-2.832	0.355	0.328
	GKS	-0.802	0.354	0.224-0.897	0.448	0.023
	RTS	0.391	0.043	0.165-13.260	1.478	0.727
	ISS	0.221	0.043	1.146-1.357	1.247	<0.001
	R^2 (Cox-Snell)= 0.058 R^2 (Nagelkerke)= 0.725 Model: X^2 (2)= 136.311, p< 0.001					

GCS: Glasgow coma scale, RTS: Revised trauma scores, ISS: Injury severity scores.

cluding fractures in the skull or facial bones, contusio cerebri or intraparenchymal haemorrhage, subarachnoid haemorrhage (SAH) and epidural or subdural haematomas were present in most of the deceased individuals.

Trauma scoring systems, such as RTS and ISS, are helpful in triage, prognosis, prediction and appropriate use of resources in trauma patients. However, different results have been obtained in terms of the use of the scoring systems in the elderly population. A study by Bagi H et al. (13) has analysed data from 228 trauma patients aged 70.96 ± 5.2 years and reported that mean ISSs of hospitalised patients were 11.12 ± 4.20, whereas the same scores for the discharged patients were 9.9 ± 3.41 and that there was a significant difference between the two groups. Consistent with the present study, Bagi H et al. (13) have found in the same study that ISSs were 20.66 ± 6.68 in elderly deceased trauma patients and that the scores were significantly lower (10.55 ± 3.92) in surviving patients. Ozman et al. (14) have divided 161 trauma patients admitted to the ICU into two groups as patients aged >65 years and <65 years and found that ISSs were 38.94 ± 15.86 in the <65 years group and 43.38 ± 15.94 in the >65 years group, whereas ISSs did not differ between the two groups. Orhon et al. (15) have reported in their study on 633 trauma patients with a mean age of 39.65 ± 17.07 years that ISSs of eight deceased individuals were 24.37 ± 12.85, whereas the same scores of the surviving patients were 5.78 ± 6.71 and that there was a significant difference between the two. They have also reported a significant difference in ISSs between hospitalised and discharged patients. It has been suggested that standard injury scoring systems, such as the ISS, might be less predictive in the elderly compared to younger patients (16). Besides, Perdue et al. (17) have found that mortality rate in the elderly patients was twice that of younger patients with equivalent ISSs. In the present study, ISSs significantly increased in the hospitalised and discharged trauma patients, and the sensitivity and specificity of ISS in predicting the hospitalisation decision and mortality were high.

Bagi H et al. (13) have reported in their study that there was no significant difference in RTSs between the hospitalised and discharged patients but there was a significant difference in the scores between deceased individuals and surviving patients. Orhon et al. (15) have found that RTSs of the eight deceased individuals were 5.62 ± 1.31, whereas the same scores in the surviving patients were 7.75 ± 0.46 and that RTSs significantly decreased in the deceased individuals. They have also reported that the RTSs decreased significantly in the hospitalised patients. In the present study, both the deceased individuals and hospitalised patients had significantly lower RTSs at admission to the emergency department, and the specificity of RTS was higher in the deceased individuals.

In addition, there was a significant negative correlation between the duration of hospital stay and GCS scores and RTSs and a positive significant correlation with ISSs. Similar to the results of the present study, Orhon et al. (15) have found a positive correlation between the duration of hospital stay and ISSs and a negative correlation between the duration of hospital stay and RTSs.

GCS scores were very sensitive in predicting mortality in elderly trauma patients, whereas they were not sufficiently sensitive in predicting decisions regarding hospitalisation. The reason of the foregoing might be the fact that extremity fractures were more prevalent and the GCS scores were mostly 15 in the hospitalised patients. However, mortality rate was higher in patients with lower GCS scores at admission to the hospital.

CONCLUSION

In conclusion, although due to simple fall reasons, severe injuries that require hospitalisation are more common in elderly individuals, and mortality rate is higher. All trauma scoring systems can be used to predict hospitalisation, but the results of the present study suggest that the use of ISS and GCS in making the decision regarding mortality is more appropriate.

Limitations

There are various parameters affecting mortality in elderly trauma patients, including biochemical factors, comorbidity and the medications used. The major limitation of the present study is that these parameters were not considered as it was mostly based on triage practices.

Ethics Committee Approval: This study was approved by Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (Decision no: 2013/08/02, Date: 24.06.2013).

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ORİJİNAL ÇALIŞMA-ÖZET
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Yaşlı travmalı hastalar ve travma skorlarının yatış kararına etkisi

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ÖZET

Giriş ve Amaç: Acil servise başvuran 65 yaş ve üzeri travma hastalarının, hospitalizasyon ve mortalite tahmininde travma skorlarının kullanılmasının değerlendirilmesi amaçlandı.

Gereç ve Yöntem: Acil servise travma nedeniyle başvuran 65 yaş ve üstü hastalar değerlendirildi. Travma sebebine göre; basit düşme, araç içi trafik kazası (AİTK), araç dışı trafik kazası (ADTK), bir başkası tarafından künt travmaya maruz kalma (DARP) ve diğer hastalar (yüksekten düşme, yanık, delici kesici alet ile yaralanma) olarak gruplara ayrıldı. Hastaların temel verileri ve Glasgow Koma Skoru (GKS), *Revised* Travma Skoru (Gözden Geçirilmiş Travma Skoru) (RKS) ve *İnjury Severity* Skoru (ISS), hastaneye yatış ve mortalite durumları analiz edildi.

Bulgular: Çalışmamıza alınan 2264 hastanın 1434'ü (%63,3) kadındı. Travma mekanizmalarından en fazla basit düşme olduğu saptandı. Hospitalizasyon oranı %26 bu hastaların 16'sı exitus olmuştur. En fazla tespit edilen ölüm nedeni subaraknoid kanamaydı. Yatarak tedavi görenlerin GKS ortalaması: 14,87 ± 0,99, RTS ortalaması: 6,97 ± 0,343, ISS ortalaması: 7,22 ± 5,826 olarak bulunmuştur. Ayrıca hastanede kalma süresi ile GKS ($r= -0,158$, $p< 0,001$) ve RTS ($r= -0,133$, $p< 0,001$) ile arasında anlamlı negatif korelasyon, ISS ile ($r= 0,306$, $p< 0,001$) pozitif anlamlı korelasyon saptandı. Eksitus olan hastalarda GKS ($p< 0,001$) ve RTS ($p< 0,001$) puanları anlamlı oranda azalırken, ISS ($p< 0,001$) ise anlamlı oranda arttığı tespit edildi.

Sonuç: Hastaneye yatmayı öngörmek için tüm travma skorlama sistemleri kullanılabilir, ancak bu çalışmanın sonuçları mortalite ile ilgili karar vermede GCS'nin kullanılmasının daha uygun olduğunu göstermektedir.

Anahtar Kelimeler: Acil durumlar, geriyatri, travma, travma skorları

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ORIGINAL ARTICLE
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Effect of the pandemic on surgical procedures in a tertiary care hospital: A retrospective review

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ABSTRACT

Objective: The aim of this study was to examine the impact of performing surgeries with necessary precautions and to evaluate demographic characteristics of operated patients during novel coronavirus-2019 (COVID-19) pandemic and the infection rates during hospitalization and within 14 days after surgery.

Material and Methods: Between March 15th, 2020 and April 30th, 2020, a total of 639 patients who had been operated on in our center were retrospectively analyzed. According to the triage system, the surgical procedures were classified as emergency, time-sensitive, and elective procedures. Data including age, sex, indication for surgery, the American Society of Anesthesiologists (ASA) class, pre- and postoperative symptoms, the presence and/or absence of reverse transcriptase-polymerase chain reaction (RT-PCR) test result, type of surgery, surgical site, and documented COVID-19 infections during hospitalization and within 21 days after surgery were recorded.

Results: Of the patients, 60.4% were males and 39.6% were females with a mean age of 43.08 ± 22.68 years. Malignancy was the most common indication for surgery (35.5%), followed by trauma (29.1%). The abdominal area and head and neck region were the most frequent surgical sites in 27.4% and 24.9% of the patients, respectively. Of all surgical procedures, 54.9% were emergency and 43.9% were time-sensitive procedures. Of the patients, 84.2% were in ASA Class I-II while 15.8% patients were in ASA Class III, IV and V. General anesthesia was the most common anesthesia type in 83.9% of the patients. The overall rate of COVID-19 infection was 0.63% in the preoperative period. The rate of COVID-19 infection during and after surgery was 0.31%.

Conclusion: With similar infection rates to the general population, surgeries of all types can be performed safely taking preventive measures in the pre- and postoperative period. It would be wise to perform surgical treatment without delay in patients with an increased risk for mortality and morbidity in accordance with strict infection control principles.

Keywords: COVID-19, operative surgical procedure, demographic

INTRODUCTION

Pneumonia cases of unknown etiology were first reported in Wuhan, Hubei province of China in December 2019 and rapidly spread all over the world (1). The virus was identified as severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2), which was later named as novel coronavirus-2019 (COVID-19). The World Health Organization (WHO) declared COVID-19 a pandemic on March 11th, 2020 with a public health emergency of international concern (2).

The COVID-19 pandemic has dramatically affected healthcare services in many ways worldwide, and there is an increased need for intensive care unit (ICU) beds and workforce. With the increasing number of infected patients requiring hospitalization, the working practices has dramatically changed, and non-urgent elective surgeries and procedures have been postponed in many centers in accordance with the Republic of Türkiye, Ministry of Health. From the beginning of the pan-

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demic, surgical workforce has had to adopt new working practices to schedule both elective and emergency surgeries in a timely manner to utilize medical equipment and consumables, bed capacity, and workforce in the most effective way (3-7). Necessary measures have been implemented to minimize the risk of transmission in operating rooms, patient wards, and the other settings such as hallways, elevators, and stairs (8-10).

The impact of postponing elective surgeries during the pandemic has not yet been clearly understood; however, operation-related stress has been proposed to disrupt the immune system, making patients more vulnerable to infections and the decision-making process becomes more difficult, as the symptoms of the patient can overlap with potential COVID-19 infection (11). Nevertheless, emergency operations are time-sensitive and require prompt decisions. In previous studies, delayed treatment in cancer patients has been associated with adverse outcomes with reduced cure rates (12,13). In emergency operations, therefore, there is a consensus among surgeons that surgery should be planned without delay taking necessary precautions.

In the present study, it was aimed to examine the impact of performing surgeries with necessary precautions and to evaluate demographic characteristics of operated patients during the COVID-19 pandemic and the infection rates during hospitalization and within 14 days after surgery.

MATERIAL and METHODS

This single-center, retrospective study was conducted at the Department of General Surgery, Neurosurgery, Aesthetic, Plastic and Reconstructive Surgery, Thoracic Surgery, Orthopedics and Traumatology, Urology, Ophthalmology, and Otorhinolaryngology of Marmara University, Pendik Training and Research Hospital, İstanbul, between March 15th, 2020 and April 30th, 2020. Prior to surgery, all patients were informed about the possible risks and benefits of surgery, and a written informed consent was obtained. The study protocol was approved by Marmara University, School of Medicine, Ethics Committee with the approval no: 09.2020.706. The study was conducted in accordance with the principles of the Declaration of Helsinki.

A total of 639 patients who had been operated on in our center between the study period were included. Data including age, sex, indication for surgery, the American Society of Anesthesiologists (ASA) class, pre- and postoperative fever, dry cough, the presence and/or absence of reverse transcriptase-polymerase chain reaction (RT-PCR) testing, type of surgery (elective vs. emergency), surgical site, and documented COVID-19 infections during hospitalization and within 21 days after surgery were recorded. According to the triage system, surgical procedures were classified as follows: emergency procedures (a delay beyond four weeks would result in an increased risk of morbidity and mortality), time-sensitive procedures (a delay beyond four weeks to three months would result in an increased risk of morbidity and mortality), and elective procedures (deferrable for up to >3 months). Triage of the patients was carried out by the surgical departments included in the study in accordance with the national and international guideline recommendations. All healthcare workers complied with the donning/doffing procedures of personal protective equipment (PPE), including face mask, gloves, goggles, and face shields.

During the pandemic, cardiovascular surgeries were referred to an external center and obstetrics and gynecology procedures were carried out in a private center; therefore, these departments were excluded from the study.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) for Windows version 23.0 (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± standard deviation (SD), median (min-max) or number and frequency, where applicable. Pairwise comparisons were performed using the non-parametric Mann-Whitney U test while the Kruskal-Wallis H test was used for multiple comparisons. A p value of <0.05 was considered statistically significant.

RESULTS

Of a total of 639 patients included in this study, 60.4% were males and 39.6% were females with a mean age of 43.08 ± 22.68 (range, 0 to 97) years. Malignancy was the most common indication for surgery (35.5%), followed by trauma (29.1%). The abdominal area and head and neck region were the most frequent surgical sites in 27.4% and 24.9% of the patients, respectively. Of all surgical procedures, 54.9% were emergency and 43.9% were time-sensitive procedures. Of the patients, 84.2% were in ASA Class I-II while 15.8% patients were in ASA class III, IV and V. General anesthesia was the most common anesthesia type in 83.9% of the patients. Demographic and clinical characteristics of the patients and operative data are summarized in Table 1.

Of the 68 (10.6%) patients who needed ICU stay, 26.5% (n= 18) were operated from the head and neck region, 26.5% (n= 18) from the abdominal area, and 23.5% (n= 16) from the lower extremities. Majority of these patients were in ASA class I (33.8%) and class II (50%) and were operated under general anesthesia (85.4%). More than half of these patients (54.4%) were males.

In the preoperative period, four patients had fever and two patients had dry cough and underwent RT-PCR test. Of these patients, four tested SARS-CoV-2-positive. The overall rate of COVID-19 infection was 0.63% in the preoperative period. In addition, 4.4% (n= 28) of the patients including 2.5% (n= 16) with fever and 0.9% (n= 6) with dry cough in the postoperative period underwent RT-PCR test, and two patients tested SARS-CoV-2-positive. The rate of COVID-19 infection during and after surgery up to 21 days was 0.31% (n= 2). Demographic character-

Table 1. Demographic and clinical characteristics of the patients and operative data

		Male n (%)	Female n (%)	Total n (%)	p
Indication for surgery	Malignancy	122 (53.7)	105 (46.3)	227 (35.5)	0.032*
	Trauma	118 (63.4)	68 (36.6)	186 (29.1)	
	Acute abdomen	26 (60.5)	17 (39.5)	43 (6.7)	
	Diabetic foot	10 (90.9)	1 (9.1)	11 (1.7)	
	Urinary stone	22 (75.9)	7 (24.1)	29 (4.5)	
	Other	88 (61.5)	55 (38.5)	143 (22.4)	
Surgical site	Head-neck	92 (57.9)	67 (42.1)	159 (25)	0.904
	Thorax	46 (64.8)	25 (35.2)	71 (11.19)	
	Abdomen	107 (61.1)	68 (38.9)	175 (27.5)	
	Upper extremities	49 (62)	30 (38)	79 (12.4)	
	Lower extremities	74 (58.3)	53 (41.7)	127 (19.9)	
	Two sites	16 (64)	9 (36)	25 (3.9)	
	Three sites	1 (100)	0	1 (0.2)	
ASA Class	I	166 (60.4)	109 (39.6)	275 (43.1)	0.843
	II	157 (59.9)	105 (40.1)	262 (41.1)	
	III	55 (64.7)	30 (35.3)	85 (13.3)	
	IV	7 (50)	7 (50)	14 (2.2)	
	V	1 (50)	1 (50)	2 (0.3)	
Anesthesia type	General	320 (59.7)	216 (40.3)	536 (83.9)	0.904
	Regional	48 (62.3)	29 (37.7)	77 (12.1)	
	Local infiltration	12 (66.7)	6 (33.3)	18 (2.8)	
	Sedoanalgesia	6 (75)	2 (25)	8 (1.3)	
Triage category	Emergency	207 (59.1)	143 (40.9)	350 (54.9)	0.587
	Time-sensitive	172 (61.4)	108 (38.6)	280 (43.9)	
	Elective	6 (75)	2 (25)	8 (1.3)	
ICU need		37 (54.4)	31 (45.6)	68 (10.6)	0.348
Total		386 (60.4)	253 (39.6)	639 (100)	

*p at <0.05 indicates statistical significance. ASA: American Society of Anesthesiologists; ICU: Intensive care unit.

Table 2. Demographic characteristics and operative data of COVID-19-positive patients both in the pre- and postoperative period

	N	Age	Sex	ASA Class		Surgical site		Length of stay	ICU need
	n	Year (Mean)	F/M	Class	n		n	Day	n
Preoperative PCR (+)	4	73	3/1	III IV	1 3	Thorax Abdomen	3 1	5.5	1
Postoperative PCR (+)	2	46	0/2	II III	1 1	Thorax	2	11	None

ASA: American Society of Anesthesiologists; ICU: Intensive care unit.

istics and operative data of the COVID-19-positive patients both in the pre- and postoperative period are shown in Tables 2 and 3.

Mean ages of the patients who were scheduled for emergency surgery, time-sensitive surgery, and elective surgery were 41.08 ± 22.99 years, 45.31 ± 22.03 years, and 51.13 ± 26.07 years, respectively, indicating no statistically significant difference (p= 0.599). Surgery triage according to the age of the patients is presented in Table 4.

Table 3. Pre- and postoperative COVID-19 symptoms

	ICU Stay	PREOP Fever	PREOP Cough	PREOP PCR Test	POSTOP Fever	POSTOP Cough	POSTOP PCR Test
Yes	68	4	2	15 (4 positive)	16	6	28 (2 positive)
No	571	635	637	624	623	633	611

ICU: Intensive care unit; PREOP: Preoperative; POSTOP: Postoperative; PCR: Polymerase chain reaction.

Table 4. Surgery triage according to the age of the patients

Age		Emergency	Time-sensitive	Elective	Total	p
0-10 years	n	48	21	0	69	
	%	13.7%	7.5%	.0%	10.8%	
11-20 years	n	28	18	1	47	
	%	8.0%	6.4%	12.5%	7.4%	
21-30 years	n	40	42	2	84	
	%	11.4%	15.0%	25.0%	13.2%	
31-40 years	n	54	38	0	92	
	%	15.4%	13.6%	.0%	14.4%	
41-50 years	n	46	34	1	81	
	%	13.1%	12.1%	12.5%	12.7%	
51-60 years	n	57	40	0	97	0.182
	%	16.3%	14.3%	.0%	15.2%	
61-70 years	n	44	50	2	96	
	%	12.6%	17.9%	25.0%	15.0%	
71-80 years	n	19	28	1	48	
	%	5.4%	10.0%	12.5%	7.5%	
81-90 years	n	13	8	1	22	
	%	3.7%	2.9%	12.5%	3.4%	
>90 years	n	1	1	0	2	
	%	.3%	.4%	.0%	.3%	
Total		350	280	8	638	

Data are given in number and frequency, unless otherwise stated. p at <0.05 indicates statistical significance.

DISCUSSION

The COVID-19 pandemic has swept through the world, placing an enormous strain on many aspects of life, including social life, work, school, and family. The rapid spread of the pandemic has mainly crippled healthcare services, and elective surgeries have been postponed to allow facilities to dedicate all available healthcare resources, including healthcare workers and equipment, to the treatment of infected patients and to protect patients from being infected with the deadly virus, which is also the subject of ethics and medicolegal problems. In a study, Di Martino et al. (14) have reported the rate of COVID-19 infection after surgery as 7% among the operated patients during the pandemic while Karayiannis et al. (19) have found this rate to be 5.6%. In our study, the rate of COVID-19 infection as confirmed by RT-PCR was quite lower than the previous studies and general population (n= 2, 0.31%) within 21 days of surgery. In addition, we observed no COVID-19-related mortality in our study while Karayiannis et al. (15) have reported the mortality rate from COVID-19 as 0.8%.

In a large-scale, multi-center, cohort study, operated patients with COVID-19 infection diagnosed within seven days before or 30 days after surgery have been evaluated (16). In that study, mortality rate has been found as 23.8% in these patients and male sex, ≥70 years of age, ASA class III-V, cancer surgery, and emergency surgery have been found to increase mortality rates. In a systematic review and meta-analysis, Wang et al. (17) have reported that COVID-19-positive patients with hip fractures scheduled for surgery had ≥5 times higher risks of early mortality than COVID-19-negative patients with hip fractures. In the current study, six patients who tested COVID-19 positive

in the pre- or postoperative period needed ICU stay; however, none of the patients died. Of note, these patients were in ASA Class IV, leading to an increased rate of morbidity.

In our country, all elective surgical procedures were postponed or cancelled to prevent devastating consequences of the pandemic in accordance with the Republic of Türkiye, Ministry of Health guidelines, resulting in a rapid decline in the number of surgeries (18). Initially, healthcare workers and facilities faced many unknows and confusion regarding the prioritization of cases for emergency and elective. Later, however, the societies of each specialty issued relevant guidelines (19). In our study, surgical procedures were classified based on the triage system as emergency, time-sensitive, and elective procedures. According to the guidelines and general medical practice in pandemics, epidemics, and outbreaks, emergency surgeries are prioritized. In the present study, majority of the patients (54.9%) underwent emergency operations. Although therapeutic modifications for emergency cases were recommended, emergency procedures were performed, when indicated. Altogether, the COVID-19 pandemic forced surgeons to reschedule elective surgeries and adopt a "new normal" work schedule in order to minimize the time spent in the hospital setting and to protect patients from being infected (20). In our study, the rate of elective surgical procedures was only 1.3%, and these patients were operated within the first week of pandemic and elective procedures were postponed during the ongoing pandemic.

Timing of time-sensitive surgical procedures are still controversial. During the pandemic, hospital administrators and healthcare providers have faced certain challenges on how to utilize critical resources most effectively (i.e., hospital and ICU beds, mechanical ventilators, PPE, and blood transfusion capacity), which are all of utmost importance to protect healthcare workers and patients from viral exposure and to minimize in-hospital transmission of COVID-19. Among those scheduled for time-sensitive surgical procedures, a considerable rate of the patients (43.9%) was operated in our study. According to the triage system, time-sensitive procedures were defined as procedures which could be slightly delayed, but not beyond three months; otherwise, such a delay could result in worsening morbidity and mortality for the patient. In this group of patients, the majority of them (35.5%) were operated for malignant diseases. In particular, immunosuppressed patients, such as cancer patients, are at a higher risk for more severe forms of COVID-19 and, therefore, hospital admission of these patients should be minimized as much as possible. In our country, telemedicine technology has been in use to protect patients from being infected and to utilize healthcare resources in the most optimal way. However, time-sensitive and emergency, invasive procedures that need to be done in the operating room setting have been performed to avoid adverse consequences. Surgeons discuss the possible risk of infection with their patients and decide to treat or delay the existing pathology. In the literature, psychological distress has been reported in cancer (21) and epileptic patients (22), compared to healthy individuals, due to serious concerns about their cancelled and/or postponed surgeries. It has been well established that stress reduces the ability of the immune system to fight against infections and such a psychological stress may lead to increase the infection rates and disease progression in these patients. In a study, Rivera et al. (23) have reported that the all-cause mortality rate among cancer patients infected with COVID-19-was significantly higher than the general population (17% vs. 2-7%, respectively). In our study, however, none of the patients with cancer tested COVID-19-positive. Consistent with our results, in another study conducted by Ji et al. (24) to investigate the incidence of COVID-19 in patients undergoing elective cancer surgery, a total of 621 elective cancer surgeries from different specialties have been examined, and none of the patients has been found COVID-19-positive after surgery as confirmed by RT-PCR test during minimum 30-day follow-up period. Although this finding cannot be fully explained, one of the reasons may be the fact that the first case of COVID-19 in Türkiye was identified after a couple of weeks and months than many European, Middle East, and Far East countries, and prompt measures were taken after the first case in accordance with the global precautions and strategic plans for the pandemic. Additionally, high-risk cancer patients themselves or their relatives may have refrained from consulting a physician and being operated to avoid infection. Finally, as ICU beds have been mostly occupied by COVID-19 patients in many facilities during the pandemic, surgical treatments may have been abandoned or the patients may have been referred to an external center with available ICU beds. In our study, two patients in the time-sensitive category with COVID-19 positivity were operated for tracheal stenosis (n= 1) and sarcoidosis (n= 1). None of the patients undergoing emergency or elective surgery had COVID-19 infection.

During the pandemic, necessary measures were implemented in our facility to minimize the risk of transmission in operating rooms, patient wards, hallways, elevators, and stairs. All healthcare staff were instructed to wear PPE. The patients undergoing surgery were taken to single-patient wards, and caregivers and/or companions or visitors were not allowed. In addition, flexible working arrangements enabled surgeons of all specialties to do the same amount of work over a different period.

Nonetheless, there are some limitations to this study. First, mortality and morbidity rates were unable to be evaluated due to the relatively low number of patients with COVID-19 infection postoperatively. Second, asymptomatic cases may have been missed due to lack of RT-PCR screening from nasopha-

ryngeal swabs on a regular basis. Third, besides patients, frontline healthcare workers are also at a high risk of infection. In our study, healthcare workers who collected nasopharyngeal swabs from six COVID-19-positive patients did not undergo RT-PCR testing to confirm the presence or absence of the infection. Further studies investigating differences in the demographic characteristics of the patients operated on during the pandemic compared to the previous year would provide additional information on this topic.

CONCLUSION

In conclusion, with similar infection rates to the general population, surgeries of all types (i.e., emergency or elective cancer surgery) can be performed safely taking preventive measures in the pre- and postoperative period. It would be wise to perform surgical treatment without delay in patients with an increased risk for mortality and morbidity in accordance with strict infection control principles. Further studies are needed to elucidate the true incidence of COVID-19 infection in frontline healthcare workers.

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ORİJİNAL ÇALIŞMA-ÖZET
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COVID-19 pandemisinin üçüncü basamak sağlık kuruluşunda gerçekleştirilen cerrahi girişimlere etkisi

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ÖZET

Giriş ve Amaç: Bu çalışmanın amacı, yeni koronavirüs-2019 (COVID-19) pandemisi sürerken gerekli önlemleri alarak cerrahi operasyonları yürütmenin etkisini incelemek, cerrahi operasyon geçirmiş hastaların demografik özelliklerini ve hastaneye yatış esnasında ve operasyondan sonraki 14 gün içinde karşımıza çıkan enfeksiyon oranlarını değerlendirmekti.

Gereç ve Yöntem: Merkezimizde 15 Mart ve 30 Nisan 2020 tarihleri arasında ameliyat edilmiş toplam 639 hasta retrospektif olarak analiz edildi. Triyaj sistemine göre ameliyatlar acil, zamana duyarlı ve elektif olarak sınıflandırıldı. Yaş, cinsiyet, ameliyat endikasyonu, Amerikan Anestezistler Derneği (ASA) sınıflandırması, pre ve postoperatif semptomlar, ters transkriptaz polimeraz zincir reaksiyonu (RT-PCR) test sonucunun olup olmaması, cerrahi operasyon türü, cerrahi alan ve hastaneye yatış ile operasyon sonrası 21 gün içerisinde belgelenmiş COVID-19 enfeksiyonu hakkındaki veriler kayıt altına alındı.

Bulgular: Hastalardan %60,4'ü erkek, %39,6'sı kadın ve ortalama yaşları 43,08 ± 22,68 yıl idi. Malignite en yaygın ameliyat endikasyonu (%35,5) olmakla birlikte bunu travma (%29,1) takip etti. Hastaların sırasıyla %27,4'ünde ve %24,9'unda en sık karşılaşılan cerrahi alanlar abdominal bölge ve baş-boyun bölgesiydi. Tüm cerrahi operasyonların içerisinde %54,9'u acil ve %43,9'u zamana duyarlı operasyonlardı. Hastalardan %84,2'si ASA I-II sınıflandırmasındayken %15,8'i ASA III, IV ve V sınıflandırmasındaydı. Yüzde 83,9'luk bir oranla en yaygın anestezi türü genel anesteziydi. Preoperatif dönemde COVID-19 enfeksiyonu oranı %0,63 idi. Cerrahi operasyon esnasında ve sonrasında COVID-19 enfeksiyonu oranı ise %0,31 idi.

Sonuç: Genel popülasyona benzer enfeksiyon oranları ile her tür cerrahi operasyon preoperatif ve postoperatif dönemde gerekli önlemler alınarak güvenli bir şekilde uygulanabilir. Katı enfeksiyon kontrol ilkelerine uyarak mortalite ve morbidite riskinin yüksek olduğu hastalarda geç kalınmadan cerrahi tedavinin uygulanması akıllıca olacaktır.

Anahtar Kelimeler: COVID-19, cerrahi operasyon, demografik

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ORIGINAL ARTICLE
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The role of lower dose steroid therapy with vitamin D replacement in patients with idiopathic granulomatous mastitis

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ABSTRACT

Objective: Low-dose steroid therapy has been recommended in idiopathic granulomatous mastitis (IGM) in various studies in the literature, but the therapeutic minimum dose has not been determined yet. Furthermore, vitamin D deficiency, the effect of which is accepted in autoimmune diseases, has not been previously examined in IGM. The aim of our study was to evaluate the efficacy of lower dose steroid theraphy with adjustment of vitamin D replacement doses with measuring serum 25-hydroxyvitamin D levels in patients with idiopathic granulomatous mastitis (IGM).

Material and Methods: Vitamin D levels were evaluated in 30 IGM patients who applied to our clinic between 2017-2019. Vitamin D replacement was performed in patients with serum 25-hydroxyvitamin D level below 30 ng/mL and prednisolone was given to all patients at a dose of 0.05-0.1 mg/kg/day. Clinical recovery times of the patients were compared with the literature.

Results: Vitamin D replacement was given to 22 (73.33%) patients. Recovery time was shorter in patients receiving vitamin D replacement (7.62 ± 2.38; 9.00 ± 3.38; p= 0.680). Average recovery time was 8.00 ± 2.68 weeks.

Conclusion: Treatment of IGM can be carried out with lower dose steroid therapy, leading to less complications and lower costs. Measuring serum 25-hydroxyvitamin D level and treating it with the appropriate dose may contribute to the healing process.

Keywords: Idiopathic granulomatous mastitis, lower doses of steroid theraphy, vitamin D

INTRODUCTION

Idiopathic granulomatous mastitis (IGM) is a rare inflammatory breast disease of unknown etiology. This disease is clinically presented with erythematous mass, abscess or chronic fistulized sinus formation and may mimic the clinical characteristics of inflammatory breast carcinoma. Definitive diagnosis can only be made histopathologically by tru-cut or incisional biopsy, and the disease is accepted to be idiopathic after exclusion of all infectious and non-infectious causes of granulomatous disease (1-3).

Although surgery, drainage, corticosteroids and immunosuppressive drugs are used in the treatment of this disease, a clear consensus has not been reported yet (4-6). Recently, the healing effect of corticosteroids has been shown in this disease, but since it is rare, its therapeutic modality has not been determined. In different studies, different doses of steroids have been given, but the general opinion on corticosteroid dose has been as 0.4-0.8 mg/kg. However, long-term use of this dose has many side effects due to steroid such as glucose intolerance or Cushing's syndrome (7-10).

Recent studies have shown the effects of vitamin D not only on calcium metabolism and bone formation but also on the immune system. Vitamin D receptors are expressed in different tissues, such as the brain, heart, skin, bowel, gonads, prostate, breasts, and immune cells.

Therefore, it has increased its interest in the role of vitamin D in the treatment of inflammation and immune system (11-13). Vitamin D deficiency has occurred in the pathophysiology of various inflammatory diseases such as inflammatory bowel disease (IBD) and rheumatoid arthritis (RA), systemic lupus erythematosus (SLE),

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as well as in chronic low-grade inflammation associated with obesity, insulin resistance Type 2 diabetes (IDDM) and cardiovascular disease (14). Vitamin D deficiency is defined as a serum 25-hydroxyvitamin D level of less than 20 ng/mL (50 nmol/L), and insufficiency is defined as a serum 25-hydroxyvitamin D level of 20 to 30 ng/mL (50 to 75 nmol/L). In persons with vitamin D deficiency, treatment may include oral cholecalciferol (vitamin D_3) at 50.000 IU per week for eight weeks. After vitamin D levels normalize, experts recommend maintenance dosages of cholecalciferol (vitamin D_3) at 800 to 1.000 IU per day from dietary and supplemental sources (15,16).

In our study, we implemented low steroid dose to our patients as 0.05-0.1 mg/kg/day and evaluated the patients' responses to treatment and recovery times. In addition, we examined 25-OH vitamin D levels in these patients and performed vitamin D replacement in those with deficiency.

The primary purpose of this study was to evaluate the response to lower dose steroid therapy in patients with IGM, and the secondary aim was to evaluate the contribution of replacement therapy in the recovery process in patients with vitamin D deficiency in this disease.

MATERIAL and METHODS

This retrospective, non-randomized observational study covered 30 females with IGM who applied to the breast unit of our general surgery clinic between October 2017 and December 2019. Informed consent was obtained from the patients regarding the treatment to be given. Ethics committee approval was obtained from the ethics committee of our hospital. All patients were aged over 18 years and were not in pregnancy or breastfeeding. At first admission, anamnesis was taken and physical examination was made to all patients. Ultrasonography was performed on all of them as standard for imaging and all patients were diagnosed with IGM histopathologically by tru-cut biopsy.

The patients were also evaluated in terms of tuberculous mastitis and pyogenic infections. Tissue and abscess samples were sent to Polymerase chain reaction (PCR) testing for *Mycobacterium tuberculosis* (MT) and aerobic and anaerobic culture for other bacterial infections (17,18). All of the patients diagnosed with IGM were examined with vitamin D level, hemogram and C-reactive protein (CRP) in the blood.

Prednisolone (Prednol®, Mustafa Nevzat, İstanbul, Türkiye) was started at 4 mg/day for the first week and continued for three weeks at 2 x 4 mg/day. After starting treatment, patients were called for control at the 1st and 2nd weeks, and then at the 1st, 2nd, 3rd and 6th months.

In patients with improvement in the first month control, 4mg/day was continued for one week and the treatment was terminated. In patients without complete recovery, treatment was continued from 8 mg/day until observing clinical improvement, then the dose was reduced and completed. The average steroid dose we administered to our patients was 0.05-0.1 mg/kg/day.

Vitamin D, hemogram and CRP levels were examined in the blood of the patients diagnosed with IGM. Patients with serum 25-hydroxyvitamin D levels below 30 ng/mL were given cholecalciferol (Devit-3® oral drop, Deva Drug, İstanbul, Türkiye) 50.000 IU/ week for eight weeks, followed by 800-1000 IU daily. Adequacy of treatment was evaluated quarterly.

In addition, in the clinical follow-up of the patients, abscess drainage was performed in the presence of an abscess detected with physical examination and ultrasonography. Surgical excision was performed in patients with isolated mass image and not causing deformity.

The resolution of the patient's complaints and the disappearance of the lesion in physical examination and ultrasonography were accepted as clinical improvement.

All data were analyzed using SPSS version 23. Continuous variables were expressed as mean ± standard deviation. Mann-Whitney U test and Student's t-test were used to compare nonparametric and parametric values, respectively, between the two groups.

Statistical significance was defined as a p value of <0.05.

RESULTS

The study included 30 female patients. There were 6 (20%) patients aged 20-30 years, 18 (60%) patients aged 31-40 years, and 6 (20%) patients aged 41-50 years. The menopausal status of 28 (93.33%) patients was premenopausal and 2 (6.67%) patients were postmenopausal.

While taking anamnesis, 22 (80%) patients described pain and 8 (20%) patients stated that they had no pain. During physical examination, masses were observed in 4 (13.3%) patients, and mastitis/abscess images in 26 (86.67%) patients. Mastitis was present in the right breast of 12 (40%) patients and in the left breast of 18 (60%) patients. In ultrasonography findings, irregular hypoechoic lesions were monitored in 3 (10%) patients, ,mastitis-like inflammatory appearance in 9 (30%) and abscess/mastitis findings in 18 (60%). According to the BIRADS classification, there were 3 (10%) patients with BIRADS 3, 24 (80%) patients with BIRADS 4 and 3 (10%) patients with BIRADS 5.

There was no growth in the bacterial culture of any of the patients, and MT PCR tests were negative. There were 18 (72%) patients with high CRP and 3 (11.54%) patients with high WBC, all of whom had moderate CRP and WBC elevation (Table 1). Abscess drainage was performed in 17 (56.67%) patients and excisional biopsy in 1 (3.33%) patient. Serum 25-hydroxyvitamin D levels were <20 ng/mL in 17 (56.66%) patients, 20 to 30 ng/mL in 5 (16.67%) patients and >30 ng/mL in 8 (26.67%) patients.

Table 1. Demographic information, clinical presentation, laboratory parameters and radiological findings of patients with IGM

Age	**20-30 (n)** 6 (20%)	**31-40 (n)** 18 (60%)	**41-50 (n)** 6 (20%)
Menopausal status	**Premenopausal (n)** 28 (93.33%)	**Postmenopausal (n)** 2 (6.67%)	
Pain (n)	**Yes (n)** 24 (80%)	**No (n)** 8 (20%)	
Physical examination	**Mass (n)** 4 (13.3%)	**Mastitis/Abscess (n)** 26 (86.67%)	
Side	**Right (n)** 12 (40%)	**Left (n)** 18 (60%)	
Ultrasonographic findings	**Irregular Hypoechoic lesion (n)** 3 (10.00%)	**Mastitis-like inflammation (n)** 9 (30.00%)	**Coexistence of abscess and mastitis (n)** 18 (60.00%)
BIRADS classification	**BIRADS 3 (n)** 3 (10.00%)	**BIRADS 4 (n)** 24 (80.00%)	**BIRADS 5 (n)** 3 (10.00%)
CRP	**Normal (n)** 7 (28%)	**High (n)** 18 (72%)	
WBC	**Normal (n)** 23 (88.46%)	**High (n)** 3 (11.54%)	

Table 2. Evaluation of the response to Vitamin D replacement

	Number of patients		**Recovery time (week)**		
Serum 25-hydroxyvitamin D levels	**n**	**%**	**Mean ± sd**	**Median**	**p**
<30 ng/mL (Patients given replacement therapy)	**22**	**(73.33)**	**7.62 ± 2.38**	**7.00**	0.680
<20 ng/mL	17	(56.66)	7.63 ± 2.26	7.00	
20-30 ng/mL	5	(16.67)	7.60 ± 2.97	8.00	
>30 (Patients without replacement therapy)	**8**	**(26.67)**	**9.00 ± 3.38**	**8.00**	

Kruskal Wallis test.

Vitamin D replacement was given to 22 (73.33%) patients, 8 (26.67%) patients were not replaced.

Recovery time was shorter in patients receiving vitamin D replacement but was not statistically significant (7.62 ± 2.38; 9.00 ± 3.38; p= 0.680) (Table 2). All patients participating in the study were given low-dose steroid therapy, and the average recovery time was 8.00 ± 2.68 weeks and average follow-up time was 16.60 ± 5.83 months.

DISCUSSION

The etiopathogenesis and treatment model of IGM is not fully illuminated, and delays in diagnosis and treatment may lead to long-term pain, cosmetic and psychosocial problems. The underlying pathogenesis of IGM is unknown despite being an autoimmune disease. Pathological features of IGM include chronic granulomatous inflammation without necrosis.

Granulomas typically contain lymphocytes, plasma cells, epithelioid histiocytes, multinucleated giant cells, and rarely neutrophils, and granulomatous lesions can be observed in breast lobules or terminal ducts in any breast quadrant (9).

Administration of steroids to patients with IGM is a generally accepted treatment method, and different doses of steroid treatment (0.4-0.8 mg/kg) are recommended in various stud-

ies. DeHertogh et al., Norihiro et al., Jorgensan and Nielsen recommend steroid therapy, starting with 60 mg/day (0.8 mg/kg/day) prednisolone treatment and gradually decreasing at different doses, lasting four to six months (7,9,19). Karanlık et al. have recommended starting prednisolone at a dose of 0.5 mg/kg/day for 2-4 weeks and then tapering down slowly for four weeks (20). Jeon et al. have suggested administering the steroid at a dose of 0.4 mg/kg/day and gradually reducing the dose for one to 28 weeks (10). In our study, the average steroid dose we applied to our patients was 0.05-0.1 mg/kg/day and the average recovery time was 8.00 ± 2.68 weeks. We found that there was a similar recovery period with the literature. Current studies show that vitamin D appears to interact with the immune system, with its effects on the regulation and differentiation of lymphocytes, macrophages, natural killer cells

(NK), and its deficiency is associated with several autoimmune diseases, including IBD, RA, SLE, IDDM (12,21). Based on this, we evaluated routine serum 25-hydroxyvitamin D levels from patients with IGM who applied to our clinic and we gave vitamin D replacement in patients with serum vitamin D levels below 30 ng/mL. Although it was not statistically significant, mean recovery time in the group that received replacement therapy was shorter than the group that was not given vitamin D. We think that the limitation of the number of cases should be taken into consideration when the shortening of the recovery period is not statistically significant.

In addition, according to our clinical experience, we think that surgical interventions should be avoided in patients with IGM, except for abscess drainage and excisional biopsy in localized small, non-healing masses. The aim of our study was that in patients diagnosed with IGM, although low-dose steroid treatment is called, could the dose of 0.4-0.8 mg/kg/day steroid given for months until clinical improvement recommended in various publications still be unnecessary? To further reduce the side effect profile, we tried to look if there was a lower steroid dose range that would provide clinical improvement to similar periods. At the same time, we tried to evaluate whether vitamin D level in our patients diagnosed with IGM is a predisposing factor in this disease and contributes to the duration of clinical recovery by replacement.

CONCLUSION

In conclusion, we think that the treatment of patients with the diagnosis of IGM can be planned with steroid doses of 0.05-0.1 mg/kg daily and vitamin D replacement when deficiency is present; in accordance with literature, within acceptable time and with less side effects and cost; while avoiding extensive surgery. Still, we are aware that larger studies with better planned control groups are needed.

Ethics Committee Approval: The approval for this study was obtained from İstanbul Health Science University Kanuni Sultan Süleyman Training and Research Hospital Clinical Research Ethics Committee (Decision no: 236, Date: 11.08.2021).

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ORİJİNAL ÇALIŞMA-ÖZET
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İdiyopatik granülomatöz mastitli hastalarda D vitamini replasmanı ile daha düşük doz steroid tedavisinin rolü

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ÖZET

Giriş ve Amaç: Literatürde çeşitli çalışmalarda idiyopatik granülomatöz mastitte (İGM) düşük doz steroid tedavisi önerilmiş ancak terapötik minimum doz henüz belirlenmemiştir. Ayrıca otoimmün hastalıklar üzerinde etkisi kabul edilen D vitamini eksikliği daha önce İGM'de incelenmemiştir. Çalışmamızın amacı, idiyopatik granülomatöz mastitisli (İGM) hastalarda daha düşük dozda steroid tedavisi ile birlikte hastaların serum 25-hidroksivitamin D düzeylerini ölçerek vitamin D replasmanının etkinliğini değerlendirmektir.

Gereç ve Yöntem: 2017-2019 yılları arasında kliniğimize başvuran 30 IGM hastasında D vitamini düzeyleri değerlendirildi. Serum 25-hidroksivitamin D düzeyi 30 ng/mL'nin altında olan hastalara vitamin D replasmanı yapıldı ve tüm hastalara 0,05-0,1 mg/kg/gün dozunda prednizolon verildi. Hastaların klinik iyileşme süreleri literatür ile karşılaştırıldı.

Bulgular: Yirmi iki (%73.33) hastaya vitamin D replasmanı yapıldı. D vitamini replasmanı yapılan hastalarda iyileşme süresi daha kısaydı (7,62 ± 2,38; 9,00 ± 3,38; p= 0,680). Ortalama iyileşme süresi 8,00 ± 2,68 hafta idi.

Sonuç: İGM tedavisi daha düşük doz steroid tedavisi ile tedavi edilebilir, bu da daha az komplikasyona ve daha az maliyete neden olur. Serum 25-hidroksivitamin D düzeyinin ölçülmesi ve uygun dozda tedavi edilmesi iyileşme sürecine katkı sağlayabilir.

Anahtar Kelimeler: İdiyopatik granulomatöz mastit, daha düşük doz steroid tedavisi, vitamin D

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ORIGINAL ARTICLE
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Anti-inflammatory effects of oral and intraperitoneal administration of cerium oxide nanoparticles on experimental hepatic ischemia-reperfusion injury

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ABSTRACT

Objective: Hepatic ischemia-reperfusion (IR) injury occurs in liver surgery, resection, and transplantation. Reactive oxygen species (ROS) produced following IR starts the cascade of cell damage, necrosis/apoptosis, and proinflammatory responses by activating intracellular signaling cascade to drive hepatocellular damage. Cerium oxide nanoparticles (CONPs) act as anti-inflammatory and antioxidant agents. Thus, we evaluated the protective effects of oral (o.g.) and intraperitoneal (i.p.) administration of CONPs on hepatic IR injury.

Material and Methods: Mice were randomly divided into five groups: control, sham, IR protocol, CONP+IR (i.p.), and CONP+IR (o.g.). Mouse hepatic IR protocol was applied to the animals in the IR group. CONPs (300 µg/kg) were administered 24 hours before IR protocol. Blood and tissue samples were taken after the reperfusion period.

Results: Hepatic IR injury markedly increased enzyme activities, tissue lipid peroxidation, myeloperoxidase (MPO), xanthine oxidase (XO), nitrite oxide (NO), and tissue nuclear factor kappa-B (NF-κB) p65 levels, plasma pro-inflammatory cytokines, chemokines, and adhesion molecules while decreasing antioxidant markers and caused pathological changes in hepatic tissue. The expression of tumor necrosis factor alpha (TNF-α), matrix metalloproteinase 2 (MMP-2), and 9 increased, and tissue inhibitor matrix metalloproteinase 1 (TIMP-1) expression decreased in the IR group. Pretreatment with CONPs o.g. and i.p. 24 hours before hepatic ischemia improved the biochemical parameters above and alleviated the histopathological findings.

Conclusion: Results of the present study demonstrate a significant reduction in liver degeneration by administering CONPs via i.p. and o.g. route in an experimental liver IR model, suggesting that CONPs have the extensive potential to prevent hepatic IR injury.

Keywords: Ischemia reperfusion, cerium oxide nanoparticles (CONPs), mouse, oxidative stress, inflammation

INTRODUCTION

Hepatic ischemia-reperfusion (IR) injury is a significant complication of liver-related surgical interventions, liver transplantation, liver resection, hemorrhagic shock, and liver trauma surgery, implicating a complex cascade of cellular and humoral events leading to severe cellular injury (1,2). Although several factors are involved in hepatic IR injury, such as anaerobic and aerobic metabolism, intracellular calcium overload, oxidative stress, as well as events related to neutrophils, Kupffer cells, cytokines, and chemokines (1), there is no effective prevention or treatment found yet. Thus, new therapeutic options for preventing or alleviating hepatic IR injury during liver surgery are needed.

The early phase of hepatic IR injury comprises the period less than two hours after reperfusion, which includes oxidative stress and inflammation, while the late phase, in which neutrophil accumulation and hepatocellular injury are involved, occurs at six to 48 hours after reperfusion (2). Kupffer cells, the liver macrophages, are the source of reactive oxygen species (ROS) production in the initial phase of IR injury. In contrast, hypoxia and adenosine triphosphate (ATP) loss also contribute to the ischemic period by forming ROS and activating neutrophils to produce in-

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flammatory cytokines, further enhancing hepatocyte injury (3). Antioxidants are used to prevent excess ROS formation in the treatment of hepatic IR injury (4); these agents do not favorably target the liver.

Recent advances in nanotechnology offer promising agents that can effectively scavenge ROS and exhibit anti-inflammatory effects (5). Among these, cerium oxide nanoparticles (CONPs), also called nanoceria, are used in the biomedical field to treat pathologies involving oxidative stress and inflammatory processes (6). CONPs act superoxide dismutase (SOD) and catalase (CAT) like activities (7). Recent studies have demonstrated that the antioxidant capacity of CONPs is 9-fold higher than that of known antioxidants (5). Recently, CONPs have been shown to block interleukin-6 (IL-6) and tissue inhibitor of metalloproteinase-2 (TIMP-2) gene overexpression in cirrhotic rats (8). In addition, studies have shown that CONPs are not toxic in therapeutic doses, relatively stable, and accumulate in the liver by administration (9).

In this study, our aim was to assess the constructive effects of CONPs on oxidative and inflammatory processes observed during IR liver injury in a mouse hepatic IR model, considering the promising benefits of CONP-based therapies.

MATERIAL and METHODS

Animal Studies

The present study was performed in compliance with the Ethical Guidelines for Animal Studies and conducted with the permission of local animal ethics committee (2017/04.02). Eight to twelve week-old male mice weighed 20-30 g were used. Ketamine (100 mg/kg) and xylazine (10 mg/kg) were used (intraperitoneally-i.p.) for anesthesia in fasted mice (16 h). Following a midline laparotomy, the liver was exteriorized, and to induce approximately 70% liver ischemia in the left lateral and median lobes, blood flow was interrupted with an atraumatic clip during 45 minutes (Figure 1). The liver and intestine were kept moist, the mice kept warm at 37°C with a heating blanket. After the ischemia period, the clamp was removed, the abdomen was sutured and the mice were recovered, thus reperfusion was provided during five hours. The mice were sacrificed under anesthesia [ketamine (500 mg/kg) and xylazine (50 mg/kg) i.p] after the reperfusion period, and tissue and blood samples were obtained. Two part of the liver samples were weighed immediately. The part to be used in histopathological analyzes was placed in 10% formalin. The second part of the samples was kept at -80°C until biochemical analysis. Blood samples were obtained by cardiac puncture and put into heparinized tubes for centrifugation at 3.000 x g for 10 min. The supernatants were stored at -20°C until biochemical experiments.

Five different group of animals were used: control, sham, IR protocol, CONP+IR (i.p.), and CONP+IR [oral gavage (o.g.)]. Each group consisted of six mice. Animals in the control group received an isovolumetric vehicle of 5% dextrose solution and then were sacrificed; blood and tissue samples were obtained. In the sham group, 5% dextrose solution was administered, and mice abdomens were just opened without clamping of the liver; blood and tissue samples were taken after the reperfusion period. Hepatic IR protocol was applied in the IR group after the vehicle administration. CONPs (300 µg/kg) in 5% sterile dextrose solution was administered 24 hours before IR protocol by i.p. injection or o.g. in CONP+IR (i.p.) and CONP+IR (o.g.) groups; blood and tissue samples were taken after the reperfusion period.

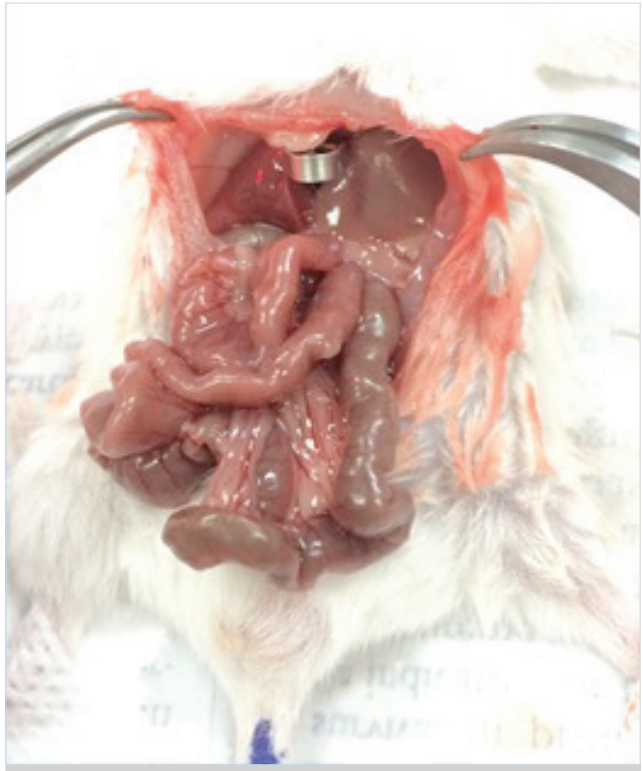

Figure 1. Partial mouse liver IR model.

The extent of liver edema was evaluated by liver/body weight (LBW) ratio. Mice in all groups were weighed. At the time of sacrifice, livers of the study groups were removed and weighed. The study groups' wet LBW was compared with that of the sham group.

Liver tissues removed from the rats were fixed in 10% formaldehyde solution for at least one day and embedded in paraffin at room temperature for 24 h. The sections of 4 µm thickness were subjected to hematoxylin & eosin staining and routine tissue monitoring. The sections were evaluated with a light microscope equipped with an image analysis program by a pathologist who was unaware of the treatment protocols. Presence of necrosis, sinus dilatation-congestion, venous congestion, inflammatory infiltration, and hepatocyte vacuolization/degeneration was considered as histopathologic evidence of liver damage (10).

Biochemical Analyses

Hepatic Enzyme Levels

Plasma transaminase and lactate dehydrogenase (LDH) levels were estimated as the markers of liver damage during hepatic IR. Plasma LDH activity was measured using an enzyme-linked immunosorbent assay (ELISA) kit (SIGMA-ALDRICH, L DH Activity Assay Kit, cat. No: MAK066); plasma alanine and aspartate aminotransferase (ALT, AST) levels were estimated using ELISA kits (SIGMA-ALDRICH, ALT Activity Assay Kit, cat. no: MAK052 and AST Activity Assay Kit, cat. no: MAK055, respectively) according to manufacturer's instructions. Results were expressed as U/L.

Oxidative Stress Parameters

Tissue malondialdehyde (MDA) level, as the indicator of lipid peroxidation, was estimated using ELISA kit (SIGMA-ALDRICH, Lipid Peroxidation (MDA) Assay Kit, cat. no: MAK085). Results were expressed as nmol/mg protein.

Tissue reduced glutathione (GSH) and oxidized (GSSG) glutathione contents were measured using glutathione assay kits (Cayman Chemicals, cat. no: 703002). Results were expressed as nmol/mg protein. GSH/GSSG ratio was calculated.

Antioxidant enzyme activities in hepatic tissue samples were determined using ELISA kits according to the manufacturer's instructions. SIGMA-ALDRICH SOD assay kit 19160 for superoxide dismutase (SOD) measurement; Glutathione Peroxidase Cellular Activity Assay Kit CGP1 for glutathione peroxidase (GPx) measurement; Glutathione S-Transferase (GST) Assay Kit CS0410 for GST measurement; Glutathione Reductase Assay Kit GRSA for glutathione reductase (GR) measurement and catalase assay kit CAT100 for catalase (CAT) measurement were used. Enzyme activities were expressed as nmol/mg protein for SOD, CAT, and GR and U/mg protein for GST and GPx.

Myeloperoxidase (MPO) Activity

Tissue MPO activities were measured using a commercially available ELISA kit (SIGMA-ALDRICH, MPO Colorimetric Activity Assay Kit, cat. no: MAK068). MPO activity was expressed as U/mg protein.

Xanthine Oxidase (XO) Activity

Since XO is the primary source of ROS at reperfusion, XO activity in liver tissues was estimated using an ELISA assay kit (SIGMA-ALDRICH, XO Activity Assay Kit cat. no: MAK078). XO activity was expressed as nmol/mg protein.

Nitric Oxide (NO)

Since it is suggested that NO mediates tissue injury during IR, reduces the harmful effects of endothelin, and improves microcirculation, liver tissue NO level was estimated using ELISA assay kit (ABNOVA, Nitric Oxide Assay, cat. no: KA1641). NO level was expressed as μM.

Tissue Nuclear Factor Kappa-B (NF-κB) p65

Since the activation of NF-κB was associated with IR injury and in vivo administration of NF-κB inhibitors reduced IR injury, in the present study, liver tissue NF-κB p65 level was determined using ELISA assay kit (MyBioSource, mouse NF-kappaB p65 ELISA Kit, catalog number MBS2508000). NF-κB p65 level was expressed as ng/mg protein.

RNA Isolation and Reverse Transcription Polymerase Chain Reaction (RT-PCR)

Total RNA was extracted using the Trizol separation method (Invitrogen). 1 μg total RNA was transcribed to cDNA with a high-capacity cDNA reverse transcription kit (Supercript II). Real-time PCR was carried out using SYBR Green PCR Master Mix (Biorad, Canada) and 100 nM of F and R primers. The relative quantity of each mRNA was normalized to the relative quantity of Glyceraldehyde 3-phosphate dehydrogenase. Primer sets used in RT-PCR experiments indicated in Table 1.

Plasma and Tissue Protein Contents

Plasma and tissue protein contents were determined using a total protein assay kit (SIGMA Total Protein kit, Micro TP0100). Protein concentration was expressed as mg/mL.

Plasma Cytokine, Chemokine, and Matrix Metalloproteinase (MMP) Levels

Since it has been reported that cytokines and chemokines contribute to the pathology of IR injury, and migration of polymorphonuclear neutrophils into damaged tissue during ischemia is facilitated by endothelial expression of adhesion molecules like intercellular adhesion molecule-1 (ICAM-1), plasma cytokine and chemokine levels were determined. IL-1-α, IL-1 β, IL-2, IL-4, IL-6, IL-10, IL-12, IL-17, tumor necrosis factor-α (TNF-α), and

Table 1. Primer sets used in RT-PCR experiments

GAPDH F: 5′ - CATCACTGCCACCCAGAAGACTG -3′ R: 5′- ATGCCAGTGAGCTTCCCGTTCAG -3′
TNF-α F: 5′ - GGTGCCTATGTCTCAGCCTCTT -3′ R: 5′ - GCCATAGAACTGATGAGAGGGAG -3′
MMP-2 F: 5′ - CAAGGATGGACTCCTGGCACAT -3′ R: 5′- TACTCGCCATCAGCGTTCCCAT -3′
MMP-9 F: 5′ - GCTGACTACGATAAGGACGGCA -3′ R: 5′- TAGTGGTGCAGGCAGAGTAGGA -3′
TIMP-1 F: 5′ - TCTTGGTTCCCTGGCGTACTCT -3′ R: 5′- GTGAGTGTCACTCTCCAGTTTGC -3′
F: Forward primer, R: Reverse primer.

interferon-γ (IFN-γ) levels were estimated using ELISA Multiplex assay kit (Invitrogen ProcartaPlex™ Multiplex Immunoassay) according to the manufacturer's instructions. Cytokine levels were expressed as pg/mL. Plasma IL-8 level was determined using ELISA assay kit (MyBioSource Rat IL8 ELISA Kit cat. no: MBS025179. IL-8 level was expressed as pg/mL. Plasma ICAM-1 level was measured using an ELISA assay kit (Thermo Fisher Scientific, Rat ICAM-1 ELISA Kit, ERICAM1). ICAM-1 level was expressed as pg/mL. Plasma MMP-2 and MMP-9 levels were determined using Mouse MMP 2 ELISA Kit (MyBioSource cat. no: MBS454416) and Mouse MMP 9 ELISA Kit (MyBioSource cat. no: MBS720876). MMP levels were expressed as pg/mL. Plasma TIMP-1 level was determined using ELISA assay kit (ABCAM mouse TIMP1 SimpleStep Cat. No. ab196265). TIMP-1 level was expressed as pg/mL

Statistical Analysis

All results were expressed as mean ± standard error of mean (SEM) of at least three independent experiments and analyzed by Prism 6.0 software for MacOS. Mann-Whitney U test and Kruskal-Wallis were used for comparison of groups of the variables. Correlations between variables were assessed with Pearson's correlation coefficients (r), and $p< 0.05$ was considered statistically significant.

RESULTS

Effects of CONPs on Liver Edema

Liver edema was assessed by the LBW ratio. LBW was significantly increased in the IR group compared to that of the sham group. However, administration of CONP orally and intraperitoneally significantly inhibited IR-induced increase in hepatic LBW ratio ($p< 0.01$) (Figure 2).

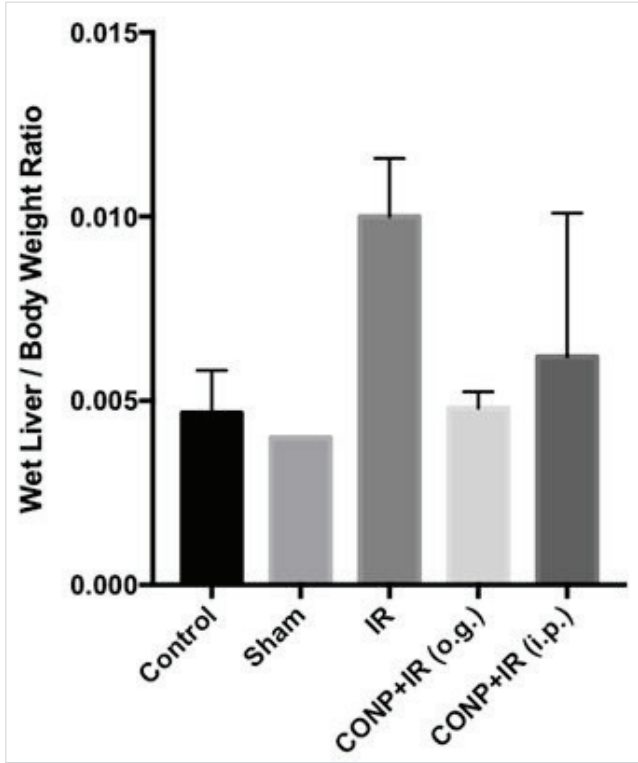

Figure 2. Liver/body weight ratio in the study groups. Results are presented as mean ± SEM (n= 6). (**p< 0.01 vs. Sham; ΨΨp< 0.01 vs. IR groups).

Effects of CONPs on Histopathological Findings

No histopathological findings were found in the liver tissue of the sham group (Figure 3A). On the contrary, the IR group showed histological changes reflecting severe hepatocellular injuries, such as loss of liver parenchyma due to hepatocyte necrosis accompanying severe polymorphonuclear leukocyte infiltration (Figure 3B), cytoplasmic vacuolization, and sinusoidal congestion. These histopathological findings were found to be highly consistent with our biochemical findings (plasma LDH, ALT, AST activities; tissue MDA content). However, morphological appearance significantly returned to almost normal in CONP+IR (i.p.) and CONP+IR (o.g.) groups (Figures 3C, 3D, respectively), indicating that treatment with CONPs ameliorates liver injury that occurred during hepatic IR in mice.

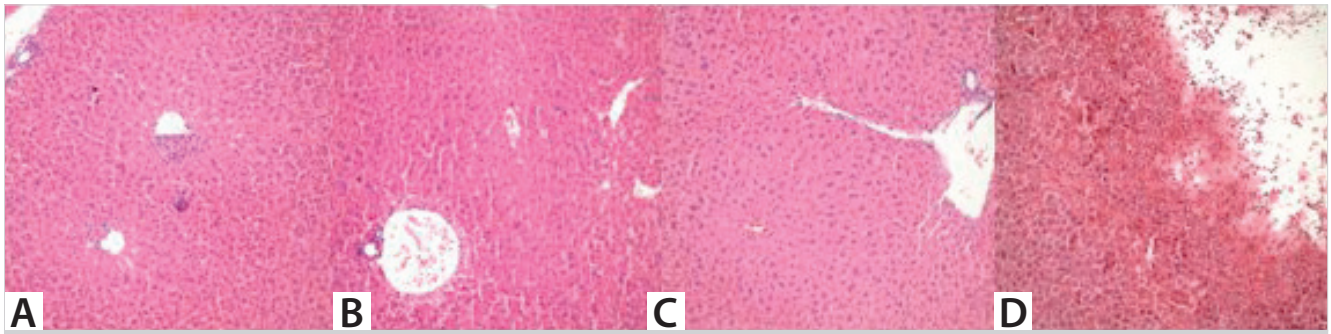

Figure 3. Hepatic histological changes in hematoxylin&eosin-stained liver sections of study groups (Original magnification: ×200). **(A)** Sham group: No pathological changes were observed. **(B)** IR group: Severe hepatocyte necrosis leading to loss of liver parenchyma with accompanying neutrophils was seen. **(C)** CONP+IR (i.p.) group: Almost normal liver parenchyma with minimal sinusoidal and venous congestion. **(D)** CONP+IR (o.g.) group: Few small necro-inflammatory foci and moderate sinusoidal congestion were present. There is no massive necrosis seen in the IR group.

Effects of CONPs on Hepatic Enzyme Levels

Plasma LDH and transaminase levels are estimated as liver damage markers during hepatic IR. Plasma LDH levels were almost four times increased in the IR group than the sham group, while CONP administration led to a significant decrease in these levels (p< 0.001). No statistically significant difference was observed between the administration of CONPs by i.p. or o.g. However, pretreatment with CONP via intraperitoneally significantly reduced the enzyme levels almost towards the levels of the sham group, which demonstrates that i.p. administration of CONPs may be helpful to reverse the tissue damage that occurred in hepatic IR (Table 2). Plasma AST and ALT activities were significantly increased after hepatic IR, and CONP administration markedly decreased the plasma levels of these liver injury indicators (p< 0.001) (Table 2). No statistically significant difference was observed between the administration of CONPs by i.p. or o.g. in terms of hepatic enzyme levels.

Table 2. Biochemical parameters in plasma and hepatic tissue samples of the study groups

	Control	Sham	IR	CONP+IR (i.p.)	CONP+IR (o.g.)
Plasma LDH (U/L)	516.11 ± 60.64	519.89 ± 42.87	1950.24 ± 183.85 ***	517.44 ± 61.17 ^^^	538.69 ± 50.54 ^^^
Plasma ALT (U/L)	19.55 ± 3.04	19.82 ± 5.58	95.55 ± 7.87 ***	20.73 ± 5.95 ^^^	22.44 ± 4.25 ^^^
Plasma AST (U/L)	38.57 ± 9.47	42.23 ± 5.69	316.97 ± 39.40 ***	43.86 ± 9.37 ^^^	46.82 ± 9.39 ^^^
Tissue MDA (nmol/mg protein)	6.56 ± 0.69	6.52 ± 0.49	30.18 ± 2.61 ***	6.87 ± 0.56 ^^^	7.06 ± 0.50 ^^^
Tissue GSH (nmol/mg protein)	75.87 ± 4.68	75.38 ± 5.45	15.84 ± 3.76 ***	75.30 ± 6.90 ^^^	75.50 ± 4.81 ^^^
Tissue GSSG (nmol/mg protein)	7.27 ± 0.79	7.46 ± 1.16	34.14 ± 4.08 ***	7.49 ± 0.85 ^^^	7.67 ± 1.12 ^^^
Tissue GSH/GSSG	10.51 ± 1.08	10.29 ± 1.54	0.46 ± 0.12 ***	10.38 ± 1.55 ^^^	10.22 ± 1.42 ^^^
Tissue SOD (nmol/mg protein)	19.19 ± 1.48	20.83 ± 3.56	6.97 ± 0.41 ***	16.07 ± 3.22 ^^^	18.18 ± 2.46 ^^^
Tissue CAT (nmol/mg protein)	7.32 ± 0.38	7.67 ± 0.44	3.07 ± 0.46 ***	7.49 ± 0.58 ^^^	7.67 ± 0.53 ^^^
Tissue GR (nmol/mg protein)	34.84 ± 3.97	32.94 ± 5.19	9.60 ± 1.10 ***	29.45 ± 3.58 ^^^	30.19 ± 5.64 ^^^
Tissue GST (U/mg protein)	4.87 ± 0.29	4.24 ± 0.51	1.67 ± 0.30 ***	4.83 ± 0.32 ^^^	4.82 ± 0.72 ^^^
Tissue GPx (U/mg protein)	3.08 ± 0.30	3.28 ± 0.38	0.83 ± 0.30 ***	2.64 ± 0.22 ^^^	2.61 ± 0.31 ^^^
Tissue MPO activity (U/mg protein)	0.40 ± 0.07	0.43 ± 0.05	2.19 ± 0.25 ***	0.43 ± 0.12 ^^^	0.42 ± 0.12 ^^^
Tissue XO activity (nmol/mg protein)	0.53 ± 0.04	0.53 ± 0.04	1.65 ± 0.12 **	0.52 ± 0.07 ^^	0.50 ± 0.06 ^^
Tissue NO level (μM)	0.50 ± 0.06	0.44 ± 0.06	1.14 ± 0.10 **	0.57 ± 0.05 ^^	0.56 ± 0.08 ^^
Tissue NF-κB p65 level ng/mg protein	0.32 ± 0.03	0.35 ± 0.06	1.29 ± 0.12 **	0.35 ± 0.05 ^^	0.34 ± 0.04 ^^

Values are presented as mean ± SEM (***p< 0.001 vs. Sham; **p< 0.01 vs. Sham; ^^^p< 0.001 vs. IR; ^^p< 0.01 vs. IR)
CONP+IR (i.p.): Cerium oxide nanoparticle + ischemia reperfusion (intraperitoneally).
CONP+IR (o.g.): Cerium oxide nanoparticle + ischemia reperfusion (oral gavage).
LDH: Lactate dehydrogenase, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, MDA: Malondialdehyde, GSH: Reduced glutathione, GSSG: Oxidized glutathione, SOD: Superoxide dismutase, CAT: Catalase, GR: Glutathione reductase, GST: Glutathione S-transferase, GPx: Glutathione peroxidase, MPO: Myeloperoxidase, XO: Xanthine oxidase, NO: Nitric oxide, NF-κB: Nuclear factor kappa-B

Effects of CONPs on Oxidative Stress Parameters

Since oxidative stress is involved in hepatic ischemic damage, tissue oxidative stress parameters were estimated in control and study groups. Tissue level of MDA produced as a secondary product of lipid peroxidation was increased in the IR group compared to control and sham groups ($p< 0.001$). Treatment with CONPs decreased tissue lipid peroxidation levels significantly ($p< 0.001$) compared to those of the IR group. (Table 2). The administration of CONPs i.p. detected the most significant reduction in tissue MDA level, suggesting that CONPs, o.g. administration may be beneficial to the recovery of hepatic IR injury.

Liver GSH content was significantly decreased, GSSG content was increased, and GSH/GSSG ratio was decreased in the IR group compared to control and sham groups while GSH level and GSH/GSSG ratio were increased and GSSG level was decreased in the treatment groups ($p< 0.001$) (Table 2). Since tissue glutathione levels approached the levels of the control and sham groups with the treatment with CONPs, CONPs are presented as a promising therapeutic agent for the improvement of the impaired oxidative stress status during hepatic IR injury. The administration route of CONPs showed no statistical difference in terms of glutathione levels.

Tissue antioxidant enzyme activities were significantly decreased in liver tissues of the IR group and elevated in the treatment groups ($p< 0.001$). Thus, CONPs may be introduced as promising agents to recover the deteriorated antioxidant capacity during hepatic IR injury (Table 2). However, the administration route of CONPs did not show a statistical difference in antioxidant enzyme levels.

Table 3. Plasma proinflammatory cytokines and chemokines in the study groups

	Control	Sham	IR	CONP+IR (i.p.)	CONP+IR (o.g.)
TNF-α pg/mL	2.49 ± 0.49	2.41 ± 0.51	73.89 ± 5.12 ***	3.50 ± 0.80 ^^^	3.79 ± 1.24 ^^^
IL-1α pg/mL	4.76 ± 0.89	4.80 ± 1	17.21 ± 3.56 ***	5.82 ± 1.28 ^^^	5.60 ± 1.18 ^^^
IL-1β pg/mL	2.79 ± 0.48	3.02 ± 0.31	11.65 ± 1.69 ***	2.90 ± 1.30 ^^^	4.75 ± 0.86 ^^^
IL-2 pg/mL	18.01 ± 2.81	20.22 ± 3.94	67.66 ± 9.38 ***	24.17 ± 3.46 ^^^	27.49 ± 5.81 ^^^
IL-4 pg/mL	40.91 ± 3.14	42.34 ± 7.39	57.88 ± 11.07 *	45.91 ± 8.71 ^	41.79 ± 8.73 ^
IL-6 pg/mL	8.56 ± 0.82	8.14 ± 1.37	168.83 ± 21.24 ***	10.84 ± 1.55 ^^^	12.27 ± 2.55 ^^^
IL-8 pg/mL	112.37 ± 15.66	108.62 ± 16.17	503.34 ± 78.65 ***	124.52 ± 15.96 ^^^	144.46 ± 17.47 ^^^
IL-10 pg/mL	161.80 ± 16.38	172.63 ± 12.57	51.22 ± 1.07 ***	169.40 ± 7.66 ^^^	170.00 ± 6.80 ^^^
IL-12 pg/mL	116.41 ± 12.90	122.43 ± 18.31	1194.46 ± 129.99 ***	138.99 ± 24.66 ^^^	151.27 ± 32.20 ^^^
IL-17A pg/mL	47.67 ± 7.15	43.36 ± 7.94	435.46 ± 59.70 ***	50.98 ± 4.83 ^^^	55.22 ± 7.56 ^^^
ICAM-1 ng/mL	194.15 ± 2.62	194.39 ± 4.82	551.56 ± 77.01 ***	202.22 ± 6.15 ^^^	208.02 ± 6.12 ^^^
MMP-2 pg/mL	71.05 ± 14.23	71.04 ± 12.45	244.62 ± 147.25 ***	74.57 ± 16.64 ^^^	85.23 ± 11.60 ^^^
MMP-9 pg/mL	63.58 ± 2.90	66.21 ± 3.00	562.03 ± 16.03 ***	100.99 ± 23.08 ^^^	116.17 ± 18.07 ^^^
TIMP-1 pg/mL	57.25 ± 1.45	56.34 ± 1.90	12.30 ± 2.00 ***	58.08 ± 2.20 ^^^	60.11 ± 3.55 ^^^

Data are presented as mean ± SEM (***$p< 0.001$ vs. sham; *$p< 0.05$ vs. sham; ^^^$p< 0.001$ vs. IR; ^$p< 0.05$ vs. IR).
TNF- α: Tumor necrosis factor, IL: Interleukin, ICAM-1: Intercellular adhesion molecule, MMP: Matrix metalloproteinase, TIMP: Tissue inhibitor of metalloproteinase.

Effects of CONPs on Tissue MPO Activity

MPO activity, a biomarker to indicate the degree of neutrophil accumulation and inflammatory response, was elevated in the IR group compared to control and sham groups ($p< 0.001$). Conversely, CONP administration significantly decreased hepatic MPO activity than the IR group ($p< 0.001$) (Table 2).

Effects of CONPs on Tissue XO Activity

XO activity in liver tissue was significantly increased in the IR group in comparison with the control and sham groups. On the other hand, CONP administration significantly suppressed the hepatic XO activity ($p< 0.01$) (Table 2).

Effects of CONPs on Tissue NF-κB Activity

NF-κB activity in liver tissue was found to be dramatically increased in the IR group, whereas this level was importantly increased in CONP treatment groups ($p< 0.01$) (Table 2). The administration route of CONPs did not show a statistical difference in hepatic NF-κB levels.

Effects of CONPs on Plasma Cytokine Levels

IR injury causes a complex inflammatory immune response and is associated with a marked increase in inflammatory mediators and chemotactic proteins (11). In accordance with the previous studies, it was observed that IR injury significantly altered serum inflammatory proteins (Table 3). Plasma TNF-α, IL-1α, IL-1β, IL-2, IL-4, IL-6, IL-8, IL-12, IL-17A, ICAM-1 levels were markedly increased, and IL-10 was decreased in the IR group while pretreatment with CONPs approached the altered cytokine/chemokine/adhesion molecule levels of control and sham groups ($p< 0.001$) (Table 3). In addition, the tissue expression of TNF-α was increased in IR group and decreased in the treatment groups ($p< 0.001$) (Figure 4), indicating that CONP administration reduces the enhanced TNF-α production.

Effects of CONPs on Plasma MMP Levels

Since hepatic IR is associated with MMP activation and release, plasma MMP-2, MMP-9, and TIMP-1 levels were measured in control and study groups. Plasma MMP-2 and MMP-9 levels were significantly higher in IR group compared to the values of control and sham groups ($p< 0.001$). Conversely, MMP expression and plasma levels were markedly decreased in the CONPs administration groups ($p< 0.001$). (Figure 5).

DISCUSSION

Hepatic IR injury represents a clinical problem associated with many surgical interventions. The induction of Kupffer cell after reperfusion is the initial phase of liver and followed by ROS release, which generates oxidative stress, parenchymal and vascular injuries, as well as hepatocyte damage via lipid peroxidation or straightly enhancing neutrophil microcirculation (12). Cytokines released by activated Kupffer cells and aggregated neutrophils play a crucial role in IR injury (13).

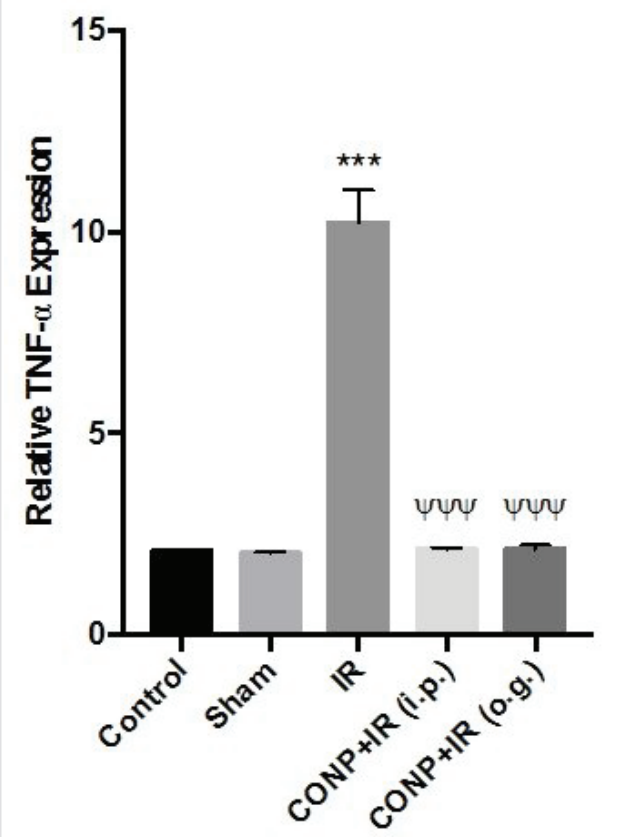

Figure 4. Gene expression of TNF-α in liver tissue of study groups. Values are presented as mean ± SEM (n= 6). (***$p< 0.001$ vs Sham; ΨΨΨ$p< 0.001$ vs IR).

CONPs have shown to display several antioxidant behaviors, including SOD activity, CATmimetic activity, NO radical scavenging, hydroxyl radical scavenging, radiation-protective anti-inflammatory, and neuroprotective effects (14). It has been reported that CONPs might be used to treat sepsis, cardiomyopathy, stroke, obesity, ovarian cancer, hepatic steatosis, and cancer (7,15-18). Previous studies have suggested that CONPs show SOD-like, CAT-like, and peroxidase activity and NO scavenging ability, leading to reduced ROS production in macrophages (19).

Treatment of hepatic IR injury with antioxidants has exhibited encouraging results in vivo but has not been successful in clinical applications resulting from insufficient antioxidant levels. Thus, targeted drug delivery would provide better outcomes. The studies have demonstrated that upon i.v. injection, before translocating to the organs, CONPs stay in circulation for a short period (t1/2 is 7.5 min) (9). The Kupffer cells enclose CONPs within the liver. Since reperfusion is followed by a dramatically increased oxidative stress, administering CONPs 1 h before ischemia results in bioaccumulation of the particles in the liver that scavenge ROS that are formed during reperfusion (20). In the present study, hepatic IR caused a dramatic elevation in

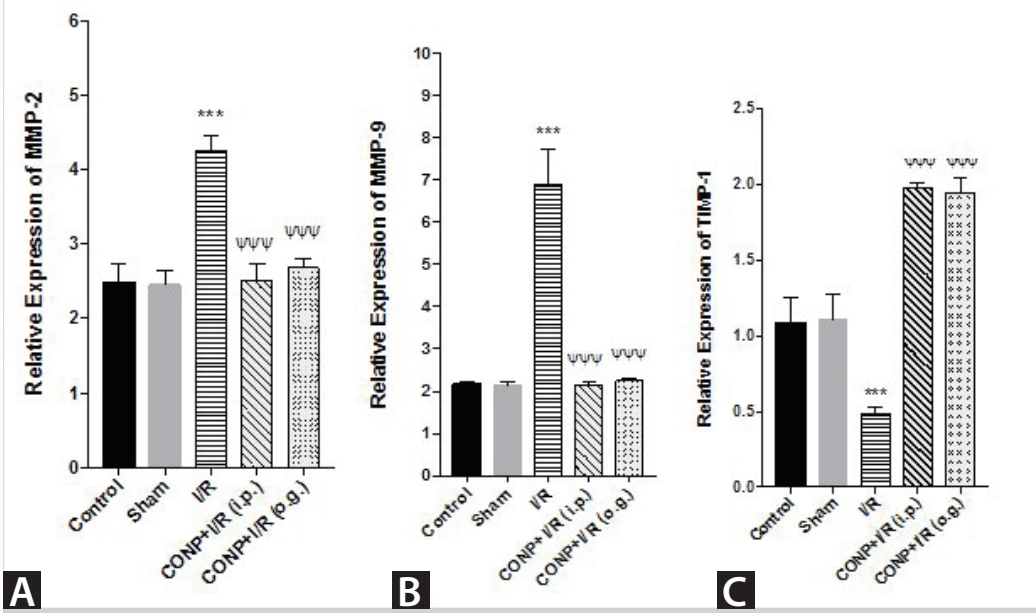

Figure 5. Gene expressions of MMP-2 **(A)** MMP-9 **(B)** and TIMP-1 **(C)** in liver samples of study groups. Values are presented as mean ± SEM (n= 6). (***p< 0.001 vs Sham; ΨΨΨp< 0.001 vs IR).

plasma ALT, AST, and LDH enzymes due to IR-induced hepatic cell injury. Treatment with CONPs 24 hours before the IR in the liver attenuated increases in plasma ALT-AST and LDH activities, indicating that CONP administration has the benefit of reducing hepatocellular injury during IR. CONP administration also reduced the elevated levels of MDA, GSSG while increasing the levels of GSH and antioxidant enzymes. Severe hepatocyte swelling, alongside vacuolar degeneration and multiple necrotic areas, are common findings during the histological analysis of the tissues with IR injury. Conversely, treatment with CONPs recovered these changes supporting the findings that CONPs in oxidized form transits between cerium (III) oxide (Ce^{3+}) and Ce^{4+} oxidative states, allow regenerative redox cycling and free radical scavenging (21).

During IR injury, NO production is compromised because of constitutive endothelial NO synthase dysfunction. It has been shown that NO reduces macrophage and neutrophil infiltration and neutralizes the superoxide anion. It also inhibits apoptosis, protects the sinus structure of liver and microcirculatory blood flow, increases hepatic oxygenation, and diminishes oxidative stress injury (1). In our study, tissue NO level was increased in the hepatic IR group and decreased in CONP administration groups, possibly due to the antioxidative properties of CONPs.

XO, a rate-limiting enzyme of purine catabolism, operates as a ROS source in IR injury (22). Under ischemic conditions, XO occurs with proteolysis from xanthine dehydrogenase (XDH). In normoxic conditions, XDH produces urate from hypoxanthine and xanthine, and XO, whose expression is the highest in the liver, is responsible for the ROS generation under hypoxic and IR conditions (23). Our data confirmed that CONP administration reduced the plasma levels of XO and ICAM-1 and ameliorated the cellular liver damage during hepatic IR.

It has been demonstrated that NF-κB activation endorses the levels of cytokines such as TNF-α, and IL-6, in the initial phase of the injury in the Kupffer cells (12). In this study, tissue NF-κB level was elevated in the IR group and reduced in CONP administration groups, demonstrating that CONP administration has a beneficial effect on regulating NF-κB levels and oxidative unbalance in hepatic IR.

Studies have indicated that MMPs and their TIMPs play significant roles in the extracellular matrix remodeling in liver damage (24). Proteases are delivered from injured cells, when healthy cells deliver TIMPs. A high ratio of MMP/TIMP indicates the activated MMPs, whereas a low ratio of MMP/TIMP hints at the contrary. MMP-2 and MMP-9, significantly ensured in the degradation of fibronectin and collagen IV, may cause damage in the liver to altering the sinusoidal cells and remodeling of the stromal structure (25). The tissue expressions and plasma levels of MMP-2 and -9 were increased while tissue expression and plasma level of TIMP-1 decreased in the IR group, demonstrating a high MMP/TIMP ratio hepatic IR injury in this study. Since CONP administration reversed this unbalanced status, it was concluded that CONPs administration prevents the activation of matrix proteinases and protects the liver from IR injury.

Hepatic IR injury causes an enhancement in proinflammatory mediators and chemotactic proteins (9). In accordance with previous studies, we found that hepatic IR injury led to increased plasma inflammatory proteins such as plasma TNF-α,

IL-1α, IL-1β, IL-2, IL-4, IL-6, IL-8, IL-12, IL-17A, ICAM-1 levels and decreased plasma IL-10 level compared to control and sham groups. However, the changes in inflammatory markers are diminished and returned almost to the baseline controls via treatment with CONPs. Additionally, TNF-α increases the expression of adhesion molecules like ICAM-1, vascular cell adhesion protein (VCAM-1), and P-selectin on vascular endothelial cells (6). Reducing tissue TNF-α expression and plasma TNF-α level is suggested to improve hepatic IR injury by suppressing inflammatory response (26).

CONCLUSION

CONPs scavenge reactive oxygen and nitrogen species by altering the enzymes in favor of antioxidation or non-enzymatic ways through scavenging hydroxyl and NO radicals. Most experimental studies related to CONPs are principally focused on animal or human cells in vitro; thus, more in vivo studies are needed.

This preliminary study demonstrates a significant reduction in liver degeneration by administering CONPs via i.p. and o.p. route in an experimental liver IR model. Presented data suggest that CONPs have the potential for the prevention of hepatic IR injury. However, the details of the mechanism of the cytoprotective effect produced by CONPs should be further investigated. Furthermore, cytokine and MMP levels examined at the protein level should also be examined at the gene level to determine whether the effect is at the gene level or the protein level, so the details of the mechanism should be clarified.

Main Points

- Hepatic ischemia-reperfusion (IR) injury is a complication of liver-related surgical interventions.
- Cerium oxide nanoparticles (CONPs) are used to treat oxidative stress and inflammation-related processes.
- Preoperative treatment with CONPs reduces the increased oxidative stress, pro-inflammatory mediators, and extracellular matrix components in hepatic IR.
- CONPs may be considered as promising therapeutic agents for preventing IR injury.

Ethics Committee Approval: The approval for this study was obtained from Dumlupınar University Animal Experiments Local Ethics Committee with the Decision no: 2017.04-02, Date: 06.04.2017).

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Author Contributions: Concept – A.Z., A.E., G.T.; Design – A.Z., A.E., G.T.; Supervision – G.U., M.C.A., B.G.; Materials – A.Z., A.E., G.T.; Data Collection and/ or Processing – K.K., G.T.; Analysis and/or Interpretation – G.U., M.C.A., B.G.; Literature Search – A.Z., K.K.; Writing Manuscript – A.Z., G.U., K.K.; Critical Reviews – G.U., M.C.A., B.G.

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ORİJİNAL ÇALIŞMA-ÖZET
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Deneysel karaciğer iskemi-reperfüzyon hasarında cerium oksidin oral ve intraperitoneal uygulanmasının anti-enflamatuvar etkisi

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ÖZET

Giriş ve Amaç: Hepatik iskemi-reperfüzyon (IR) hasarı karaciğer cerrahisi ve transplantasyonda meydana gelir. IR hücre hasarı kaskadını, nekroz/ apopitoz ve hepatosellüler hasarı yöneten intrasellüler sinyal kaskadını aktive olmasıyla oluşan proenflamatuvar cevaplar ile reaktif oksijen radikalleri (ROS) üretilir. Cerium oksit nanopartikülleri (CONPs) anti-enflamatuvar ve antioksidan ajan gibi davranmaktadır. Bu yüzden, CONPs'nin oral (o.g.) ve intraperitoneal (i.p.) uygulanmasının hepatic IR hasarındaki koruyucu etkisini değerlendirdik.

Gereç ve Yöntem: Fareler rastgele kontrol, sham, IR protocol, CONP+ IR (i.p.) ve CONP (o.g.) olarak beş gruba ayrıldı. Fare hepatik IR protokolü IR grubundaki hayvanlara uygulandı. IR protokolünden 24 saat önce CONPs (300 µg/kg) uygulandı. Reperfüzyon periyodu sonrası kan ve doku örnekleri alındı.

Bulgular: Hepatik IR hasarı, doku lipid peroksidasyonunu, miyeloperoksidaz (MPO), ksantin oksidaz (XO), nitrit oksit (NO) ve doku nükleer faktör kappa-B(NF-κB) p65 enzim aktivitelerinin seviyelerini belirgin şekilde arttırdı; plazma proenflamatuvar sitokinler, kemokinler ve adezyon molekülleri antioksidan belirteçleri azaltırken karaciğer dokusunda patolojik değişikliklere neden olmuştur. IR grubunda tümör nekroz faktör alfa (TNF-α), matriks metalloproteinaz 2 (MMP-2) ve 9 ekspresyonu artmış, doku inhibitörü matriks metalloproteinaz 1 (TIMP-1) ekspresyonu azalmıştır. Hepatik iskemiden 24 saat önce o.g. ve i.p. olarak uygulanan CONP'ler ile yukarıda belirtilen biyokimyasal parametreleri düzeldi ve histopatolojik özellikleri hafifletti.

Sonuç: Bu çalışmanın sonuçları, deneysel bir karaciğer IR modelinde i.p. ve o.g. yoluyla CONP'lerin uygulanmasıyla karaciğer dejenerasyonunda önemli bir azalma olduğunu göstermektedir, bu da CONP'lerin hepatik IR hasarının önlenmesi için geniş bir potansiyele sahip olduğunu göstermektedir.

Anahtar Kelimeler: İskemi reperfüzyon, cerium oksit, nanopartiküller (CONPs), fare, oksidatif stres, enflamasyon

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ORIGINAL ARTICLE
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The utility of surgical Apgar score in predicting postoperative morbidity and mortality in general surgery

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ABSTRACT

Objective: Many surgical scoring systems are used to predict operative risk but most are complicated. The aim of the study was to determine the utility of the Surgical Apgar Score (SAS) in predicting post operative mortality and morbidity in general surgical cases.

Material and Methods: This was a prospective observational study. All adult patients for emergency and elective general surgical procedures were included. Intraoperative data was collected, and post operative outcomes were followed up till 30 days. SAS was calculated from intraoperative lowest heart rate, lowest MAP and blood loss.

Results: A total of 220 patients were included in the study. All consecutive general surgical procedures were included. Sixty of the 220 cases were emergency and the rest were elective. Forty-five (20.5%) of the patients developed complication. Mortality rate was 3.2% (7 out of 220). The cases were divided into high risk (0-4), moderate risk (5-8) and low risk (9-10) based on SAS. Complication and mortality rates were 50% and 8.3% in the high risk group, 23% and 3.7% in the moderate risk and 4.2% and 0 in the low risk group, respectively.

Conclusion: The surgical Apgar score is a simple and valid predictor of postoperative morbidity and 30-day mortality among patients undergoing general surgeries. It is applicable to all types of surgeries for emergency and elective cases and irrespective of the patient general condition and type of anesthesia and surgery planned.

Keywords: Surgical Apgar score, postoperative risk, surgical mobidity

INTRODUCTION

Determination of patient condition after any surgery is important for post operative monitoring and follow up. Various scores such as Acute Physiologic Assessment and Chronic Health Evaluation II (APACHE II), Physiologic and Operative Severity Score for the enUmeration of Mortality (POSSUM) and Simplified Acute Physiology Score (SAPS) have been used for predicting outcomes (1,2). These scoring systems are complicated and depend upon various laboratory parameters for calculation. These are not commonly used in surgical practice and hence, there is a need for simple scoring systems to facilitate adequate post operative monitoring.

Gawande et al. have developed a simple scoring tool inspired by the pediatric Apgar score called the Surgical Apgar Score (SAS) (3). This is a 10-point score based on three clinical parameters: lowest heart rate, lowest mean arterial blood pressure measured intraoperatively and total estimated blood loss at the end of surgery (3). Lower score for the patient has been found to be associated with more chances of major complications and mortality.

SAS can determine need for monitoring and is especially beneficial in deciding shifting the patient to the intensive care unit (ICU) in a set up with limited resources and paucity of facilities. Melis et al. have validated the score in a retrospective cohort of 2125 patients having undergone general surgical procedures including cancer surgeries, and overall mortality and 30-day morbidity has been found to be inversely proportional to SAS (4). The authors have also found a low SAS score to be strong predictor of ICU need.

The score was initially developed for general surgical and vascular surgeries but since then has been extensively studied and applied across various surgeries; how-

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ever, the strength of correlation between various surgical specialty procedures and score prediction varies (2,5,6). The validity has been established in most of the situation barring a handful like orthopedic surgeries and Ivor Lewis esophagectomies (7,8). Modifications of the score have also been studied in gastrectomies and liver transplant surgeries, and the modified scores have been validated (9,10). Pearson et al. have replaced the estimated blood loss parameter with volume of packed red blood cells transfused among patients undergoing liver transplantation and found it correlated better than outcomes than the original score. This is likely due to the fact liver transplant usually has significant blood loss but transfused volume to maintain physiological balance is more accurate indicator of condition in these patients (9). Miki et al. have modified the score among gastrectomy cases due to the observation that gastrectomy is usually associated with lower blood loss then other major gastrointestinal surgeries and reduced the cut off for the blood loss variable to range between 147 to 525 mL instead to 100 to 1000 mL in the original score, only to find a better association of the modified score with patient outcomes (10).

However, the score has not been evaluated in the setting of general hospital which caters to all routine general surgical procedures ranging from simple to complicated in the elective as well as emergency setting to see if the applicability can be generalized. This was the aim of our study to assess the utility of the score in predicting post operative mortality and morbidity in all general surgical procedures at a district hospital in Southwestern India.

MATERIAL and METHODS

Study Setting

The study was carried out at two teaching hospitals affiliated to the authors' medical college comprising of a district level government hospital and a tertiary care private hospital.

Study Design

This was a prospective observational study.

Study Duration

The study was conducted from September 2019 to January 2021 until the required sample size was completed.

Inclusion Criteria

All adult (aged >18 years) patients presenting to the department of general surgery and undergoing both elective and emergency surgeries were included in the study after taking adequate informed consent. Only patients undergoing surgery under general anesthesia or spinal anesthesia were included.

Exclusion Criteria

The patients excluded from the study included those with polytrauma requiring any other surgical procedure apart from or in addition to general surgery, those undergoing surgery under local anesthesia or peripheral nerve blocks, discharged against medical advice, presenting with head injury, who refused consent and whose 30-day follow up could not be completed.

Sample Size Calculation

The minimum sample size required was 217 with a rate of complication estimated to be 18% (11), 5% error rate and 5% level of significance. Considering a 10% patient drop out rate, a total of 240 patients were initially enrolled.

Outcomes Measurement

Outcomes were taken as patient condition in the hospital till discharge and follow up until 30 days postoperatively. All major and minor complications of surgery were recorded including death and graded as per the Clavien Dindo classification of surgical complications (12). Among the patients who had more than one complication, the complication with the highest grade was included for analysis. Concordance of surgical Apgar score with occurrence of complications was calculated at the end of the study.

Data Collection

Patients' general details were collected from hospital records. Variables for calculation of the SAS were collected from anesthesia records for the heart rate and mean arterial pressure and surgeons notes to categorize blood loss (estimated blood loss). Preoperative and post operative hemoglobin and packed cell volume (PCV) were measured for each patient to calculate blood loss using the following formula.

Blood loss= $[(EBV \times (H_i - Hf) / \{(Hct_i + Hctf) /2\}] + (500 \times T_u)$ (13,14).

[Estimated blood volume (EBV) is assumed to be 70 cm^3/kg, H_i and Hf represent pre- and postoperative hemoglobin 24 hrs after surgery respectively, Hct_i and Hctf represent pre- and postoperative hematocrit 24 hrs after surgery respectively, T_u is the sum of autologous whole blood (ABW), packed red blood cells (PRBC), and cell saver (CS) units (FFP, Cryoprecipiatate) transfused].

The individual score for each patient was calculated using the variables with the standard cut offs given by Gawande et. al (Table 1) (3).

Follow Up

Post operative follow up was done by the investigators till discharge and till one month through telephonic conversation and OPD review. Any major or minor complications were recorded in the patient proforma.

Statistical Analysis

Data were analyzed using SPSS version 25.0 using univariate and multivariate analysis with $p< 0.05$. Categorical variables

Table 1. The 10 point Surgical Apgar score (SAS) (3)

	0	1	2	3	4
Estimated blood loss (mL)	>1000	601-1000	100-600	≤100	-
Lowest mean arterial pressure (mmHg)	<40	40-54	55-69	≥70	-
Lowest heart rate (beats/min)	>85*	76-85	66-75	56-65	≤55

*Occurrence of pathologic bradyarrhythmia, including sinus arrest, atrioventricular block or dissociation, junctional or ventricular escape rhythms, and asystole also receive 0 pts for lowest heart rate.

were expressed as frequencies and percentages and continuous normally distributed variables were expressed as mean ± standard deviation, and non normally distributed variables were expressed as median (interquartile range Q1-Q3). Univariate and Bivariate analyses were done by Chi-square test and Student's t-test. Spearman correlation index was calculated to determine individual risk factors and significance of the same. Receiver operating characteristics (ROC) curves were plotted, and area under the curve (AUC) was calculated to identify the cut off score and sensitivity.

RESULTS

A total of 240 patients were included into the study as per the study protocol accounting for about 10% drop out. All consecutive patients at the affiliated hospitals who consented for the study were included, and recruitment was stopped once the sample size was achieved. Of the included 240 cases, 20 were excluded as the 30-day follow up could not be completed and the final analysis was done on 220 cases.

Among the total 220 patients, 133 were males (60.5%). Mean age of the study subjects was 47 years (± 14.6). Among the study population, hypertension was the most common comorbidity being present in 25% (55/220) of the patients, with diabetes being second most common in 19.5% (43/220). None of the comorbidities and baseline factors were found to be statistically significant and associated with development of complications (Table 2).

The list of all surgeries performed is detailed in Table 3. Among the study population, open hernioplasty was the most common surgery performed for ventral or groin hernias. Among the total 220 surgeries, 60 were emergency and the rest were elective. Of the 160 elective cases, 30 patients (18.8%) developed any grade of complication in the postoperative period while 15 of the 60 emergency cases (25%) had no complication. This difference was not found to be statistically significant (p= 0.3). Similarly, no significant difference was seen in the patients requiring postoperative ICU care and 30-day mortality in both groups.

Table 2. Population baseline characteristics showing presence of comorbidities among the study sample

Comorbidities	Total Study Sample - 220		Complication Rate	Chi-square/ Fisher's Exact Test
	No of Patients	Percentage		
Diabetes	43	19.5%	12 (27.9%)	0.18
Hypertension	55	25.0%	12 (21.8%)	0.77
IHD	9	4.1%	1 (11.1%)	0.48
Stroke	3	1.4%	2 (66.7%)	0.05
TB	4	1.8%	1 (25%)	0.82
Asthma	3	1.4%	2 (66.7%)	0.05
COPD	4	1.8%	2 (50%)	0.14
CLD	2	0.9%	0	0.47
Renal failure	4	1.8%	2 (50%)	0.14
Hypothyroidism	7	3.2%	2 (28.6%)	0.59
Previous surgery	44	20.0%	13 (29.5%)	0.09
Previous admission	94	42.7%	27 (28.7%)	0.009
Smoking	28	12.7%	6 (21.4%)	0.89
Alcohol	14	6.4%	3 (21.4%)	0.93
Drug abuse/tobacco	8	3.6%	2 (25%)	0.74

IHD: Ischemic heart disease, TB: Tuberculosis, COPD: Chronic obstructive pulmonary disease, CLD: Chronic kidney disease.

Table 3. Surgeries included in the final cohort of 220 patients

Surgeries	Number of Cases
Above knee amputation	4
Adhesiolysis	2
Anterior resection	3
Below knee amputation	6
Cytoreductive surgery	7
Distal gastrectomy	1
Drainage of perianal abscess	4
Feeding gastrostomy/jejunostomy	4
Fistulectomy	1
Gastrojejunostomy	3
Grahams patch repair	7
Hemithyroidectomy	1
Hemorrhoidectomy	3
Hernioplasty-ventral and groin	29
Jaboulays procedure	3
Laparoscopic appendicectomy	13
Laparoscopic cholecystectomy	27
Laparoscopic hernia repair	6
Laparoscopic ovarian cyst excision	1
Major debridement	8
Modified radical hysterectomy	1
Modified radical mastectomy	10
Omental biopsy	2
Open appendicectomy	14
Open cholecystectomy/cholecystostomy	3
Peritoneal lavage	3
Pilonidal sinus excision with flap	1
Radical mastectomy	1
Ray amputation	1
Rectopexy	1
Right hemicolectomy	5
Small bowel resection anastomosis	16
Split skin grafting	7
Subtotal mastectomy/lumpectomy	2
Superficial parotidectomy	2
Thoracotomy and repair-diaphragmatic hernia	1
Total thyroidectomy	5
Transhiatal esophagectomy	1
Trendlenberg's procedure	1
Wide local excision for sarcoma	2
Wide local excision of oral malignancy with neck dissection	8

Among the total 220 surgeries, 167 (75.9%) were done under general anesthesia and 53 under spinal anesthesia. Thirty-six of the 167 patients (21.6%) under general anesthesia developed some complications compared to 9 of the 53 (17%) patients under spinal anesthesia. This difference was not found to be statistically significant (p= 0.47).

The overall complication rate was 20.5% (45/220 patients). Eight patients (40%) had grade I complication, 9 (20%) grade II, 4 (9%) grade III, 7 (16%) grade IV and 7 (16%) grade V including death. Twenty-one out of the 220 patients (9.5%) required postoperative ICU admission for various durations. Thirty-one patients (14%) required blood or blood product transfusion of which the most common product was packed red cells followed by fresh frozen plasma. In our study, surgical site infection was the most common complication and seen in 19 out of 220 patients (Table 4).

Among all patients, there was a total of seven deaths (3.2%). Of the seven deaths, two patients died of massive pulmonary thromboembolism, two patients due to intraabdominal sepsis secondary to anastomotic leak and peritonitis, one due to post op myocardial infarction (MI), one due to disseminated intravascular coagulopathy (DIC) and one due to post op hemorrhage and shock.

Mean lowest heart rate was 72 (± 15) and median (IQR) SAS score for lowest heart rate was 2.0 (1.0-3.0) (Table 5). The lowest mean arterial pressure was 81 (± 13) mmHg and median score

Table 4. Types of complications

Complication	Frequency
Surgical site infection	19
Flap necrosis	5
Wound dehiscence	2
Exacerbation of COPD	2
Renal failure	2
Pulmonary embolism	2
Stump infection	2
Septic shock	2
Anastomotic leak	2
Hemorrhage	1
Ascending gangrene	1
Post op Ileus	1
Pneumonia	1
Post op fever	1
DIC	1
Myocardial infarction	1
Total	45

COPD: Chronic obstructive pulmonary disease, DIC: Disseminated intravascular coagulopathy.

Table 5. Operative baseline characteristics for the study population

Patient Baseline Characteristics Factors (Units)	Mean/Median	Std. Deviation/
Duration of surgery (minutes)#	120	80-150
Lowest HR (beats per minute)*	72	15.4
Lowest MAP (mmHg)*	80.8	13.1
Estimated blood loss (mL)*	200	80-250
Pre op HB (gm/dL)*	12.7	2.1
Post op HB (gm/dL)*	11.6	2.1
Pre op PCV (%)*	38	6
Post op PCV (%)*	35	6
Patient Weight (kg)*	65.3	11.1
Calculated blood loss (mL)#	150	65-255
Median SAS for lowest heart rate#	2.0	1.0-3.0
Median SAS for lowest MAP#	3.0	3.0-3.0
Median SAS for calculated blood loss#	2.0	2.0-3.0
Median SAS for estimated blood loss#	2.0	2.0-3.0
Median Total SAS#	7.0	6.0-8.0

HR: Heart rate, MAP: Mean arterial pressure, HB: Hemoglobin, PCV: Packed cell volume, SAS: Surgical Apgar score.
*values expressed as mean ± SD, #values expressed as Median (25-75 IQR).

was 3.0 (3.0-3.0). Our data revealed that the median estimated blood loss (EBL) was 200 (80-250) mL and the calculated blood loss (CBL) was 150 (65-255) mL, which was not found to be statistically different. The assigned median score to estimated blood loss and calculated blood loss was both 2.0 (2.0-3.0). Total median SAS was 7.0 (6.0-8.0) in our study population. Median scores for complication group (n= 45) were found to be significantly lower for heart rate, calculated and estimated blood loss and total SAS and these parameters were found to individually correlate with presence of complications.

Median SAS was 5.0 in the complication group as compared to 8.0 in the no complication group (p= 0.00). Spearman correlation between SAS and grade of complication was also found to be -0.49 (p= 0.001), which was statistically significant and indicated a higher grade of complication associated with a lower SAS score. The Receiver Operating Characteristic (ROC) curve for the SAS had an area under the curve (AUC) of 0.8 (95% CI - 0.72-0.88) (Figure 1). A cut off of 7 for the score had a sensitivity of 82% to predict risk of complications post operatively.

Median SAS for patients requiring ICU care was five as compared to eight for those who did not (p= 0.00). The ROC curve for ICU need correlating to SAS (Figure 2) showed an area under the curve of 0.89 (95% CI 0.84 - 0.95). At a cut off value of 7, the score had a 90% sensitivity in predicting the need for ICU care.

Total number of deaths in our study was seven out of 220 (3.2%). This was the total 30-day mortality and was found to be associated significantly with lower mean values of score for heart rate, blood loss and SAS. Median SAS for the patients who died was 5 as compared to 7.0 for those who did not (p= 0.001). The ROC curve for 30-day mortality correlating to SAS (Figure 3) showed an area under the curve of 0.88 (95% CI 0.81 - 0.94).

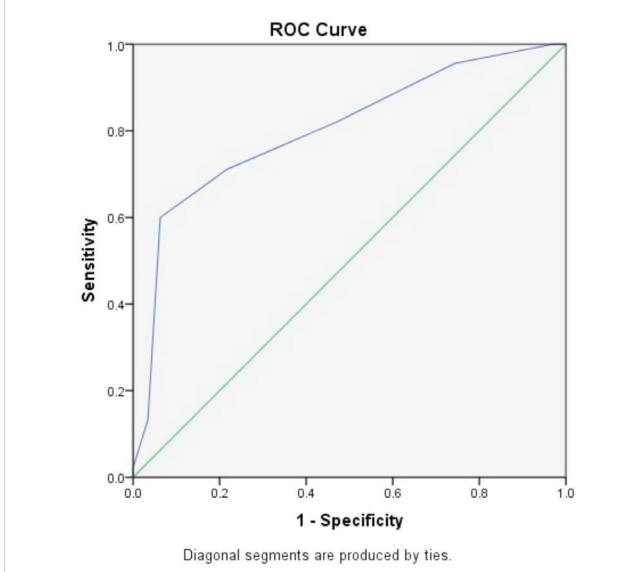

Figure 1. Receiver operating characteristic (ROC) curve for SAS against presence of complication (AUC - 0.8, 95% CI - 0.72-0.88).

The cases were stratified into three groups (Table 6) with High risk (0-4), moderate risk (5-8) and low risk (9-10), and the distribution of complications, need for ICU care and death were all found to be significantly higher in the high-risk group with 50%

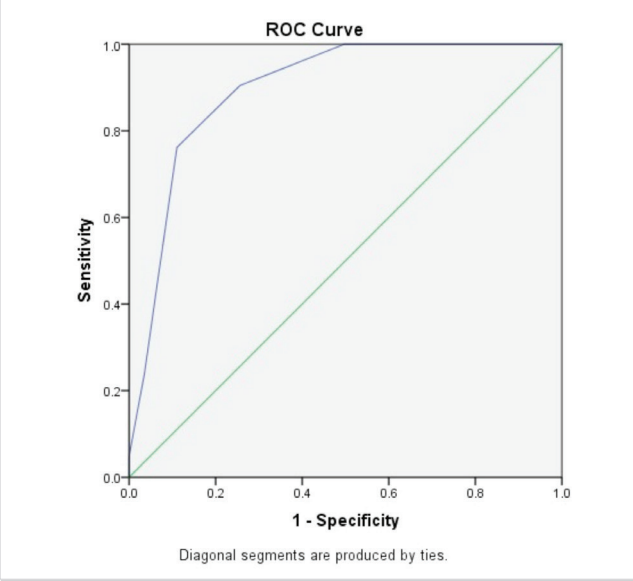

Figure 2. ROC curve for SAS against ICU need (AUC - 0.89, 95% CI - 0.84 -0.95).

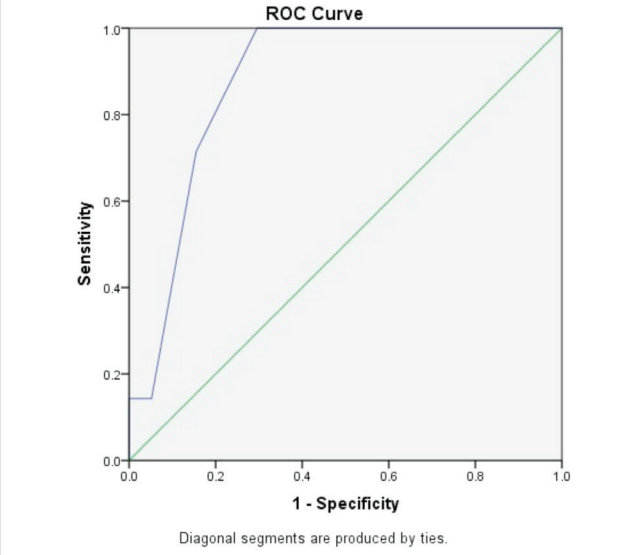

Figure 3. ROC curve for SAS against death (AUC – 0.88, 95% CI – 0.81 -0.94).

risk of 30 day morbidity and 8.3% risk of mortality compared with 4.3% and 0% in the low risk groups.

DISCUSSION

Our study was done on 220 patients under the general surgery department at our hospitals and included all elective and emergency cases. There was no significant difference in the baseline characteristics of the patients who did and did not develop complications. This finding was similar to the ones reported previously (4,15) where comorbidities did not affect the 30-day mortality and morbidity.

All major and minor general surgical procedures routinely carried out at a tertiary care district hospital were included, and repair of ventral and groin hernias was the most common surgery followed by laparoscopic cholecystectomy (Table 3). There were other major cases as well including gastrectomy, colonic and rectal resection, small bowel resection anastomosis and major lower limb amputation. There were also oncological procedures including wide local excision of soft tissue tumors, mastectomy, hysterectomy, ovarian cytoreductive surgery and wide local excision with neck dissection for oral malignancies. Such wide variety of cases have been only reported in a few studies previously where the authors have included all general surgical cases (11,16,17). However, the sample size was lesser than our study in two of these studies and one study included orthopedic procedures also with general surgical procedures comprising about 50% of the sample size (16).

Although our study included all types of cases ranging from minor to major, the results indicated that the score hold true irrespective of the magnanimity of the procedure. The parameters were based on intra operative heart rate, blood pressure and blood loss and were affected by the patients' state of health and response to surgical and anesthetic stress which reflected the likely post operative recovery. The heterogeneity of the cases offered a unique insight into the utility of the score in regular practice on a larger scale and validated its accuracy.

Among the total 220 surgeries in our cohort, 60 were emergencies (27%) and rest of them were electives. Twenty-five percent of the patients undergoing emergency surgery developed complications and 18.8% in the ones undergoing elective surgery. This difference was not statistically significant, and mean SAS in the two groups was also similar. The two groups were included together for the final analysis of the score as there were no statistical differences between them (p= 0.3). Literature suggests that emergency surgeries are generally associated with higher risk of complications due to under resuscitated patients

Table 6. Association between SAS and outcomes

SAS	No of Patients	Complications	ICU Need	Death
0-4	12	6 (50%)	5 (41.6%)	1 (8.3%)
5-8	161	37 (23%)	16 (9.9%)	6 (3.7%)
9-10	47	2 (4.2%)	0 (0)	0 (0)

and worse intraoperative conditions, the score seems to be applicable here as well (13,17,18). Shaikh et al. have reported a complication rate of 94% among emergency laparotomies, which is higher than that found in our study at 25% but this difference may be due to types of surgeries included in our study with not only laparotomies but also other procedures (13).

We included cases done under both general and regional anesthesia, and 76% of them were under general anesthesia with the rest under spinal anesthesia. The rates of complications and mean SAS for both types of anesthesia was not found to be statistically different and outcomes were similar. This is different than the results by Urrutia et al. and Nair et al., who have found that patients undergoing surgery under spinal anesthesia do not have a good correlation of the SAS to the outcomes (2,7). They hypothesize that the score maybe unreliable in cases of regional anesthesia as majority of procedures on the lower limbs are performed under spinal anesthesia which causes vasodilation induced hypotension and is easily corrected by crystalloid boluses but may not necessarily affect the surgical outcome (2). However, these authors have included orthopedic procedures in their studies whereas our cohort consisted of general surgical patients. Our results confirm the ability of the score to predict the outcomes irrespective of the type of anesthesia used.

The overall 30-day morbidity in our study was 20.5% with 45 of the 220 subjects developing some grade of complication. The overall complication rates have been variably reported in the literature ranging from 14-40% depending on the type of surgeries included (5,11,19). Among the studies reporting emergency surgeries and laparotomies, complication rates have been reported as high as 40-60% (13,17). Most studies have not mentioned the complications encountered but surgical site infections, pneumonia and sepsis are commonly reported (13,20,21).

Median SAS in our study was 7.0 (IQR 6-8). We also compared blood loss using the surgeons estimation post operatively and also calculated blood loss using a standardized formula (13,14). There has been a differing opinion regarding blood loss estimation and interobserver variability in previously conducted studies, and authors have always commented on the fallibility of this component of the score. To overcome this shortcoming, few authors have calculated blood loss from pre and postoperative blood parameters and shown this score to be valid. However, no previous studies have compared the methods of blood loss estimation and calculation and shown if any of them was superior. Our study attempted to correct this lacuna in the existing literature, and we demonstrated the two methods to be equally useful and accurate in calculating the score. The difference between the median estimated and calculated blood loss was not statistically significant, and there was a good interobserver agreement between the two values (κ 0.82).

In our study population, majority of the patients (161/220) fell in the moderate risk group followed by 47 in low risk and 12 in the high risk groups (Table 6). This distribution is similar to what is commonly observed in clinical practice, with most patients having an uneventful to a mildly turbulent post operative period whereas a small proportion of patients have a high risk of mortality and morbidity as seen in our high risk group. We did not categorise the surgeries by major or minor and the complications or SAS was not assessed for individual surgeries, which is a limitation of our study. However, the authors believe that the score is appropriate to all cases and can be applied in general practice in any hospital set-up.

Univariate analysis of the individual components and the score against the incidence of complications showed that the median score was lower (5) among the patients who developed any grade of complication as compared to eight among those with no complications. The lowest heart rate and blood loss also individually correlated with risk of complications with statistically significant lower mean values. Receiver operating characteristic (ROC) curve showed an area under the curve (AUC) of 0.8 (95% CI - 0.72-0.88) (Figure 1) indicating a good association between the score and chance of complication. The curve showed a cut off of 7 being able to predict risk of complication with 80% sensitivity. These findings are at par with previous studies that have shown similar AUC and predictive value of the score (19,22). We also assessed the association between the score and the grade of complication and was found to be inversely proportional. Bivariate analysis showed a negative Spearman correlation (-0.49), which was statistically significant (p= 0.001), and indicated a lower score being inversely associated with a higher grade of complication.

Of the study population, 21 patients required ICU admission and the median score among these patients was five as compared to eight in those who did not require ICU admission (p= 0.00). The ROC curve showed that SAS was significantly associated with prediction of ICU need with AUC of 0.89 (Figure 2). Similar results have been demonstrated previously and a cut of value of 7 has been suggested. In our study, a cut off value of <7 from the ROC curve had a 90% sensitivity in predicting postoperative ICU need. Among our subjects, high risk group (0-4) had 41.6%, moderate risk (5-8) had 10% and low risk (9-10) had 0% chance of ICU admission (Table 3). In a study by Melis et. al, low SAS has been shown to be a strong predictor of ICU need. High risk score 0-4 was associated with 79% chance of ICU admission compared to 17% if the score was 9-10 (23).

Mortality rate in our study was 3.2% (7 out of 220), and median SAS was significantly lower in these patients. The ROC curve also showed a good correlation with AUC of 0.88 (Figure 3). This is in line with previous studies where SAS has been inversely as-

sociated with linearly increasing risk of 30-day mortality (6). The score can be categorized into low risk (9-10), moderate risk (5-8) and high risk (0-4). Complication and mortality rates were 50% and 8.3% in the high risk group, 23% and 3.7% in the moderate risk and 4.2% and 0 in the low risk group respectively (Table 6), which can help as a simple guide to predict postoperative risk and plan care.

Regenbogen et al. have validated the score across all surgical procedures and found it to predict post operative outcomes with significant accuracy (18). Similarly, the score has also been studied in patients undergoing surgery for traumatic brain injuries, head and neck squamous cell carcinomas, gynecological surgeries, radical prostatectomy (14,20,21,24). Our findings show the applicability of the score across all general surgical procedures that are carried out at a secondary and tertiary care center. In majority of our set ups, intensive and critical care unit availability is limited, and judicious use of these resources is of utmost importance for optimal patient care. In such a scenario, a simple and effective tool like the SAS can help clinicians predict the need for ICU admission for patients and prioritize bed allotment.

The score is not fallible and multiple queries have been raised about its accuracy due to the dynamic nature of vital parameters used in calculation of the score and their labile nature. For instance, single run of arrythmia during surgery may warrant a low score or transient bradycardia may lead to a high score which may not reflect the entire duration of surgery and can cause inaccurate final assessment. Similarly, anesthetic drug induced hypotension during induction can lead to false MAP recording and alter the score. In addition, as the score is only calculated postoperatively, it cannot be used to plan preoperative counselling and assess risk (25).

There are significant concerns regarding SAS and include its exclusion of parameters like patient age, comorbidities, existing comorbidities, operative time, blood transfusions, use of intravenous fluids in surgery and other factors that have significant bearing on the outcome of the patient. Although majority of the studies are from single centers and represent homogenous type of procedures, the score holds true even when applied to a heterogenous population across all surgical procedures as demonstrated in our set-up. The score has stood the test of time and showed to be useful despite being simplistic and that is its greatest strength (6).

CONCLUSION

The Surgical Apgar score is a simple and valid predictor of postoperative morbidity and 30-day mortality among patients undergoing general surgeries. It is applicable at district hospital level to all types of surgeries and can be applied for emergency and elective cases and irrespective of the patient general condition and type of anesthesia and surgery planned.

Ethics Committee Approval: This study was approved by Kasturba Medical College Institutional Ethics Committee (Decision number: 10-19/480 Date: 16.10.2019).

Peer-review: Externally peer-reviewed.

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ORİJİNAL ÇALIŞMA-ÖZET
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Cerrahi Apgar Skorunun postoperatif morbidite ve mortaliteyi öngörmedeki faydası

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ÖZET

Giriş ve Amaç: Ameliyat riskini tahmin etmek için birçok cerrahi skorlama sistemi kullanılır, ancak çoğu karmaşıktır. Bu çalışmanın amacı, genel cerrahi vakalarında cerrahi sonrası mortalite ve morbiditeyi öngörmede Cerrahi Apgar Skorunun (CAS) faydasını belirlemektir.

Gereç ve Yöntem: Bu ileriye dönük gözlemsel bir çalışmaydı. Acil ve elektif genel cerrahi işlemler için tüm yetişkin hastalar dahil edildi. İntraoperatif veriler toplandı ve postoperatif sonuçlar 30 güne kadar takip edildi. CAS, intraoperatif en düşük kalp hızı, en düşük ortalama arter basıncı (OAP), ve kan kaybından hesaplandı.

Bulgular: Toplam 220 hasta çalışmaya dahil edildi. Tüm ardışık genel cerrahi prosedürler dahil edildi. 220 olgunun 60'ı acil ve geri kalanı elektifti. Hastaların 45'inde (%20,5) komplikasyon gelişti. Mortalite oranı %3,2 idi (220'den 7'si) ve olgular SAS'a göre yüksek risk (0-4), orta risk (5-8) ve düşük risk (9-10) olarak ayrıldı. Komplikasyon ve mortalite oranı yüksek risk grubunda %50 ve %8,3, orta risk grubunda %23 ve %3,7 ve düşük risk grubunda %4,2 ve 0 olarak bulundu.

Sonuç: Cerrahi Apgar Skoru, genel cerrahi geçiren hastalarda postoperatif morbidite ve 30 günlük mortalitenin basit ve geçerli bir göstergesidir. Hastanın genel durumu ve planlanan anestezi ve ameliyat türü ne olursa olsun, acil ve elektif vakalarda her türlü ameliyata uygulanabilir.

Anahtar Kelimeler: Cerrahi Apgar Skoru, postoperatif risk, cerrahi hastalık

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The relationship between self-esteem, body dissatisfaction, and eating attitudes in bariatric surgery candidates

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ABSTRACT

Objective: Considering the effects of self-esteem, eating attitudes and body satisfaction on obesity and bariatric surgery outcomes, psychiatric evaluation is important for the identification and treatment of psychopathology, improvement of self-esteem, eating attitudes and body satisfaction. In this study, it was aimed to determine the relation between eating behaviors, body dissatisfaction, self-esteem and psychological symptoms in patients seeking bariatric surgery. Our second aim was to determine whether depressive symptoms and anxiety had a mediating role in the relationship between body satisfaction and self-esteem and eating attitudes.

Material and Methods: The study included 200 patients. Patients' data were retrospectively evaluated. Psychometric evaluation performed during the preoperative period included psychiatric examination and administration of the Beck Depression Inventory, Beck Anxiety Inventory, Rosenberg Self-Esteem Scale, Body-Cathexis Scale, and Dutch Eating Behaviors Questionnaire.

Results: There was a positive correlation between self-esteem and body satisfaction and a negative correlation between self-esteem and emotional eating ($r= 0.160$, $p= 0.024$; $r= -0.261$, $p< 0.001$ respectively). Body satisfaction had an effect on emotional eating mediated by depression and an effect on external and restrictive eating mediated by anxiety. Furthermore, anxiety mediated the relations between self-esteem and external and restrictive eating behaviors.

Conclusion: Our finding indicating that depression and anxiety have mediator effects on the relation between self-esteem, body dissatisfaction, and eating attitudes is significant since screening for these entities and their treatment is relatively more practical in clinical settings.

Keywords: Depression, anxiety, eating attitudes, self esteem, body image

INTRODUCTION

Obesity is a significant public health problem associated with depression, impaired body image, low self-esteem, eating disorders, and poor quality of life (1,2), and a multifaceted approach is required for its successful treatment. Bariatric surgery is known as the most effective treatment for patients with morbid obesity and is becoming increasingly prevalent worldwide (3). However, it has been reported that weight loss is lower than expected in some cases, and weight returns to preoperative levels in some cases. These studies have also shown that a thorough preoperative psychological assessment could positively affect surgical outcomes (3).

Since eating disorders and unhealthy eating attitudes are closely related to obesity, they have become a focus of interest for several researchers in bariatric surgery and psychiatry (3). According to these authors, emotional eating behavior is characterized by eating for coping with negative emotions despite not being hungry. Another unhealthy eating behavior defined in these studies is restrictive eating to maintain or lose weight. This behavior is unhealthy because prolonged restrictive eating can be interrupted by excessive eating episodes (4). On the other hand, external eating is characterized by an inability to resist the physical characteristics of food, such as aroma and appearance, and consumption of food even when not hungry (5).

In addition to unhealthy eating attitudes, mood and anxiety disorders are frequently encountered in patients with obesity (3). It has been reported that there are positive correlations between depression, emotional and external eating behaviors (6). A positive correlation has also been found between anxiety and these unhealthy

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eating attitudes (7). Conversely, while some authors have found no association between restrictive eating, depression, and anxiety disorders, others detected a negative correlation between restrictive eating and depression in obese individuals (3,6,7). In addition to mood and anxiety disorders, low self-esteem is common in obese patients (1). It has been noted that the severity of eating disorders is negatively correlated with self-esteem (8,9). Another factor closely related to self-esteem is body dissatisfaction which is an important concept that should be evaluated, as it is has been postulated that there is a relation between body dissatisfaction and disordered eating (2,10).

Few studies regarding the relations between mood and anxiety disorders, eating attitudes, body satisfaction, and self-esteem in obese individuals have reported inconsistent findings (11,12). It has been noted that depression and self-esteem mediate the effects of body dissatisfaction and body image on eating attitudes (11). In addition, it has been observed that body shame has a mediating role on low self-esteem and unhealthy eating attitudes (12).

Recently, studies conducted with overweight or obese individuals have focused on the associations between eating disorders and body satisfaction, increased attention to weight, depression, anxiety, and self-esteem rather than the prevalence of the eating disorders (9). This study aimed to determine if depressive symptoms and anxiety played a mediating role in the relation between body satisfaction, self-esteem, and eating attitudes in obese patients seeking bariatric surgery.

MATERIAL and METHODS

This project was approved by the ethics review committee of our institution (2019/69-08). All patients gave written and verbal consent for this study. The study was conducted in accordance with the principles of the Declaration of Helsinki. Patients who presented to the general surgery department of our hospital between July 2018 and July 2019 and were referred to the psychiatry department for preoperative assessment were the target population of this study. Patients with incomplete data were excluded. In our center, all bariatric surgery candidates undergo psychiatric evaluation via Structured Clinical Interview for DSM-5 Diagnosis (SCID-5-CV) (13) by psychiatrists working at the center and psychometric assessment via administration of Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Rosenberg Self-Esteem Scale (RSES), Body-Cathexis Scale (BCS), and Dutch Eating Behaviors Questionnaire (DEBQ), which are all self-assessment scales. All scales' validity and reliability study had been done for their Turkish versions (14-18).

Sociodemographic data form was used to collect data including age, sex, education level, marital status, body mass index (BMI), psychiatric history, current use of psychiatric drugs, and descriptive information about obesity. BAI was developed in 1988 (19). Higher scores indicate relatively more severe anxiety. BDI was developed in 1961 (20), and it measures the severity of depressive symptoms. RSES was developed to evaluate self-esteem (21). Ten items included in the self-esteem subscale were used in this study. BCS assesses the degree of a person's satisfaction with various parts or aspects of her/his body (22). Higher scores indicate a greater degree of body satisfaction. DEBQ consists of 33 items in three subscales: restrictive eating, emotional eating, and external eating (23). Higher scores indicate a greater degree of that eating behavior.

Psychiatrists routinely evaluate all bariatric surgery candidates at our institution. The assessments and questionnaires mentioned above are performed during these evaluations, and the relevant data are stored in patient folders. The relevant forms are reviewed by psychiatrists and psychologists. In the context of our study, we retrospectively reviewed the patient folders and results of these assessments to investigate the impact of the body dissatisfaction and self-esteem assessed by RSES and BCS on eating attitudes to reveal the potential mediating effect of anxiety and depression assessed by BDI and BAI in this relationship.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows v.25.0 (IBM Corp., Armonk, NY). Data were given as numbers (n) or percentages (%) for categorical (i.e., qualitative) variables and mean ± standard deviations (SD) for numerical (i.e., quantitative) variables. The relations between scale scores were analyzed using Pearson's and Spearman's correlation tests. Comparison of obesity variables according to scale scores was performed using the t-test, and the mediation hypotheses were tested by Hayes Process v3.3 macro (SPSS Statistics for Windows v.25.0).

RESULTS

Two hundred patients were included in this study. Sociodemographic and clinical data of the patients are shown in Table 1. Mean scale scores of these patients are displayed in Table 2. Our analysis revealed no significant relationship between BMI, and BDI, BAI, DEBQ subscale scores (Restrictive eating, emotional eating and external eating), or BCS and RSES scores ($p= 0.902$, $p= 0.793$, $p= 0.295$, $p= 0.442$, $p= 0.631$, $p= 0.153$, $p= 0.624$ respectively) (Table 2).

Results of the statistical analysis regarding the relations between the BCS, RSES, and DEBQ subscale scores are presented in Table 3. This analysis elucidated a positive correlation between the RSES and BCS scores and a negative correlation between the RSES and DEBQ emotional eating subscale scores ($p= 0.024$, $p< 0.001$ respectively). While the correlations between these subscale scores were analyzed, the potential impact of BDI and BAI was controlled. Performance of the same analysis without controlling this potential impact revealed relatively higher correlation coefficients.

Table 1. Sociodemographic and clinical characteristics of the patients

Variable	Mean ± SD	n (%)
Age, years	36.61 ± 11.16	
Body mass index (BMI)	45.18 ± 7.65	
Level of education	Less than primary school	4 (2)
	Primary school	49 (24.5)
	Secondary school	33 (16.5)
	High School	66 (33)
	University	46 (23)
Sex	Female	160 (80)
	Male	40 (20)
Marital status	Single	61 (30.5)
	Married	131 (65.5)
	Widow/Divorced	8 (4)
Physical illness	Yes	80 (40)
History of psychiatric presentation	Yes	69 (34.5)
History of psychiatric drug use	Yes	64 (32)
DSM-5 diagnosis (excluding eating disorders)	Depressive disorders	15 (7.5)
	Adjustment disorder	7 (3.5)
	Anxiety disorders	5 (2.5)
	Obsessive compulsive disorder	2 (1.0)
	Bipolar disorder	2 (1.0)
	Attention deficit-hyperactivity disorder	1 (0.5)
	Substance related disorder	1 (0.5)
	Dysthymia	1 (0.5)
	Social phobia	1 (0.5)
Eating disorders and eating attitudes	Pica	2 (1.0)
	Restrictive eating	5 (2.5)
	Binge eating disorder	17 (8.5)
	Night eating syndrome	30 (15)
	Grazing	35 (17.5)
	Emotional eating	65 (32.5)

Table 2. Scales scores and their relation to BMI

		BMI	
	Mean ± SD	**r**	**p**
BAI	12.34 ± 9.42	0.019	0.793
BDI	14.22 ± 8.49	-0.009	0.902
RSES	20.06 ± 5.17	0.035	0.624
BCS	125.66 ± 25.02	-0.101	0.153
DEBQ - Restrictive Eating	27.83 ± 6.91	0.074	0.295
DEBQ - Emotional Eating	29.97 ± 13.14	-0.055	0.442
DEBQ - External Eating	27.68 ± 7.54	-0.034	0.631

*p< 0.05 and **p< 0.01 (Pearson's correlation test).
BAI: Beck Anxiety Inventory, BDI: Beck Depression Inventory, RSES: Rosenberg Self-Esteem Scale, BCS: Body-Cathexis Scale, DEBQ: Dutch Eating Behaviors Questionnaire.

Table 3. The correlation between body satisfaction, self-esteem, and eating attitude scores (Anxiety and depression were controlled)

		RSES	BCS
RSES	r	1	0.160
	p		0.024
DEBQ-Restrictive Eating	r	0.091	0.059
	p	0.200	0.408
DEBQ-Emotional Eating	r	-0.261	-0.046
	p	0.000	0.524
DEBQ-External Eating	r	-0.075	-0.071
	p	0.292	0.322

RSES: Rosenberg Self-Esteem Scale, BCS: Body-Cathexis Scale, DEBQ: Dutch Eating Behaviors Questionnaire.

Also, other significant associations were detected between these subscales at the uncontrolled state, such as relationships between emotional eating and body satisfaction (r= -0.236 and p= 0.001), external eating and self-esteem (r= -0.209 and p= 0.003), and external eating and body satisfaction (r= -0.204 and p= 0.004).

Analysis regarding mediation hypothesis revealed that anxiety mediated the effect of body dissatisfaction on restrictive eating, depression mediated the effect of body dissatisfaction on emotional eating, anxiety mediated the effect of body dissatisfaction on external eating, anxiety mediated the effect of low self-esteem on restrictive eating, and anxiety mediated the effect of low self-esteem on external eating (Figures 1,2). However, other models analyzing these parameters detected no significant mediation effects.

DISCUSSION

This study aimed to determine the effects of body satisfaction and self-esteem on eating behaviors and whether or not anxiety and depression mediated this relationship. It showed a positive correlation between self-esteem and body satisfaction and a negative correlation between self-esteem and emotional eating. Additionally, body satisfaction had an effect on emotional eating mediated by depression and an effect on external and restrictive eating mediated by anxiety. Furthermore, anxiety mediated the relationships between self-esteem and external and restrictive eating behaviors.

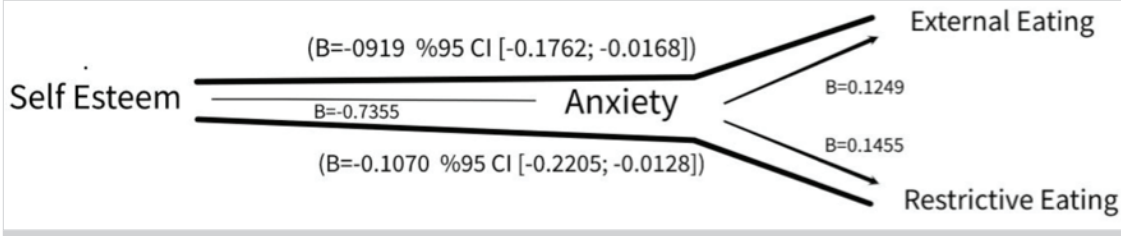

Figure 1. Anxiety as a mediator of the association between self-esteem, external eating and restrictive eating.

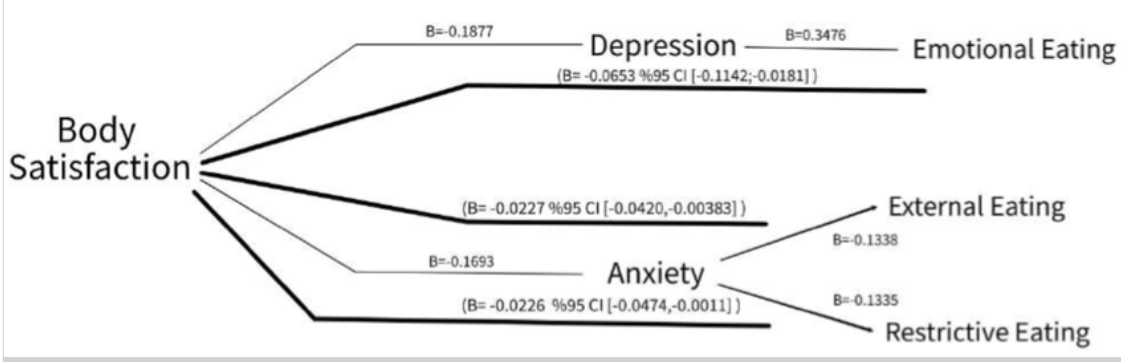

Figure 2. Anxiety and depression as mediators of the association between body satisfaction, external eating, restrictive eating and emotional eating.

Although bariatric surgery is the most effective obesity treatment, it is known that 30% of bariatric surgery patients do not achieve optimal weight loss or regain weight after surgery. It was suggested that psychosocial status and functionality had an essential role in these outcomes (2,24), and it is widely accepted that all bariatric surgery candidates should undergo a psychological assessment (24).

Approximately 17.5% of our patients had psychopathologies other than eating disorders, which is in line with the previous reports (24). Depression was the most common diagnosis in these patients followed by adjustment and anxiety disorders. It has been reported that severe depression is a risk factor for regaining weight and a predictor for inadequate weight loss following bariatric surgery (2). It has also been suggested that there is a positive correlation between obesity and anxiety (7) and it has been reported that the presence of an anxiety disorder preoperatively is predictive for a postoperative anxiety disorder and negatively influences postoperative weight losing process (25).

We used DSM-5 criteria for evaluating our patients regarding eating disorders (26). They were also evaluated with psychometric tests to investigate eating attitudes. Data reported in the literature regarding eating attitudes are both limited and controversial (27). Although it has been shown that eating disorders are more frequent in bariatric surgery candidates than in the general patient population, the range of prevalence figures is relatively wide (27). This variation is probably due to the methodological differences between these studies. On the other hand, all of these studies agree that preoperative evaluation of these patients concerning eating attitudes is critical considering that disordered eating had adverse effects on post-bariatric surgery weight losing process (27,28).

Our study focused on the relationships of self-esteem and body satisfaction with eating attitudes, depression, anxiety, and BMI. We found no correlation between BMI, self-esteem, or body satisfaction in our study. However, as expected, there was a positive correlation between self-esteem and body satisfaction (29).

It is widely accepted that the relation between self-esteem and BMI is complex (1). While some studies have shown that being obese or overweight is associated with low self-esteem, others have found no relation between these variables when body dissatisfaction is controlled (12,30). The absence of a relation between BMI and self-esteem and body dissatisfaction in the present study might have been because the potential mediators affecting this relationship were not included in our analysis.

It has been previously shown that low self-esteem, body dissatisfaction, and unhealthy eating attitudes are prevalent in obese individuals, and they are all associated with the psychopathological status of the patients (31). Therefore, our study aimed to determine whether depression and anxiety mediated the effects of low self-esteem and body dissatisfaction on dysfunctional eating. Our analysis revealed a correlation between low self-esteem and emotional eating. We found that body dissatisfaction did not directly affect eating attitudes, and depression and anxiety mediated the effects of body dissatisfaction on emotional, restrictive, and external eating. Furthermore, the effects of low self-esteem on restrictive and external eating were mediated by anxiety as per our analysis.

It is known that negative emotions such as stress and depressive thoughts that contribute to weight gain are associated with body dissatisfaction and low self-esteem (30,32). Although some studies have suggested that self-esteem is related to vulnerability to eating disorders, others have reported no relation between self-esteem and eating disorders (12). Since emotional eating is a strategy to cope with negative emotions or to experience positive emotions, negative emotions caused by body dissatisfaction and low self-esteem can trigger emotional eating (30). In line with this, it has been noted that there is a significant relation between depression and emotional eating (33). Emotional eating has also been shown to mediate the relationship between depression and obesity (4). These findings indicate that eating attitudes and mood disorders have variable effects on patient weight. Our study found a direct relation between self-esteem and emotional eating. While we did not find a direct relation between body satisfaction and emotional eating, we found that body satisfaction was related to emotional eating via the mediation of depression.

External eating is an eating attitude depending on external stimuli (5). In the literature, although there is no direct relationship between depression and external eating, it is known that there is a relationship between impulsivity and external eating, and depression affects impulsivity (33). In addition, it has been reported that depression is related to increased fast-food intake via external eating (5). Previous reports have also suggested that stress could increase responsiveness to external food cues and stimulate eating in individuals with external eating (33). In our study, we found that body satisfaction and self-esteem had an effect on external eating mediated by anxiety. While it could be suggested that stress, impulsivity, or other factors contribute to this mediatory effect, the exact mechanism could not be elucidated due to the retrospective design of our study.

Restrictive eating is more common in obese than non-obese individuals (13,34). As it is known that there is a relationship between body dissatisfaction and restrictive eating pattern, it can be suggested that obese individuals will resort to this strategy to lose weight and alleviate negative emotions (34). It has been reported that body dissatisfaction and depression have partial effect on the development of bulimic disposition and restrictive eating (4). On the other hand, there is limited data on the relation between self-esteem and restrictive eating (8). A study regarding eating disorders has reported that patients with re-

strictive eating have higher self-esteem than those with binge or purge behavior or bulimia nervosa (8). Although it is widely accepted that body dissatisfaction is associated with weight loss, restrictive eating, and bulimia, a negative affect has been found to mediate the relation between body dissatisfaction and restrictive eating in adult females, but not in adult males (35). It has been reported that depression and self-esteem mediate the effect of body dissatisfaction on eating disorders, especially in patients with bulimic and restrictive eating and compensatory behaviors, while they only partially mediate the effect of body image on eating disorders (11). In the light of the present findings, it can be stated that the relations between low self-esteem, body dissatisfaction, and eating attitudes are multifaceted and complex. Further research is required to delineate these relations and fully understand the mediation effects of depression and anxiety on these relations.

This study has some limitations which need to be considered. First, it included obese patients who presented for bariatric surgery, and thus, its findings cannot be generalized to a broader patient population. Second, it employed self-report scales, and it should be considered that some patients might have given socially acceptable answers. Also, the cross-sectional nature of the study represents another limitation.

CONCLUSION

Bariatric surgery is considered the most effective obesity treatment, and psychiatric evaluation is of great importance in bariatric surgery candidates to identify and treat psychopathologies and improve self-esteem, eating attitudes, and body satisfaction. Assessment of these patients regarding self-esteem, body dissatisfaction, and eating attitudes necessitates a more comprehensive work-up than screening for depression and anxiety. Furthermore, treatments given after these assessments are not always readily available. Our study found that depression and anxiety had mediator effects on the relationship between self-esteem, body dissatisfaction, and eating attitudes. Our findings indicate that interventions for depression and anxiety can affect eating attitudes with their mediator roles and show that there are complex relations between self-esteem, body image, psychopathology, and eating attitudes.

Ethics Committee Approval: This study was approved by Turkish Ministry of Health University of Health Sciences Dışkapı Yıldırım Beyazıt Training and Research Hospital Clinical Research Ethics Committee (Decision no: 69/08, Date: 05.08.2019).

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ORİJİNAL ÇALIŞMA-ÖZET
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Obezite cerrahisi adaylarında benlik saygısı, beden memnuniyetsizliği ve yeme tutumları arasındaki ilişki

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ÖZET

Giriş ve Amaç: Benlik saygısı, yeme tutumları ve beden memnuniyetinin obezite ve bariyatrik cerrahi sonuçları üzerindeki etkileri göz önüne alındığında, psikiyatrik değerlendirme, psikopatolojinin belirlenmesi ve tedavisi, benlik saygısı, yeme tutumları ve beden memnuniyetinin iyileştirilmesi için önemlidir. Bu çalışmada, bariyatrik cerrahi arayışında olan hastalarda yeme davranışları, beden memnuniyetsizliği, benlik saygısı ve psikolojik belirtiler arasındaki ilişkileri belirlemek amaçlanmıştır. İkinci amacımız beden memnuniyeti ve benlik saygısı ile yeme tutumları arasındaki ilişkide depresif belirtiler ve anksiyetenin, aracı rolü olup olmadığının belirlenmesidir.

Gereç ve Yöntem: Bu çalışma 200 hasta içermektedir. Hastaların verileri geriye dönük olarak değerlendirildi. Ameliyat öncesi dönemde yapılan psikometrik değerlendirme, psikiyatrik muayene ve Beck Depresyon Envanteri, Beck Anksiyete Envanteri, Rosenberg Benlik Saygısı Ölçeği, Vücut Algısı Ölçeği ve Hollanda Yeme Davranışı Anketi'nin uygulanmasını içeriyordu.

Bulgular: Benlik saygısı ile beden memnuniyeti arasında pozitif, benlik saygısı ile duygusal yeme arasında negatif yönde bir ilişki vardı ($r= 0,160$, $p= 0,024$; $r= -0,261$, $p< 0,001$ sırasıyla). Beden memnuniyeti, duygusal yeme üzerinde depresyon aracılığıyla ve dışsal ve kısıtlayıcı yeme üzerinde anksiyete aracılığıyla etkiye sahipti. Ayrıca benlik saygısı ile dışsal ve kısıtlayıcı yeme davranışları arasındaki ilişkilere anksiyetenin aracılık etkisi saptandı.

Sonuç: Depresyon ve anksiyetenin benlik saygısı, beden memnuniyetsizliği ve yeme tutumları arasındaki ilişkide aracı etkisinin olduğuna dair bulgularımız, bu özelliklerin klinik ortamlarda taranması ve tedavileri nispeten daha pratik olduğu için önemlidir.

Anahtar Kelimeler: Depresyon, anksiyete, yeme tutumları, benlik saygısı, beden algısı

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ORIGINAL ARTICLE
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COVID-19 infection frequency and clinical course in patients with liver transplantation: Results of a single transplant center in Türkiye

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ABSTRACT

Objective: In this paper, it was tried to determine the incidence of COVID-19, course of the disease, and mortality rate in liver transplant patients by evaluating all patients operated on in our center. In addition, the results of liver transplantation performed in our center during the pandemic period were also presented.

Material and Methods: All patients who had undergone liver transplantation in our liver transplant center were questioned about their history of COVID-19 either at their routine controls in the clinic or by phone interview.

Results: Our liver transplant unit had 195 registered liver transplantation patients (2002-2020), and 142 of these were still alive and under follow-up. During the pandemic period, 80 patients referred to our outpatient clinic for follow-up, and their records were evaluated retrospectively in January 2021. Among 142 liver transplant patients, a total of 18 (12.6%) COVID-19 patients were identified. While 13 of these patients were males, mean age of the patients at the time of interviews was 48.8 years (22-65 years). Nine of the patients had living donor liver transplant, and the rest had cadaveric liver transplant. The most common COVID-19 associated symptom in the patients was fever. During the pandemic period, 12 liver transplant operations were performed in our center. Nine of them were living donor liver transplantation and the remainder were cadaveric liver transplantations. Two of our patients got COVID-19 positive during this period. One of them who was transplanted after COVID treatment was followed-up in intesive care for a long time and was lost not related to COVID-19.

Conclusion: The incidence of COVID-19 is higher in liver transplant patients than in the general population. Nonetheless, mortality rates are low. During the pandemic period, liver transplantation can be continued by following general precautions.

Keywords: COVID-19 infection, liver transplantation, clinical course

INTRODUCTION

Due to the effects of the pandemic on health system, many elective surgical procedures have been delayed or postponed, and health services associated with coronavirus disease 2019 (COVID-19) have been tried to be sustained. However, patients needing emergent surgery cannot be delayed due to their current vital risks, and oncological surgery patients can not tolerate too much delay due to the risk of progression of their existing diseases. Unlike these, a group of affected surgical patients in the pandemic period was both patients awaiting organ transplantion and those having undergone organ transplantation.

Undoubtedly, liver transplantation has also been affected considerably during the pandemic period. It has been observed that there has been a significant decrease in the number of liver transplantation in many parts of the world since the beginning of the pandemic period (1-3). Serious concerns have arisen among patients awaiting organ transplantation, both about being operated during the pandemic period and the increase in waiting time (4).

Patients with liver transplantation must receive lifelong immunosuppression therapy and therefore live at risk of both communal and opportunistic infections throughout their lives. Although COVID-19 is known to mainly start with fever

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and respiratory symptoms, it can also occur with many different symptoms. However, there is limited information on how COVID-19 disease onset may occur in patients who have undergone liver transplantation or risk factors and course of the disease due to their current immunosuppressive conditions. While some publications regarding the effects of coronavirus on these patients have reported a mortality rate of up to 30% (5,6), some publications have reported similar mortality rates compared to non-transplant coronavirus-positive patients with similar comorbidities (7). At this point, it is not clear whether immunosuppression is an advantage or a disadvantage in these patients. Some studies provide recommendations for reducing immunosuppression in patients with liver transplantation (8,9). However, the fact that the short-term results in patients receiving immunosuppression are the same as the general population also suggests that immunosuppression may have a protective effect in these patients (10-12). Because of these differences of opinion, transplant centers should monitor their own patients and manage their patients according to these results.

In this paper, it was tried to determine the incidence of COVID-19, course of the disease, and mortality rate in liver transplant patients by evaluating all patients operated on in our center, which is a liver transplant center and provides tertiary health services. In addition, the results of liver transplantation performed in our center during the pandemic period as of March 2020 were also presented.

MATERIAL and METHODS

This study was conducted in January 2021 in gastroenterology surgery clinic. All patients who had undergone liver transplantation in our liver transplant center were questioned about their history of COVID-19 either at their routine controls in the clinic or by phone interview. Information was obtained from them or their relatives regarding whether they had COVID-19 disease or not, their initial symptoms, whether they were hospitalized or not, duration of their treatment, the treatment they received and their ventilator needs. Laboratory results obtained during this period were again obtained from the patients or their relatives. Death information of the patients was obtained from their relatives. Before this interview, patients or their relatives were informed about the study and their verbal consent was obtained. The consent was obtained for the study from the Republic of Türkiye, Ministry of Health. The study was conducted in accordance with good clinical practice principles and the Declaration of Helsinki. Statistical analysis was carried out by a statistician using IBM SPSS Statistics (version 22) software as appropriate.

RESULTS

Ankara City Hospital liver transplant unit had 195 registered liver transplantation patients (2002-2020), and 142 of these patients were still alive and under follow-up. During the pandemic period (as of March 2020), 80 patients referred to the transplant outpatient clinic for follow-up. COVID-19-related records of these patients were prospectively kept and these records were evaluated retrospectively in January 2021. In addition, COVID-19 related data of the remaining 62 patients were collected by phone call and added to other records during January 2021. Besides, the records of new liver transplant patients who had undergone surgery at our transplant center between March 2020 and January 2021 were also retrospectively evaluated.

Among 142 liver transplant patients, a total of 18 (12.6%) COVID-19 patients were identified through both control examinations and telephone interviews. While 13 of these patients (72.2%) were males, mean age of the patients at the time of the interviews was 48.8 years (22-65 years). Nine of the patients had a living donor liver transplant and the rest had cadaveric liver transplant. While the oldest patient was operated in 2003, the newest patient had liver transplantation in 2020. All patients were under immunosuppressive therapy (tacrolimus, everolimus or mycophenolat mofetil). The patients in the first six months of transplantation were also receiving steroid therapy.

Ten of the patients (55.5%) had at least one initial symptom. The most common COVID-19 associated symptom in the patients was fever. High fever response was observed in seven patients, cough in four patients, myalgia in two patients, dyspnea, nausea/vomiting and headache in one patient each. PCR positivity was detected in all but one of the sypmtomatic patients. Also, in seven of the symptomatic patients, COVID-19 compatible findings were detected in computed tomography of the thorax while the examination was interpreted as normal in three of them. The remaining eight patients were asymptomatic. It was understood that six of these patients had a history of COVID-19 after COVID IgG and IgM antibody tests were found to be positive in control tests. PCR and thorax CT findings were negative in these six patients, as well. While only CT positivity was detected in one of the remaining two patients, there was no symptom in the other patient although both PCR and CT were positive for COVID-19.

Six patients who were diagnosed with antibody positivity continued to be followed up in their current state without the need for treatment. Other two asymptomatic patients were hospitalized due to their CT findings and PCR positivity in one patient. Nine of the symptomatic patients were hospitalized and followed up in the COVID unit while one was followed in the COVID intensive care unit. However, the patient who was followed up in the intensive care unit was taken into intensive care because of existing liver functions, not because of the symptoms of COVID-19. Total hospitalization rate was 66.6%. Except for the patients whose diagnosis was confirmed with antibody positivity, in 12 patients (including asymptomatic patients), immunosuppressive therapy was stopped if the patient was re-

Table 1. Symptom, examination and treatment data of COVID-19 positive liver transplant patients

	Trans.	Symptoms	CT finding	PCR	Antibody	Treatment
Patient 1	CLT	Fever Nausea Vomiting	None	Positive	-	Hydroxychlorine
Patient 2	LDLT	Fever Cough	Positive	Negative	-	Favipiravir Hydroxychlorine
Patient 3	CLT	None	None	Negative	Positive	None
Patient 4	CLT	None	None	Negative	Positive	None
Patient 5	LDLT	None	None	Negative	Positive	None
Patient 6	CLT	Cough Dyspnoea	Positive	Positive	-	Favipiravir Hydroxychlorine
Patient 7	LDLT	Coguh	None	Positive	-	Favipiravir Hydroxychlorine
Patient 8	LDLT	Fever Cough Myalgia	Positive	Positive	-	Favipiravir Hydroxychlorine
Patient 9	LDLT	Fever Cough	None	Positive	-	Favipiravir Hydroxychlorine
Patient 10	LDLT	Fever Cough	Positive	Negative	-	Favipiravir Hydroxychlorine
Patient 11	LDLT	None	Positive	Negative	-	Favipiravir
Patient 12	LDLT	None	Positive	Positive	-	Favipiravir Hydroxychlorine
Patient 13	CLT	None	None	Negative	Positive	None
Patient 14	CLT	Fever	Positive	Positive	-	Favipiravir
Patient 15	CLT	Fever Cough	Positive	Positive	-	Favipiravir Hydroxychlorine
Patient 16	CLT	None	None	Negative	Positive	None
Patient 17	CLT	None	None	Negative	Positive	None
Patient 18	LDLT	Headache	Positive	Positive	-	Favipiravir

LDLT: Living donor liver transplantation, CLT: Cadaveric liver transplantation.

ceiving mycophenolate mofetil, and other immunosuppressive treatments were continued to be used by reducing the daily dose without discontinuation. A standard protocol is followed in our center for the treatment of COVID-19. After laboratory values of the patients were evaluated, these patients were hospitalized and treatment was started. All patients were isolated and hospitalized in COVID units. These patients received only favipravir (standard treatment for five days) if there was pneumonic infiltration or hydroxychloroquine (standart treatment for five days) if not. Anticoagulant therapy was initiated in all patients. After the treatments were completed, if the patient's COVID-19 PCR test result was negative, COVID treatments were discontinued and immunosuppressive treatments were continued as in pre-illness doses. COVID-19 related mortality was not observed in any of the patients.

During the pandemic period, 12 liver transplant operations were performed in our center. Nine of them were living donor liver transplantation and the remainder were cadaveric liver transplantations. In these nine living donor liver transplant patients, five donors were first degree, one donor was second degree and two donors were third degree relatives while the donor of one patient was non-relative. Two of our patients got COVID-19 positive during this period. One of them was asymptomatic, but there was thorax involvement on CT scan. The other patient had COVID before transplantation and was followed up in the intensive care unit due to liver failure. Both patients received favipravir therapy. While the patient who had COVID after transplantation was discharged after COVID-19 treatment, the patient who was transplanted after COVID treatment was followed up in the intesive care for a long time and was lost

even if it was not related to COVID-19. Similarly, two donor cases had COVID-19, one pre-transplant and one in post-transplant period. Two patients were discharged after their treatment.

DISCUSSION

In patients with solid organ transplantation, the rate of COVID-19 infection is higher than the general population, which was also the result in our study (12.6%). However, despite this high rate, short-term results are similar to the general population (13,14). There is a hypothesis that immunomodulators have a protective effect against the excessive and uneven inflammatory effect of COVID-19. In the study published by Belli LS et al., tacrolimus has been associated with decreased mortality for liver transplant recipients compared to other immunosuppressants (cyclosporine, mycophenolate mofetil, mTOR inhibitors) (11). TNF antagonists, not being risk factors for severe COVID-19, also supports this opinion in inflammatory bowel patients receiving immunosuppressive therapy (15). However, it is thought that similar effects may not be present in all immunosuppressants in these studies. Almost half of the patients in our study were asymptomatic patients. Nonetheless, the reason for thigh rate of hospitalization was due to the uncertainty about the treatment approach in this patient group and the extra care shown to these patients.

There are also opposing publications stating that mortality associated with COVID-19 is high in transplanted patients (16-18). However, in these publications, different organ transplantations have been subjected to same evaluation regardless of age and other comorbidities. Again, Belli LS et al. have shown that age is the most important factor affecting mortality in transplant patients (11). Other existing comorbidities can also affect this rate. While mean age was 48.8 years in our study, there were no patients aged 65 years and over. This may have also affected our results in a good way.

Symptoms associated with COVID-19 may also vary in liver transplant patients. Although symptoms associated with fever and respiratory tract are mostly observed, atypical symptoms (diarrhea, abdominal pain) can also be observed as in the general population (19). In our study, initial symptoms of the disease were found to be similar to the general population.

During the pandemic period, the number of liver transplants has decreased all over the world. The increased risk of infection among transplant patients and the fact that the whole world is actually at risk of infection have raised concerns. However, both cadaveric and living donor liver transplantation continued partially. There are data showing that this procedure can be done safely with taking maximum precautions, but including a limited number of patients (20). Even though we do not know the long-term results, liver transplantation case reports have been reported in patients with COVID-19 infection and recovery (21). However, despite these results, mortality risk of the disease should not be forgotten, and there is still no data suggesting that transplantation can be performed safely during the pandemic period. In the literature, lethal progressive cases have also been reported (22,23). Only one of the 12 transplant patients we performed during the pandemic period was successfully treated while having COVID-19 after the transplant. One patient underwent transplantation after COVID-19 treatment but was lost even if it was not related to COVID-19. Two donor patients were also discharged after completing their treatment. There is still uncertainty in the literature in this direction. However, we think that transplant operations can be performed safely with the current precautions provided.

One of the limitations of this study is that verbal information was obtained from all patients. Since the follow-up of the patients in the periods when they were positive for COVID-19 was not performed by us, the questions about that period were asked and answers were in the form of "yes" or "no". Although information was tried to be obtained from all patients, reverse transcription-polymerase chain reaction (RT-PCR) test or antibody test was not performed in every patient. Rauber C et al. have performed a prospective screening trial for SARS-CoV-2 RNA and anti-SARS-CoV-2 IgG infection in liver transplant recipients during the COVID-19 pandemic and found a 3.7% rate of acute or past infection (24). Although this ratio is less than our series, it is also possible for patients to experience COVID-19 without symptoms. Therefore, one might say that this number does not reflect the true incidence and may be even more. Therefore, it should be reminded that this study reflects the rate of COVID-19 that can be detected in transplant patients in our liver transplant pool and that only these patients are evaluated.

CONCLUSION

The incidence of COVID-19 is higher in liver transplant patients than in the general population. Nonetheless, mortality rates are low. During the pandemic period, liver trasnplantation can be continued by following general precautions.

Ethics Committee Approval: This study was approved by Ankara City Hospital No. 1 Clinical Research and Ethics Committee (Decision no: E1/1694/2021, Date: 31.03.2021).

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ORİJİNAL ÇALIŞMA-ÖZET
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Karaciğer transplantasyonu yapılan hastalarda COVID-19 enfeksiyon sıklığı ve klinik seyri: Türkiye'de tek bir nakil merkezinin sonuçları

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ÖZET

Giriş ve Amaç: Bu yazıda bir karaciğer nakli merkezinde ameliyat edilen tüm hastaları değerlendirerek karaciğer nakli yapılan hastalarda COVID-19 insidansını, hastalığın seyrini ve ölüm oranını belirlemeye çalıştık. Ayrıca pandemi döneminde merkezimizde yapılan karaciğer nakli hastalarının sonuçları da sunuldu.

Gereç ve Yöntem: Karaciğer nakli merkezimizde karaciğer nakli yapılan tüm hastalarda klinikteki rutin kontrollerinde veya telefon görüşmesi ile COVID-19 öyküsü sorgulandı.

Bulgular: Karaciğer nakli ünitemizde kayıtlı 195 karaciğer nakli hastası (2002-2020) bulunmaktaydı ve bunların 142'si halen hayatta ve takip altındaydı. Pandemi döneminde polikliniğimize takip için başvuran 80 hasta Ocak 2021'de geriye dönük olarak değerlendirildi. 142 karaciğer nakli hastası arasında toplam 18 (%12,6) COVID-19 hastası tespit edildi. Bu hastaların 13'ü erkek iken, hastaların görüşme anındaki yaş ortalaması 48,8 (22-65) idi. Hastaların dokuzuna canlı donör karaciğer nakli, geri kalanına kadavradan karaciğer nakli yapıldı. Hastalarda COVID-19 ile ilişkili en yaygın semptom ateşti. Pandemi döneminde merkezimizde 12 karaciğer nakli operasyonu yapıldı. Bunlardan dokuzu canlı vericili karaciğer nakli, geri kalanı kadavradan karaciğer nakliydi. Bu süreçte iki hastamızda COVID-19 testi pozitif çıktı. COVID tedavisi sonrası nakil yapılan bir tanesi uzun süre yoğun bakımda takip edildi ve COVID-19'a bağlı olmaksızın kaybedildi.

Sonuç: Karaciğer nakli hastalarında COVID-19 insidansı genel popülasyona göre daha yüksektir. Buna rağmen ölüm oranları düşüktür. Pandemi döneminde genel önlemlere uyularak karaciğer nakline devam edilebilir.

Anahtar Kelimeler: COVID-19 enfeksiyonu, karaciğer nakli, klinik seyir

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ORIGINAL ARTICLE
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Duration of operation and diagnosis of hepatitis B (HBV) is an independent risk factor for surgical site infections after liver transplantation

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ABSTRACT

Objective: Surgical site infections (SSI) are the most common complications after liver transplantation (LT). Although there are some risk factors known in the literature after LT, the available data is insufficient for routine use. In the present study, it was aimed to define the parameters that may be used to clearly determine the risk of SSI after LT in our clinic.

Material and Methods: In the present study, we evaluated 329 patients who underwent liver transplantation with regard to risk factors for surgical site infections. The relation between demographic data and SSI was evaluated using SPSS, Graphpad, and Medcalc statistical programs.

Results: In a total of 329 patients, SSIs were determined in 37 (11.24%). Among the 37 patients, 24 were classified as organ space (64.9%) and 13 as deep SSI (35.1%). None of these patients developed superficial incisional infection. SSI showed statistically significant relation with operation time (p= 0.008), diabetes (p= 0.004), and cirrhosis due to hepatitis B (p< 0.001).

Conclusion: As a result, deep and organ space infections are much more observed in patients undergoing liver transplantation with hepatitis B, diabetes mellitus and prolonged surgery. This is thought to have developed because of chronic irritation and increased inflammation. Since data on hepatitis B and duration of surgery are limited in the literature, this study is considered to be a contribution to the literature.

Keywords: Surgical site infection, liver transplantation, operation time

INTRODUCTION

Liver transplantation (LT) is one of the most effective therapeutic options for patients with liver diseases. However, complications constitute most of the previously reported causes of death in these patients. Postoperative infections are the most common complications after LT (1-8). Hospital infections, which occur as a result of invasive procedures and applications in the hospital, lead to prolonged hospital stay and cause significant morbidity and mortality. Surgical site infections (SSIs) constitute a significant part of hospital infections (2). SSIs are divided into three distinct types as superficial incisional, deep incisional and organ space. Although advances have been made in infection control practices, including improved operating room ventilation, sterilization methods, surgical technique, and availability of antimicrobial prophylaxis, SSIs remain a substantial cause of morbidity, prolonged hospitalization, and mortality (3).

Previous studies have documented increased risk for SSI based on patient and operative characteristics (3-5). Studies have shown that MELD score, diabetes, hyperglycemia, age, operation time, high volumes of blood transfusion are risk factors for SSI (5-7). The aim of this study was to determine and understand the risk factors of SSI in patients undergoing LT in our general surgery department.

MATERIAL and METHODS

Patients who underwent transplantation for chronic liver disease at Bursa Uludağ University from January 2007 and August 2020 were included in the current study. Ethics approval of the study was obtained from the local institutional ethics committee (No: 2011-KAEK-26/413, Date: 20.07.2020).

The same immunosuppression regimen was applied to all patients included in the study, which consisted of tacrolimus, steroid and mycophenolate mofetil (MMF).

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Standard dose steroid and MMF were used, and tacrolimus doses were checked daily to keep them within a certain range. Perioperative antibacterial prophylaxis consisted of ampicillin and sulbactam for the first 48 hours after transplantation. Anti-fungal and anti-viral prophylaxis included a combination of nystatin swish-and-swallow, micafungin, fluconazole, ganciclovir and valganciclovir for 3-6 months, depending on the risk profile. Post-transplantation antimicrobial therapy was changed on an individual basis considering clinical factors and speciation of microbiology results.

Surgical site infections were classified according the centers for disease control and prevention classification system as follows:

(a) superficial incisional involving only the skin or subcutaneous tissue of the incision;

(b) deep incisional involving the fascia and/or muscular layers in the primary incision (deep incision primary) in a patient who had an operation involving one or more incisions and an SSI identified in the secondary incision (deep incision secondary) in an operation with more than one incision; and

(c) organ-space involving any part of the body opened or manipulated during the procedure excluding the skin incision, fascia, or muscle layers. In the presence of more than one SSI type, the more complex SSI type was selected. Patients' demographic information, operative details, post-operative outcomes and infection outcomes were collected from the archive of the department of general surgery. SSIs were defined by using standardized Centers for Disease Control and Prevention's National Healthcare Safety Network.

The relation between demographic data and SSI was analyzed using SPSS, Graphpad, Medcalc statistical programs. Chi-square test was used between types of organism and source of infection. Overall survival details were presented for each of the three different SSI groups. The Kaplan Meier method was used to determine the effect of SSI on survival. Multivariate analyses were performed using a Cox proportional hazards regression model to investigate associations of patients features, operative information and postoperative complications within 30 days of liver transplantation with development of SSI after liver transplantation. Logistic regression analysis was performed to analyze the risk factors. Student's t-test was used for comparison of quantitative outcome parameters.

Table 1. Patient demographics

Features	Number
Sodium MELD score	18 (15-30)
Age (years, median)	51.4 (5-76)
BMI	27 (18-33)
Sex	
Male	215 (89.9)
Female	114 (34.7)
SSI	
None	292 (88.7)
Organ Space	24 (7.3)
Deep	13 (4.0)
Underlying Diseases	
HBV	126 (38.3)
HCV	21 (6.4)
NASH	24 (7.3)
PBC	16 (4.9)
Cryptogenic	43 (13.1)
Wilson	24 (7.3)
Others	75 (22.8)

RESULTS

The present study included 329 unrelated patients who had undergone LT. Of these patients, 215 were males and 114 were females, with a median age of 51.4 years (range 5-76 years). Median body mass index was 27 (Range 18-33), and median model for end-stage liver disease (MELD) score was 18 (range 15-30). The most common principal liver disease diagnosis was chronic hepatitis B (n= 126, 38.3%). Median operative time was 238 min (range 100-747 min). SSIs were determined in 37 (11.3%) patients. Among the 37 patients, 24 was classified as organ space (64.9%) and 13 (35.1%) as deep (Table 1). None of these patients developed superficial incisional infection. As reported in Table 2, the highest SSI incidence rates were observed in HBV-infected

Table 2. Diagnosis and SSI

Diagnosis	None (n= 292)	Organ Space (n= 24)	Deep (n= 13)	Total (n= 329)
HBV	105 (83.3%)	16 (12.7%)	5 (4.0%)	126
HCV	17 (81.0%)	1 (4.8%)	3 (14.2%)	21
NASH	24 (100%)	0 (0.0%)	0 (0.0%)	24
PBC	16 (100%)	0 (0.0%)	0 (0.0%)	16
Cryptogenic	42 (97.6%)	0 (0.0%)	1(2.4%)	43
Wilson	24 (100%)	0 (0.0%)	0 (0.0%)	24
Others	40 (85.4%)	7 (9.3%)	4 (5.3%)	75

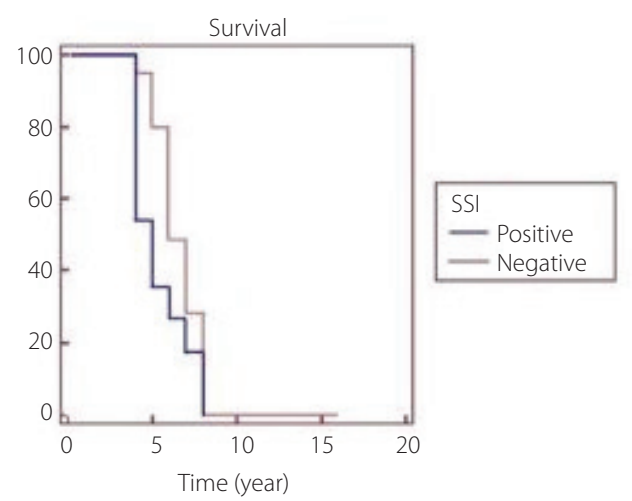

Figure 1. The effect of SSI on overall survival.

patients (56.8%; 95% CI 4.5-9.2). The growth of various bacterial pathogen was determined in 29 patients, and fungal pathogen was determined in eight. The most common micro-organisms isolated was *Escherichia coli* in 20 of 37 (54.0%) patients.

First, the relation between SSI and prognosis was investigated by Kaplan Meier analysis, and the effect of SSI development on short overall survival was determined (Log-rank, p= 0.003, HR= 4.614, Figure 1).

In our study, SSI was 22 in males and 15 in females, and no statistically significant relation was found (p> 0.05). In single variable analysis, there was an association between HBV-infection and SSI (p= 0.001). SSI, which was associated with poor prognosis, showed a statistically significant relation with operation time (p= 0.008), diabetes (p= 0.004), HBV-infection p< 0.001).

In our study, the operative time lasted longer than two hours, which resulted in an increase in the risk of SSI (Table 3). In the study, 21 of the 94 patients with diabetes mellitus developed SSI. In the modeling based on logistic regression analysis with all parameters showing significance, operative time and HBV diagnosis were determined as independent risk factors for SSI (Table 4).

DISCUSSION

SSI is an important cause of morbidity in the early post-transplant period due to the complexity of the surgery, immunosuppression and patient comorbidities (8). Although progress has been made in infection control practices, SSI remains one of the most common health-related infections (8).

The incidence of SSI following liver transplantation ranges between 8.8% and 37.6%, depending on the definition of SSI and the differences in follow-up times (5,8-11). Softness et al., in their single center experience with 252 patients, have found SSI rate to be 9.5% (9). RA Oliveira et al. have determined an SSI rate of 26.9% in their study (10). In the study of Freire MP et al. in 2021, SSI rate was 30.1% (11). In our retrospective study, the incidence of SSI was 11.24% (37/329) and was consistent with the literature.

We observed solid evidence of a strong association between diagnosis, operative time and SSI, and these relationships were independent of other variables. As stated in many studies in the literature, operative time is closely related with surgical site infection. In the results of our study, operative time was found to be an independent risk factor in terms of surgical site infection, which was consistent with the literature (8-11).

In our study, the relation of SSI with diabetes mellitus was not statistically significant. According to a meta-analysis published by Martin et al in 2016, surgical site infections were found to be closely related to diabetes mellitus. According to this analysis, pre and post hyperglycemia and a history of diabetes mellitus were found to be risk factors for the development of surgical site infection, and our study is consistent with this result (12).

Table 3. Operative time and SSI

Operative Time (hour)	95% CI	p	Total (n= 329)
<2	0.93 to 1.56	0.956	24
2-4	1.23 to 2.01	0.025	47
4-5	0.88 to 1.77	<0.001	100
>6	1.25 to 2.20	<0.001	16

Table 4. Risk factors for SSI using logistic regression analysis

Features	OR	95%	p
Operation Time (>2 vs <2)	2.5	2.01-5.43	0.022
Diabetes (Yes vs. No)	-	-	0.066
HBV-mediated (Yes vs. No)	2.01	1.02-7.23	0.002

In our patient group who developed surgical site infection, the duration of intensive care and hospital stay increased in the postoperative period, but this result was not statistically significant.

Sangrasi et al. have shown the duration of postoperative stay as a risk factor for SSI, and hospitalization of the group with SSI was 16.2 days while the hospitalization period of the group without SSI was 6.3 days. In this study, it was shown that hospitalization time increased more than two times in patients who developed infection (13).

According to a study conducted by Işık et al. in 2015, operation time exceeding four hours was found to be a risk factor for the development of SSI (14). Our study was consistent with the results of this study. In our study, the operative time lasted longer than two hours and resulted in an increase in the risk of SSI. Malone et al. have compared patients with a duration of operation <2 hours, 2-4 hours, and >4 hours and found that as duration increased, so did the rates of SSI (2.1%-3.3%-6.4%, respectively) (15).

There is no reported relation between surgical site infection and hepatitis B in the literature. Although mechanisms that trigger the development of cirrhosis in the liver are thought to be induced by chronic inflammation, the current literature on the mechanisms of surgical site infection is insufficient, and more studies are needed. According to the findings of our study, the development of surgical site infection was found to be significantly higher in patients who had undergone liver transplantation due to hepatitis B cirrhosis compared to the other groups. According to this result, the determination of hepatitis B as an independent risk factor for the development of surgical site infection is a significant contribution to the literature.

Risk factors for the development of SSI have been determined in previous studies. In our study, risk factors of the patient were associated with increased operative time and hepatitis B. As a result of our work with this data, it can be changed to prevent the development of SSI, and intervention of predictable factors can be evaluated. However, studies that evaluate risk factors and have more patients are needed.

Our study has several limitations. As our study was a cohort study, we did not check the interventions that could have affected the results. Clinical parameters in the study are few.

In conclusion, we found that HBV-infection and operative time were associated with an increased risk of SSI. In order to reduce the rate of SSI in patients with LT, studies should be increased.

Ethics Committee Approval: The approval for this study was obtained from Uludağ University Faculty of Medicine Clinical Research Ethics Committee (Decision no: 2020-12/17, Date: 08.07.2020).

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ORİJİNAL ÇALIŞMA-ÖZET
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Hepatit B (HBV) tanısı ve operasyon süresi karaciğer transplantasyonu sonrası cerrahi alan enfeksiyonları için bağımsız bir risk faktörüdür

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ÖZET

Giriş ve Amaç: Cerrahi alan enfeksiyonları (CAE), karaciğer nakli (KN) sonra en sık görülen komplikasyonlardan biridir. Literatürde KN sonrası bilinen bazı risk faktörleri olmasına rağmen, mevcut veriler rutin kullanım için yetersizdir. Bu çalışmada, kliniğimizde KN sonrası CAE riskini açıkça belirlemek için kullanılabilecek parametrelerin tanımlanması amaçlanmıştır.

Gereç ve Yöntem: Bu çalışmada, KN uygulanan 232 hastayı değerlendirdik. Demografik veriler ve CAE arasındaki ilişki SPSS, Graphpad, Medcalc istatistik programları kullanılarak analiz edilmiştir.

Bulgular: Toplam 232 hastada 26 (%11,26) CAE saptandı. 26 hastanın 16'sı organ boşluk 16 (61,5) ve 10'u (39,5) derin CAE olarak sınıflandırıldı. Bu hastaların hiçbirinde yüzeysel cerrahi alan enfeksiyonu gelişmedi.Derin ve organ boşluk SS, operasyon süresi (p= 0,01), diyabet (p= 0,004), HBV enfeksiyonu (p= 0,001) arasında istatistiksel olarak anlamlı ilişki saptandı.

Sonuç: Sonuç olarak, karaciğer nakli uygulanan hepatit B tanısı olan, diyabetik ve ameliyat süresi uzayan hastalarda daha fazla derin ve organ boşluk enfeksiyonu geliştiği görülmektedir. Bunun da kronik irritasyon ve artmış enflamasyon sonucunda geliştiği düşünülmüştür. Literatürde hepatit B ve ameliyat süresi ile ilgili veriler kısıtlı olduğundan bu çalışmanın literatüre katkı sağlayabileceği düşünülmüştür.

Anahtar Kelimeler: Cerrahi alan enfeksiyonu, karaciğer nakli, operasyon süresi

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CASE SERIES
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A case series of choledochal cyst with pancreatic divisum: A rare association

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ABSTRACT

Choledochal cysts (CC) are congenital cystic dilations of the biliary tree usually associated with abnormal pancreaticobiliary ductal junction (APBDJ), but its association with pancreatic divisum has been rarely described. We encountered four cases of CC associated with pancreatic divisum (PD). Three had Type 3 PD and one had Type 1 PD. Two cases presented with pancreatic complications, with one case requiring preoperative minor papilla sphincterotomy for recurrent pancreatitis. The association of CC with PD is infrequent, and the variable presentation alters management strategy. PD may be one of the factors responsible for complications associated with CC.

Keywords: Choledochal cyst, pancreatic divisum, abnormal pancreaticobiliary junction

INTRODUCTION

Choledochal cysts (CC) are congenital cystic dilation of the biliary tree predominantly reported in the first decade of life (1). The pathogenesis of CC remains unclear. However, the most accepted theory is the presence of anomalous pancreaticobiliary duct junction (APBDJ) and long common channel (2). This is hypothesized to cause the reflux of pancreatic enzymes into the common bile duct leading to inflammation and duct ectasia, and reflux into the pancreatic duct causing pancreatitis (3,4). Pancreatic divisum (PD) is the most common congenital anomaly of the pancreas, which results when the embryological ventral and dorsal buds fail to fuse (complete PD) or fuse partially (incomplete PD). Although rare, PD can cause intraductal hypertension leading to abdominal pain and recurrent pancreatitis (5). The co-existence of CC and PD and the associated complications are rare, with less than ten documented cases in the literature (6). This report reviews our experience of four cases of CC with PD.

Case 1

A 20-year-old female patient presented with a history of epigastric pain for seven days. On clinical examination, the patient had tachycardia and epigastric tenderness. Her serum amylase and lipase levels were 900 IU/L and 726 IU/L, which was more than three times above the normal limits. Ultrasonography (USG) of the abdomen showed dilated common bile duct (CBD) of two centimeters with edematous pancreatitis which responded to conservative management. On MRCP, diagnoses of Todani Type IV A CC (7) with APBDJ and Type 3 pancreatic divisum were made. The patient underwent elective complete CC excision six weeks after recovery from pancreatitis. Postoperative course was uneventful. On follow-up for five years, the patient is doing well.

Case 2

A 28-year-old male patient presented with recurrent episodes of pain abdomen for 12 months. The patient had recurrent episodes of mild acute pancreatitis for which he was evaluated with MRCP and found to have Type I CC (two centimeters) with Type 1 PD and underwent minor papilla sphincterotomy elsewhere (Figure 1). Three months after acute pancreatitis attack, the patient underwent CC excision.

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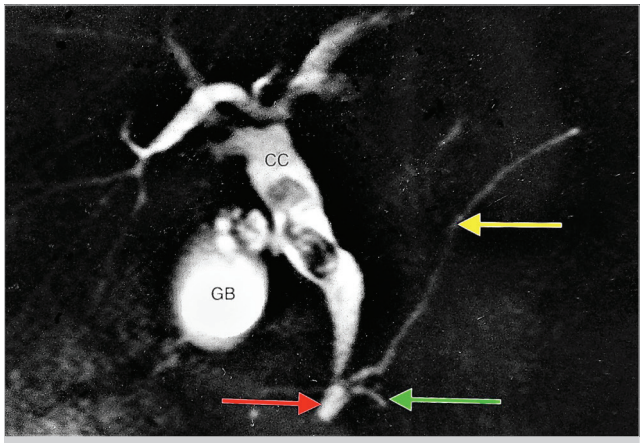

Figure 1. Magnetic resonance cholangiopancreatography (MRCP) of choledochal cyst (CC) with pancreatic divisum (PD). Yellow arrow; dorsal pancreatic duct draining separately into the minor papilla with no communication with the ventral duct (green arrow) suggestive of complete PD. Red arrow; long common channel formed by common bile duct and ventral duct draining into the major papilla.

On postoperative day (POD) two, he developed acute pancreatitis with peripancreatic necrosis with a computed tomography severity index (CTSI) score of ten. On POD ten, the patient developed haemobilia with jaundice and melena, requiring two units of blood transfusion. Conventional angiogram did not reveal any active source of the bleed, and eventually, melena subsided with no drop in hemoglobin over the subsequent days. He developed sepsis with a total leukocyte count of 35.000 cells/mm^3. Necrosis was drained percutaneously. Drain fluid culture showed multi-drug resistant *Escherichia coli*. The patient did not respond to these interventions; a step-up approach was followed, and on POD 23 underwent surgical necrosectomy and drainage. Following surgery, the patient required prolonged ICU care with ventilator assistance. He eventually improved and was discharged on POD 44 in stable condition, but the patient was lost to follow up.

Case 3

A 12-year-old girl, with pain in the abdomen and vomiting ongoing for one month, was diagnosed with Type IV A CC of two centimeters with complete PD on MRCP and normal biochemical investigations. The patient underwent complete cyst excision with an uneventful postoperative course. She was discharged on POD six. The patient is currently doing well after five years of follow-up.

Case 4

A 35-year-old female patient presented with pain in the abdomen ongoing for 15 days. MRCP showed Type I CC with incomplete Type 3 pancreatic divisum (Figure 2). The patient underwent complete excision of the cyst but developed a low output biliary leak, which was managed conservatively. The patient has been on regular follow-up and asymptomatic at five months of follow-up.

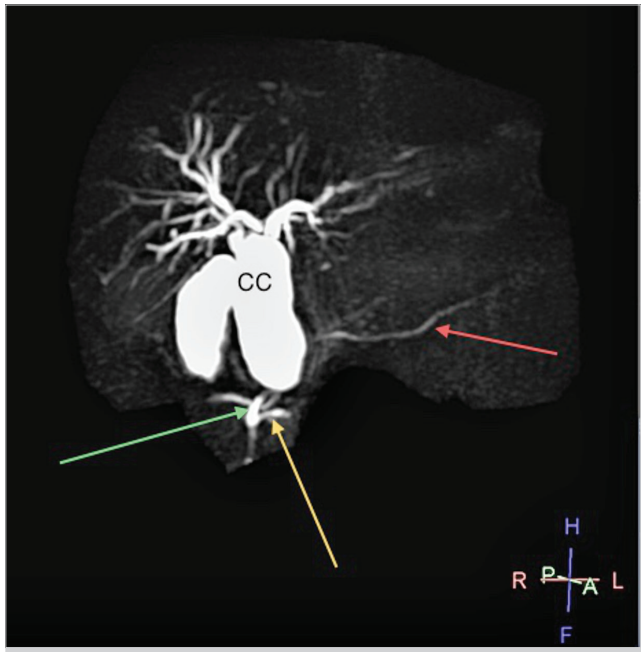

Figure 2. Magnetic resonance cholangiopancreatography (MRCP) choledochal cyst (CC) with incomplete (Type 3) pancreatic divisum (PD). Red arrow; dorsal pancreatic duct draining separately into the minor papilla with filamentous communication with the ventral duct (yellow arrow) suggestive of incomplete PD. Green arrow; long common channel formed by common bile duct and ventral duct draining into the major papilla.

DISCUSSION

The presence of pancreatic divisum rules out APBDJ as the only cause of CC as most of the pancreatic juice drains through the dorsal duct into the minor papilla, which has no communication with the biliary system (8,9).

Although cases with PD rarely cause any symptoms, they have been implicated with acute pancreatitis in 25-38% of the patients (8). In addition, Cotton et al. have suggested the importance of the co-existence of stenotic accessory pancreatic duct along with PD in the causation of pancreatitis (10). The risk factors mentioned above for acute pancreatitis, although rare, also increase the risk of postoperative pancreatitis (11). In our study, one case with preoperative pancreatitis developed severe necrotizing pancreatitis in the postoperative period requiring operative intervention, which is a rare complication and has not been reported previously.

The incidence of acute pancreatitis with CC is 0% to 70.6% in children and 10% to 54.5% in adults (11). The incidence of acute pancreatitis in our series of adult CC was 3.7%. The causative factors described for acute pancreatitis with CC are fusiform dilatation with a non-stenotic distal bile duct above the common

channel, a dilated common channel, and protein plugs in the common channel, which leads to reflux of bile into the pancreatic duct, and therefore leading to increased incidence of acute pancreatitis (11-13).

As there is an uncertainty of PD being a causative factor in acute/chronic pancreatitis and the risks associated with the treatment options, the approach to the management of PD should be based on the clinical presentation. Treatment options available are endoscopic sphincterotomy or surgical sphincterotomy with sphincteroplasty.

A few authors have managed PD associated with Type 3 CC (choledochocele) with either endoscopic sphincteroplasty or sphincterotomy as therapeutic modality (14). Hackert et al. have reported a case treated with bile duct resection, papillectomy, hepaticojejunostomy, and jejunal reinsertion of the uncinate pancreatic duct, which is an infrequently performed procedure (15). Other types of CC associated with PD could be managed with preoperative minor papilla sphincterotomy with or without stenting or trans-duodenal papillectomy followed by CC excision (6,9,16,17). In our study, two patients with CC and PD presented with acute pancreatitis. Only one patient required preoperative minor papilla sphincterotomy due to recurrent pancreatitis.

CONCLUSION

In conclusion, CC with PD is a rare congenital anomaly. PD may be an additional factor along with APBDJ for complications associated with CC, but larger sample size studies are required to prove this. Management strategy of these cases varies with the presence of complications.

Ethics Committee Approval: This study was approved by Nizam's Institute of Medical Sciences Institutional Ethics Committee (Decision no: EC/NIMS/2940/2022, Date: 25.01.2022).

Informed Consent: Informed consent was obtained from the son of the patients.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.K.P.; Supervision - B.N., P.K.N., A.K.B.; Data Collection and/or Processing - A.K.P., P.K.N., A.K.B.; Literature Search - P.K.N., B.N., A.K.P.; Writing Manuscript - A.K.P., P.K.N.; Critical Reviews - B.N., P.K.N.

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OLGU SERİSİ-ÖZET
Turk J Surg 2022; 38 (3): 294-297

Pankreas divisum ile birlikte koledok kisti olgu serisi: Nadir bir birliktelik

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ÖZET

Koledok kistleri (KK), genellikle anormal pankreatikobiliyer duktal bileşke (APBDB) ile ilişkili olan safra kanallarının konjenital kistik dilatasyonlarıdır ve pankreas divisum (PD) pankreas divisum ile ilgisi nadir bildirilmiştir. Serimizde PD ile ilişkili dört KK olgusu bulunmaktadır. Bu dört olgunun üçünde Tip 3 PD, birinde ise Tip 1 PD vardı. İki olgu pankreatik komplikasyonlar geliştirirken bunlardan biri rekürren pankreatit açısından preoperatif minör papilla sfinkterotomisi gerektirdi. KK ile PD ilişkisi nadir olmakla birlikte değişken başvuru şekilleri yönetim stratejisini değiştirmektedir. PD, KK ile ilişkili komplikasyonlardan sorumlu bir faktör olabilir.

Anahtar Kelimeler: Koledokal kist, pankreas divisum, anormal pankreatikobiliyer bileşke

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CASE REPORT
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Microperforation after colonic endoscopic submucosal dissection, air in 5 separate locations

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ABSTRACT

Endoscopic submucosal dissection (ESD) and endoscopic mucosal dissection (EMD) are recognized treatment procedures for mucosal lesions. There will always be a risk for complications even if they are performed by experienced specialists. In this study, we aimed to present a 58-year-old male patient in whom lesion was detected in the proximal part of the descending colon during a colonoscopy. Histopathological examination of the lesion revealed intramucosal carcinoma. The lesion was removed by ESD but after the intervention, bilateral pneumothoraxes, pneumoperitoneum, pneumoretroperitoneum, pneumomediastinum and pneumoderma complications observed. It is quite unlikely to encounter all of these complications together in one patient. In this paper, we would like to highlight the potential for complications after ESD, even for the rare and unexpected ones, to contribute to their recognition and treatment.

Keywords: ESD colorectal, pneumoderma, pneumomediastinum, pneumoperitoneum, pneumoretroperitoneum, pneumothorax

INTRODUCTION

Endoscopic submucosal dissection (ESD) and endoscopic mucosal resection (EMR) provide favorable and precise solutions for gastrointestinal mucosal lesions. As perforation is the main complication with endoscopic resections, ESD use is controversial to some extent due to high complication rates, long learning curve, and long procedural duration (1). Intraperitoneal air has been observed at unexpectedly high frequencies when computerized tomography (CT) imaging is performed after the procedure although it is not required in the routine clinical practice (2). In our paper, it was aimed to present the clinical management and outcome of bilateral pneumothoraxes, pneumomediastinum, pneumoperitoneum, pneumoretroperitoneum, and pneumoderma diagnosed after an ESD intervention in the descending colon.

CASE REPORT

This is a 58-year-old patient with no diagnosed health problems. During a colonoscopy intervention due to the complaint of rectal bleeding, a sessile lesion was detected in the proximal part of the descending colon and biopsy samples were collected. The outcome of the histopathological examination revealed intramucosal carcinoma developing on tubular adenoma. The patient's laboratory (carcinoembryonic antigen 0.5 ng/mL) and radiological findings revealed no positive findings and the colonoscopy examination was repeated by us. The lesion was observed to be 25 mm in diameter with a wide base. It was protuberant and owned a micronodular surface (Figure 1A). After the intervention, the patient was informed of the polyps in the colon, of his lesion, and of possible treatment options. The lesion was removed by ESD via a colonoscope (Pentax, EPK-i5000, Tokyo, Japan) after obtaining informed consent of the patient. The intervention took 43 minutes to be completed. Two endoclips (Olympus QuickClip2TM, Tokyo, Japan) were placed due to the deepening of the lesion in some regions, extending till muscularis propria (Figure 1B). Due to the complaint of pain developing after the intervention, the patient was hospitalized. Laboratory tests resulted in a C-reactive protein (CRP) level

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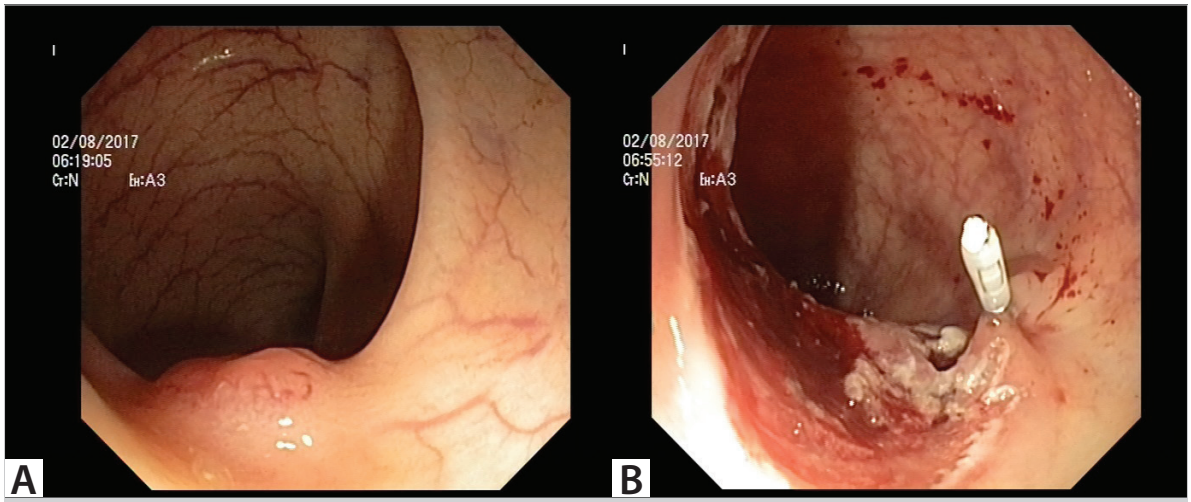

Figure 1. A. View of the lesion before ESD, **B.** Resected area and endoclip application after ESD.

of 2.93 mg/dL and leukocyte count of 13.11 K/uL. As the pain complaint was not resolved, an abdominal CT (Siemens, Berlin, Germany) was performed demonstrating bilateral pneumothoraxes, pneumomediastinum, pneumoperitoneum, pneumoretroperitoneum, and pneumoderma (Figures 2A-B). The general condition of the patient was good and his vital signs were stable. Oral intake was stopped and the patient started fluids, electrolytes, and antibiotics intravenously. Blood gas analysis results were as follows: pH 7.4, lactate 0.7 mmol/L. The respective 6-hour and 12-hour laboratory test outcomes were CRP 9.44-17.16 mg/dL, and leukocytes 14.39-12.79 K/uL. On consulting with the chest diseases and thoracic surgery departments for pneumothoraxes and pneumomediastinum, close monitoring of the patient and antibiotic treatment were recommended. During clinical monitoring of the patient, the complaint of pain was sustained. The abdomen was distended. Laboratory test values in the 24-hour laboratory values were 20.59 mg/dL for CRP and 12.03 K/uL for leukocyte count. An ultrasound-guided 8F drainage catheter was placed intra-abdominally by the interventional radiology department. Abundant amounts of air were aspirated through the drainage catheter and then it was allowed for free drainage. Abdominal pain relieved on the third day. Leukocyte count and CRP levels were 10.84 K/uL and CRP 18.41 mg/dL, respectively. The patient started oral intake of food. The patient was uneventful on the fourth and fifth days of monitoring. He was discharged from the hospital with a normal leukocyte count and with CRP levels of 5.32 mg/dL. Histopathological examination of the tissue sample obtained by ESD revealed a moderately differentiated tumor limited to the mucosa. All surgical margins were reported to be intact. A control

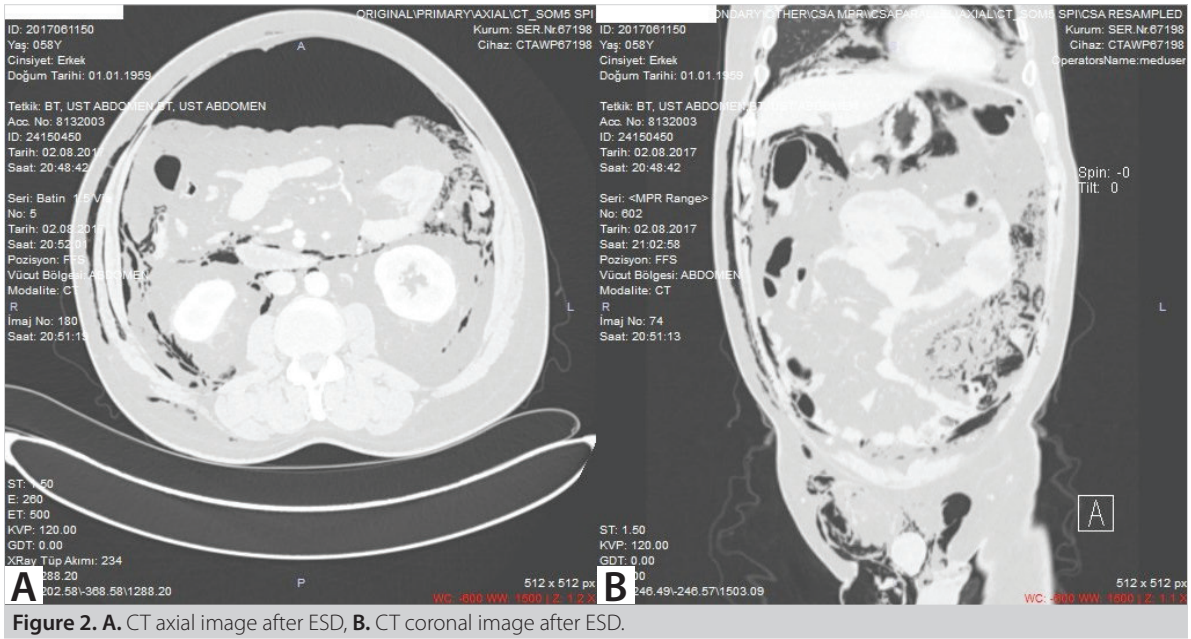

Figure 2. A. CT axial image after ESD, **B.** CT coronal image after ESD.

endoscopy, performed one month later, demonstrated that the resection area was intact.

DISCUSSION

Endoscopic submucosal dissection is an alternative method to surgery in the treatment of eligible cases (2,3). It provides more advantages in mucosal cancers compared to the conventional endoscopic mucosal resection (EMR) (2). Therefore, ESD was applied to our patient as the diagnosis was intramucosal carcinoma. However, compared to conventional (EMR), ESD takes a longer period of time to perform and has higher rates of complication such as bleeding and perforations (4,5). Main complications associated with ESD are perforations and bleeding (4). The duration of the intervention was not prolonged and no perforations or bleeding was observed in our patient during the procedure. However, perforations after ESD can be classified into two as macro-perforations and micro-perforations (2). Macro-perforation is defined as a hole, which can be recognized easily by endoscopy. Micro-perforation is a kind of perforation which is diagnosed by the presence of free air observed in the direct radiogram after the intervention (2). There are some explanations on the causes of micro-perforations that they can occur after a small puncture by an injector or they can be caused by some transmural air leakage due to a mild injury of muscularis propria without a visible hole (2,6). In addition, excessive tool manipulation, longer durations of electrocauterization, and keeping the electrocautery close to the muscular layer may result in transmural burns, and eventually, perforations (7). Although there was not a macro-perforation in our patient, thermal damage in the muscularis propria layer was observed and closed with endoclips. A perforation can usually be treated immediately by placing metallic endoclips. The pneumoperitoneum, which was detected after the intervention, was decided not to require surgery after monitoring the patient for 24 hours. Then intraabdominal catheter was placed and decompression was performed. Surgery should be performed in cases where endoscopic closure of the perforation is not ensured or the patient is not stable.

The presence of air in five different localizations (pneumoperitoneum, pneumoretroperitoneum, pneumomediastinum, pneumothorax, and pneumoderma) developing after ESD is a very rare complication. Retroperitoneal air arose directly from the retroperitoneal perforation of the colon or from the air leakage to the mesentery and retroperitoneum all the way through the dissected colon wall (7). The retroperitoneal air moves to the mediastinum along the fascial planes. Following the eventual rupture of the mediastinal pleura, it is transferred to the pleural spaces ending up with pneumothorax (7). If dyspnea or pneumoderma develops during or after the procedure, chest radiography or thoracoabdominal CT should be performed for diagnostic purposes (3). As it was predicted that a chest tube insertion might be necessary, the patient was treated with intermittent oxygen therapy and antibiotics after the CT scan of the pneumothorax.

CONCLUSION

After an ESD intervention, we may unexpectedly encounter the insufflated air, for colonic lumen expansion, in the form of pneumoperitoneum, pneumoretroperitoneum, pneumomediastinum, bilateral pneumothorax, and pneumoderma. However, before radiological findings, the clinical course of the patient should be considered first. For this reason, if there is no evidence of peritonitis or respiratory distress in a patient after ESD, identifying the presence of free air radiologically will not require changes in treatment strategies.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – F.C.; Design – K.E.K.; Supervision – F.C., V.C.; Data Collection and/or Processing – F.C., V.C., H.T.C.; Analysis and/or Interpretation – F.C., V.C., K.E.K., H.T.C., M.H.; Literature Search – F.C., K.E.K., M.H.; Writing Manuscript -F.C. K.E.K.; Critical Reviews – F.C., K.E.K., M.E.

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OLGU SUNUMU-ÖZET
Turk J Surg 2022; 38 (3): 298-301

Kolonik endoskopik submukozal diseksiyon sonrası mikroperforasyon, 5 ayrı lokalizasyonda hava

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ÖZET

Mukozal lezyonlar için endoskopik submukozal diseksiyon (ESD) ve endoskopik mukozal diseksiyon (EMD) kabul görmüş bir tedavi prosedürüdür. Deneyimli uzmanlar tarafından gerçekleştirilse bile, her zaman komplikasyon riski vardır. Yazımızda kolonoskopi sırasında inen kolonun proksimalinde lezyon saptanan, 58 yaşında bir erkek hastayı sunduk. Lezyonun histopatolojik incelemesinde intramukozal karsinom saptandı. Lezyon ESD ile çıkarıldı ancak girişim sonrası bilateral pnömotoraks, pnömoperiton, pnömoretroperiton, pnömomediastinum ve pnömoderma komplikasyonları izlendi. Bu komplikasyonların hepsine bir hastada karşılaşılması pek olası değildir. Bu yazımızda ESD sonrası nadir ve beklenmedik komplikasyonların olasılığını vurgulamak, bu komplikasyonların tespit ve tedavisine katkıda bulunmaktır.

Anahtar Kelimeler: Kolorektal ESD, pnömoderma, pnömomediastinum, pnömoperitoneum, pnömoretroperitoneum, pnömotoraks

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CASE REPORT
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Diagnostically challenging rupture of pancreaticoduodenal artery aneurysm: A case report

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ABSTRACT

Splanchnic artery aneurysms are rare vascular lesions with a high risk of rupture regardless of their size. Symptoms may vary from simple abdominal pain or vomiting to morbid conditions like haemorrhagic shock; however, most aneurysms are asymptomatic and difficult to diagnose. In this study, it was aimed to present the case of a 56-year-old female with a ruptured pancreaticoduodenal artery aneurysm treated by coil embolization.

Keywords: Aneurysm, coil embolization, angiography, pancreaticoduodenal artery

INTRODUCTION

Splanchnic artery aneurysms (SAA) are rare vascular lesions. The first case of SAA was described by Ferguson in 1895 (1), and approximately 3000 cases have been reported since 1960 (2). SAA ruptures are difficult to diagnose and could cause mortality. Accurate and rapid diagnosis is critical in case of rupture. In this study, it was aimed to present a case of ruptured pancreaticoduodenal artery aneurysm (PDAA) treated with coil embolization. Written consent was obtained from the patient.

CASE REPORT

A 56-year-old female presented to the emergency department with acute abdominal pain, vomiting and nausea. The patient complained of epigastric and left upper quadrant pain. While the patient did not have a history of any surgery, trauma or biliopancreatic disease, she was taking salbutamol 200 µg, valsartan 160 mg and hydrochlorothiazide 25 mg for chronic obstructive pulmonary disease and hypertension, respectively. On examination, the patient's blood pressure was 155/90 mmHg, heart rate 78 bpm and body temperature 37.2°C. Her abdominal examination did not reveal any signs of rigidity, rebound or pulsatile mass. Complete blood count (CBC) revealed a white blood count (WBC) of 14,550 cells/mm^3 (4.600-10.200 cells/mm^3) and haematocrit level of 32% (40%-54%). Her electrolytes, liver function tests, blood urea nitrogen and creatinine were normal. Plain abdominal X-ray and ultrasonography did not reveal any abnormality. Intravenous contrast-enhanced computed tomography (CT) scan revealed paraduodenal heterogeneity and fluid with an aneurysm that was 18 mm in diameter arising from the pancreaticoduodenal artery (Figure 1).

As the patient was haemodynamically stable and the diameter of the aneurysm was <20 mm, surgery was not considered. An urgent selective angiography of the coeliac artery was performed, and an actively bleeding PDAA was demonstrated. Additionally, stenosis of the celiac artery was observed. Aneurysm was selectively catheterised, and embolization of the proximal and distal parts was performed using multiple coils to block inflow and outflow blood flow (Figure 2).

During the period of hospitalisation, her vital signs were normal. In CBC, WBC decreased to 12.300/mm^3 and haematocrit was 30% at 12 hours after embolization.

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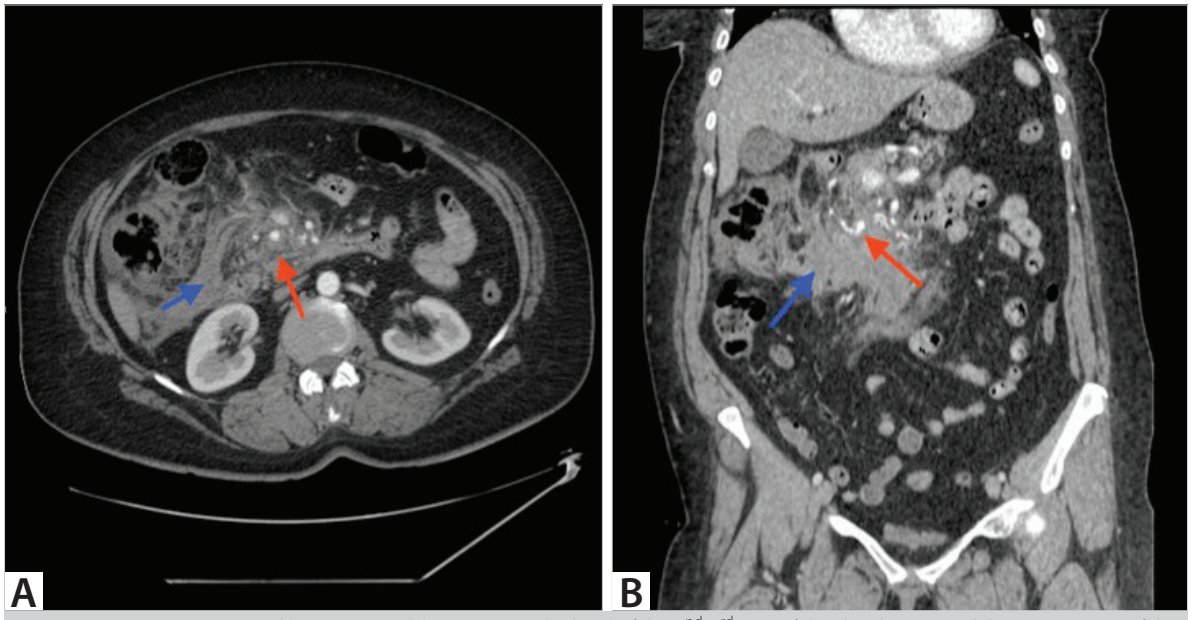

Figure 1. A-B. Retroperitoneal haematoma (blue arrow) at the level of the 2nd-3rd part of the duodenum and the appearance of the aneurysm originating from the pancreaticoduodenal artery at this level (red arrow).

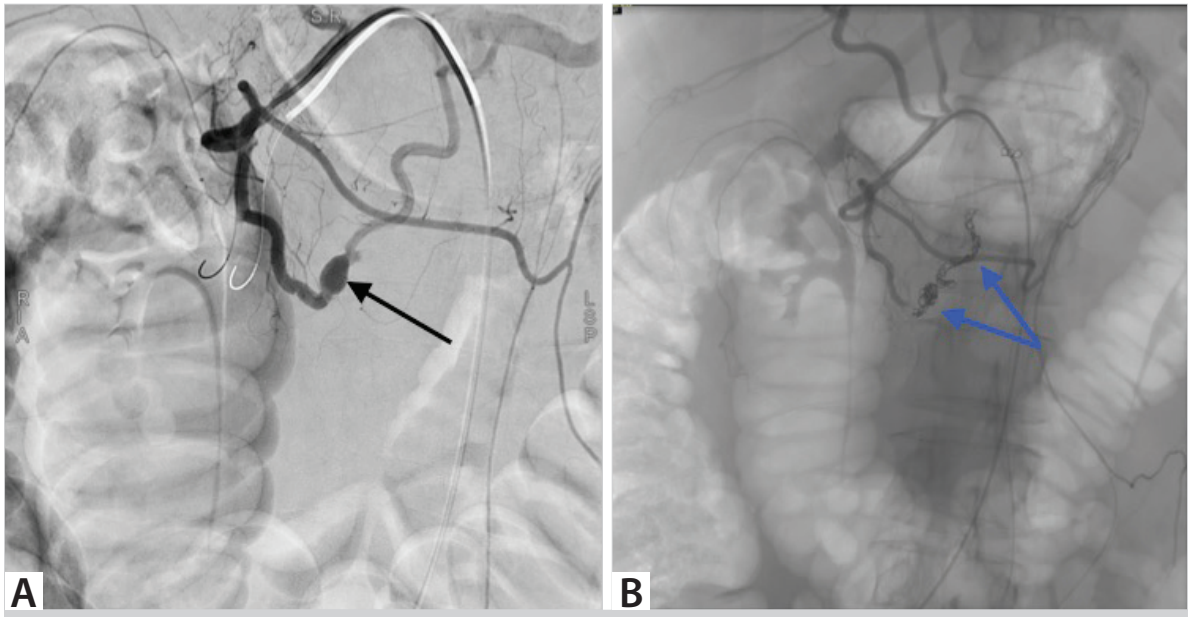

Figure 2. A. Appearance of the aneurysm on digital subtraction angiography (black arrow), **B.** After coil embolization (blue arrow).

On the second day, her WBC returned to normal levels and haematocrit remained stable. She was started on an oral liquid diet on the second day and given a normal salt-free diet on the third day. Her haematocrit level was 32%, and liver function tests, blood urea nitrogen, creatinine and electrolytes were normal on the third day. She was discharged on the fourth day of admission. She returned to our department one month later for follow up CT, which revealed resorption of the retroperitoneal haematoma with no signs of bleeding or aneurysm.

DISCUSSION

Aneurysms involving all layers of the arterial wall are defined as 'true aneurysms', which occur along with the narrowing of occlusive coeliac artery. If the aneurysm is caused by a breach in the inner layer of the arterial wall, it is called a 'pseudoaneurysm'. Congenital collagen deficiency and atherosclerosis are the most common causes of true aneurysms. False aneurysms may result from pancreatic inflammation, trauma and hepatobiliary vascular surgery (3,4). Our patient did not have a history of

any disease or surgery that could cause an aneurysm; however, she had stenosis of the celiac artery.

Clinical presentation of aneurysm varies. Abdominal pain is the most common symptom (52%), followed by gastrointestinal bleeding (24%), hypotension (22%) and pulsatile abdominal mass (6%). Nonspecific symptoms, including vomiting, nausea and diarrhoea are observed in 13% of the patients (2). Our patient had abdominal pain, mild hypotension, nausea and vomiting. Nevertheless, other common symptoms, such as bleeding of the gastrointestinal tract or pulsatile mass, were not seen. Only 26.6% of the patients with SAA are admitted to hospitals with symptoms, and 56.4% of these have ruptured aneurysms (5). Mortality rates are up to 30% in cases of rupture or emergent treatment of SAA (6,7).

Aneurysms can be diagnosed using CT, angiography or magnetic resonance imaging. Widespread use of cross-sectional imaging studies in the past decade has increased the number of patients diagnosed with aneurysm; however, most aneurysms are asymptomatic and are incidentally diagnosed (8). Our patient was diagnosed using a combination of CT and angiography.

Treatment indications for asymptomatic true SAA are aneurysm diameter >2 cm or three times greater than the normal arterial diameter and expansion of >0.5 cm/year, patients undergoing orthotropic liver transplantation, symptomatic patients and childbearing age women. Alternatively, false aneurysms should be treated immediately after diagnosis regardless of their characteristics because of the high risk of rupture. Watch and wait treatment can be used for incidentally diagnosed, non-complicated true aneurysms. False aneurysms have a 76.3% risk of rupture, whereas in true aneurysms, the risk is 3.1% (5). Our patient had a symptomatic aneurysm which was ruptured.

Multiple treatment modalities are used to treat aneurysms, including coil or glue embolization, stent grafting, Amplatzer plug, artery ligation, aneurysm resection, vascular resection with catheter bypass and en-bloc resection of adjacent organs. Non-surgical treatments have become more prevalent in recent years (5). Before 1980, the ratio of non-surgical treatment methods was approximately 3%. In lthe ast decades, non-surgical treatment options have increased; the rate of surgical treatment methods has been reduced due to technical difficulties and high morbidity. Embolization is more frequently used in contemporary practice. Due to difficulties in identifying and isolating aneurysms of the peripancreatic arteries intraoperatively, non-surgical treatment methods, including coil embolization or stent graft placement, have emerged as treatments of choice for most patients (2). If non-surgical techniques fail or the patient is haemodynamically unstable, surgical intervention should be considered as part of the preliminary plan. Since our patient had stable haemodynamic parameters and the aneurysm diameter was <20 mm, we preferred non-surgical treatment methods in accordance with the literature.

CONCLUSION

Developments in endovascular treatment methods have revolutionised the treatment of aneurysmal diseases. Difficult surgical approaches lead surgeons to less invasive, non-surgical treatment methods. This report demonstrates that diagnosis of SAA can be difficult and cause considerable mortality if diagnosed late.

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OLGU SUNUMU-ÖZET
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Pankreatikoduodenal arter anevrizması rüptürü, teşhisi zor, tedavisi zor: Bir olgu sunumu

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ÖZET

Splanknik arter anevrizmaları, boyutlarından bağımsız olarak yüksek rüptür riski taşıyan nadir vasküler lezyonlardır. Belirtiler basit bir karın ağrısından veya kusmadan, hemorajik şok gibi morbidite oluşturan duruma kadar değişebilir. Ancak anevrizmaların çoğu asemptomatiktir ve teşhis edilmesi güçtür. Burada coil embolizasyon ile tedavi edilen pankreatikoduodenal arter anevrizması rüptürü olan 56 yaşındaki bir kadın olguyu sunmaktayız.

Anahtar Kelimeler: Anevrizma, anjiyografi, coil-embolizasyon, pankreatikoduodenal arter, rüptür

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CASE REPORT
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Femoral artery aneurysm developed on intimal sarcoma: Case report

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ABSTRACT

Intimal angiosarcoma is a rare vascular malignancy, and diagnosis is very difficult due to nonspecific symptoms. There are controversial points regarding the diagnosis, treatment and follow-up of intimal angiosarcomas. The purpose of this case report was to evaluate the diagnosis and treatment process of a patient diagnosed with femoral artery intimal angiosarcoma. Furthermore, in line with previous studies, it was aimed to illuminate controversial points. A 33-year-old male patient, who had been operated on due to ruptured femoral artery aneurysm, was diagnosed with intimal angiosarcoma with the pathology result. Recurrence was observed during clinical follow-up, and the patient was treated with chemotherapy and radiotherapy. Since there was no response to treatment, the patient underwent aggressive surgery including the surrounding tissues. No recurrence or metastasis was observed in the patient's 10th month follow-up. Although intimal angiosarcoma is rare, it should be considered in differential diagnosis when femoral artery aneurysm is detected. The most important step in treatment is aggressive surgery, but adding chemo-radiotherapy to the treatment should be considered.

Keywords: Intimal angiosarcoma, surgery, chemo-radiotherapy

INTRODUCTION

Vascular malignancies are observed rarely, and angiosarcoma constitutes less than one percent of them, consisting of two subtypes: intimal type and mural type (1-3). Intimal angiosarcoma originates from the intimal layer of the arterial wall. It can develop at any level of the aorta and manifests different symptoms depending on its levels. Symptoms usually emerge as a result of stenosis, obstruction or thromboembolic events (3-5). It is difficult to diagnose intimal angiosarcoma due to nonspecific clinical presentation. In addition, intimal sarcoma diagnosed with femoral artery aneurysm is a very rare case. Surgery with negative tumour margins is a cornerstone of the intimal angiosarcoma treatment (6-7). It becomes apparent that chemotherapy and radiotherapy play a role in sarcoma treatment, but less attention has been paid to specific angiosarcoma treatment (8-13).

This case report attempted to shed light on how an intimal angiosarcoma case should be handled and addressed a number of dilemmas regarding diagnosis, treatment options and follow-up methods.

CASE REPORT

A 33-year-old male presented with a complaint of swelling and pain in the right groin for a month. His medical history and family history were not remarkable. On physical examination, the pulses of bilateral lower extremities were palpable, and the ankle arm pressure index was measured as 1.2 on the right and 1.3 on the left. Arterial Doppler ultrasound and Computed Tomography (CT) imaging revealed a ruptured right femoral artery aneurysm that was located 5.5 x 4.5 cm periphery of the right main femoral artery and was measured 7 mm at its thickest site (Figure 1).

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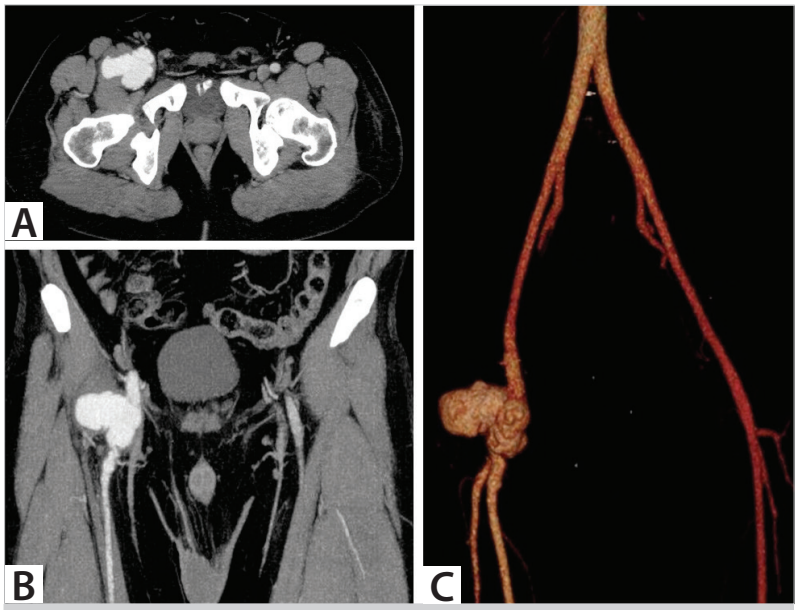

Figure 1. A. In the arterial phase extremity CT angiography, pseudo-aneurysm is observed in the right common femoral artery with an irregular wall in the right common femoral artery in the arterial phase at the level of the femoral neck. **B.** In the coronal CT reformat maximum intensity projection image, the contours and extension of the pseudo-aneurysm in the common femoral artery. **C.** In 3-D CT reformat image, the relationship between pseudo-aneurysm, neck and common femoral artery can be observed.

The abdominal aorta, main iliac and external iliac arteries were detected normal. The patient was investigated for systemic autoimmune diseases and vasculitis, and no remarkable result was obtained. In addition, the patient had no history of trauma.

The patient underwent aneurysmectomy, and common femoral artery reconstruction was performed with a synthetic ringed polytetrafluoroethylene (PTFE) graft by preserving the external iliac and deep femoral arteries. After the operation, distal pulses of the patient were palpable and the ankle arm pressure index was measured as 1.2 on the right. Pathological examination of the specimen revealed pleomorphic-undifferentiated sarcoma originating from the intima with Vimentin (+) and a margin greater than 1 cm (Figure 2). Thoracic CT and Positron Emission Tomography (PET) showed no distant metastasis. The patient was evaluated by the oncology unit after the surgery, and clinical follow-up was decided due to tumour free margin and no metastasis. In the third month of follow-up, the patient complained about swelling and pain in the right groin. Femoral artery pulses could not be measured on the right lower extremity. Magnetic Resonance Imaging (MRI) and PET imaging showed a relapse of sarcoma that was measured as 9 x 7 cm. Recurrent sarcoma was found to extend the iliac muscle at the level of the right iliac crest and encircled the deep and superficial femoral arteries 360 degrees. In addition, a 37 x 27 mm metastatic lesion at the level of the collum femoris and trochanter minor was detected (Figure 3). Chemo-radiotherapy was decided in order to perform surgical resection with a wider tumour negative margin.

Two cycles of chemotherapy at three-week intervals (150 mg Adriablastin + 6000 mg ifosfamide plus + 3000 mg mesna) and 28 Gy/8 fr radiotherapy were administered to the patient. During chemo-radiotherapy, deep vein thrombosis developed within the right femoral vein and subcutaneous enoxaparin sodium 2 x 8000 IU was initiated at the treatment dose. Surgery was decided since the MRI revealed no regression in the relapse lesion and metastatic lesions after chemotherapy, and surgical resection was considered possible in preoperative evaluation. Eight months after the first operation, the skin including the previous incision line, subcutaneous tissue, proximal femur and neighbouring muscles, external iliac artery and vein, and superficial femoral artery and vein were removed en bloc, and then vein ligation was performed (Figure 4). A femur prosthesis was placed for reconstruction and by-pass was performed with a synthetic ringed PTFE graft at the level of bifurcation between the main iliac artery proximally and superficial femoral artery distally. The femoral vein and main iliac vein were ligated (Figure 5). Plastic and reconstructive surgery was also included in the reconstruction part of the operation. A vertical pedicular rectus abdominis flap was removed to rideand left side of the deep inferior epigastric artery. The flag was transposed to the

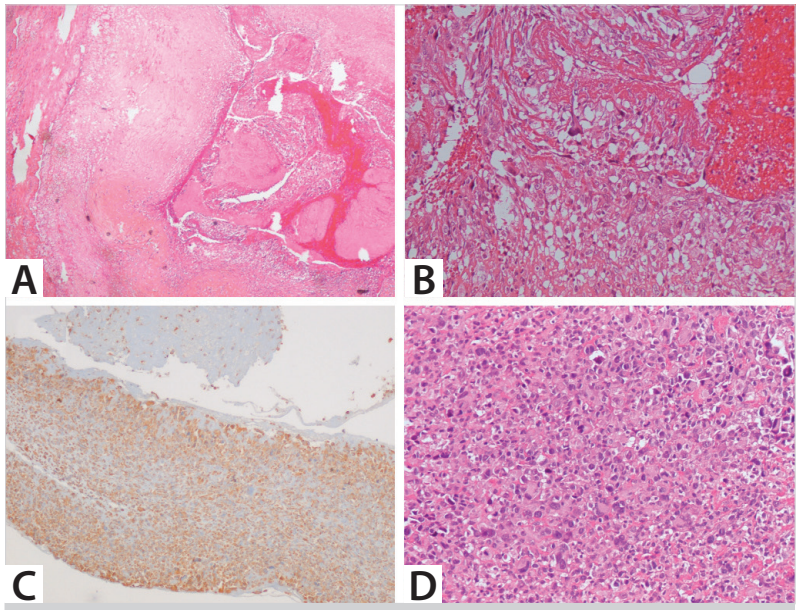

Figure 2. Thrombus in the vessel lumen and endovascular tumour with intimal component. **A.** Hematoxylin and eosin (HE), x100, **B.** HE, x200, **C.** Vimentin (+), x100, **D.** Pleomorphic malignant tumour cells (HE, x200).

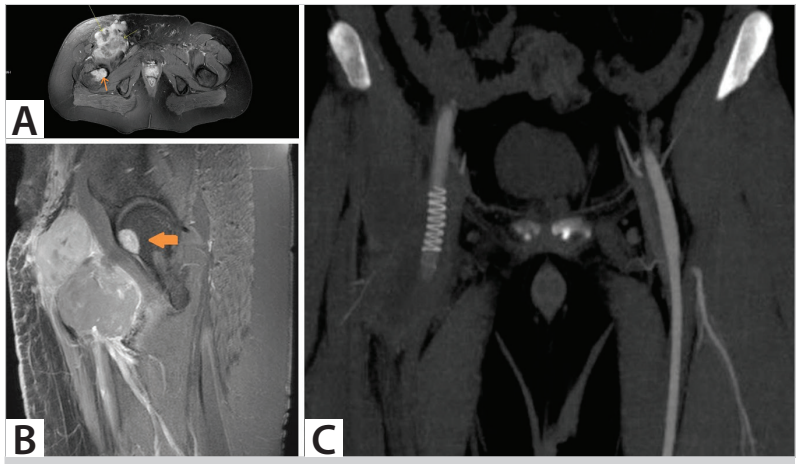

Figure 3. A. In contrast-enhanced MRI scan, in the axial MRI view of T1A sequence post contract fat suppression, common femoral artery (short yellow arrow), the central cystic-necrotic infiltrative mass lesion with dense heterogeneous contrast involvement in the pseudo-aneurysm region (long yellow arrow), metastatic lesion is observed in the medulla-trabecular area with intense contrast enhancement (orange arrow). **B.** In contrast-enhanced MRI scan, in the sagittal MRI view of T1A sequence post contract fat suppression, infiltrative, heterogeneous contrasting mass lesion and femoral head metastatic lesion (orange arrow). **C.** In the arterial phase extremity CT angiography, after endovascular stent graft inserted in the common femoral artery, the stent lumen open and the pseudo-aneurysm sac with thrombosis.

oncologic resection area. The flap of the left rectus abdominal muscle, skin and subcutaneous tissue, anterior region of the femoral prosthesis and the resection region were closed primarily (Figure 6).

Postoperatively, all pulses of the right lower extremity were palpable, and the ankle arm pressure index was measured as 1. In postoperative follow-up, flap circulation was good. Postoperatively, oral acetylsalicylic acid 100 mg, subcutaneous enoxaparin sodium 4000 IU and intermittent pneumatic compression

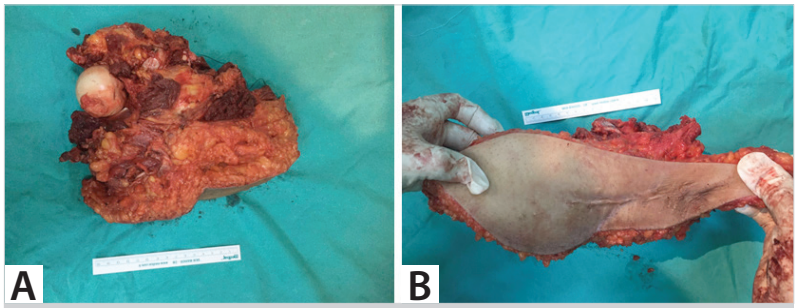

Figure 4. A. The clinical appearance of the wide resection specimen with the proximal part of the femur. **B.** The clinical appearance of the wide resection specimen with the proximal part of the femur.

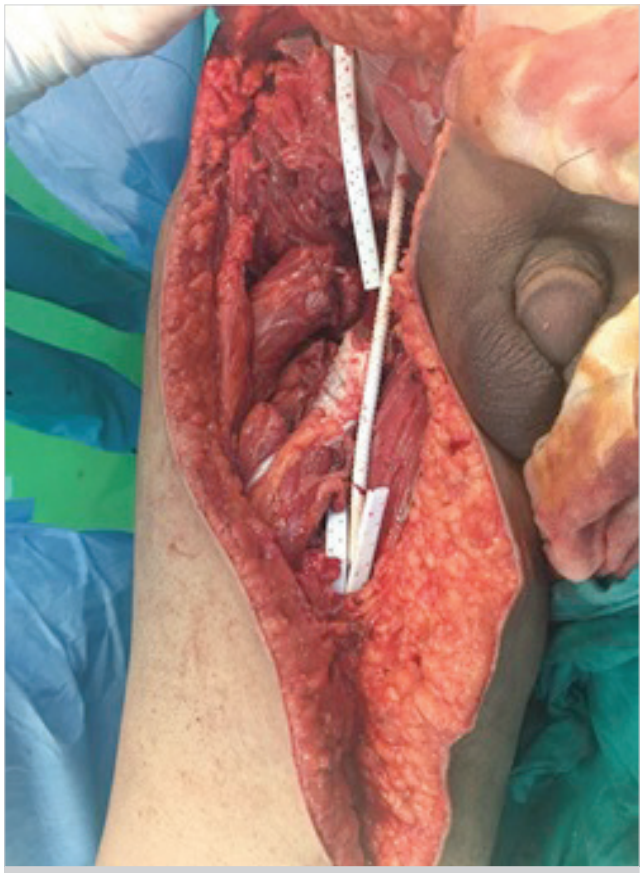

Figure 5. Postoperative picture of the resection area. Synthetic ringed polytetrafluoroethylene (PTFE) graft was placed between iliac artery and superficial femoral artery. The femoral vein and main iliac vein were ligated.

on bilateral lower extremities were initiated for DVT prophylaxis. Pathological examination reported an undifferentiated high grad sarcoma with 85% necrosis and negative surgical margins in vascular, soft tissue, bone tissue structures. The patient was discharged on postoperative day 10 with oral acetylsalicylic acid 100 mg/day. On control, distal pulses of the right lower extremity were palpable and ankle arm pressure index was 1.1.

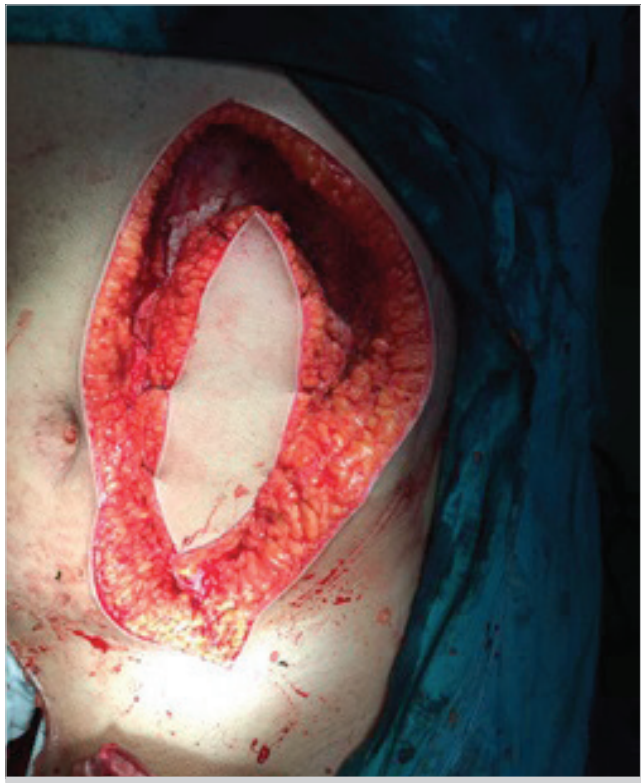

Figure 6. The flap of left rectus abdominal muscle, skin and subcutaneous tissue, anterior region of femoral prosthesis and resection region were closed primarily.

Two months after the second operation, the patient received paclitaxel 150 mg/week treatment for 12 weeks. No local relapse and distant metastasis were detected in the follow up control visit performed in the tenth month.

DISCUSSION

Intimal sarcomas are quite rare undifferentiated pleomorphic sarcomas originating from the tunica intima (1-3). According to the results of a review by Sebenik et al., 90% of intimal sarcomas originate from the aorta and 10% of them originate from the iliac and femoral arteries (4). Clinical findings vary depending

on the level of the affected vessel, whether there is stenosis in the aortic lumen or not, or whether thromboembolic metastasis developed or not. Intimal sarcomas form polypoid masses growing toward the lumen, which causes more commonly obstruction or thrombo-emboli symptoms (1-5). Diagnosis of intimal angiosarcoma is difficult due to non-specific clinic presentation and extreme rarity. Aortic angiosarcoma presents as an asymptomatic thoracic aneurysm, dyspnea, sudden death or distal embolization. However, the case of intimal sarcoma diagnosed with femoral artery aneurysm and/or arterial rupture is very rare in the literature. The present case was admitted to our clinic with non-specific complaints and was primarily investigated for vasculitis. Diagnostic approach for intimal angiosarcoma is based on a high degree of suspicion. An alternative explanation is that in the differential diagnosis of an aneurysm, which is not associated with vasculitis and traumatic status, intimal sarcomas should be considered.

While planning the treatment of intimal sarcoma, MRI is important for the assessment of local invasion and determining resectability whereas intravenous contrast CT is important in assessing distant metastasis. There are insufficient data on the use of PET scans in this type of tumour (5,6,13). Although there is no defined algorithm for the treatment of intimal sarcoma, aggressive surgical resection including neighbouring tissues is recommended in non-metastatic cases. Obtaining negative surgical margin is the most important factor for the prevention of relapse, which is fostered by some local recurrence studies (6,7). From this point of view, it appears that frozen section (FS) examination is also recommended for the assessment of resection intra-operatively. In the first operation, FS was not performed because it was not evaluated as intimal sarcoma. Diagnosis of intimal sarcoma was made after surgery, and no additional surgical intervention was considered since the surgical margin was greater than 1 cm. In a study conducted by Alamanda et al., positive surgical margin has been shown to increase relapse rates by 12-38% over a six-year follow-up (7). Re-resection should be performed, if possible, in patients with surgical margin positivity. Administration of radiotherapy is recommended if re-resection is not possible (8,9).

The efficacy of radiotherapy and chemotherapy in case of intimal sarcomas is contradictory. However, there are studies indicating that chemotherapy and radiotherapy administered after surgery have positive effects on survival (10,11). In addition, recent literature on extremity soft tissue sarcoma stresses that preoperative chemo-radiation improved overall survival and disease-free survival, but it is not a standard treatment (10). Beane JD et al. have shown that postoperative RT improves local control in high-grade lesions such as intimal sarcoma tumours, but its effect on overall survival has not been demonstrated (12). On the other hand, previous research has mostly tended to focus on soft tissue sarcoma rather than on intimal angiosarcoma. In our case, it was decided to continue with adjuvant chemotherapy and radiotherapy after early recurrence, but a satisfactory response could not be obtained. Therefore, en bloc resection including bone, soft tissue and vessels was performed.

There is limited data available in the literature on surveillance strategies for intimal angiosarcoma. There is no exact data about which imaging method is better for follow-up. During the first-year follow-up, MRI for local recurrence and CT for distant metastasis may be preferred every four to six months. In this case, no evidence of relapse was found in the 10-month follow-up period.

CONCLUSION

We presented a rare femoral angiosarcoma case, which was treated with chemo-radiotherapy and was operated aggressively to achieve tumour negative margins. When femoral artery aneurysm is detected in patients with non-specific symptoms, intimal sarcoma should be considered in differential diagnosis. The most important step in treatment is aggressive surgery, but adding chemo-radiotherapy to the treatment should be considered.

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Femoral arter anevrizmasından gelişen intimal anjiyosarkom: Olgu sunumu

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ÖZET

İntimal anjiyosarkom nadir görülen vasküler bir malignitedir ve spesifik olmayan semptomlar nedeniyle tanı konulması oldukça zordur. İntimal anjiyosarkomların tanısı, tedavisi ve takip süreciyle ilgili tartışmalı noktalar bulunmaktadır. Bu olgu sunumunun amacı femoral arter intimal anjiyosarkom tanısı konulan hastanın tanı ve tedavi sürecini değerlendirmek ve daha önce yapılmış olan çalışmalar doğrultusunda tartışmalı noktaları aydınlatabilmektir. Rüptüre femoral arter anevrizma saptanarak ameliyat edilen 33 yaşında erkek hastanın patoloji sonucu intimal anjiyosarkom olarak geldi. Takiplerinde nüks gelişen hasta öncelikle kemoterapi ve radyoterapi tedavisi gördü. Tedaviye yanıt alınamaması üzerine hastaya çevre dokuları da içerecek şekilde agresif bir cerrahi yapıldı. Hastanın 10. ay kontrollerinde nüks ve metastaz saptanmadı. İntimal anjiyosarkom nadir görülse de femoral arter anevrizması saptandığında ayırıcı tanıda akla getirilmelidir. Tedavide agresif cerrahi önemlidir ancak kemo-radyoterapinin de tedaviye eklenmesi düşünülmelidir .

Anahtar Kelimeler: İntimal anjiyosarkom, cerrahi, kemo-radyoterapi

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The use of Bakri balloon to reduce the anastomosis tension in hepaticojejunostomy

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ABSTRACT

One of the factors that impair anastomosis healing in patients undergoing hepaticojejunostomy is tension of the anastomosis. There may be tension, especially in cases with a short mesojejunum. In cases where the jejunum cannot be brought higher, positioning the liver a little lower may be a solution. We placed a Bakri balloon between the liver and diaphragm to position the liver to a lower level. Here we present a successful hepaticojejunostomy case in which we placed a Bakri balloon to decrease the anastomosis tension.

Keywords: Bakri balloon, hepaticojejunostomy, anastomosis tension

INTRODUCTION

Performing a hepaticojejunostomy operation has certain difficulties, especially in cases with a short mesojejunum. Although it is tried to be performed at the most proximal site as possible where the mesojejunum is longest, this mesojejunum may not be sufficient to perform a tension-free anastomosis in some patients. As it is known, the tightness of the anastomosis in hepaticojejunostomy operations increases the rate of postoperative bile leakage (1). Therefore, additional methods may be required to reduce anastomotic pressure. Placing a sterile gauze between the liver and the diaphragm during anastomosis is one of the methods that facilitates anastomosis. However, removing this sterile gauze after anastomosis has taken place will cause an increase in tension in the anastomosis. Therefore, there is a need for a tool that can be driven behind the liver and removed later, not only during the anastomosis but also after the operation, until the anastomosis heals.

CASE REPORT

Bakri balloon is a device that can be used vaginally in uterine bleeding. This intrauterine balloon is kept in the uterus during bleeding and acts as a tamponade to stop the bleeding (2). We also thought of placing the Bakri balloon between the liver and the diaphragm since it is large, can be easily placed during the operation and can be easily removed after the operation when desired. To reduce the tension of the anastomosis, it was inflated with 500 cc saline intraoperatively by placing it between the liver and the diaphragm in a patient with a short mesojejunum (Figure 1). In this way, the distance between the liver and the jejunum was shortened, and the anastomosis could be performed without tension. Operation was terminated by leaving the Bakri balloon in place. No complications developed during the follow-ups, and no bile leakage was observed (Figure 2). The Bakri balloon was completely emptied and withdrawn on the seventh day of the operation. The patient was discharged, and no problems were observed in the follow-ups of the patient.

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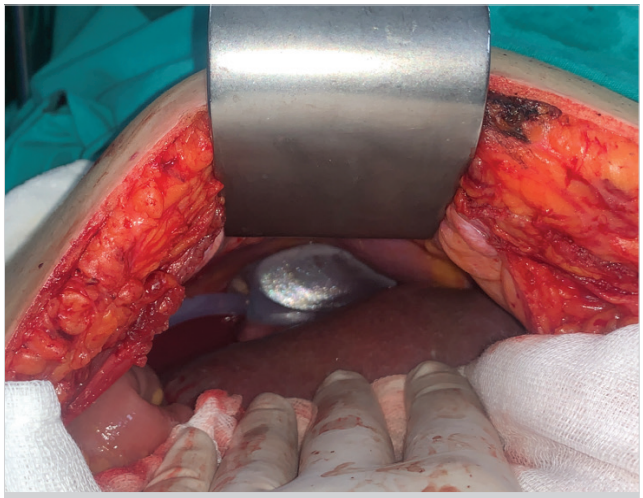

Figure 1. Bakri balloon placed between the diaphragm and the liver.

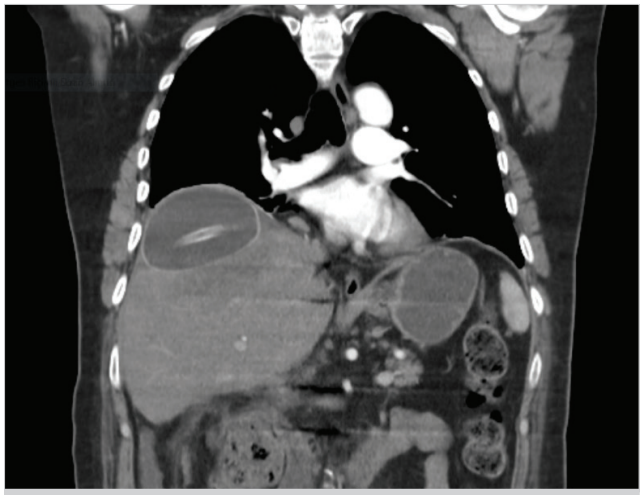

Figure 2. Postoperative CT image showing the Bakri balloon between the diaphragm and the liver.

DISCUSSION

We assert that this method can be used safely in anastomosis with a tension, especially in patients with a short mesojejunum.

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CERRAHİ TEKNİK-ÖZET
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Hepatikojejunostomi anastomoz gerginliğini azaltmak için Bakri balon kullanımı

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ÖZET

Hepatikojejunostomi yapılacak olgularda anastomoz iyileşmesini bozan faktörlerden birisi de anastomozun gergin olmasıdır. Özellikle kısa mezojejunumu olan olgularda gergnilik olabilmektedir. Jejunumun daha yukarı getirilemediği durumlarda karaciğeri bir miktar aşağıya konumlamak bir çözüm olabilir. Karaciğeri daha aşağı bir seviyeye konumlandırmak için karaciğer ile diyafram arasına bir Bakri balonu yerleştirdik. Burada anastomoz gerginliğini azaltmak için Bakri balonu yerleştirdiğimiz başarılı bir hepatikojejunostomi olgusunu sunmaktayız.

Anahtar Kelimeler: Bakri balon, hepatikojejunostomi, anastomoz gerginliği

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