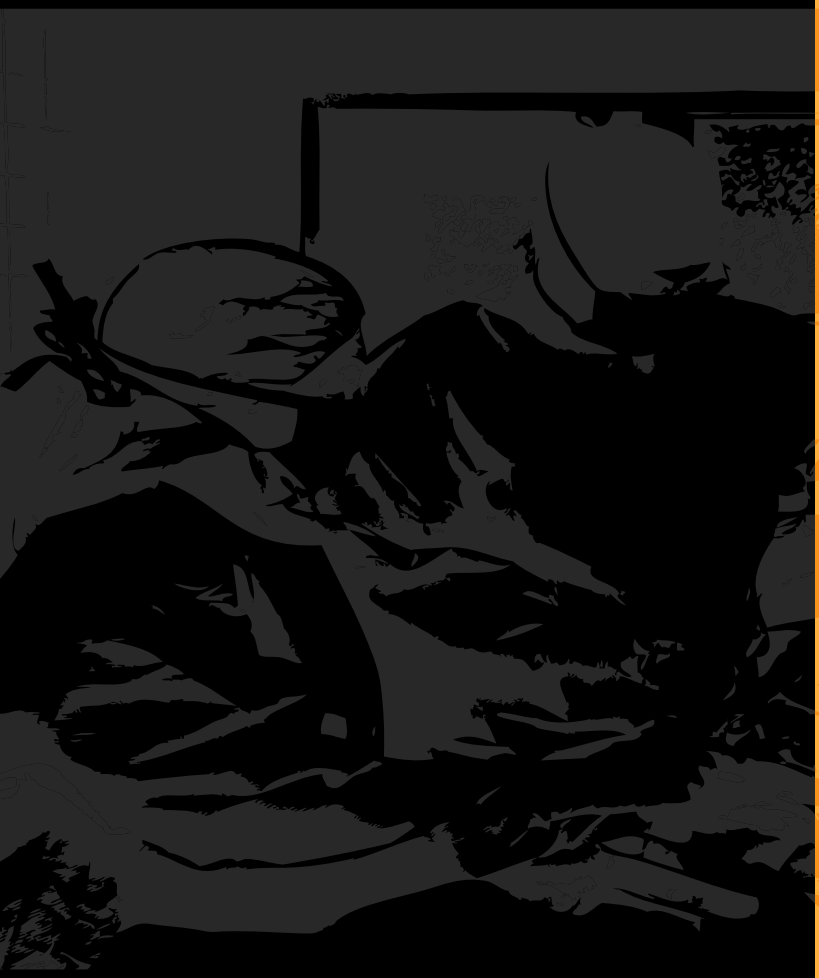
ISSN 2564-6850
E-ISSN 2564-7032

Indexed in PubMed, Web of Science and Scopus

TURKISH JOURNAL OF SURGERY



VOL. 34 | ISSUE 4
DECEMBER 2018

turkjsurg.com

TURKISH JOURNAL OF SURGERY

Türk Cerrahi Derneği adına sahibi ve Sorumlu Yazı İşleri Müdürü/Owner on behalf of the Turkish Surgical Association and Responsible Manager: Seher Demirer • Yayın türü / Publication Type: Yerel süreli / Local periodical • Basım yeri / Printed at: Matsis Matbaa Hizmetleri San. ve Tic.Ltd.Şti, Tevfikbey Mah., Dr. Ali Demir Cad. No: 51, 34290 Sefaköy, Turkey (+90-212-624 21 11) • Basım tarihi / Printing Date: Aralık 2018 / December 2018 • Türk Cerrahi Derneği tarafından yayınlanmaktadır / Published by Turkish Surgical Association, Koru Mah. Ihlamur Cad. No:26 Çayyolu-Çankaya, Ankara, Turkey +90 (312) 241 99 90

Contact
Address: Koru Mah. Koru Sitesi, Ihlamur Cad. No: 26 06810 Çayyolu, Ankara, Türkiye
Phone: +90 312 241 99 90 Fax: +90 312 241 99 91 editor@turkjsurg.com

Publisher / Yayıncı
İbrahim KARA

Publication Director
Ali ŞAHİN

Finance and Administration
Zeynep YAKIŞIRER

Deputy Publication Director
Gökhan ÇİMEN

Editorial Development
Gizem KAYAN

Publication Coordinators
Betül ÇİMEN
Özlem ÇAKMAK
Okan AYDOĞAN
İrem DELİÇAY
Nergis KALKAN
Arzu YILDIRIM

Project Assistants
Ecenur ASLIM
Doğan ORUÇ
Sinem KOZ

Graphics Department
Ünal ÖZER
Deniz DURAN
Beyzanur KARABULUT

Contact:
Adres/Address: Büyükdere Cad. 105/9
34394 Mecidiyeköy, Şişli, İstanbul
Telefon/Phone: +90 212 217 17 00
Faks/Fax : +90 212 217 22 92
E-posta/E-mail: info@avesyayincilik.com

TURKISH JOURNAL OF SURGERY

International Editorial Board

TURKISH JOURNAL OF SURGERY

TURKISH JOURNAL OF SURGERY

TURKISH JOURNAL OF SURGERY

TURKISH
JOURNAL
OF SURGERY

TURKISH JOURNAL OF SURGERY

Aims and Scope

Turkish Journal of Surgery (Turk J Surg) is the official, peer reviewed, open access publication organ of the Turkish Surgical Association, Turkish Hepatopancreatobiliary Surgery Association and Turkish Association of Endocrine Surgery (TAES). The financial expenses of the journal are covered by the Turkish Surgical Association. The journal is published quarterly on March, June, September and December and its publication language is English.

The aim of 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, ethics, surgical education and forensic medicine fields are included in the journal.

The journal is a surgical journal that covers all specialities and its target audience includes academicians, practitioners, specialists and students from all specialities 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).

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

Processing and publication are free of charge with the journal. No fees are requested from the authors at any point throughout the evaluation and publication process. All manuscripts must be submitted via the online submission system, which is available at www.turkjsurg.com. The journal guidelines, technical information, and the required forms are available on the journal's web page.

All expenses of the journal are covered by the Turkish Surgical Association.

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 Association, editors, editorial board, and/or publisher; the editors, editorial board, and publisher disclaim any responsibility or liability for such materials.

All published content is available online, free of charge at www.turkjsurg.com.

The journal is printed on an acid-free paper.

OPEN ACCESS

Editor in Chief: Prof. Mustafa ŞAHİN
Address: Koru Mah. Koru Sitesi, Ihlamur Cad. No: 26 06810 Çayyolu, Ankara, Turkey
Phone: +90 (312) 241 99 90
Fax: +90 (312) 241 99 91
E-mail: editor@turkjsurg.com

Publisher: AVES
Address: Büyükdere Cad. 105/9 34394 Mecidiyeköy, Şişli, İstanbul, Turkey
Phone: +90 212 217 17 00
Fax: +90 212 217 22 92
E-mail: info@avesyayincilik.com
Web page: avesyayincilik.com

TURKISH JOURNAL OF SURGERY

Instructions to Authors

Turkish Journal of Surgery (Turk J Surg) is the official, peer reviewed, open access publication organ of the Turkish Surgical Association, Turkish Hepatopancreatobiliary Surgery Association and Turkish Association of Endocrine Surgery (TAES). The financial expenses of the journal are covered by the Turkish Surgical Association. The journal is published quarterly on March, June, September and December and its publication language is English.

The aim of 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, ethics, surgical education and forensic medicine fields are included in the journal.

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

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 that have been submitted to another journal for evaluation and rejected for publication. The submission of previous reviewer reports will expedite the evaluation process. Manuscripts that have been presented in a meeting should be submitted with detailed information on the organization, including the name, date, and location of the organization.

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

An approval of research protocols by the Ethics Committee in accordance with international agreements (World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects," amended in October 2013, www.wma.net) 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 should be included that shows that written informed consent of patients and volunteers was obtained following a detailed explanation of the procedures that they may undergo. 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, the 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 the patients' anonymity. For photographs that may reveal the identity of the patients, releases signed by the patient or their legal representative should be enclosed.

All submissions are screened by a similarity detection software (iThenticate by CrossCheck).

In the event of alleged or suspected research misconduct, e.g., plagiarism, citation manipulation, and data falsification/fabrication, the Editorial Board will follow and act in accordance with COPE guidelines.

Each individual listed as an author should fulfill the authorship criteria recommended by the International Committee of Medical Journal Editors (ICMJE - www.icmje.org). The ICMJE recommends that authorship be based on the following 4 criteria:

1- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
2- Drafting the work or revising it critically for important intellectual content; AND
3- Final approval of the version to be published; AND
4- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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 specific other 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.

Turkish Journal of Surgery requires corresponding authors to submit a signed and scanned version of the authorship contribution form (available for download through www.turkjsurg.com) during the initial submission process in order to act appropriately on authorship rights and to prevent ghost or honorary authorship. If the editorial board suspects a case of "gift authorship," the submission will be rejected without further review. As part of the submission of the manuscript, the corresponding author should also send a short statement declaring that he/she accepts to undertake all the responsibility for authorship during the submission and review stages of the manuscript.

Turkish Journal of Surgery requires and encourages the authors and the individuals involved in the evaluation process of submitted manuscripts to disclose any existing or potential conflicts of interests, including financial, consultant, and institutional, that might lead to potential bias or a conflict of interest. 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.

The Editorial Board of the journal handles all appeal and complaint cases within the scope of COPE guidelines. In such cases, authors should get in direct contact with the editorial office regarding their appeals and complaints. When needed, an ombudsperson may be assigned to resolve cases that cannot be resolved internally. The Editor in Chief is the final authority in the decision-making process for all appeals and complaints.

When submitting a manuscript to Turkish Journal of Surgery, authors accept to assign the copyright of their manuscript to Turkish Surgical Association. If rejected for publication, the copyright of the manuscript will be assigned back to the authors. Turkish Journal of Surgery requires each submission to be accompanied by a Copyright Transfer Form (available for download at www.turkjsurg.com). When using previously published content, including figures, tables, or any other material in both print and electronic formats, authors must obtain permission from the copyright holder. Legal, financial and criminal liabilities in this regard belong to the author(s).

Statements or opinions expressed in the manuscripts published in Turkish Journal of Surgery reflect the views of the author(s) and not the opinions of the editors, the editorial board, or the publisher; the editors, the editorial board, and the publisher disclaim any responsibility or liability for such materials. The final responsibility in regard to the published content rests with the authors.

MANUSCRIPT PREPARATION

The 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 the 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 where the editorial office staff will 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:

- Copyright Transfer Form,
- Author Contributions Form, and
- ICMJE Potential Conflict of Interest Disclosure Form (should be filled in by all contributing 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 and this page 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, and Tables, Figures, Images, and other media are not included.

Review Articles: Reviews prepared by authors who have extensive knowledge on a particular field and whose scientific background has been translated into a high volume of publications with a high citation potential 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 stud-

ies. 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 that constitute challenges in diagnosis and treatment, those offering new therapies or revealing knowledge 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.

Surgical Methods: Images of remarkable, striking and rare cases that emphasize the basic mechanisms of diagnosis and treatment of diseases, express discrepancies and extraordinary situations and explain new treatment techniques and options are evaluated for publication. Display items are important in this type of manuscripts and supporting the manuscript with video (in WMV, AVI or MPEG formats) images can facilitate a faster evaluation process and increase the possibility of publication.

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, and Tables, Figures, Images, and other media should not be included. The text should be unstructured. The manuscript that is being commented on must be properly cited within this manuscript.

Tables

Tables should be included in the main document, presented after the reference list, and they should be 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 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 they should be 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. 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." In the main text of the manuscript, references should be cited using Arabic numbers in parentheses. 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: 709-711.

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

Book Section: Suh KN, Keystone JS. Malaria and babesiosis. Gorbach SL, Barlett JG, Blacklow NR, editors. Infectious Diseases. Philadelphia: Lippincott Williams; 2004.p.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/ncidodIEID/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.

Editor in Chief: Prof. Mustafa ŞAHİN
Address: Koru Mah. Koru Sitesi, Ihlamur Cad. No:26 06810 Çayyolu, Ankara, Turkey
Phone: +90 (312) 241 99 90
Fax: +90 (312) 241 99 91
E-mail: editor@turkjsurg.com

Publisher: AVES
Address: Büyükdere Cad. 105/9 34394 Mecidiyeköy, Şişli, İstanbul, Turkey
Phone: +90 212 217 17 00
Fax: +90 212 217 22 92
E-mail: info@avesyayincilik.com
avesyayincilik.com

TURKISH JOURNAL OF SURGERY

Contents

Original Investigations

Case Reports

TURKISH JOURNAL OF SURGERY

TURKISH JOURNAL OF SURGERY

Editorial

Dear Colleagues,

With the publication of the December 2018 issue of the Turkish Journal of Surgery, its 34th volume has been completed. In order to enable our journal to be scanned in national and international indices and to be followed by our colleagues from either our country or abroad, we made some decisions 2 years ago and changed the journal format and publishing approach.

Firstly, the journal was started to be published completely in English. Some measures were taken to facilitate the submission process of the manuscripts and to speed up the evaluation process of these studies. Both domestic and international colleagues were contacted and the number of articles submitted to our journal was increased.

As a result of the studies and practices, the journal's being followed on the internet increased 4-fold and significant increases were observed in the flow of manuscripts. Essentially, there have been a significant increase in citation rate of the articles published in our journal.

At this point, our esteemed colleagues have a great share. We urge you to continue to give us the support that you have given so far by sending your clinical and experimental studies to our journal and by referring to the articles published in our journal.

The fact that our journal is being followed and scanned in international indices in the surgical branch and in scientific publishing will be the common success of all of us.

I would like to express my gratitude to the Editorial Board, reviewers, the staff of the association, AVES employees for their contribution to the problem-free and successful publications and to the executive board of the Turkish Association of Surgery for their financial support they provide.

I wish everyone a happy new year with the hope that the future will be more beautiful than the past.

Best regards,

Prof. Dr. Mustafa ŞAHİN
Editor in Chief

Turk J Surg 2018; 34(4): 259-263
DOI: 10.5152/turkjsurg.2018.4019

Original Article

Gastrointestinal stromal tumors: A clinical and histopathological presentation of 27 cases

Doğan Gönüllü[1], Okan Demiray[1], Serkan İlgün[1], Ufuk Mete Yıldız[1], Mehmet Lari Gedik[2], Muzaffer Er[1], Ayşenur İğdem[3], Elife Kimiloglu[3], Ferda N. Köksoy[1]

ABSTRACT

Objective: Gastrointestinal stromal tumors (GISTs) are mesenchymal tumors that express type 3 tyrosine kinase receptors and are thought to develop from the neoplastic transformation of the interstitial Cajal cells. The present study was performed to morphologically and immunohistologically evaluate GISTs, to compare their qualities using a GIST risk categorization system, and to identify the diagnostic and prognostic parameters of GISTs.

Material and Methods: A total of 27 patients with GISTs underwent treatment and were followed up at the Gaziosmanpaşa Taksim Training and Research Hospital. Descriptive statistics was used to calculate the mean and median values. Survival analysis was performed by the Kaplan–Meier method. The analyses were performed using the SPSS version 22.0 software.

Results: The mean follow-up time was 3.5 (5 months to 13 years) years. The mean age was 60.4 (29–82) years. The tumors were localized in the stomach (62.9%), extraintestinal areas (14.8%), intestine (7.4%), esophagus (7.4%), and rectum (7.4%). Twenty-four patients were classified according to the Fletcher system. Of these patients, 7 (25.9%) were classified as very low risk, 8 (29.6%) as low risk, 7 (25.9%) as intermediate risk, and 2 (7.4%) as high risk. Twenty-four patients underwent surgery. Of the 3 patients who did not undergo surgery, 1 had metastatic disease at the time of diagnosis, and 2 had mini- or micro-GISTs in the stomach. On endoscopic surveillance, all tumors remained stable. Three out of the 27 patients were lost to follow-up. Two patients developed recurrence, and 1 patient died of GIST.

Conclusion: We analyzed the clinical and pathological characteristics of GIST. The most common site of tumor origin was the stomach. The size, mitotic index, and Ki-67 values were to be found high in intermediate- and high-risk groups and metastatic diseases.

Keywords: Gastrointestinal stromal tumor, interstitial Cajal cells, mesenchymal tumors, tyrosine kinase receptor mutation

ORCID IDs of the authors:
D.G. 0000-0002-8232-5209;
O.D. 0000-0001-6920-7585;
S.İ. 0000-0002-4862-2891;
U.M.Y. 0000-0002-4482-0225;
M.L.G. 0000-0002-0440-9394;
M.E. 0000-0001-8578-1229;
A.İ. 0000-0002-3047-1546;
E.K. 0000-0002-2708-1272;
F.N.K. 0000-0002-5878-7489.

Cite this paper as:
Gönüllü D, Demiray O, İlgün S, Yıldız UM, Gedik ML, Er M, et al. Gastrointestinal stromal tumors: A clinical and histopathological presentation of 27 cases. Turk J Surg 2018; 34(4): 259-263.

[1]Department of General Surgery, University of Health Sciences, Gaziosmanpaşa Taksim Training and Research Hospital, İstanbul, Turkey

[2]Department of General Surgery, Ministry of Health, Fatsa State Hospital, Ordu, Turkey

[3]Department of Pathology, University of Health Sciences, Gaziosmanpaşa Taksim Training and Research Hospital, İstanbul, Turkey

This study was presented at the 36th Congress of the European Society of Surgical Oncology, 14-16 September 2016, Krakow, Poland.

Corresponding Author
Doğan Gönüllü
e-mail: dogangonullu@yahoo.com

Received: 08.11.2017
Accepted: 07.02.2018
Available Online Date: 11.09.2018

INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are mesenchymal tumors that express type 3 tyrosine kinase receptors and are thought to develop from the neoplastic transformation of the interstitial Cajal cells (intestinal pacemaker cells on the intestinal wall) or their precursors (1-3). Mutation of the tyrosine kinase receptor (c-Kit/CD117) in precursor tumors causes uncontrolled growth. Approximately 95% of sporadic GISTs are positive for CD117, 60% to 70% positive for CD34, and 30% to 40% positive for smooth muscle actin, whereas negative for S100 protein and desmin (3, 4). KIT gene mutation is specific to gastric stromal tumors in the intramembranous component of the tyrosine kinase receptor (exon 11) and in the extramembranous component (exon 9) as well as to tumors located in the intestines and colon, which reportedly have a worse prognosis (3, 5-7). Patients with exon 11 mutation (63.0%–83.5%) have been shown to have better responses to imatinib (Gleevec; Novartis Pharma AG, Basel, Switzerland) than patients with exon 9 mutation (34.0%–47.8%) (3, 8, 9). In patients without KIT mutation, platelet-derived growth factor receptor-alpha (PDGFRα) mutation should be considered, and these types of stromal tumors frequently have epithelioid qualities (5, 10). GISTs positive for both KIT and PDGFRα mutations have not been reported; however, tumors that are negative for both markers reportedly constitute approximately 10% of all GISTs and are predominantly located in the stomach (2, 5, 9). A highly specific marker, DOG1 (discovered on GIST-1), has been started to be used for c-Kit-negative stromal tumors (2).

The purpose of the present study was to morphologically and immunohistochemically evaluate GISTs, to compare their qualities using the GIST risk categorization table established by Fletcher et al. (11), and to determine the important parameters for the diagnosis and prognosis of GISTs.

MATERIAL AND METHODS

In total, 27 patients with GISTs underwent surgical treatment and were followed up at the Gaziosmanpaşa Taksim Training and Research Hospital from 2002 to 2016. The study was conducted in accordance with the ethical standards set by the Declaration of Helsinki. Informed consent was obtained from all individual

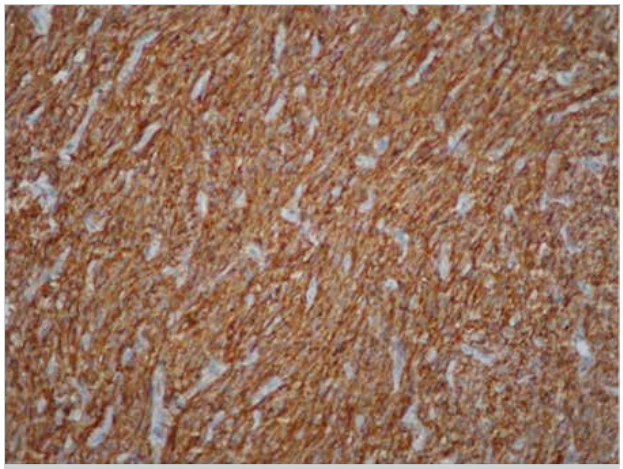


Figure 1. CD117 staining of a gastrointestinal stromal tumor (×200 magnification)

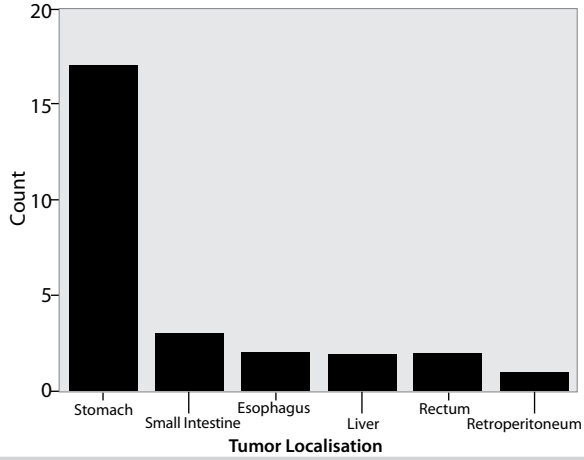


Figure 2. Locations of gastrointestinal stromal tumors

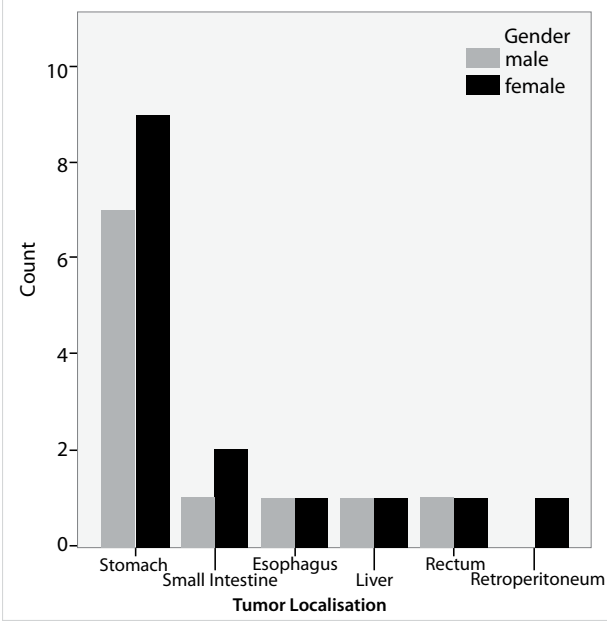


Figure 3. Risk groups according to the Fletcher classification

participants included in the study. Hematoxylin and eosin staining and immunohistochemical markers, such as c-Kit, CD34, and Ki-67, were used to diagnose GISTs (Figure 1). Risk groups and other prognostic parameters were reported (Figure 1). On clinical presentation, the median follow-up time was 3.5 (5 months to 13 years) years. Patients in the high-risk group were monitored using an abdominal ultrasonography and a computed tomography every 3 to 6 months for the first 3 years and every 6 months for the following 5 years. Descriptive statistics was used to calculate the mean and median values. Survival analysis was performed by the Kaplan–Meier method. The analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 22.0 software (IBM Corp., Armonk, NY, USA).

RESULTS

The female-to-male ratio was 5:4. The mean age was 60.4 (29–82) years. Five tumors were incidentally diagnosed in patients undergoing surgery for other reasons, such as gastric cancer, sigmoid volvulus cancer, colon cancer, renal cancer, and ovarian cancer. Seventeen (62.9%) tumors were localized in the stomach, 4 (14.8%) in the extraintestinal areas (2 in the mesentery and 2 in the liver), 2 (7.4%) in the intestine, 2 (7.4%) in the esophagus, and 2 (7.4%) in the rectum (Figure 2). Twenty-four patients were classified according to the Fletcher system (3 patients were classified as stage 4). Of all 27 patients, 7 (25.9%) were classified as very low risk, 8 (29.6%) as low risk, 7 (25.9%) as intermediate risk, and 2 (7.4%) as high risk (Figure 3).

The mean Ki-67 of the patients with stage 4 cancer was 15.6 (7–25), whereas it was 9.6 (2–25) for both intermediate and high-risk patients. The Ki-67 level was >7% in all patients with metastatic GISTs but in only 6 (54%) of the intermediate and high-risk patients. The Ki-67 staining ratio was <1% for 7 (25.9%) patients, 2%–7% for 13 (48.1%) patients, and >7% for 7 (25.9%) patients. Staining was not observed in >7% of the tumors located in the esophagus; however, staining >7% was observed in only 1 patient among those with intestinal tumors (Figure 4).

The mean tumor diameter was 5.45 (0.5–18) cm, and the largest tumors were observed among those with an extraintestinal localization (average tumor diameter: 13.2 (8–18) cm) (Figure 5). Seven tumors were <2 cm, 3 were classified as micro-GISTs (<1 cm), and 4 were classified as mini-GISTs (1–2 cm).

Fifteen (55.5%) tumors were spindle cell tumors, 7 (25.9%) were epithelioid tumors, and 5 (18.5%) were mixed form tumors (Figure 6). Nine of the 17 GISTs located in the stomach were spindle cell tumors. All esophageal tumors were epithelioid tumors, and tumors localized in the colon or extraintestinal regions were either spindle cell tumors (75%) or epithelioid tumors (25%).

Three out of the 27 patients were lost to follow-up. Two patients developed recurrent disease, and one died of GIST. The 5-year survival rate was 89.3% (Figure 7). Twenty-four (88.8%) patients underwent surgery. Of the 3 patients who did not undergo surgery, 1 had metastatic disease at the time of diagnosis, and 2 had a mini- or micro-GIST localized in the stomach. On endoscopic surveillance, the tumors remained stable. All patients with high-risk disease and metastatic disease underwent imatinib treatment.

DISCUSSION

Gastrointestinal stromal tumors are rare and constitute <1% of the primary tumors of the gastrointestinal system, 2.2% of the stomach tumors, 13.9% of the intestinal tumors, and 0.1% of the colorectal tumors (12). GISTs are most frequently located in the stomach (50%–60%), intestine (20%–30%), colon and rec-

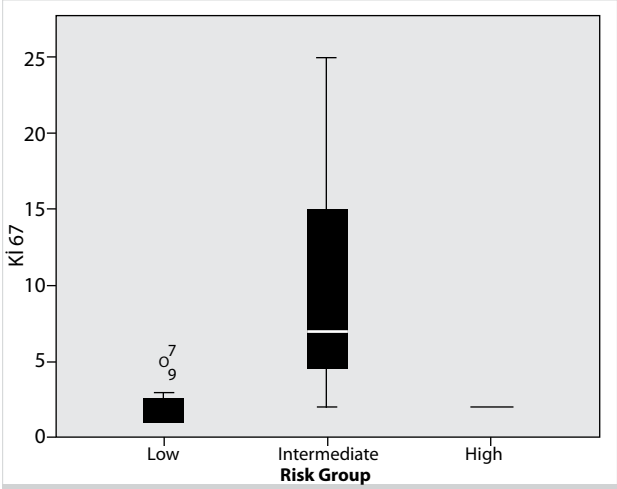


Figure 4. Correlations between Ki-67 index and risk group

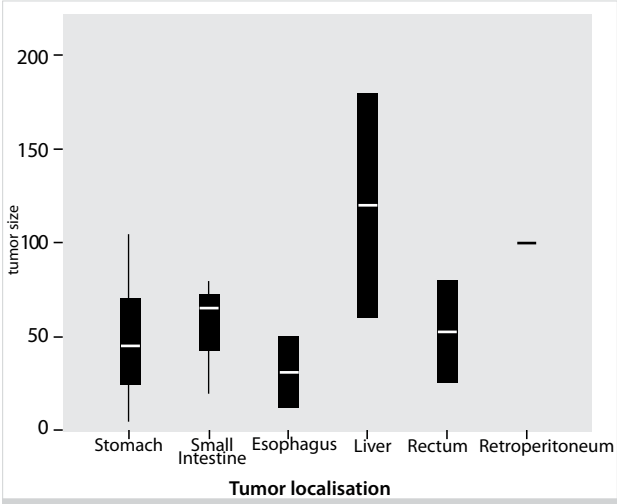


Figure 5. The mean size of gastrointestinal stromal tumors

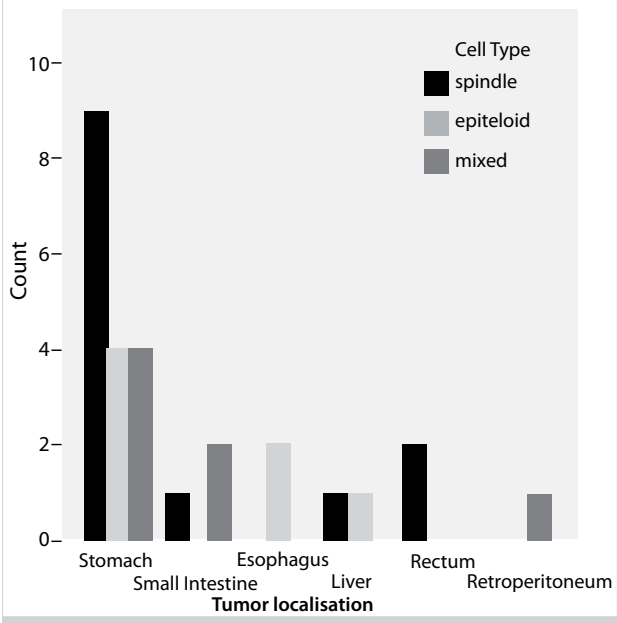


Figure 6. Histological types of gastrointestinal stromal tumors

tum (10%), and esophagus (5%). They are rarely located in the extraintestinal regions, such as the mesentery, omentum, and retroperitoneum (5%) (13). GISTs in the bladder and gallbladder have only been described in case reports (14). Consistent with the literature, most GISTs in our series were localized in the stomach (62%), yet our high ratio of extraintestinal GISTs (14.8%, 4 liver and retroperitoneal tumors) is a different finding.

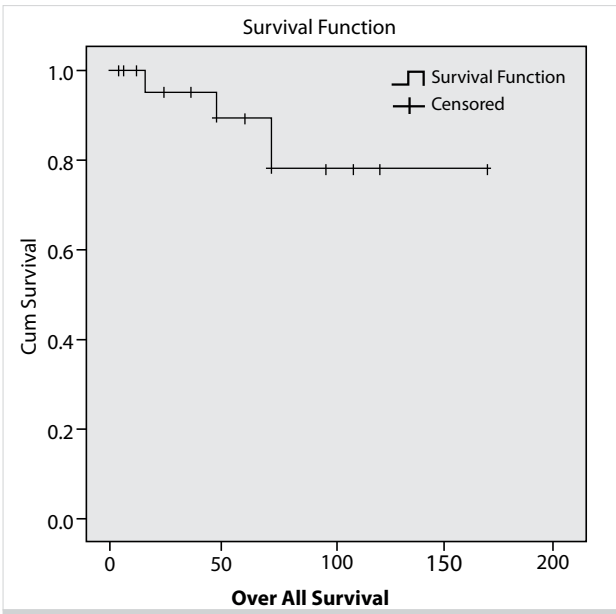


Figure 7. The 5-year survival rate

Gastrointestinal stromal tumors are equally observed in both sexes. They are more frequent between aged 50 and 70 years. However, the development of GISTs in pediatric patients has also been reported (9). The incidence of GISTs in a Swedish study was 13 per million (15). In other studies, the annual incidence in North America was 3.2 to 7.0 per million, whereas that in Hong Kong was 15 to 20 per million (2). Most GISTs (80%) are found incidentally; only a small ratio is observed as a component of a familial disease (e.g., neurofibromatosis type 1 and Carney complex) (9).

Gastrointestinal stromal tumors were historically classified as soft tissue sarcomas (e.g., leiomyosarcoma, leiomyoma, and leiomyoblastoma) owing to their CD34 staining, but the c-Kit mutation was demonstrated in 1990, after which the term "GIST" began to be used more frequently as a tumor group separate from leiomyosarcoma, schwannoma, and neurofibroma, all of which are c-Kit-negative (4). The Armed Forces Institute for Pathology reviewed 1765 patients who were diagnosed with smooth muscle tumors from 1979 to 1996 and classified 94% of them as GISTs (2, 3).

Histologically, GISTs are classified as spindle cell tumors (70%), epithelioid cell tumors (20%), and mixed-type tumors, which are rarely observed. Spindle cell tumors are large in volume, most frequently localized in the stomach and intestines, exhibit KIT and PDGFRα mutations, and respond well to treatment with imatinib mesylate. In contrast, the epithelioid subtype is less frequently observed, does not exhibit KIT and PDGFRα mutations, and co-occurs with lymph node metastases. Spindle cell tumors were observed in 55.5% (n=15) of the patients, epithelioid in 25.9% (n=7) of the patients, and mixed in 18.5% (n=5) of the patients in the present study. Nine of the 17 GISTs were spindle cell tumors, whereas all esophageal tumors were epithelioid. Of those located in the colon or extraintestinally,

75% were spindle cell tumors, and 25% were epithelioid tumors. In contrast to previous studies, mixed tumors had larger volumes in the present study (average diameter: 6.8 cm). c-Kit and CD34 were positive in 86.6% of the spindle cell tumors, and CD34 was negative in 2 tumors. Additionally, 54.1% of the epithelioid tumors were positive for both c-Kit and CD34. One case was c-Kit-negative, and the other case was CD34-negative. Among the mixed tumors, c-Kit/CD34 staining was positive in 80% of the cases, whereas 1 tumor was CD34-negative.

The prognosis and prognostic factors of GISTs have long been the subject of debates. Many parameters have been discussed, but four risk groups were recently accepted based on the tumor size and mitotic index (11). In addition to these two parameters, mucosal invasion, presence of tumor necrosis, increased cellularity, and immunohistochemical markers of cell proliferation (Ki-67, MIB-I, PCNA, and DOG) have been considered as other potentially effective factors in the evaluation of malignancy risk.

The Ki-67 proliferative index is not included among the accepted prognostic factors, yet many studies (15, 16) have revealed that it is more valuable than the mitotic index. Nilsson et al. (16) found that in patients with a Ki-67 index >7, GIST recurrence is observed in 63%, and 47% die of this tumor. On the other hand, in patients with a Ki-67 index <7, the recurrence rate was only 4%, and only 1% died of the tumor. Zhao et al. (15) suggested that patients with a Ki-67 index >8 respond less to treatment with tyrosine kinase inhibitors. In our series, the Ki-67 index was >7% in 7 patients who were classified as low risk (n=1), intermediate risk (n=3), high risk (n=1), and phase 4 (n=2) based on the Fletcher stratification.

Extraintestinal GISTs develop from multipotent stem cells, which are the precursors of the interstitial Cajal cells. Immunohistochemical studies have shown that they are CD117-positive, and according to a previous study, they constitute 10% of all GISTs (17). In the 2012 San Francisco Gastrointestinal Cancers Symposium, Guye et al. (18) reported that based on the Surveillance, Epidemiology and End-Results records, 261 out of the 2951 patients who underwent surgery from 1996 to 2008 had extraintestinal GISTs with a higher average diameter and were in advanced stages. The 5-year survival rate was 32% for extraintestinal GISTs and 49% for GISTs (18). Their report suggested that extraintestinal localization is an independent factor for a poor prognosis. In our series, 4 patients had extraintestinal tumors, 3 had spindle cell tumors, and 1 had an epithelioid stromal tumor. All cases were CD34- and CD117-positive, with an average diameter of 13.2 (8–18) cm. Two had necrosis, and the Ki-67 ratio was 14.8% (2%–25%). Two were localized in the liver (one was intermediate risk and the other was stage 4 with lung and adrenal metastases). Three were localized in the retroperitoneum or mesentery (intermediate and high risk). Recurrence was observed after 1 year in 1 patient with an intermediate-risk tumor. These patients were followed up for an average of 4 (1–6) years, and all were alive at the time of the present study.

Although GISTs reach a larger volume than other gastrointestinal tumors with adenocarcinoma qualities, they do not lead to lymphatic metastasis, making surgical procedures easier and the prognosis more favorable (8). Their biological behavior varies; only 10% to 30% of all GISTs progress to malignancy (13). There is still a lack of consensus on prognostic factors, but the risk classification described by Fletcher et al. (11) is an accepted guideline (18). Tumors displaying malignant behaviors are assessed by tumor size and the mitotic index per 50 high power field (HPF). When the tumor diameter alone is evaluated, a diameter <5 cm generally indicates a good prognosis, whereas a diameter >5 cm signifies a malignant prognosis. A mitotic index >5/50 HPF suggests malignancy. However, these parameters have been shown to vary according to localization, and Miettinen et al. (19) of the Armed Forces Institute of Pathology added the GIST localization to the parameters indicated by Fletcher et al. (11). In our series, the use of the Fletcher classification revealed that 25.9% (7/27) of the cases were very low risk, 29.0% (8/27) were low risk, 25.9% (7/27) were intermediate risk, and 7.4% (2/27) were high risk.

The Memorial Sloan–Kettering Cancer Clinic has developed prognostic nomograms for calculating the 2-year and 5-year recurrence-free rates by evaluating the tumor diameter, mitotic index, and localization findings (2, 3).

The fundamental treatment method for most GISTs is surgical resection with clear surgical margins. The extreme fragility of the tumor requires special attention to prevent its rupture (8, 13) during the procedure with resultant intra-abdominal seeding. If the tumor ruptures, and if there is no indication for the tyrosine kinase inhibitor imatinib, then it should be noted as an epicrisis and brought to the oncologist's attention; such cases are considered for imatinib treatment regardless of the Fletcher classification (8). Since the possibility of lymphatic metastasis is low in patients with sporadic GISTs (8, 13), lymphadenectomy is not necessary (2, 8, 13, 20, 21). However, case reports have indicated that the rate of lymph node metastasis is higher in pediatric patients with GISTs that are c-Kit- and PDGFRα-negative, multifocal, or familial (22-24).

Laparoscopic procedures are not recommended for especially large tumors (8). Radiotherapy is ineffective (9). After surgical treatment, recurrence is observed mostly in the peritoneum (50%), liver (65%), or both (13). A review of the previous study suggests that omental tumors recur frequently, and this may be due to rupture and unseen implants. De Matteo et al. (25) reported that among their patients who underwent R0 resection, 35% have local recurrence, and 44% had local recurrence with liver metastases. The tumor diameter is more important than the surgical margin negativity for local recurrence according to their results. We observed recurrence in 2 of the patients. In the first patient, a Fletcher low-risk epithelioid tumor in the stomach fundus was treated by proximal gastrectomy, and recurrence developed at the resection line 4 years later despite the fact that the surgical margin was negative. In the second patient who was determined to have a retroperitoneal spindle cell tumor with intermediate risk, recurrence developed 1 year later and displayed high-risk tumor qualities. Interestingly, two neuroendocrine tumors, each with a diameter of 1 cm, were incidentally detected in the intestine of the second patient.

The 5-year overall survival rate was 63% for patients with low-risk tumors (<5 cm) and 34% for those with high-risk tumors (>10 cm) in the present study (26).

Patients with high-risk tumors (>5 mitoses/50 HPF, tumor diameter >5 cm, tumor rupture during surgery, or R1-type resection and exon 11 mutation) are considered for adjuvant treat-

ment (8). In the present series, 5 out of the 27 patients had high-risk stage 4 GISTs according to the Fletcher classification and received imatinib treatment.

We were able to surgically treat 88.8% (24/27) of the patients, and the 5-year survival rate was 89.3%. Most of the tumors were resectable at the point of diagnosis. Most of the tumors (62.9%) were located in the stomach, and 81.4% (22/27) of the patients were classified as very low, low, or intermediate risk based on the Fletcher criteria. All of these factors can explain the high survival rate. De Matteo et al. (25) reported a 54% survival rate and 45% 5-year remission rate following radical surgery (R0).

CONCLUSION

We analyzed the clinical and pathological characteristics of GIST admitted and treated during the past 13 years. The most common site of tumor origin was the stomach. The size, mitotic index, and Ki-67 values were found to be high in intermediate- and high-risk groups and metastatic diseases.

Ethics Committee Approval: Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects" (amended in October 2013).

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - D.G., O.D., S.I.; Design - D.G., O.D., A.I., E.K.; Supervision - M.E., F.N.K., M.L.G.; Resource - D.G., O.D., E.K.; Materials - D.G., A.I., E.K., M.L.G.; Data Collection and/or Processing - F.N.K., S.I., M.L.G., O.D.; Analysis and/or Interpretation - D.G., F.N.K., S.I.; Literature Search D.G., O.D., F.N.K., A.İ.; Writing Manuscript - D.G., O.D., S.I.; Critical Reviews - M.E., A.İ., E.K.

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

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

REFERENCES

1. Pidhoreeky I, Chency RT, Kraybill WG, Gibbs JF. Gastrointestinal stromal tumors:current diagnosis, biologic behavior, and management. Ann Surg Oncol 2000: 7; 705-712. [CrossRef]
2. Valsangkar N, Sehdev A, Misra S, Zimmers TA, O'Neil BH, Koniaris LG. Current management of gastrointestinal stromal tumors: Surgery, current biomarkers, mutations, and therapy. Surgery 2015; 158: 1149-1164. [CrossRef]
3. Lai EC, Lau SH, Lau WY. Current management of gastrointestinal stromal tumors-A comprehensive review. Int J Surg 2012; 10: 334-340. [CrossRef]
4. Fletcher CD, Berman JJ, Corless C, Gorstein F, Lasota J, Longley BJ, et al. Diagnosis of Gastrointestinal Stromal Tumors: A consensus Approach. Human Pathology 2002; 33: 459-465. [CrossRef]
5. Neeta Somaiah. Gastrointestinal stromal tumors: optimizing therapy throughout the course of disease. Available from URL: www.clinicaloptions.com/oncology. 2015
6. Lasota J, Corless CL, Heinrich MC, Debiec-Rychter M, Sciot R, Wardelmann E, et al. Maria Debiec-Rychter, Sciot R, Eva W. Clinicopathologic profile of gastrointestinal stromal tumors (GISTs) with primary KIT exon 13 or exon 17 mutations: a multicenter study on 54 cases. Mod Pathol 2008; 21: 476-484. [CrossRef]
7. Taniguchi M, Nishida T, Hirota S, Isozaki K, Ito T, Nomura T, et al. Effect of c-kit Mutation on Prognosis of Gastrointestinal Stromal Tumors. Cancer Res 1999; 59: 4297-4300.
8. Anna Nasierowska-Guttmejer. Gastrointestinal stromal tumors. In Rutkowski P, ed. Soft Tissue Sarcomas. Copyright Via Media: 2016, p: 126-52.
9. Gabriella A. Expression profiling of gastrointestinal stromal tumors biomarkers for prognosis and therapy (MSD Thesis). University of Gothenburg; 2012.
10. Local treatment for gastrointestinal stromal tumors. Available from URL: www.up to date.com
11. Fletcher CD, Berman JJ, Corless C, Gorstein F, Lasota J, Longley BJ, et al. Diagnosis of gastrointestinal stromal tumors: a consensus approach. Int J Surg Pathol 2002: 10: 81-89. [CrossRef]
12. Thomas RM, SobinLH. Gastrointestinal cancer incidence and prognosis by histologic type, SEER population based data 1973-1983. Cancer 1995: 75; 154-170. [CrossRef]
13. Michael S, Emmanouel D, Charikleia S, Panagiotis S, Electra P, Georgia L, Michael S. Gastrointestinal stromal tumor. W J of Surg Oncol 2009; 7: 61. [CrossRef]
14. Ortiz-Hidalgo C, de Leon Bojorge B, Albores Saavedra J. Stromal tumor of the gallblader with phenotype of interstitial cells of Cajal. A previous unrecognized neoplasm. Am J Surg Pathol 2000: 24: 1420-1423. [CrossRef]
15. Zhao WY, Xu J, Wang M, Zhang ZZ, Tu L, Wang CJ, et al. Prognostic value of Ki 67 index in gastrointestinal stromal tumors. Int J Clin Exp Pathol 2014; 7: 2298-2304.
16. Nilsson B, Bümming P, Meis-Kindblom JM, Oden A, Dortok A, Gustavsson B, et al. Gastrointestinal stromal tumors :the incidence, prevalence, clinical course, and prognostication in the prematinibmesylat era, a population based study in western Sweden. Cancer 2005; 15; 103; 821-829. [CrossRef]
17. Xiao-Li Luo, Dan Liu, Jian-Jun Yang, Min-Wen Zheng, Jing Zhang, Xiao-Dong Zhou. Primary gastrointestinal stromal tumor of the liver: A case report. World J Gastroenterol 2009; 7; 15: 3704-3707. [CrossRef]
18. Guye ML. Extraintestinal location for primary non-metastatic GIST associated with increased risk for death. 2012 Gastrointestinal Cancers Symposium. San Fransisco.
19. Miettinen M, Leslie H. Sobin, Maarit Sarlomo-Rikala. Immunohistochemical Spectrum of GISTs at Different Sites and Their Differential Diagnosis with a Reference to CD117 (KIT). Mod Pathol 2000; 13: 1134-1142. [CrossRef]
20. Fletcher CD. Risk aggressive behavior in GIST's. Human Pathology 2002; 33: 459-65. [CrossRef]
21. D'Amato G, Steinert DM, McAuliffe JC, Trent JC. Update on biology and therapy of gastrointestinal stromal tumours. Cancer Control 2005; 12: 44-56. [CrossRef]
22. Shafizad A, Mohammadianpanah M, Nasrolahi H, Mokhtari M, Mousavi SA. Lymph Node Metastasis in Gastrointestinal Stromal Tumor (GIST): to Report a Case. Iranian J of Cancer Prevention 2014: 7: 171-175.
23. Otto C, Agaimy A, Braun A, Rädecke J, Hoeppner J, Illerhaus G, et al. Multifocal gastric gastrointestinal stromal tumors (GISTs) with lymph node metastases in children and young adults: A comparative clinical and histomorphological study of three cases includinga new case of Carney triad. Diagn Pathol 2011; 6: 52. [CrossRef]
24. Agaimy A, WünschPH. Lymph node metastasis in gastrointestinal stromal tumours (GIST) occurs preferentially in young patients <or=40 years: An overview based on our case material and the literature. Langenbecks Arch Surg 2009: 394: 375-381. [CrossRef]
25. DeMatteo RP, Lewis JJ, Leung D, Mudan SS, James M W, Brennan MF. Two Hundred Gastrointestinal Stromal Tumors Recurrence Patterns and Prognostic Factors for Survival. Ann Surg 2000: 231: 51-58. [CrossRef]
26. Besana-Ciani I, Boni L, Dionigi G, Benevento A, Dionigi R. Outcome and long term results of surgical resection for gastrointestinal stromal tumors (GIST). Scand J Surg 2003; 92: 195-199. [CrossRef]

Turk J Surg 2018; 34(4): 264-270
DOI: 10.5152/turkjsurg.2018.3888

Original Article

Management of iatrogenic bile duct injuries: Multiple logistic regression analysis of predictive factors affecting morbidity and mortality

Ela Ekmekcigil[1], Ömer Ünalp[1], Alper Uğuz[1], Ruslan Hasanov[1], Halil Bozkaya[2], Timur Köse[3], Mustafa Parıldar[2], Ömer Özütemiz[4], Ahmet Çoker[1]

ABSTRACT

Objective: Iatrogenic bile duct injuries remain a challenge for the surgeons to overcome. The predictive factors affecting morbidity and mortality are important for determining the best management modality.

Material and Methods: The patients who referred to Ege University Faculty of Medicine after laparoscopy associated iatrogenic bile duct injury are grouped according to Strasberg–Bismuth classification system. The type and number of prior attempts, concomitant complications, and treatment modalities are analyzed using the SPSS version 18 (IBM, Chicago, IL, USA). The variables with $p<0.10$ were considered for univariate analysis and then evaluated for predictive factors by forward Logistic Regression method using multiple logistic regression analysis.

Results: According to the analysis of 105 patients who were referred during 2004–2014, the type and number of prior attempts are considered predictive factors in sepsis. In multiple logistic regression analysis, abscess formation, concomitant vascular injury, and serum bilirubin level are significantly effective in predicting mortality.

Conclusion: The management of iatrogenic bile duct injuries should be carefully planned with a multidisciplinary approach. The predictive factors affecting morbidity and mortality are important in determining the best modality for managing iatrogenic bile duct injuries. Abscess formation, vascular injury, and serum bilirubin level are the potential risk factors. Therefore, we can strongly recommend immediate assessment of patients for prompt diagnosis and referring to an HPB center, to avoid further injuries.

Keywords: Bile duct injury, laparoscopy, predictive factors

Cite this paper as: Ekmekcigil E, Ünalp Ö, Uğuz A, Hasanov R, Bozkaya H, Köse T, et al. Management of iatrogenic bile duct injuries: Multiple logistic regression analysis of predictive factors affecting morbidity and mortality Turk J Surg 2018; 34(4): 264-270.

[1]Department of General Surgery, Ege University University School of Medicine, İzmir, Turkey

[2]Department of Interventional Radiology, Ege University University School of Medicine, İzmir, Turkey

[3]Department of Biostatistics and Medical Informatics, Ege University University School of Medicine, İzmir, Turkey

[4]Department of Gastroenterology, Ege University University School of Medicine, İzmir, Turkey

This study was presented at the 11th E-AHPBA congree in Manchester 21-24 August 2015, United Kingdom.

Corresponding Author
Ela Ekmekcigil
e-mail: eekmekcigil@gmail.com

Received: 25.10.2017
Accepted: 30.11.2017
Available Online Date: 28.08.2018

INTRODUCTION

Iatrogenic bile duct injuries (IBDI) are important and serious complications that develop during laparoscopic cholecystectomy. Currently, more than 75% of cholecystectomies are performed laparoscopically and the frequency of IBDI is observed between 0.3% and 1.4% (1-6).

The prognosis of the injury has a broad spectrum. The clinical process that is observed with mild symptoms may lead to an increase in morbidity in which the survival expectancy decreases and the quality of life deteriorates (7, 8). What determine the prognosis in IBDI are the predictive factors that are effective on perioperative morbidity and mortality (9). The experience of the surgeon, advanced age and male gender, the presence of biliary duct anomalies, and local findings accompanied by severe inflammation and fibrosis are the risk factors known to cause IBDI (10, 11). The introduction of effective factors on the injury process will guide the surgeons in determining a distinguished treatment method. The aim of our study is to make a contribution to the optimum treatment approach in this regard by presenting effective risk factors on morbidity and mortality.

MATERIAL AND METHODS

In the Department of General Surgery, Ege University, Faculty of Medicine where the study was conducted; an average of 200 hepatopancreatobiliary patients including liver transplants, tumor resections and reconstructions are performed each year. The study was performed retrospectively with 105 patients who were transferred to our clinic as a tertiary center from multiple centers due to IBDI which developed during laparoscopic cholecystectomy between 2004 and 2014. Our study has been carried out in accordance with the Helsinki declaration.

Obtaining the Data

The patients' data were reached through the computer-registry system with hospital data-base. Data base was established on the basis of demographic data, initial symptoms, surgical interventions applied in patients prior to the admission to our center after injury, level and type of injury, accompanying complications, and perioperative outcomes obtained with the treatment methods that were applied at the tertiary center.

Patient Groups

Injuries following the interventions in biliary tract (such as ERCP, PTC), injuries caused by trauma and malignant disease, blunt/penetrant injuries, and injuries caused by hepatectomy/gastrectomy were not included in our study group. The patients undergoing laparoscopic cholecystectomy due to cholelithiasis were included in the study.

Patients were divided into three groups based on the number of interventions applied at the external center and on the appropriate treatment method chosen afterwards.

Group 1: Patients transferred to our clinic with the diagnosis of bile duct injury after laparoscopic cholecystectomy.
Group 2: Patients who were transferred to our clinic after surgical intervention in an external center for repair due to bile duct injury.
Group 3: Patients who were transferred to our clinic due to bile duct injury and treated with endoscopic and percutaneous methods.

Surgical methods were performed in the patients of the first group for therapeutic purposes in our clinic. Patients in the second group are the patients who were transferred after one or more surgical interventions for the purpose of repair and who were reoperated for treatment. The third group consisted of patients in whom non-surgical techniques (ERCP, PTC) were performed for treatment (Table 1).

Clinical Features

Findings that enabled the surgeon to notice the condition of injury in the postoperative period were analyzed through physical examination features and by grouping the data obtained from the imaging methods.

Parameters were established with gender characteristics, age-average and age groups (≤60, >60y), serum bilirubin values and bilirubin scoring index (<2 mg/dL, 2-10 mg/dL, >10 mg/dL). The effect of complication development (abscess development, hepatic and vascular injury, intestinal organ injury) on the prognosis was analyzed in the postoperative treatment period. Sepsis status was identified in the presence of clinical and microbiological infection and analyzed in patients with systemic inflammatory response syndrome (SIRS) criteria (12).

Surgical methods applied by the hepatobiliary surgeon for the purpose of repair before and after the transfer were analyzed and evaluated in terms of the effect on prognosis in the postoperative period.

Classification

The cases were classified according to the injury type and anatomic location on the basis of the Strasberg - Bismuth classification system (13). The prognostic effect of the level of injury was evaluated and the data used in the statistical analysis were grouped. Groups were formed as minor injuries (type A and type D), as major (types E1 and E2) and as complicated major injuries (type E3, type E4 and type E5).

The patients who were examined in terms of vital function findings and single / multiple organ failure were assessed with the Clavien - Dindo scoring system in order to determine the severity of complications according to postoperative treatment plan (14).

Surgical Treatment

The operation methods we preferred in our clinic for repair after the transfer of the patients and the methods performed in the external center before the transfer were analyzed in order to provide homogeneous analysis in the statistical evaluation by creating the same groups.

Non-surgical methods (such as PTC, ERCP) were primarily used for therapeutic purposes in minor type injuries in which main biliary duct continuity is mostly protected. In case of failure; T-tube placement with choledochotomy was preferred in limited injuries in the lateral surface of the duct in the distal part of the main hepatic duct (type D). In major injuries; in cases with proximal location and in which hepatic junction is preserved (type E1-E2), Roux-en-Y hepaticojejunostomy was performed. Roux-en-Y hepaticojejunostomy was performed to maintain the continuity of bilio-enteric tract in more proximal injuries (type E3-type E4-type E5) in which the integrity of main hepatic duct junction deteriorated. However, if there was a distance bigger than 1 cm between the mouths of injured hepatic duct, the ducts were made ready for anastomosis by bringing them together with sutures on the same plane using the 'double barrel technique'. In the case of complicated injuries in which the hilar sheath integrity deteriorated, hepaticojejunostomy was performed using the 'segment 3 approach'.

The mouth of the hepatic duct to be anastomosed was prepared taking into account the principle that the injured hepatic duct mucosa should reach the proximal end, where it is sufficiently vascularized. Intestinal orifice prepared narrower than the diameter of hepatic duct on the antimesenteric face of jejunum with distance at 20th cm from ligamentum of Treitz.Hepatic duct mouth was anastomosed one by one using 4/0-5/0 absorbable monofilament suture material to establish an integrity with the jejunum mucosa without any tension on the line using end-to-side anastomosis technique, and routine use of biliary stent was not preferred in the cases.

Statistical Analysis

Clinical parameters generated by computer-based data recording system were analyzed using SPSS-PASW statistics version 18.0 for Windows (SPSS Inc.; Chicago, IL, USA). Numerical variables of the groups were compared with the Kruskal Wallis and Mann Whitney U tests. The data were analyzed with Pearson x2 test and Fisher's exact test in univariate analysis. Nonparametric factors were calculated with Spearman's correlation coefficient test. In the statistical analysis, $p<0.05$ was considered significant. The data accepted as significant in univariate analysis were taken into multiple logistic regression analysis with forward LR method. A p value of <0.10 was accepted as significant in the selection of the risk factors whose efficacy would be assessed with multiple logistic regression analysis.

RESULTS

Among the 105 patients, the ratio of female/male was 83/22 in terms of gender distribution. There were 30 patients over

Table 1. Group of patients and clinical features

Characteristics of 105 patients:		Group A: n (%): (Primary referral)	Group B: n (%): (Secondary referral)	Group C: n (%): (interventional Treatment)
Gender	Female	37 (78.7)	25 (78.1)	21 (80.8)
	Male	10 (21.3)	7 (21.9)	5 (19.2)
Age (years)	<60	33 (70.2)	23 (71.9)	19 (73.1)
	>60	14 (29.8)	9 (28.1)	7 (26.9)
Blood Biluribin level (mg/dL)	<2	25 (54.3)	12 (38.7)	25 (96.2)
	2-10	18 (39.1)	13 (41.9)	1 (3.8)
	>10	3 (6.5)	6 (19.3)	0 (0)
Mean value (mg/dL)		3.4	5.75	1.09
İnitial procedure(s)				
Lap. Cholecystectomy:		47 (100)	-	23 (88.5)
Conversion +/- Choledochotomy+T-tube:		-	23 (71.9)	2 (7.7)
Hepaticojejunostomy:		-	3 (9.4)	1 (3.8)
HJ.+Hepatectomy/Vascular/Intestinal repair:		-	6 (18.8)	-
Repair procedure(s)				
Interventional&medical treatment*:		-	4 (12.5)	26 (100)
Conversion +/- Choledochotomy+T-tube:		10 (21.3)	1 (3.1)	-
Hepaticojejunostomy:		30 (63.8)	22 (68.8)	-
HJ.+Hepatectomy/Vascular/Intestinal repair:		7 (14.9)	5 (15.6)	-

* ERCP: Endoscopic Retrograde Cholangiopancreatography; PTC: Percutaneous Transhepatic Cholangiography; HJ: Hepaticojejunostomy

Table 2. Predictive effect of the injury level according to Strasberg-Bismuth classification on the development of mortality and sepsis

		Mortality		Sepsis	
Level of Injury:		RR:	%95 CI:	RR:	%95 CI:
Type A-D*	Type E1-E2	2.81 (NS)	0.24-32.6 (NS)	6.0	1.45-24.9
	Type E3-E4-E5	8.86	1.03-76.06	6.78	1.74-26.43

*Reference group
*RR: Relative Risk; 95% CI: 95% Confidence Interval; NS: Nonspecific

the age of 60 with an average age of 46.2 years (range 20-78 years) (Table 1).

While, in Group 1, there were forty-seven patients (47, 45%) who were transferred to our clinic with the diagnosis of injury after laparoscopic cholecystectomy applied in an external center, there were thirty-two patients (32, 31%) who underwent surgery before the transfer to our clinic in Group 2. There were twenty-six patients (26, 24%) treated with non-surgical (ERCP, PTC) methods for minor injuries in group 3. While the mortality rate in 105 patients was 9.5% (10 patients), the rate of sepsis development was 23.8% (25 patients).

Univariate Analysis of Demographic Findings

Age groups were grouped as below and over 60 years. When the reference group was under 60 years old, there was an increased risk of mortality in patients over 60 years of age ($p<0.05$, RR: 4.43, 95% CI: 1.15-17.0). However, no difference was observed between male and female patients in terms of mortality ($p>0.05$, RR: 1.7%, 95% CI: 0.40-7.25).

Univariate Analysis of Serum Bilirubin Values

It was observed that the mean serum bilirubin level was 3.0 mg/dL and biluribin level was an independent risk factor for sepsis development ($p<0.05$). Statistical analysis performed with Mann Whitney U test showed that while the median bilirubin level was 3.48 mg/dL (0.42-25 mg/dL) in the sepsis group, the median value was 1.33 mg/dL (0.1-19) ($p<0.001$) in the non-sepsis group.

In the grouping that was made according to the bilirubin scoring index, the group with serum bilirubin level <2 mg/dL was compared as a reference with the other groups. There was a significant risk increase in the group with 2-10 mg/dL serum bilirubin level in terms of mortality (RR: 14.78% 95% CI: 1.73-123.3) and in terms of sepsis (RR: 6.07% 95% CI: 2.21-16.6).

Univariate Analysis of Injury Level

Minor injuries were compared with major injury groups as reference. There was a significant mortality risk increase in the group with complicated major injuries (type E1-E2-E3) (RR: 8.86% 95% CI: 1.03-76.06). It was observed that the level of injury caused a significant increase in the risk of sepsis development (RR: 6.0 95% CI: 1.45-24.9 in type E1-E2-E5 injuries; RR: 6.78 95% CI: 1.74-26.43) (Table 2).

Univariate Analysis of Previous Surgical Interventions

After the injury, the effect of surgical methods performed before transfer of patients was evaluated for determining the prognosis after injury. There was a significant increase in the risk of sepsis (RR: 2.86%, 95% CI: 1.01-8.11) in patients in whom conventional cholecystectomy was preferred or in whom cholecystectomy and choledochotomy – T-tube were performed

Table 3. Predictive effect of the post-injury surgical methods applied at the external center on sepsis development and its relation with the frequency of vascular injuries

	Sepsis		Frequency of Vascular Injury	
Method of Surgery:	**RR:**	**95% CI:**	**Rate:**	**%:**
Conventional cholecystectomy ± Choledochotomy T-tube placement:	2.86	1.01-8.11	5/25	20%
Hepaticojejunostomy	1.69	0.16-17.85 (NS)	1/4	25%
Hepaticojejunostomy ± Hepatic Injury ± Vascular Injury ± Intestinal Injury	10.18	1.66-62.6	2/6	33%

*RR: Relative Risk; 95% CI: 95% Confidence Interval; NS: Nonspecific

Table 4. Calculation of the risk coefficient for mortality and sepsis development by comparing the repair methods applied by the HPB surgeon in the Tertiary center with those treated by interventional methods

		Mortality		Sepsis	
Method of Repair:		**RR:**	**95% CI:**	**RR:**	**95% CI:**
Interventional Treatment Methods (ERCP-PTC)*	Conventional Cholecystectomy ± Choledochotomy T-tube placement :	6.44 (NS)	0.52-79.6	2.0 (NS)	0.28-14
	Hepaticojejunostomy	1.77 (NS)	0.17-17.8	3.25 (NS)	0.84-12.5
	Hepaticojejunostomy ± Hepatic Injury ± Vascular Injury ± Intestinal Injury	14.5	1.42-148	12.6	2.40-65.9

*Reference group, ERCP: Endoscopic Retrograde Cholangiopancreatography, PTC: Percutaneous Transhepatic Cholangiography
*RR: Relative Risk; 95% CI: 95% Confidence Interval; NS: Nonspecific

due to injury. Hepaticojejunostomy (HJ) was performed in 10 of 105 patients after injury by the primary surgeon, but there was a significant increase in the risk of sepsis (RR: 10.1, 95% CI: 1.66-62.6) with accompanying injuries (hepatic injury, intestinal injury, vascular injury) in 6 of them (Table 3).

Thirty-two patients who were in group 2 and underwent multiple surgical interventions prior to the transfer to the EUFM general surgery clinic were re-operated by hepatobiliary surgeon. The number of previous surgical interventions was also analyzed in terms of risk increase and it was observed that the increase in the number of interventions applied was an effective predictor of sepsis development (>1 intervention RR: 3% 95% CI: 1.11-8.05). In 61 cases (58%) referred with drainage catheter, there was no significant relationship between the presence of catheter and the development of mortality and sepsis (p>0.05).

Univariate Analysis of Surgical Methods Performed by Hepatobiliary Surgeon

The effect of surgical approaches applied to the patients who were admitted to our clinic on the development of mortality and sepsis was analyzed. It was observed that the most preferred method of repair was hepaticojejunostomy (HJ) (64 patients, 85.3%). The patients treated with non-surgical methods (ERCP-PTC) (group 3) were accepted as the reference group and compared with the surgical methods applied by hepatobiliary surgeon. As a result of the analysis, it was observed that there was no risk increase in terms of the mortality and sepsis development (RR: 1.77% 95% CI: 0.17-17.8). However, in the presence of comorbid complications (hepatic-intestinal-vascular injuries), there was an increase in risk in terms of mortality and sepsis development (RR: 14.5 95% CI: 1.42-148.5) (Table 4).

Factors Affecting Hospitalization Period

While the mean hospitalization period was 19.7 days, the longest hospitalization period was 24.5 days in group 2. It was revealed that there was no statistically significant difference among the three groups in terms of hospitalization duration (p>0.05). It was observed that the development of biloma, abscess, biliary fistula and biliary stenosis did not statistically affect the hospitalization period (p>0.05). The analysis that was made using Spearman's correlation coefficient showed that the time until the transfer of the patients to the tertiary center (r: 0.221 p: 0.0028) after the laparoscopic cholecystectomy, and the number of applied percutaneous drainage (r: 0.430 p<0.001) affected the hospitalization duration. However, accompanying complications (hepatic-intestinal-vascular injuries) were observed not to be statistically significant (p>0.05).

Univariate Analysis of Clinical Findings and Complications

Twenty-seven of the 105 patients (27, 25.7%) were diagnosed during laparoscopic cholecystectomy. There were thirty-nine patients (39, 37.1%) who had the symptoms of abdominal pain on admission to our clinic, only 10 patients (10, 9.5%) with jaundice findings and two patients (2, 1.9%) with gastrointestinal hemorrhage. Among the parameters formed as a result of the analysis, it was observed that abdominal pain was the risk factor for the development of sepsis (RR: 5.72 95% CI: 1.25-26.24).

When the accompanying complications were evaluated; it was observed that there were thirty-five patients (35, 33%) who had abscess formation, ten patients (10, 42.8%) with intestinal injuries and 17 patients (17, 16%) with vascular injuries. In the result of the risk analysis; abscess formation (RR: 3.73 95% CI: 1.43-9.7), intestinal injury (RR: 3.79% 95% CI: 1-14.45) and vascular injury (RR: 14.4 95% CI: 4.29-48.25) were independent predictors in terms of sepsis and mortality. It was also observed through radiological methods that there was a significant risk of sepsis development in patients with biliary stenosis (RR: 3.73, 95% CI: 1.44-9.69) and biliary fistula (RR: 13.90, 95% CI: 1.78-108.43).

Clavien-Dindo Classification System

When the severity of complications was assessed with the Clavien - Dindo scoring system, the risk of sepsis development was also observed to have increased in relation to classification (RR: 6.44 95% CI: 2.86-14.51).

Multiple Logistic Regression Analysis of the Factors effective on Sepsis and Mortality Development

Among all independent predictors, the Clavien-Dindo classification system was not included in the analysis in order to provide the analysis of the most effective factors. The efficiency of the variables was revealed by calculating the corrected coefficients (CC).

It was observed that the most powerful predictors of sepsis were abscess development (CC: 6.74 95% CI: 1.21-37.60), accompanying vascular injury (CC: 29.41 95% CI: 4.15-208.07) and serum bilirubin level (CC: 4.25 95% CI: 1.034 -17.47).

When the factors were evaluated in terms of mortality, abscess development (CC: 38.25 95% CI: 2.61-558.8), accompanying vascular injury (CC: 17.595% CI: 1.45-211.8) and serum bilirubin level (CC: 23.6 95% CI: 1.58- 352.6) were found to be significant predictors (Table 6).

Table 5. Univariate analysis of risk factors in sepsis development

Univariate Analysis of Predictive Factors:	RR:	95% CI:
Abdominal Pain	5.72	1.25–26.24
Biliary Fistula	13.90	1.78–108.43
Abscess formation	3.73	1.43–9.7
Intestinal Injury	3.79	1–14.45
Vascular Injury	14.4	4.29–48.25

RR: relative risk; 95% CI: 95% confidence interval

DISCUSSION

Bile duct injuries are the complications that cause unexpected results for surgeons and negatively affect their occupational life. Likewise, they cause extremely hard situations for the repairing surgeon from a technical point of view. Even in the case of successful repair, it leaves a negative effect on the quality of life of the patients. While young populations frequently expect a quality of life postoperatively, it leads to consequences which may require intensive care support and result in mortality, which are difficult for the patients and relatives to understand, and difficult for us, the surgeons, to explain.

In bile duct injuries which have a distinctive importance among all postcholecystectomy complications, the first step is provided by the surgeon's awareness. We can define awareness as the particular importance that is given to the possibility of injury in patients with acute or chronic inflammation findings during operation, and in potential situations such as adhesion of infundibulum to the cystic duct, difficult dissection of the cystic duct, failure to reveal the anatomy, the presence of large stone in the Hartmann's pouch, or short cystic duct. Approximately 85% of IBDI is not diagnosed during primary iatrogenic surgery. According to the literature, the rate of diagnosis during operation is 15-30% (15, 16). In our study, the rate of the patients diagnosed during the operation and referred to our clinic is 25.7%. The most common symptom in the postoperative period was abdominal pain (37.1%) and there was a significant relation with the development of sepsis in the course of prognosis. However, it was observed that there was no risk increase in patients in whom drainage was placed into the abdomen and referred due to the suspicion of injury. Abdominal pain, high fever, findings of abdominal distension suggesting biliary leakage in the postoperative period, and the presence of excess drainage with biliary characteristics in the patient in whom drainage was placed due to intraoperative suspicion are the clues that allow the surgeon to quickly recognize the condition of injury.

In our study, the risk of sepsis development was observed to increase even in patients in whom cholecystectomy +/- choledochotomy T-tube drainage was performed by the primary surgeon for the purpose of repairing. It was observed that, among the preferred methods, hepaticojejunostomy was performed in few cases, and that the risk of mortality and sepsis did not increase as long as there was no accompanying complication, but as seen in table 3, the risk of vascular injury increased along with the progress of the surgical technique applied for repair. While Buell and Koffron published in their study that hepatic artery injury occurred in patients who had postcholecystectomy bile duct injury and in whom

Table 6. Scheme of the predictive factors that are observed in the final model through multiple logistic regression analysis

	Mortality				Sepsis			
Risk Coefficients of Predictive Factors:	RR:	95% CI:	CO:	95% CI:	RR:	95% CI:	CO:	95% CI:
Vascular Injury	11.18	2.7–45.9	17.5	1.45–211.8	14.4	4.29–48.25	29.4	4.1–208
Abscess formation	5.42	1.3–22.48	38.25	2.61–558.8	3.73	1.43–9.7	6.74	1.2–37.6
Serum Bilirubin Level	14.7	1.77–123.39	23.6	1.58–352.62	6.071	2.21–16.66	4.25	1.03–17.4

RR: relative risk; 95% CI: 95% Confidence Interval; CO: Corrected Odds

the primary treatment management failed (17, 18), it was observed in our study that repeated interventions (>1 trial: RR: 3 CI: 1.11-8.05) for the purpose of repair before the transfer to tertiary center increased the risk of sepsis in the postoperative period. Stewart & Way showed that the success rate of repair interventions performed by the primary surgeon who conducted cholecystectomy was 17%, but it reached 94% when applied by an experienced hepatobiliary surgeon (19-21). In univariate analysis of complications; intestinal injuries were revealed as the causative predictor (Table 5) in 10 of 105 patients and with multiple logistic regression analysis abscess formation was also shown as one of the strongest predictors (Table 6). In the literature; while major complications occurred after reconstructive surgery in 21% of the patients who underwent intervention for repair at the center where they were transferred from, the complication rate was observed to be 6% in the patients transferred without intervention (22). The fact that combined biliary and vascular injuries are associated with serious complications such as hepatic necrosis and abscess development after reconstructive surgery and that they increase the likelihood of late recurrent stenosis (23, 24) suggests that patients who are to undergo complicated hepatobiliary surgery should be transferred to tertiary centers (25-28).

In the result of multiple logistic regression analysis, we observed that the value of serum bilirubin was a significant predictor in order to obtain good postoperative outcomes and to take necessary precautions against single/multiple organ failure in patients scheduled for repair surgery. In the analysis performed with the serum bilirubin values of the patients at the admission; when the bilirubin level was lower than 2 mg/dl, it did not lead to a risk increase; however, when it reached the range of 2-10 mg/dL, the risk of sepsis development (Corrected Odds CO: 4.25 CI: 1.034 - 17.47) and mortality (CO: 17.5 CI: 1.45 - 211.8) significantly increased; but, similarly, there was no increase in the patients with the values higher than 10 mg/dL. The time until the transfer of the patients to the tertiary center and the increase in the number of percutaneous drainage, which are among the factors prolonging the hospitalization period, caused an increase in morbidity in patients whose transfer was delayed. At this point, the evaluation of the patients in a tertiary center where gastroenterologists, interventional radiologists and HPB surgeons are available is important in terms of prognosis (29, 30).

When we evaluated the mortality rates, the average rate was 9.5% for all patients, it was observed to be 7.1% for the patients transferred after single intervention, and 14.2% for the patients receiving multiple interventions.

CONCLUSION

Iatrogenic bile duct injuries are complications in which the treatment management should be determined through a careful planning with a multidisciplinary approach. Quick decisions taken with missing data can cause to worsen the current picture. The best treatment approach should be provided in the light of predictive factors that are effective on mortality and morbidity. The development of abscess, vascular injury and the increase in the serum bilirubin level are potential risk factors affecting the prognosis. With the recognition of the injury and avoiding the complications with recurrent interventions, the arrangement of treatment approaches in the light of predictive factors that are effective on prognosis will increase the survival expectancy.

Ethics Committee Approval: The authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects.

Informed Consent: Informed consent was not received due to the retrospective nature of the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept A.Ç.; Design - A.Ç., E.E.; Supervision - A.Ç., Ö.Ö.; Resource - Ö.Ü., A.U.; Materials - E.E., R.H.; Data Collection and/or Processing - E.E., H.B.; Analysis and/or Interpretation - E.E., T.K., A.Ç.; Literature Search - Ö.Ü., M.P.; Writing Manuscript - E.E.; Critical Reviews - A.Ç., M.P., Ö.Ö.; Other - M.S.

Acknowledgements: Special thanks to Prof. Dr. Murat Sözbilen for his great effort in performing surgeries.

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

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

REFERENCES

1. Fletcher DR, Hobbs MS, Tan P, Valinsky LJ, Hockey RL, Pikora TJ, et al. Complications of cholecystectomy: risks of the laparoscopic approach and protective effects of operative cholangiography: a population-based study. Ann Surg 1999; 229: 449-457. [CrossRef]
2. Calvete J, Sabater L, Camps B, Verdû A, Gomez-Portilla A, Martin J, et al. Bile duct injury during laparoscopic cholecystectomy: myth or reality of the learning curve? SurgEndosc 2000; 14: 608-611. [CrossRef]
3. MacFadyen BV Jr, Vecchio R, Ricardo AE, Mathis CR. Bile duct injury after laparoscopic cholecystectomy. The United States experience. Surg Endosc 1998; 12: 315-321. [CrossRef]
4. Go PM, Schol F, Gouma DJ. Laparoscopic cholecystectomy in the Netherlands. Br J Surg 1993; 80: 1180-1183. [CrossRef]
5. Gouma DJ, Go PM. Bile duct injury during laparoscopic and conventional cholecystectomy. J Am Coll Surg 1994; 178: 229-233.
6. Richardson MC, Bell G, Fullarton GM. Incidence and nature of bile duct injuries following laparoscopic cholecystectomy: an audit of 5913 cases. Br J Surg 1996; 83: 1365-1360. [CrossRef]
7. Flum DR, Cheadle A, Prela C, Dellinger EP, Chan L. Bile duct injury during cholecystec- tomy and survival in medicare beneficiaries. JAMA 2003; 290: 2168-2173. [CrossRef]
8. Boerma D, Rauws EA, Keulemans YC, Bergman JJ, Obertop H, Huibregtse K, et al. Impaired quality of life 5 years after bile duct injury during laparoscopic cholecystectomy: a prospective analysis. Ann Surg 2001; 234: 750-757. [CrossRef]
9. Savader SJ, Lillemoe KD, Prescott CA, Winick AB, Venbrux AC, Lund GB, et al. Laparoscopic cholecystectomy-related bile duct injuries: a health and financial disaster. Ann Surg 1997; 225: 268-273. [CrossRef]
10. Goor DA, Ebert PA. Anomalies of the biliary tree. Report of a repair of an accessory bile duct and review of the literature. Arch Surg 1972; 104: 302-309. [CrossRef]
11. Strasberg SM, Hertl M, Soper NJ. An analysis of the problem of biliary injury during laparoscopic cholecystectomy. J Am Coll Surg 1995; 180: 101-125.

12. Fry DE. Sepsis Syndrome. Am Surg 2000; 66: 126-132.
13. Strasberg SM, Hertl M, Soper NJ. An analysis of the problem of biliary injury during laparoscopic cholecystectomy. J Am Coll Surg 1995; 180: 101-125.
14. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004; 240: 205-213. [CrossRef]
15. De wilt LT, Rauws EA, Gouma DJ. Surgical management of iatrogenic bile duct injury. Scand J Gastroenterology Suppl 1999; 230: 89-94.
16. Gouma DJ, Obertop H. Management of bile duct injuries: treatment and long-term results. Dig Surg 2002; 19: 117-122. [CrossRef]
17. Koffron A, Ferrario M, Parsons W, Nemcek A, Saker M, Abecassis M. Failed primary management of iatrogenic biliary injury: incidence and significance of concomitant hepatic arterial disruption. Surg 2001; 130: 722-731. [CrossRef]
18. Buell JF, Cronin DC, Funaki B, Koffron A, Yoshida A, Lo A, et al. Devastating and fatal complications associated with combined vascular and bile duct injuries during cholecystectomy. Arch Surg 2002; 137: 703-710. [CrossRef]
19. Johnson AG, Lyon IM, Blumgart LH. Stricture of common hepatic duct after right hepatic lobectomy treated by Longmire's operation. J R Soc Med 1979; 72: 136-139. [CrossRef]
20. Stewart L, Way LW. Bile duct injuries during laparoscopic cholecystectomy: factors that influence the results of treatment. Arch Surg 2003; 130: 1123-1128. [CrossRef]
21. Stewart L, Way LW. Laparoscopic bile duct injuries: timing of surgical repair does not influence success rate. A multivariate analysis of factors influencing surgical outcomes. HPB (Oxford) 2009; 11: 516-522. [CrossRef]
22. de Reuver PR, Grossmann I, Busch OR, Obertop H, van Gulik TM, Gouma DJ. Referral Pattern and Timing of Repair Are Risk Factors for Complications After Reconstructive Surgery for Bile Duct Injury. Ann Surg 2007; 245: 763-770. [CrossRef]
23. Gupta N, Solomon H, Fairchild R, Kaminski DL. Management and outcome of patients with combined bile duct and hepatic artery injuries. Arch Surg 1998; 133: 176-181. [CrossRef]
24. Schmidt SC, Langrehr JM, Hintze RE, Neuhaus P. Long-term results and risk factors influencing outcome of major bile duct injuries following cholecystectomy. Br J Surg 2005; 92: 76-82. [CrossRef]
25. Flum DR, Cheadle A, Prela C, Dellinger EP, Chan L. Bile duct injury during cholecystectomy and survival in medicare beneficiaries. JAMA 2003; 290: 2168-2173. [CrossRef]
26. Carroll BJ, Birth M, Phillips EH. Common bile duct injuries during laparoscopic cholecystectomy that result in litigation. Surg Endosc 1998; 12: 310-313. [CrossRef]
27. Gordon TA, Burleyson GP, Tielsch JM, Cameron JL. The effects of regionalization on cost and outcome for one general high-risk surgical procedure. Ann Surg 1995; 221: 43-49. [CrossRef]
28. Savader SJ, Lillemoe KD, Prescott CA, Winick AB, Venbrux AC, Lund GB, et al. Laparoscopic cholecystectomy related bile duct injuries: a health and financial disaster. Ann Surg 1997; 225: 268-273. [CrossRef]
29. Sicklick JK, Camp MS, Lillemoe KD, Melton GB, Yeo CJ, Campbell KA, et al. Surgical management of bile duct injuries sustained during laparoscopic cholecystectomy: perioperative results in 200 patients. Ann Surg 2005; 241: 786-792. [CrossRef]
30. Fischer CP, Fahy BN, Aloia TA, Bass BL, Gaber AO, Ghobrial RM. Timing of referral impacts surgical outcomes in patients undergoing repair of bile duct injuries. HPB (Oxford) 2009; 11: 32-37. [CrossRef]

Turk J Surg 2018; 34(4): 271-275
DOI: 10.5152/turkjsurg.2018.4018

Original Article

Colorectal cancer surgery in octogenarians

Barış Gülcü, Tuncay Yılmazlar, Özgen Işık, Ersin Öztürk

ABSTRACT

Objective: The incidence of colorectal cancer becomes higher among octogenarians as the life expectancy increases. Whether advanced age is a risk factor for colorectal surgery is a matter of debate. In the present study, the clinical results of octogenarians who underwent colorectal cancer surgery are discussed to find an answer to this question.

Material and Methods: Data of 63 octogenarians who were operated in a tertiary colorectal surgery department between January 1, 2010 and December 31, 2013 were reviewed retrospectively. Demographic data and preoperative, peroperative, and postoperative parameters were evaluated.

Results: Overall, 57.2% of the patients were men. The median age was 81 (80–89) years. Cancer was located at the right colon in 17.5%, left colon in 50.8%, and rectum in 31.7%. Eleven patients underwent emergency surgery (17.5%). The most common surgical procedure was low anterior resection in elective (22.2%) and Hartmann's procedure in the emergency setting (9.5%). Stoma creation was more frequent among patients undergoing emergency procedures (42% vs. 6.8%; p=0.0018). Histopathological diagnosis was adenocarcinoma in 90.5% of the patients, and 34.9% of the patients had stage IIIB disease. Surgical morbidity was significantly higher among patients who underwent rectal resection (66% vs. 10.2%; p=0.0124). Medical morbidity was observed in 10 (15.9%) patients. Preoperative blood transfusion was a risk factor for morbidity (83.4% vs. 29.8%; p=0.0170). Length of total hospital stay was 14 (3–39) days. Surgical (p=0.0004) and medical (p=0.0288) morbidity prolonged the length of total hospital stay. The overall mortality rate was 1.6%.

Conclusion: Colorectal surgery may be safely performed in octogenarians with acceptable morbidity and mortality in specialized centers.

Keywords: Colorectal, morbidity, mortality, octogenarian, surgery

ORCID IDs of the authors:
B.G. 0000-0002-9754-8755,
T.Y. 0000-0003-1924-0795,
Ö.I. 0000-0002-9541-5035,
E.Ö. 0000-0001-8593-5101.

Cite this paper as:
Gülcü B, Yılmazlar T, Işık Ö, Öztürk E. Colorectal cancer surgery in octogenarians. Turk J Surg 2018; 34(4): 271-275

Department of General Surgery, Uludag University School of Medicine, Bursa, Turkey

This study was presented at the 15th National Colon and Rectal Surgery Congress, May 19-23, 2015, Antalya, Turkey.

Corresponding Author
Barış Gülcü
e-mail:drbarisgulcu@hotmail.com

Received:10.11.2017
Accepted: 26.01.2018
Available Online Date: 18.09.2018

INTRODUCTION

The average life span was 50 years in the 1900s; it has increased to 75 years in 2000. Currently, compared with the previous century, there are three times more people who are aged over 70 years and ten times more people aged over 80 years. The increasing life expectancy and increased number of elderly people are accompanied by an increasing number of elderly patients with cancer who require surgery owing to the increasing cancer incidence with advanced age (1). The majority of this group comprises patients with colorectal cancer, as half of all cases with colorectal cancer are present in patients over 70 years (2).

Octogenarians, whose population has been increasing the most in society, are also the patient group with the most increased colorectal cancer rates. Limited functional reserves, comorbid diseases, and frequent acute surgical problems of these patients make surgeons avoid performing an operation on them (3). However, several studies report promising outcomes for octogenarians (4, 5).

Since it is the only fully equipped and experienced tertiary center in our region, our clinic performs a remarkable number of surgeries on elderly patients. The outcomes of octogenarians were similar to those of younger patients after all general surgical procedures. The aim of the present report was to study the clinical outcomes of octogenarians who had operations in our clinic with a diagnosis of colorectal cancer.

MATERIAL AND METHODS

Octogenarian patients who underwent surgery for colorectal cancer in the Uludag University Department of General Surgery between January 1, 2010 and December 31, 2013 were retrospectively evaluated. Approval for the study was obtained from the local ethics committee. Informed consent was obtained from all patients to participate in the study. All of the procedures were performed by high-volume colorectal surgeons. Inclusion criteria comprised patient age ≥80 years, diagnosis of colorectal cancer, and complete postoperative follow-up.

Data on demographics, comorbid diseases, American Society of Anesthesiologists (ASA) score, tumor localization, admission type (emergency/elective), symptom duration time, need for preoperative blood transfusion, intent of the surgical procedure (palliative/curative), resection type, surgical procedure, stoma creation, histopathological diagnosis, disease stage, morbidity (surgical/medical), length of total hospital stay (LOS), and mortality development of the patients were documented. The ASA score was identified by an anesthesiologist preoperatively.

Surgical procedures were classified into three groups: right colon, left colon, and rectum. Colon from the ileocecal valve to the mid-transverse colon within the insertion of the middle colic artery was defined as the right colon. Colon from the mid-transverse colon to the rectosigmoid junction but not involving the rectum was defined as the left colon. Disease staging was performed based on the tumor node metastasis stage, which was most recently updated in 2009 and originally reported by both the American Joint Committee on Cancer and the Union for International Cancer Control in 1954.

We classified perioperative complications as surgical (surgical site infection, anastomotic leak, eventration, intra-abdominal abscess, and peroperative injury) or medical (atrial fibrillation, pneumonia, and urinary tract infection). All mortalities within 30 days after surgery, even if it was not associated with the performed surgical procedure, and all mortalities related to the surgery or any surgical complications were documented as mortality.

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) for windows version 10.0 (SPSS Inc.; Chicago, IL, USA). Data were presented as mean±standard deviation or median (min–max) values. Ratios between the groups that were created according to various variables were compared using the Pearson's chi-square test and the Kolmogorov–Smirnov test. The magnitudes of the values between the groups were compared using the Mann–Whitney U test. A p value <0.05 was considered as statistically significant in all analyses.

RESULTS

In total, 63 (8.2%) of the 768 patients who underwent surgery for colorectal cancer in our clinic between January 1, 2010 and December 31, 2013 were octogenarians. There were 36 (57.2%) men and 27 (42.8%) women. The median age was 81 (80–89) years. There were 14 (22.2%) patients who did not have any comorbid diseases. Fifteen patients had only cardiac comorbid diseases. However, the overall rate of cardiac comorbid diseases was 57.1% (alone in 15 patients and with other comorbid diseases in 21 patients). Only one patient was classified as ASA I, 71.5% were ASA II, and 26.9% were ASA III.

The primary tumor was located at the right colon in 11 (17.5%), left colon in 32 (50.8%), and rectum in 20 (31.7%) patients. Rectal cancer was the most frequent type of cancer, followed by sigmoid (22.2%) and rectosigmoid colon cancer (17.5%). The median duration of symptoms was 40 days for patients with colon cancer throughout the colon, 90 days for right colon cancer, 40 days for left colon cancer, and 30 days for rectal cancer.

Palliative procedures were performed in only 2 (3.2%) patients, whereas curative surgery was performed in 61 (96.8%) of them. The performed palliative procedures were bypass and transanal local excision. R0 resection was performed in 61 (96.8%) patients, whereas R1 resection was performed in 1 (1.6%) patient. There was only one patient with an unresectable mass. Eleven (17.5%) patients underwent emergency procedures. Table 1 presents the performed surgical procedures. Hartmann's procedure and low anterior resection (LAR) were most frequently performed in emergency and elective operations, respectively.

A stoma was created in 19 (30.1%) patients. End stoma was created in 14 (73.7%) of them, whereas a diverting stoma with an anastomosis was created in 5 (26.3%) patients. The rate of stoma creation was significantly higher in emergency operations (p=0.0018). Adenocarcinoma with a rate of 90.5% was the most predominant pathological diagnosis. Table 2 shows the distribution of the disease stages. Stage IIIB was the most predominant stage with a rate of 34.9%.

Six patients received blood transfusion in the preoperative period, and 5 (83.4%) of them experienced postoperative morbidity. Receiving blood transfusion in the preoperative period was a risk factor for morbidity (p=0.0170). Twelve (19%) patients had surgical morbidity. Surgical site infection was the most common surgical morbidity. Surgical morbidity was significantly higher in patients who underwent rectal surgery (p=0.0124). Ten (15.9%) patients experienced medical morbidities. The most common medical morbidity was atrial fibrillation (7.9%) (Table 3). The median LOS was 14 (3–39) days. Development of surgical morbidity (p=0.0004) and medical morbidity (p=0.0288) was the factor that negatively affects the LOS.

There was only 1 (1.58%) perioperative mortality. This patient underwent LAR for rectal cancer after completion of neoadjuvant chemo radiotherapy, and he was reoperated for anastomotic leak on postoperative day 6. The patient died as a result of intra-abdominal sepsis on postoperative day 21.

DISCUSSION

The number of elderly people within the population has been progressively growing parallel to the increasing life expectancy. According to the World Health Organization, describing ages over 80 years old as "very old," the very old group appears to be the most prevalently growing group among the population (6). The very old people represent 1.03% of the total population in 2007, and its number increased 1.5-fold to 1.52% in 2013 (7).

In the present study, 8.2% of the patients who underwent operations due to colorectal cancer were octogenarians. This ratio was 9.6% in the study performed by Nyam et al. in Singapore (8) and 15.4% in the multicenter study performed by Marusch et al. (9) in Germany. As society becomes older, surgeons more frequently encounter octogenarians. The number of octogenarians undergoing operations for colorectal cancer in countries with a long life expectancy and a large elderly population, such as Germany, is nearly two-fold that of countries such as Turkey and Singapore.

Table 1. Distribution of the procedures

Surgical Procedure (n, %)	Emergency (n=11)	Elective (n=52)	Total (n=63)
Right hemicolectomy	1 (1.6)	9 (14.3)	10 (15.9)
Left hemicolectomy	1 (1.6)	5 (7.9)	6 (9.5)
Anterior resection	-	12 (18)	12 (18)
Low anterior resection	-	14 (22.2)	14 (22.2)
Abdominoperineal resection	-	4 (6.3)	4 (6.3)
Hartmann	6 (9.5)	3 (4.8)	9 (13.3)
Total*/subtotal colectomy	3 (4.8)	2 (3.2)	5 (8)
Turnbull–Cutait	-	1 (1.6)	1 (1.6)
Bypass	-	1 (1.6)	1 (1.6)
Transanal local excision	-	1 (1.6)	1 (1.6)

*Total colectomy was necessary in one patient with synchronous colorectal tumor
Datas are presented as n (%)

Table 2. Characteristics of cancer

	n	Rate (%)
Pathological diagnosis of colorectal cancer		
Adenocarcinoma	57	90.5
Mucinous adenocarcinoma	3	4.8
Signet ring cell carcinoma	1	1.59
Malign melanoma	1	1.59
Lymphoma	1	1.59
Distribution of the disease stage (adenocarcinoma)		
Stage I	6	10
Stage IIA	14	23.4
Stage IIIB	22	36.6
Stage IIIC	8	13.3
Stage IVA	10	16.6

AJCC: American Joint Committee on Cancer (7th edition)

The rate of ASA III patients was 26.9% in our study, whereas it was 59.8% in the study by Ming-gao et al. (2) and 81% in the study performed by Tsar'kov et al. (10). Neither the ASA score nor the corresponding presence of concomitant diseases affected morbidity or mortality. However, the low rate of ASA III patients, the predominance of ASA II patients, and the lack of ASA IV, V, and VI patients limited the evaluation of the effect of the ASA score on postoperative outcomes in our study. Nonetheless, previous studies from our department found that there is a correlation between mortality and ASA score (11, 12).

Ong et al. (13) reported rates of 55% for right colon cancer, 19% for left colon cancer, and 26% for rectal cancer. Additionally, these rates were 20% for right colon cancer, 46% for left colon cancer, and 34% for rectal cancer in the study, and they varied in different cultures (3, 9, 14–16). Many studies from Western countries have shown that the number of right-sided cancers progressively increases as age increases (17). Zhang et al. (18) reported that the rate of right colon cancer in patients aged over 75 years is 34.6%, whereas it is 20% in patients younger than 75 years. The right-sided tumor rate was 17.5% in the present study. Although our department is a referral center in the region, those patients might be referred less frequently due to the lower complexity of right colectomy compared with left colectomy and rectal resections.

Table 3. Morbidities and their treatments

Morbidity	n	Rate (%)	Treatment
Surgical morbidities	12	19	
Iatrogenic splenic injury	1	1.6	Splenectomy
Intra-abdominal abscess	1	1.6	Percutaneous drainage
Eventration	2	3.2	Reoperation
Anastomotic leak	3	4.7	Reoperation (all were rectal resections)
Surgical site infection	5	7.9	Debridement and antibiotherapy
Medical morbidities*			
Urinary tract infection	1	1.6	
Pneumonia	3	4.7	
Atrial fibrillation	5	7.9	
Pneumonia+atrial fibrillation	1	1.6	

*No medical morbidities required surgical intervention

Preoperative blood transfusion was detected as a risk factor for increasing postoperative morbidity. Halabi et al. (19) reported that blood transfusion increases the mortality, morbidity, and LOS in 27,120 patients who underwent operations for colorectal cancer in California. We believe that the need for blood transfusion is also a factor that reflects the complexity of the case.

Stoma creation was necessary in 19 (30.1%) patients, and 42% of them were admitted as emergency cases. The reported stoma creation rates were higher in a previous study (2). While 50.8% of the tumors were localized at the left colon and 31.7% at the rectum, the rate of patients who underwent a Hartmann's procedure was 13.3%. The complication rates of the Hartmann's procedure have been reported to vary between 20% and 69% in different series (20). Most importantly, the difficulty of the Hartmann's procedure necessitates another intervention to sustain intestine continuity. Higher stoma reversal failure rate is the major disadvantage of the Hartmann's procedure. Sücüllü et al. (21) stated that the Hartmann's procedure must be performed very selectively, especially for elderly patients with cancer, and that in general, it must be considered as a possible permanent procedure.
In our study, most of the patients were Duke C patients, whereas one-third of the study population represented Duke A and B patients. Half of the patients in developed countries, such as France, United Kingdom, Germany, and Japan, are Duke A and

B patients, with a predominance of Duke B patients. In these countries, half of the patients do not need adjuvant treatment after surgery. Therefore, the burdens on patients, doctors, and the economy decrease as both the toxic effects of adjuvant treatment on patients and the utilization of treatments that are used to reduce these effects decrease.

In the present study, 19% of the patients experienced surgical morbidity, and it was significantly frequent in patients who underwent surgery for rectal cancer. It must be noted that limited number of ASA III–IV patients, limited number of emergency procedures, and patients with advanced stage tumors may yield false negative results. Although a multicenter study from Germany (9) observed a surgical morbidity rate of 20%, the ASA score, emergency surgery, and presence of concomitant diseases (cardiac, respiratory, and renal) affected morbidity. In another study, the rate of surgical morbidity was 8.8%, and the only factor affecting morbidity was emergency admission (13). Almost 16% of the patients experienced medical morbidity. Although it was not a significant variable in the development of medical morbidity, studies have associated surgery itself with medical morbidity (17). Additionally, the ASA score and emergency admission were reported to be other risk factors (9).

Length of total hospital stay was another variable in our study. The mean LOS was 14 days in our series. The factors that affect the LOS were medical and surgical morbidities. Unfortunately, the number of studies evaluating the effects of age on the LOS is limited (22). Advanced age may be a factor lengthening the LOS since surgeons are more comfortable when they monitor the elderly patients longer before hospital discharge. Methodological studies focusing on this issue are needed to identify why elderly patients have a longer duration of hospitalization and to determine the factors that affect this duration.

In the present study, the rate of perioperative mortality was 1.58%. The rate ranges from 5.2% to 10% according to previous studies (8, 17, 23). Similar to previous data, the morbidity and mortality rates were reduced in our center since patients were operated by surgeons who were specialized in colorectal surgery (24). Evaluation of the patient-related factors that affect mortality is not appropriate owing to the presence of only one mortality; however, Grosso et al. (25) and Öztürk and Yılmazlar (11) from our clinic stated that the ASA score and concomitant diseases are factors that affect mortality.

The major limitation of the present study was its retrospective design. A low number of ASA III and IV patients may be another limitation that can affect the results. On the other hand, this is one of the largest series studied outcomes of colorectal cancer surgery in octogenarians from our country.

CONCLUSION

The number of octogenarian patients in society increases as life expectancy increases. The most important risk factor for colorectal cancer is age, and its incidence will continue to increase as societies become older. Surgeons tend to avoid operating on octogenarians since advanced age is considered as a risk factor. However, as demonstrated in our study, colorectal cancer surgery can be performed safely with acceptable morbidity and mortality rates in specialized centers.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Uludag University School of Medicine.

Informed Consent: Informed consent was not received due to the retrospective nature of the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - B.G., T.Y.; Design - B.G., T.Y.; Supervision - E.Ö., T.Y.; Resource - B.G., Ö.I.; Materials - B.G., Ö.I., E.Ö.; Data Collection and/or Processing - B.G., Ö.I.; Analysis and/or Interpretation - B.G., Ö.I., E.Ö.; Literature Search - B.G., Ö.I.; Writing Manuscript - B.G., Ö.I., T.Y.; Critical Reviews - E.Ö., T.Y.

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

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

REFERENCES

1. Vignali A, Di Palo S, Tamburini A, Radaelli G, Orsenigo E, Staudacher C. Laparoscopic vs. open colectomies in octogenarians: a case-matched control study. Dis Colon Rectum 2005; 48: 2070-2075. [CrossRef]
2. Ming-Gao G, Jian-Zhong D, Yu W, You-Ben F, Xin-Yu H. Colorectal cancer treatment in octogenarians: elective or emergency surgery?, World J Surg Oncol 2014; 12: 386. [CrossRef]
3. Tan KY, Chen CM, Ng C, Tan SM, Tay KH. Which octogenarians do poorly after major open abdominal surgery in our Asian population? World J Surg 2006: 547-552. [CrossRef]
4. Baek SJ, Kim SH, Kim SY, Shin JW, Kwak JM, Kim J. The safety of a "fast-track" program after laparoscopic colorectal surgery is comparable in older patients as in younger patients. Surg Endosc 2013; 27: 1225-1232. [CrossRef]
5. Pawa N, Cathcart PL, Arulampalam TH, Tutton MG, Motson RW. Enhanced recovery program following colorectal resection in the elderly patient. World J Surg 2012; 36: 415-423. [CrossRef]
6. Aging and life course. Available from URL: http://www.who.int/ageing/about/facts/en/. Access Date: 02 October 2014.
7. İstatistikle Yaşlılar. Available from URL: http://www.tuik.gov.tr/PreHaberBultenleri.do?id=16057. Access Date: 04 October 2014.
8. Nyam DCNK, Tang CB, Ang M, Ho YH, Leong AFPK, Seow-Choen F. Surgery for colorectal cancer in the octogenerians. Tech Coloproctol 1999: 23-26. [CrossRef]
9. Marusch F, Koch A, Schmidt U, Steinert R, Ueberrueck T, Bittner R, et al. The impact of the risk factor "age" on the early postoperative results of surgery for colorectal carcinoma and its significance for peroperative management. World J Surg 2005; 29: 1013-1021. [CrossRef]
10. Tsar'kov PV, Nikoda VV, Stamov VI, Markar'ian DR, Tulina IA. The efficacy of the multidisciplinary approach in colorectal cancer surgery in elderly patients. Khirurgiia (Mosk) 2012: 4-13.
11. Ozturk E. Yilmazlar T. Factors affecting the mortality risk in elderly patients undergoing surgery. ANZ J Surg 2007; 77: 156-159. [CrossRef]
12. Yilmazlar T, Guner O, Yilmazlar A. Criteria to consider when assessing the mortality risk in geriatric surgery. Int Surg 2006; 91: 72-76.
13. Ong ES, Alassas M, Dunn KB, Rajput A. Colorectal cancer surgery in the elderly: acceptable morbidity?. Am J Surg 2008; 195: 344-348. [CrossRef]

14. Leong QM, Aung MO, Ho CK, Sim R. Emergency colorectal resections in Asian octogenarians: factors impacting surgical outcome. Surg Today 2009; 39: 575-579. [CrossRef]
15. Barrier A, Ferro L, Houry S, Lacaine F, Huguier M. Rectal cancer surgery in patients more than 80 years of age. Am J Surg 2003; 185: 54-57. [CrossRef]
16. Smith JJ, Lee J, Burke C, Contractor KB, Dawson PM. Major colorectal cancer resection should not be denied to the elderly. Eur J Surg Oncol 2002; 28: 661-666. [CrossRef]
17. Gurevitch AJ, Davidovitch B, Kashtan H. Outcome of Right Colectomy for Cancer in Octogenerians. J Gastrointest Surg 2009: 100-104. [CrossRef]
18. Zhang B, Fattah A, Nakama H. Characteristics and survival rate of elderly patients with colorectal cancer detected by immunochemical occult blood screening. Hepatogastroenterology 2000; 47: 414-418.
19. Halabi WJ, Jafari MD, Nguyen VQ, Carmichael JC, Mills S, Pigazzi A, et al. Blood transfusions in colorectal cancer surgery: incidence, outcomes, and predictive factors: an American College of Surgeons National Surgical Quality Improvement Program analysis. Am J Sur 2013; 206: 1024-1032. [CrossRef]
20. Desai DC, Brennan EJ Jr, Reilly JF, Smink RD Jr. The Utility of the Hartmann Procedure. Am J Surg 1998; 175: 152-154. [CrossRef]
21. Sücüllü İ, Demirbaş S, Yücel E, Filiz İ, Kurt Y, Akın L. Hartmann's Procedure: Should it be Performed? Kolon Rektum Hast Derg 2007; 17: 26-30.
22. Fazio VW, Tekkis PP, Remzi F, Lavery IC. Assessment of operative risk in colorectal cancer surgery: the Cleveland Clinic Foundation colorectal cancer model. Dis Colon Rectum 2004; 47: 2015-2024. [CrossRef]
23. Kunitake H, Zingmond DS, Ryoo J, Ko CY. Caring for octogenarian and nonagenarian patients with colorectal cancer: what should our standards and expectations be?. Dis Colon Rectum 2010; 53: 735-743. [CrossRef]
24. Çolak T, Türkmenoğlu Ö, Dağ A, Gündoğdu R, Aydın S. Does establishment of colorectal surgical unit improve colorectal operations? Ulus Cerrahi Derg 2009; 25: 49-52.
25. Grosso G, Biondi A, Marventano S, Mistretta A, Calabrese G, Basile F. Major postoperative complications and survival for colon cancer elderly patients. BMC Surgery 2012; 12: 20. [CrossRef]

Turk J Surg 2018; 34(4): 276-281
DOI: 10.5152/turkjsurg.2018.3975

Original Article

Effects of subjective sleep quality on the quality of life in patients with chronic anorectal disorder

Bülent Devrim Akçay[1], Vahit Onur Gül[2], Serhat Özer[3], Duygu Akçay[4], Onur Eyigün[5]

ABSTRACT

Objective: The aim of the present study was to evaluate the subjective sleep quality in patients with anorectal disorder, to determine the factors associated with subjective sleep quality, and to explore the relationship between subjective sleep quality and quality of life.

Material and Methods: This descriptive study was conducted between April 8, 2015 and April 12, 2016. The research population consisted of 284 patients who attended the general surgery outpatient clinics of Konya Military Hospital and were subsequently diagnosed with one of the four most common anorectal disorders (hemorrhoidal disease, anal fissure, anorectal abscess/fistula, and sacrococcygeal pilonidal disease). Data were collected from 114 patients who volunteered to participate in the study. After establishment of the diagnosis based on proctological anamnesis and physical examination, the Pittsburgh Sleep Quality Index, Short-Form Health Survey, Beck Anxiety Inventory, and Beck Depression Inventory were administered to the patients, along with a questionnaire on sociodemographic data, via a face-to-face interview technique.

Results: Ninety-six (84.2%) patients had poor sleep quality, whereas 18 (15.8%) patients had good sleep quality. Among the patients with poor sleep quality, 16 were diagnosed with anorectal abscess and fistula (100.0%), 40 with hemorrhoidal disease (90.9%), 16 with sacrococcygeal pilonidal disease (80.0%), and 24 with anal fissure (70.6%). Overall, all patients with poor sleep quality (n=96) had low scores in all subcomponents of the quality of life scale.

Conclusion: The sleep quality in patients with chronic anorectal disorder is significantly impaired, thus negatively affecting quality of life. Therefore, improvement in quality of life by improving sleep quality should be one of the main objectives in treating chronic anorectal disorders.

Keywords: Chronic anorectal disorder, sleep disturbance, sleep quality, quality of life

ORCID IDs of the authors:
B.D.A. 0000-0002-6308-9327;
V.O.G. 0000-0001-9071-0732;
S.Ö. 0000-0003-3468-1839;
D.A. 0000-0001-9030-6879;
O.E. 0000-0002-3736-9122.

Cite this paper as:
Akçay, BD, Gül VO, Özer S, Akçay D, Eyigün O. Effects of subjective sleep quality on the quality of life in patients with chronic anorectal disorder. Turk J Surg 2018; 34(4): 276-281.

[1]Department of Psychiatry, Gülhane Training and Research Hospital, Ankara, Turkey
[2]Department of General Surgery, Gülhane Training and Research Hospital, Ankara, Turkey
[3]Unit of Intensive Care, Gülhane Training and Research Hospital, Ankara, Turkey
[4]Ministry of National Defense, Ankara, Turkey
[5]Department of Psychiatry, Edremit State Hospital, Ankara, Turkey

Corresponding Author
Bülent Devrim Akçay
e-mail: drbulentakcay@yahoo.com

Received: 30.08.2017
Accepted: 02.01.2018
Available Online Date: 13.09.2018

INTRODUCTION

Sleep is a physiological need in humans. Humans spend approximately one-third of their lifetime sleeping. Sleep follows a regular pattern; provides energy; promotes growth, development, learning, and relaxation; and is affected by many internal and external factors (1-3). Humans have physical, social, intellectual, and emotional needs. Therefore, fulfillment of the basic physical and mental needs is essential to maintain well-being. Sleep, as a fundamental need, is an important parameter that affects the quality of life (QOL) and well-being (4, 5). Some diseases may cause sleep disorder by inducing physical and psychological stress. Moreover, other factors, such as dietary habits, lifestyle, medication use, smoking, alcohol consumption, and illicit drug use, along with psychological and environmental factors, may affect sleep patterns (6).

Chronic diseases constitute one of the causes of sleep disorders. Chronic disease is a long-term medical condition or disease that shows slow progression and requires regular and continuous treatment and follow-up owing to its potential to cause irreversible structural or functional impairment or disability (7). Acute phases or exacerbations of chronic diseases are treated in a hospital setting, whereas most of the treatment and care is provided at home. There are many aspects that influence QOL in patients with chronic diseases. Therefore, increasing a patient's QOL is one of the fundamental objectives in the treatment of chronic diseases (8).

Chronic anorectal disorders are conditions that require continuous treatment and care, along with self-management to prevent acute complications and minimize long-term effects. Currently, chronic anorectal disorders frequently encountered in the general population emerge as an important surgical problem with a risk of recurrence and becoming chronic following both surgical and medical therapies. They also have the tendency to decrease QOL owing to poor prognosis and related complications. Among the frequently diagnosed anorectal disorders, the prevalence of chronic anal fissure is 6%–7%, chronic hemorrhoidal disease is 45%, chronic sacrococcygeal pilonidal disease is 3%–4%, and chronic anal abscess/fistula is 4%–5% (9, 10). Sleep—a state in which the tissues in the body undergo regeneration—is one of the fundamental daily life activities that affect the individuals' QOL and health. Chronic

anorectal disorders may cause sleep problems by causing pain and physical disorders, resulting in anxiety and depression in the long term (11, 12). A review of the literature shows that whereas the relationship between sleep disorders and various other disorders is investigated, there is no sufficient research on the effects of sleep quality on QOL in patients with chronic anorectal disorders. The aim of the present study was to assess sleep quality in patients with chronic anorectal disorders, to determine the factors that might be associated with sleep quality, and to explore the relationship between sleep quality and QOL.

MATERIAL AND METHODS

This descriptive study was conducted between April 8, 2015 and April 12, 2016. The research population was composed of 284 patients who were admitted to the surgical outpatient clinics of Konya Military Hospital and who were subsequently diagnosed with one of the four most frequent anorectal disorders. Anorectal disorders comprised hemorrhoidal disease, anal fissure, anorectal abscess/fistula, and sacrococcygeal pilonidal disease. Participants who were male and female, aged ≥18 years, and who had the level of education and the mental status sufficient to complete the assessment scales and questionnaires were included in the study. Informed consent was obtained from all of the patients. Data were collected from 114 patients who volunteered to participate in the study. The ethics committee approved the study (approval date: April 7, 2015; decree no. 2015/01-9). Following the diagnosis based on proctological anamnesis and physical examination conducted in the surgical outpatient clinics, the Pittsburgh Sleep Quality Index (PSQI), Short-Form Health Survey (SF-36), Beck Anxiety Inventory, and Beck Depression Inventory were administered to the patients, along with a questionnaire on their sociodemographic data, via face-to-face interviews.

Sociodemographic data included gender, age, income, marital status, educational level, medical history, alcohol consumption, smoking, and possible physical complaints. The SF-36 is used to assess QOL and was designed for use in clinical practice by the Rand Corporation in 1992 (13). It is a 36-item questionnaire with physical and mental components. The physical component consists of general health perceptions, physical functioning, role limitations because of physical health, and bodily pain subscales, whereas the mental component consists of emotional well-being, role limitations because of personal or emotional problems, energy/fatigue, and social functioning subscales. Each subscale is scored on a scale from 0 to 100 points, where "0" indicates a poor health status. It contains items on the perceived change in health during the past 4 weeks and past week. The validity and reliability of the Turkish version of the SF-36 were assessed by Koçyigit et al. (14).

Pittsburgh Sleep Quality Index was used to evaluate the sleep quality of patients. It was developed by Buysse et al. (15) consisting of 19 questions and 7 components to assess sleep quality during the past month. The total score is calculated using 18 items and 7 components. Each item is rated on a 0–3 scale, and component scores are summarized to create a total PSQI score with a range of 0–21, with higher scores indicating poor sleep quality. A total PSQI score of <5 indicates good sleep quality, whereas a total score of ≥5 indicates poor sleep quality (15). Ağargün et al. (16) evaluated the validity and reliability of the index and found that it is applicable to the Turkish population. The sensitivity of the test is 89.6%, and the specificity is 86.5%.

Statistical Analysis

Frequency distribution, descriptive statistics, and cross-tabulations were created using the Statistical Package for the Social Sciences (SPSS) version 15.0 software (SPSS Inc., Chicago, IL, USA). Demographic data, descriptive findings related to disease, and PSQI and QOL scores were expressed in frequency and percentages. The chi-square test was used to assess the relationship between diagnosis and sleep quality. The independent sample t-test was used to compare different subscales of the QOL scale and sleep quality in groups. A level of 0.05 was statistically significant.

RESULTS

Table 1 shows the sociodemographic data of the participants in the study and descriptive findings related to the disease. With regard to patient demographics, 89.5% of the participants were males, 52.6% were in the 22–30-year age group, 82.5% had moderate income, and 49.5% had undergraduate degrees. Of the patients, 38.6% were diagnosed with chronic hemorrhoidal disease, 29.8% with chronic anal fissure, 17.5% with chronic sacrococcygeal pilonidal disease, and 14.0% with chronic anorectal abscess and fistula. Of the 58 patients, 28 complained of bleeding, whereas 30 had constipation and diarrhea. With regard to treatment, 47.4% of the patients had previously undergone surgery, and 71.9% had received medical therapy (Table 1). The relationship between sleep quality and sociodemographic and descriptive variables (smoking, alcohol consumption, surgical history, and medical therapy) was evaluated using the chi-square test. There was no statistically significant relationship between sleep quality and sociodemographic and descriptive characteristics ($p>0.05$). The findings show that among the patients with poor sleep quality, 45.8% suffered from pain, 29.2% from constipation, and 25% from bleeding.

The findings show that 96 (84.2%) patients had poor sleep quality, whereas 18 (15.8%) had good sleep quality. Among the participants of the study, 24 out of 34 patients diagnosed with chronic anal fissure (70.6%), 40 out of 44 with chronic hemorrhoidal disease (90.9%), 16 out of 20 with chronic sacrococcygeal pilonidal disease (80.0%), and 16 with chronic anorectal abscess and fistula (100.0%) had poor sleep quality. There was a statistically significant difference between patients with poor sleep quality and patients with good sleep quality ($p<0.05$; Table 2).

The findings also show that 59.65% of the patients had no anxiety, whereas 24.56% had mild, 8.77% had moderate, and 7.02% had severe anxiety. In addition, 57.9% of the patients had no depression, whereas 33.33% had mild, 7.02% had moderate, and 1.75% had severe depression. The chi-square test showed that chronic anorectal disorders, such as chronic anal fissure, chronic hemorrhoidal disease, chronic sacrococcygeal pilonidal disease, and chronic anorectal abscess and fistula, did not show a significant relationship with anxiety and depression ($p>0.05$). Moreover, 77.8% of the patients with good sleep quality based on the PSQI scores had no depression, whereas 22.2% had moderate depression. On the other hand, 43.8% of the patients with poor sleep quality had no depression, whereas 29.2% had

mild, 22.9% had moderate, and 4.2% had severe depression (χ^2=0.023, p<0.05). Additionally, 55.6% of the patients with good sleep quality according to the PSQI scores had no anxiety, whereas 33.3% had mild, and 11.1% had moderate anxiety. Moreover, 33.3% of the patients with poor sleep quality had no anxiety, whereas 20.8% had mild, 25.0% had moderate, and 20.8% had severe anxiety (χ^2=0.044, p<0.05).

Table 1. Sociodemographic and descriptive data of participants

Gender	**n**	**%**
Female	12	10.5
Male	102	89.5
Age(years)		
18–21	30	26.3
22–30	60	52.6
31–45	22	19.3
≥45	2	1.7
Income level		
Low	10	8.8
Moderate	94	82.5
High	10	8.8
Educational level		
Primary school	24	21.1
High school	22	19.3
Undergraduate	56	49.1
Postgraduate	12	10.5
Duration of disease	**Min/max**	**Mean±SD**
	1/5	2.74±1.48
Diagnosis	**n**	**%**
Chronic hemorrhoidal disease	44	38.6
Chronic anal fissure	34	29.8
Chronic sacrococcygeal pilonidal disease	20	17.5
Chronic anorectal abscess and fistula	16	14.0
Complaints		
Pain	56	49.1
Constipation/diarrhea	30	26.4
Bleeding	28	24.6
Surgical history		
Yes	54	47.4
No	60	52.6
Medical therapy		
Yes	82	71.9
No	32	28.1
Total	114	100

Table 3 shows the distribution of the patients' PSQI scores according to their diagnoses. When all patients with chronic anorectal disorders are evaluated based on their total PSQI scores, it was found that the average PSQI scores of patients in all the diagnosis groups were >5 points. The mean PSQI scores were 9.82±4.8 points in patients diagnosed with chronic anal fissure, 11.27±3.37 points in patients diagnosed with chronic hemorrhoidal disease, 10.15±3.80 points in patients diagnosed with chronic sacrococcygeal pilonidal disease, and 14.00±2.78 points in patients diagnosed with chronic anorectal abscess and fistula (Table 3).

Table 4 shows the distribution of the patients' QOL scores based on their diagnoses. Various subscale scores that comprise the QOL scale are as follows: physical functioning subscale with 25.6±4.20, role limitations because of physical health problems subscale with 6.33±1.44, bodily pain subscale with 7.33±2.34, perceived change in health subscale with 19.59±5.05, energy/fatigue subscale with 14.82±4.71, social functioning subscale with 7.12±2.08, role limitations because of personal or emotional problems subscale with 4.57±1.27, and emotional well-being subscale with 18.91±5.06. In terms of QOL, all groups of patients with anorectal disorders suffered from bodily pain, energy/fatigue, impaired social functioning, and poor emotional well-being. Among these subgroups, patients with chronic sacrococcygeal pilonidal disease particularly suffered from bodily pain, whereas patients diagnosed with anorectal abscess and fistula particularly suffered from energy/fatigue, impaired social functioning, and poor emotional well-being (Table 4).

The mean QOL scores in patients with poor sleep quality (n=96) were below average in all subscales of the QOL scale. There was a significant relationship between sleep quality and scores in physical functioning, role limitations because of physical health problems, bodily pain, perceived general health, and emotional well-being subscales (p<0.005, p<0.05, p<0.05, p<0.05, and p<0.001, respectively; Table 5).

DISCUSSION

The present study found that 84.2% of the participants had poor sleep quality. Sleep quality was considerably impaired in all diagnosis groups, patients in all diagnosis groups scored

Table 2. Sleep quality of patients based on their diagnoses

	Good sleep quality		**Poor sleep quality**		**Total**	
Diagnosis	**n**	**%**	**n**	**%**	**n**	**p**
Chronic anal fissure	10	29.4	24	70.6	34	0.023
Chronic hemorrhoidal disease	4	9.1	40	90.9	44	<0.05*
Chronic sacrococcygeal pilonidal disease	4	20.0	16	80.0	20	
Chronic anorectal abscess and fistula	0	–	16	100.0	16	
Total	18	15.8	96	84.2	114	

*Chi-square test

Table 3. Distribution of the PSQI scores of patients based on their diagnoses

	Chronic anal fissure (n=34)	Chronic hemorrhoidal disease (n=44)	Chronic sacrococcygeal pilonidal disease (n=20)	Chronic anorectal abscess and fistula (n=16)		
PSQI*	**Mean±SD**	**Mean±SD**	**Mean±SD**	**Mean±SD**	**Min/max**	**Mean±SD**
Sleep efficiency	1.00±1.15	1.00±1.09	0.70±1.12	1.00±1.15	0/3	0.95±1.12
Sleep disturbance	1.97±0.90	2.31±0.70	2.40±0.68	2.87±0.34	0/3	2.31±0.77
Use of sleep medication	1.03±0.67	1.02±0.50	1.15±0.81	1.25±0.68	0/3	1.08±0.64
Daytime dysfunction	1.79±0.77	2.36±0.65	1.95±0.94	2.75±0.44	0/3	2.18±0.78
Sleep onset latency	1.32±0.87	1.54±0.72	1.50±0.82	2.12±0.61	0/3	1.55±0.81
Duration of sleep	0.97±1.05	1.11±0.99	0.70±0.92	1.50±1.26	0/3	1.05±1.05
Subjective sleep quality	1.73±0.86	1.90±0.86	1.80±1.00	2.50±0.73	0/3	1.92±0.89
Total PSQI score	9.82±4.83	11.27±3.37	10.15±3.80	14.00±2.78	0/19	11.03±4.05

PSQI*: Pittsburgh Sleep Quality Index

Table 4. Distribution of the quality of life scores of patients based on their diagnoses

	Chronic anal fissure (n=34)	Chronic hemorrhoidal disease (n=44)	Chronic sacrococcygeal pilonidal disease (n=20)	Chronic anorectal abscess and fistula (n=16)	Total score	
SF-36 Health Survey*	**Mean±SD**	**Mean±SD**	**Mean±SD**	**Mean±SD**	**Min/max**	**Mean±SD**
Physical functioning	26.06±3.04	25.73±4.77	25.3±5.33	24.38±2.73	12/30	25.6±4.20
Role limitations because of physical health problems	6.59±1.26	6.41±1.61	6.20±1.58	5.75±1.00	4/8	6.33±1.44
Bodily pain	7.78±2.56	7.44±2.34	6.59±2.17	7.04±1.92	2/12	7.33±2.34
General health perceptions	21.55±3.87	19.33±5.21	19.44±6.00	16.35±3.93	9/30	19.59±5.05
Energy/fatigue	15.30±3.82	15.60±5.33	14.80±5.16	11.75±2.72	4/24	14.82±4.71
Social functioning	7.41±2.11	7.27±2.00	7.00±2.15	6.25±2.11	2/10	7.12±2.08
Role limitations because of personal or emotional problems	4.64±1.34	4.77±1.32	4.50±1.05	4.00±1.15	3/6	4.57±1.27
Emotional well-being	19.23±4.14	20.09±5.31	18.10±6.48	16.00±2.73	5/30	18.91±5.06

*Short-Form Health Survey

Table 5. Comparison of sleep quality and various subscales of the quality of life scale

	Good sleep quality (n=18)	Poor sleep quality (n=96)		
SF-36 Health Survey	**Mean±SD**	**Mean±SD**	**F**	**p***
Physical functioning	28.00±1.82	25.10±4.33	11.485	0.001
Role limitations because of physical health problems	6.55±1.19	6.29±1.48	5.790	0.018
Bodily pain	8.22±3.18	7.17±2.12	6.619	0.011
General health perceptions	21.67±6.69	19.21±4.63	5.565	0.020
Energy/fatigue	15.56±6.29	14.68±4.38	3.694	0.057
Social functioning	7.88±2.54	6.98±1.97	1.049	3.694
Role limitations because of personal or emotional problems	5.00±1.45	4.50±1.23	2.781	0.098
Emotional well-being	20.33±8.33	18.65±4.20	19.049	0.000

*Independent sample t-test

>5 points in PSQI, and their scores in all components of the QOL scale were below average (Tables 2-4). The mean scores of the patients with poor sleep quality were below average in all subscales of the QOL scale compared with those of patients with good sleep quality (Table 5). Sleep quality is one of the most important factors that affect QOL (17). According

to the study by Griffin et al. (24), nonsurgical therapies have a positive effect on QOL in patients diagnosed with anal fissure (18). Another study found that treatment of chronic anal fissure with topical diltiazem improves patients' QOL (19). Ortiz et al. (20) reported significant improvement in QOL in patients with chronic anal fissure following internal lateral sphincterotomy. In the present study, the findings suggested that impairment in sleep quality negatively affected QOL in patients with chronic anorectal disorders.

Age, gender, smoking, and alcohol consumption are among the many factors that affect sleep quality (21-23). However, sociodemographic characteristics and descriptive features (smoking, alcohol consumption, surgical history, and medical therapy) do not significantly affect sleep quality in patients with chronic anorectal disorders. In other words, sociodemographic characteristics and descriptive features are not among the factors that affect sleep quality in patients who participated in the present study.

Another factor that affects sleep quality is the presence of comorbid psychopathology in patients with chronic anorectal disorders. A study conducted among the patients with chronic anal fissure found high rates of comorbid psychopathological disorders. The same study also reported that QOL is negatively affected by the severity of depression and anxiety, and that stress acts as both triggering and aggravating factors in patients with chronic anal fissure (18). One of the most frequent complaints in patients with psychiatric disorders is the changes in sleep quality and quantity. In addition to the concurrence of various sleep problems with psychiatric disorders, sleep problems may emerge as a characteristic symptom of psychiatric disorders. Furthermore, sleep problems are among the diagnostic features of depressive and anxiety disorders. Previous studies have indicated that 80%–85% of the patients with depressive disorder suffer from insomnia, whereas 15%–20% suffer from hypersomnia. Patients with anxiety disorder may experience problems in sleep onset latency and duration of sleep (22). In the present study, 84.21% of the participants had no or mild anxiety, and 91.23% had poor mild depression. These rates suggest that the majority of the participants had no comorbid psychiatric disorder. Therefore, it would be reasonable to argue that anxiety and depression were not among the factors that affect sleep quality in the participants of the study.

Complaints, such as pain, constipation/diarrhea, and bleeding, that result from chronic inflammatory disease in patients with chronic anorectal disorders are distressful symptoms that impair sleep quality and considerably decrease QOL (24). One study on patients with chronic anal fissure evaluated the SF-36 QOL scale and demonstrated that the intensity of pain and bleeding has a negative effect on bodily pain and role limitations because of personal or emotional problems (18). Another study on patients with chronic anal fissure reported pain in 96.7% and bleeding in 83.3% of the patients (18). A study conducted by Griffin et al. (24) on the effects of nonsurgical treatment on the QOL of patients with anal fissure demonstrated that in patients who had nonsurgical treatment, there is a significant reduction in pain, bleeding, and irritation symptoms. Another study found that symptoms, such as pain and irritation in patients with anal fissure, negatively affect the SF-36 scores before treatment, whereas successful treatment of anal fissure decreases pain and improves QOL (19). In the present study, 49.12% of the patients had complaints of pain, 24.56% had bleeding, and 26.3% had constipation and diarrhea (Table 1). Therefore, we suggest that the effects of chronic diseases on QOL must be evaluated along with their effects on individuals in treatment planning, and the treatment approach must also incorporate interventions toward increasing the patients' QOL (25). In the present study, the fact that pain was the main complaint among the patients (45.8%) with poor sleep quality suggests that sleep quality is directly associated with patients' complaints.

CONCLUSION

The current findings demonstrate that impairment in sleep quality negatively affects QOL in patients with chronic anorectal disorder. Therefore, improvement in sleep quality must be one of the main objectives in treating patients with chronic anorectal disorder to improve their QOL. Future research on the subject should conduct randomized, controlled studies on larger samples using polysomnography as an objective measure to assess sleep quality.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Konya Military Hospital (07.04.2015-2015/01.1-9).

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - B.D.A., V.O.G.; Design - B.D.A., V.O.G.; Supervision - B.D.A.; Resource - B.D.A., V.O.G., S.Ö., D.A.; Materials - B.D.A., V.O.G.; Data Collection and/or Processing - B.D.A., V.O.G., O.E.; Analysis and/or Interpretation - D.A.; Literature Search - B.D.A., V.O.G.; Writing Manuscript - B.D.A.; Critical Reviews - B.D.A.

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

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

REFERENCES

1. Karadağ M. Classification of sleep disorders (ICSD-2). Turkiye Klinikleri Arch Lung 2007; 8: 88-91.
2. Öztürk L. An old question to be answered: Why do we sleep? İst Tıp Fak Derg 2007; 70: 114-121.
3. Özgen F. Sleep and Sleep Disorders. Psikiyatri Dünyası 2001; 5: 41-48.
4. Karadağ MG, Aksoy M. Sleep regulation and nutrition. Göztepe Tıp Derg 2009; 24: 9-15.
5. Kal HE. Sleep problems and associated factors in women in menopausal period (Doctoral dissertation. Selçuk Üniversitesi Sağlık Bilimleri Enstitüsü. 2011.
6. Çeviri T. The effect of passive music therapy on sleep quality in elders living in nursing facilities. J Psych Nurs 2016; 7: 55-60.
7. Özdemir Ü, Taşçı S. Psychosocial problems and care in chronic diseases. ERÜ Sağlık Bilimleri Fakültesi Derg 2013; 1: 57-69.
8. Kumsar AK, Yılmaz FT. An overview of quality of life in chronic patients. ERÜ Sağlık Bilimleri Fakültesi Derg 2014; 2: 62-70.
9. Okuş A, Karahan Ö, Eryılmaz MA, Ay AS, Sevinç B, Aksoy N. Bodur S, Halıcı AH. The prevalence and distribution of pilonidal disease in society according to age and sex. Selçuk Tıp Derg 2013; 29: 120-122

10. Çayır Y. Common anorectal disorders. Türkiye Klinikleri J Family Med Spec Top 2015; 6: 78-82.
11. Menteş, Bulut, Alabaz, Leventoğlu. Türk Kolon ve Rektum Cerrahisi Derneği Benign disorders of anorectal diseases. İvedik, Ankara: 2011.
12. Goligher JC. Surgery of the anus, rectum, and colon. 5th ed. London: Balliere, Tindall; 1984
13. Bowling A. Measuring health: A review of quality of life measurement scales. 2nd ed. Philadelphia: Open University Press; 1997.
14. Koçyigit H, Aydemir O, Olmez N&Memis. The validity and reliability of SF-36 in Turkey. Ege Fiz Ted Reh Derg 1999; 12: 102-106.
15. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. Psychiatry res 1989; 28: 193-213. [CrossRef]
16. Ağargün YM, Kara H, Anlar Ö. The validity and reliability of Pittsburg Sleep Index. Türk Psikiyatri Dergisi 1996; 7: 107-111.
17. Nurcan Arat, Yıldırım N, Altay H, Şahin O, Sökmen Y. Sabah İ. Clinical and echocardiographic parameters related with the physical activity habitude and sleep quality index in patients with compensated heart failure. Türkiye Klinikleri J Cardiovasc Sci 2006; 18: 196-205.
18. Arısoy Ö, Şengül N, Çakir A. Stress and psychopathology and its impact on quality of life in chronic anal fissure (CAF) patients. Int J Colorectal Dis 2016; 4: 2732-2731.
19. Tsunoda A, Kashiwagura Y, Hirose K, Sasaki T, Kano N. Quality of life in patients with chronic anal fissure after topical treatment with diltiazem. World J GastrointestSurg 2012; 4: 251-255. [CrossRef]
20. Ortiz H, Marzo J, Armendariz P, De Miguel M. Quality of life assessment in patients with chronic anal fissure after lateral internal sphincterotomy. Br J surg 2005; 92: 881-885. [CrossRef]
21. Roehr T, Roth T. Sleep, alcohol, and quality of life: sleep and quality of life in clinical medicine. In: Verster JC, Pandi- Perumal SR, Streiner DL eds. Totowa, USA: Humana Press; 2008.
22. Aydın H. Sleep and its disorders. Hekimler Yayın Birliği Ankara: 2007.
23. Abdülkadiroğlu Z, Bayramoğlu F, İlhan N. Sleep and sleep disorders. Genel Tıp Derg 1997; 7: 161-166.
24. Griffin N, Acheson AG, Tung P, Sheard C, Glazebrook C, Scholefield JH. Quality of life in patients with chronic anal fissure. Colorectal Dis 2004; 6: 39-44. [CrossRef]
25. Ucan O, Ovayolu N. Relationship between diabetes mellitus, hypertension and obesity, and health-related quality of life in Gaziantep, a central south-eastern city in Turkey. J clinnurs 2010; 19: 2511-2519. [CrossRef]

Turk J Surg 2018; 34(4): 282-285
DOI: 10.5152/turkjsurg.2018.3981

Original Article

Does hyperthermic preconditioning affect the rate of surgical site infection rate and inflammatory reaction in colorectal cancer patients? A prospective randomized clinical trial

Wafi Attaallah[1], Leyla Semiha Şen[1], Ahmet Özdemir Aktan[1], Emel Demiralp Ekşioğlu[2], Zeynep Eti[3], Sertaç Ata Güler[1], Asım Cingi[1]

ABSTRACT

Objective: Hyperthermic preconditioning has been shown to protect against different insults in experimental studies. However, clinical studies assessing its effects remain limited. The aim of this study was to investigate the effects of hyperthermic preconditioning on the rate of surgical site infection and inflammatory reaction in patients undergoing elective colorectal cancer surgery.

Material and methods: Patients with colorectal cancer, scheduled to undergo elective surgery were enrolled in this prospective randomized study. Patients were randomly assigned to either the hyperthermic preconditioning group or control group. Postoperative superficial and deep surgical site infection were recorded. Blood samples were collected from all the patients in the hyperthermic preconditioning group prior to the application of hyperthermia 12 h before surgery, immediately prior to surgery, and 4 h and 24 h postoperatively. For the control group, blood samples were obtained within the same periods without the application of hyperthermia. Levels of interleukin-1, IL-6, and tumor necrosis factor-α were measured from blood samples.

Results: Twenty patients were randomized to the hyperthermic preconditioning group and 21 to the control group. No significant difference was found in deep or superficial surgical site infection between the groups. No significant difference in the tumor necrosis factor-α, interleukin-1, and IL-6 levels was found in serum samples collected before hyperthermia, during the operation, and postoperatively.

Conclusion: This study showed that hyperthermic preconditioning has no effect on the surgical site infection and cytokine response in patients undergoing elective surgical intervention for colorectal cancer.

Keywords: Colorectal cancer, hyperthermic preconditioning, inflammatory reaction, surgical infection

Cite this paper as:
Attaallah W, Şen LS, Aktan AÖ, Demiralp Ekşioğlu E, Eti Z, Güler SA, et al. Does hyperthermic preconditioning affect the rate of surgical site infection rate and inflammatory reaction in colorectal cancer patients? A prospective randomized clinical trial. Turk J Surg 2018; 34(4): 282-285.

[1]Department of General Surgery, Marmara University School of Medicine, İstanbul, Turkey
[2]Department of Immunology, Marmara University School of Medicine, İstanbul, Turkey
[3]Department of Anesthesia, Marmara University School of Medicine, İstanbul, Turkey

Corresponding Author
Wafi Attaallah
e-mail: drwafi2003@yahoo.com

Received: 08.09.2017
Accepted: 01.11.2017
Available Online Date: 11.09.2018

INTRODUCTION

Hyperthermic preconditioning (HP) has been shown to be protective against different insults in experimental studies. HP protects against stress conditions in the small intestine, liver, kidney, hippocampus, forebrain, and heart (1, 2). Animal studies have shown that hyperthermia protects against intestinal ischemia/reperfusion injury and the lethal effects of endotoxin (3, 4) and decreases intestinal permeability in septic mice (5). HP can improve the immune response and subsequently might play a protective role in reducing the severity of fecal peritonitis and sepsis in rats (6, 7).

Hyperthermia (HT) induces heat-shock protein (HSP) expression and decreases pancreatic injury. It has also been shown to improve survival in cases of necrotizing pancreatitis (8). The protective effect of HT has been commonly related to the induction of HSPs. Systemic HT is currently used in the treatment of certain malignant diseases (9-11). The positive effect of fever on survival during infections has been well known for several years (12-14). However, despite positive results of experimental studies, the effectiveness of HP in clinical studies remains limited. This prospective randomized study aimed to investigate the effects of HP on surgical site infection (SSI) rates and inflammatory reaction in colorectal cancer patients.

MATERIAL AND METHODS

Colorectal cancer patients undergoing elective surgery with a curative intent were enrolled in this prospective randomized study at Marmara University Hospital between May 2007 and February 2009. The Marmara University Research Ethics Committee approved the study, and all the subjects provided informed consent before participating in the study.

Patients with colorectal cancer, scheduled to undergo elective surgery with a curative intent, having American Society of Anesthesiologists (ASA) I-II scores were included in the study. Patients with metastatic or disseminated disease, obstruction, and perforation were excluded. Patients not tolerating HT, having ASA scores above II, and those who did not give informed consent were also excluded. The sample size was determined by a power analysis owing to the assumption that HP will decrease infection rate.

By using an internet randomization table, patients were randomly assigned to either of these groups:

1. HP group: Patients were exposed to heat for 1 h using a heating blanket (39°C) 12 h before surgery. After the heating procedure was completed, patients were followed until surgery at normal room temperature.

2. Control group: Patients were kept at room temperature.

Patients were randomized according to their application dates to our clinic. One of the authors (AC) enrolled participants and assigned them to interventions after generating the random allocation sequence. The participants were blinded after being assigned to interventions according to the randomization table. Duration of postoperative stay in the hospital, number of blood transfusions, and SSI rates were recorded for all the participants. Postoperative complications, including superficial and deep SSI and anastomotic leaks, were also noted. Patients were followed for 30 days after surgery for SSIs. Low molecular weight heparin was administered to all patients for deep venous thrombosis prophylaxis, and its dose was adjusted according to body weight. The antibiotics cefazolin and metronidazole were also routinely administered.

Table 1. Patient characteristics and study results

	Hyperthermic preconditioning group n=20	Control group n=21	p[a]
Age (years)[b]	59 (30–88)	69 (36–81)	0.074[c]
Gender*			
Male	10 (50)	9 (43)	0.65[d]
Female	10 (50)	12 (57)	
ASA*			
I	14 (70)	13 (62)	0.6[d]
II	6 (30)	8 (38)	
BMI (mean)	26±2	28±5	0,012[d]
SSI*	6 (30)	5 (24)	0,87[d]
COmorbid disease*	4 (6)	1 (5)	0,83
Smoking*	4 (20)	1 (5)	0,19[f]
Alcohol*	1 (5)	2 (10)	1.0[f]
Postoperative stay in hospital[#]	5.6±2.7	6±3	0,66[d]
Anastomosis leak*	0 (0)	1 (5)	1.0[f]
Postoperative complications	45 (35–240)	59 (55–270)	0.07[c]
Tumor distance from anal verge*			
≤6 cm	24 (38)	6 (30)	0.3[d]
>6 cm	40 (62)	14 (70)	
Blood transfusion*	21 (33)	1 (5)	0,014[d]
SSI risk*	30 (47)	5 (25)	0.083[d]
Follow-up period[b]	11 (1–20)	6 (2–19)	0.21[c]

[a]Comparison between two groups
[b]Values are medians (range)
[c]Mann–Whitney U test
[d]Chi-square test
[e]t test for independent samples
[f]Fisher's exact test
*; n (%), [#]; mean±SD

ASA: American Society of Anesthesiologists; BMI: body mass index; HP: hyperthermic preconditioning; SSI: surgical site infection

Blood samples were collected from all the patients in the HP group prior to the application of hyperthermia 12 h before surgery, immediately prior to surgery, and 4 h and 24 h postoperatively. In the control group, blood samples were obtained within the same periods without the application of hyperthermia. Collected blood samples were centrifuged, and serum samples were stored at −200°C and were later used to measure isnterleukin-1 (IL-1), Interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) levels.

Isnterleukin-1 and IL-6 enzyme-linked immunosorbent assay kits were used according to the manufacturer's recommendations without any modification. A plate reader set at 450 nm was used to measure optical densities. IL-1, IL-6, and TNF-α levels in the samples were calculated from the standard curve and were multiplied by the dilution factor (expressed as pg/mL).

The trial was completed after all randomized patients finished the study protocol.

Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS; version 17.0) statistical software (SPSS, Inc., Chicago, IL, USA). Fisher's exact test and two-tailed chi-square test were used to compare categorical variables (e.g., surgical side infection and gender), whereas the independent two-sample t-test and the Mann–Whitney U test were used to analyze con-

Table 2. TNFα, IL1, and IL6 values in the study groups

	Hyperthermic preconditioning group n=20	Control group n=21	p[a]
TNF levels			
Prior to hyperthermia	5.76 (0.086–727)	6.72 (0–68.9)	0.9[a]
Prior to start operation	5.85 (0.05–497)	5.79 (0–154)	1.0[a]
Postoperative 4 h	7.0 (0.06–727)	6.0 (0–136)	0.7[a]
Postoperative 24 h	5.0 (0.05–417)	5.645 (0–96.3)	0.8[a]
IL-1 levels			
Prior to hyperthermia	0.60 (0.27–2.46)	0.68 (0.18–67)	0.18[a]
Prior to start operation	0.49 (0.17–2.07)	0.52 (0.09–26)	0.38[a]
Postoperative 4 h	0.66 (0.18–45.6)	0.61 (0.16–9.8)	0.67[a]
Postoperative 24 h	1.12 (0.13–3.0)	0.57 (0.14–4.05)	0.40[a]
IL-6 levels			
Prior to hyperthermia	1.94 (0.05–11.2)	6.7 (0.3–238)	0.075[a]
Prior to start operation	2.0 (0.05–21.5)	6.0 (0.05–59.8)	0.06[a]
Postoperative 4 h	104.0 (6.49–238)	10.65 (4.06–238)	0.16[a]
Postoperative 24 h	46.95 (6.9–97)	13.2 (4.06–238)	0.087[a]

[a]Mann–Whitney U Test
TNF-α: tumor necrosis factor-α; IL-1: interleukin-1; IL-6: interleukin-6

tinuous variables (e.g., age). All statistical tests were two-sided, and p-value <0.05 was considered to be significant.

RESULTS

Forty-one patients with colorectal carcinoma were randomized for this study. Twenty patients were randomized to the HP group and 21 to the control group. Age, gender, ASA scores, presence of comorbid disease, alcohol and cigarette consumption, and number of blood transfusions were similar in both groups, while the body mass index was higher in the control group (26±2 vs 28±5, p=0.012). Patient demographics are given in Table 1.

Superficial SSI was detected in six patients in the HP group (30%). In the control group, superficial SSI was noted in five patients (24%) at the postoperative 30-day follow-up (p=0.87). An anastomotic leak was noted in one patient in the control group, while none were detected in the HP group. Duration of the postoperative stay showed similar results (p=0.66).

The median TNF-α levels were 5.76 (0.08–727), 5.85 (0.05–497), 7.0 (0.06–727), and 5.0 (0.05–417) pg/mL prior to HT, prior to surgery, and at postoperative 4 and 24 hours, respectively. In the control group, the corresponding values were 6.72 (0–68.9), 5.79 (0–154), 6.0 (0–136), and 5.65 (0–96.3) respectively. No statistically significant difference was found among the groups.

The median IL-1 levels were 0.6 (0.27–2.46), 0.49 (0.17–2.07), 0.66 (0.18–45.6), and 1.12 (0.13–3.0) prior to HT, prior to surgery, and at 4 h and 24 h postoperatively, respectively. In the control group, the corresponding values were 0.68 (018–67.0), 0.52 (0.09–26.0), 0.61 (0.16–9.8), and 0.57 (0.14–4.0), respectively. No statistically significant difference was noted.

The median IL-6 levels were 1.94 (0.05–11.2), 2.0 (0.05–21.5), 104.0 (6.49–238), and 46.95 (6.9–97) prior to HT, prior to surgery, and at 4 h and 24 h postoperatively, respectively. In the control group, the corresponding values were 6.7 (0.3–238), 6.0 (0.05–59.8), 10.65 (4.06–238), and 13.2 (4.06–238), respectively. No statistically significant difference was found (Table 2). There was no complication or any unintended effect in each group.

DISCUSSION

In this prospective randomized study, the effect of HP was investigated in patients with colorectal carcinoma treated with a curative intent. No significant difference was found in the rate of SSI among the control and HP groups. In addition, no significant difference was found in TNF-α, IL-1, and IL-6 levels among the groups.

Most of the studies reporting the protective effect of HP in various stress states are experimental studies performed in animals, and clinical studies remain limited. However, HT has been more widely used in humans. Systemic HT is currently used in the treatment of certain malignant diseases (9-11), and the positive effect of fever on survival in infections has been well known for several years (12-14). Fever-range hyperthermia has been shown to improve the outcome of serious infections in several animal models (7, 15-17). It was suggested that fever may enhance polymorphonuclear leucocyte (PMNL) function, which is the most important defense mechanism against acute bacterial infections. In one rat model, HT was found to increase PMNL counts via the attenuation of apoptosis (18). Furthermore, better leukocyte trafficking was found, which was also associated with tumor regression (19). Therefore, despite insufficient evidence of benefit in humans, HT has been increasingly used in not only complementary or alternative medicine, but also some clinical oncology centers, as an adjunctive treatment to chemoradiotherapy and for the treatment of certain inflammatory diseases.

Previously, induction of heat-shock response was found to preserve organ function and reduce cell injury in myocardial and renal ischemia (20, 21). It has been suggested that heat therapy administered before the onset of sepsis may decrease the production of IL-1 and TNF-α and thus might reduce the harmful effects endotoxin release (22). All these positive results were obtained in experimental studies. In contrast to other studies (7, 15-17), an animal study performed by our group failed to demonstrate improvement in the rate of survival at 120 h of intra-abdominal sepsis using HP alone.

Cytokines mediate local inflammatory responses at the site of injury and infection. An exaggerated pro-inflammatory cytokine response to infectious stimuli may result in severe hemodynamic effects (i.e., septic shock) and alteration in the metabolic equilibrium (i.e., increased muscle catabolism and wasting) (23). In this clinical study, no significant difference among the groups in TNF-α, IL-1, and IL-6 levels was found in all the serum samples collected before HP, during the operation, and postoperatively (at 4 h and the 24 h).

The small number of patients is the most important limitation of this study that needs to be acknowledged. Moreover, different temperatures and different preconditioning models may leasd to different results. The duration of HT (39°C) (1 h and 12 h) before surgery, may not have been the best model. Recent research has shown that HSPs can protect isolated cells from the cytotoxic effects of IL-1 and TNF-α, which are considered to be the chief mediators of sepsis (24-26). In this study, HSPs were not investigated. However, IL-1, IL-6, and TNF-α levels were not significantly different in the control and HP groups, which provides indirect effect on the HSP response.

The pro-inflammatory cytokine response was not different among the groups and at the same time the values obtained varied widely in both groups, contributing to statistical indifference. Superficial SSI was detected in six patients in the HP group (30%) and in five patients in the control group (24%) during the postoperative 30-day follow-up. Also, one anastomotic leak was noted. The presence of infection increases pro-inflammatory cytokines, and high infection rate is probably responsible for the broad variation in cytokine values.

CONCLUSION

This study showed that HP has no effect on SSI and cytokine response in patients undergoing elective surgical intervention for colorectal cancer.

Ethics Committee Approval: The authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects.

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.C., A.Ö.A., Z.E., E.D.E.; Design - A.C., A.Ö.A., Z.E., E.D.E.; Supervision - A.C., A.Ö.A., W.A., L.S.Ş., S.A.G.; Resource - W.A., A.Ö,A., A.C., L.S.Ş., S.A.G.; Materials - W.A., L.S.Ş., S.A.G., A.C., E.D.E.; Data Collection and/or Processing - W.A. L.S.Ş.,S.A.G., E.D.E.; Analysis and/or Interpretation - W.A., A.C., A.Ö.A., Z.E.; Literature Search - W.A., A.C., A.Ö.A., Z.E., L.S.Ş.; Writing Manuscript - W.A., A.Ö.A., A.C.; Critical Reviews - L.S.Ş., Z.E., E.D.E.

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

Financial Disclosure: This study with project no SAĞ-031/131102 has been supported by Marmara University Scientific Research Projects Commission.

REFERENCES

1. Sakurai M, Aoki M, Abe K, Sadahiro M, Tabayashi K. Selective motor neuron death and heat shock induction after spinal cord ischemia in rabbits. J Thorac Cardiovasc Surg 1997; 113: 159-164. [CrossRef]
2. Flanagan SW, Ryan AJ, Gisolfi CV, Moseley PL. Tissue-specific HSP70 response in animals undergoing heat stress. Am J Physiol 1995; 268: 28-32. [CrossRef]
3. Stojadinovic A, Kiang J, Smallridge Y, Galloway R, Shea-Donohue T. Induction of heat-shock protein 72 protects against ischemia/reperfusion in rat small intestine. Gastroenterology Aug 1995; 109: 505-515. [CrossRef]
4. Hotchkiss R, Nunally I, Lindquist S, Taulien J, Perdrized G, Karl I. Hyperthermia protects mice against the lethal effects of endotoxin. Am J Physiol 1993; 265: 1447-1457. [CrossRef]
5. Wang Q, Hasselgren PO. Heat shock response reduces intestinal permeability in septic mice: potential role of interleukin-10. Am J Physiol Regul Comp Physiol 2002; 282: 669-676. [CrossRef]
6. Ozveri ES, Bekraki A, Cingi A, Yuksel M, Demiralp EE, Yegen BC, et al. The effect of hyperthermic preconditioning on the immune system in rat peritonitis. Intensive Care Med 1999; 25: 1155-1159. [CrossRef]
7. Güllüoğlu BM, Aksoy BS, Ozveri ES, Yüksel M, Demiralp EE, Aktan AO. Optimal timing and temperature for hyperthermic preconditioning in an animal model of fecal peritonitis. J of Investigative Surg 2002; 15: 117-124. [CrossRef]
8. Grise K, Kim F, McFadden D. Hyperthermia induces heat-shock protein expression, reduces pancreatic injury and improves survival in necrotizing pancreatitis. Pancreas Aug 2000; 21: 120-125. [CrossRef]
9. Bone RC. American College of Chest Physicians/Society of Critical Care of Medicine Consensus Conference:definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med 1992; 20: 864 -874 [CrossRef]
10. Robins HI, Sielaff KM, Storer B, Hawkins MJ, Borden E. Phase I trial of human lymphoblastoid interferon with whole body hyperthermia in advanced cancer. Cancer Res 1989; 49: 1609-1615
11. Trautman JA. Artificial fever therapy:a discussion of its management and a report of the complications of treatments. Arch Phys Ther 1942; 23: 196-206.
12. Covert JB, Reynolds WW. Survival value of fever in fish. Nature 1977; 267: 43-46. [CrossRef]
13. Kluger MJ. Fever role of pyrogens and cryogens. Physiol Rev 1991; 71: 93-127. [CrossRef]
14. Kluger MJ, Ringler DH, Anver MR. Fever and survival. Science 1975; 188: 166-168. [CrossRef]
15. Hotchkiss R, Nunnally I, Lindquist S, Taulien J, Perdrizet G, Karl I. Hyperthermia protects mice against the lethal effects of endotoxin. Am J Physiol 1993; 265: R1447-R1457. [CrossRef]
16. Koh Y, Lim CM, Kim MJ, Shim TS, Lee SD, Kim WS, et al. Heat shock response decreases endotoxin-induced acute lung injury in rats. Respirology 1999; 4: 325-330. [CrossRef]
17. Villar J, Ribeiro SP, Mullen JB, Kuliszewski M, Post M, Slutsky AS. Induction of the heat shock response reduces mortality rate and organ damage in a sepsis-induced acute lung injury model. Crit Care Med 1994; 22: 914-921. [CrossRef]
18. Chen HW, Hsu C, Lue SI, Yang RC. Attenuation of sepsis-induced apoptosis by heat shock pretreatment in rats. Cell Stress Chaperones 2000; 5: 188-195. [CrossRef]
19. Chen Q, Fisher DT, Kucinska SA, Wang WC, Evans SS. Dynamic control of lymphocyte trafficking by fever-range thermal stress. Cancer Immunol Immunother 2006; 55: 299-311. [CrossRef]
20. Donnelly TJ, Sievers RE, Vissern FL, Welsh WJ, Wolfe CL. HSP induction in rat hearts:a role for improved myocardial salvage after ischemia and reperfusion? Circulation 1992; 85: 769-778. [CrossRef]
21. Perdrizet GA, Heffron TG, Buckingham FC, Salciunas PJ, Gaber AO, Stuart FP, et al. Thistlethwaite JR Stress conditioning: anovel approach to organ preservation. Curr Surg 1989; 46: 23-26.
22. Hotchiss R, Nunnally I, Lindquist S, Taulien J, Perdrizet G, Karl I. Hyperthermia protects mice against the lethal effects of endotoxin. Am J Physiol 1993; 265: 1447-1457.
23. Badar V, Stephen F. Lowry. Schwartz's priciples of surgery. Ninth edition, Chapter 2. p. 20.
24. Jaatlela M, Saksela K, Saksela E. Heat shock protectes WEH1±164 target cells from the cytolysis by tumor necrosis factors alpha and beta. Eur J Immunol 1989; 19: 1413-1417. [CrossRef]
25. Larrick JW. Antibody inhibition of the immunoinflammatory cascade. J Crit Care 1989; 4: 211-221. [CrossRef]
26. Margulis BA, Sandler S, Eizirik D, Welsh N, Welsh M. Purified heat shock protein hsp 70 into rat pancreatic islets as protection against interleukin 1b-induced impaired b cell function. Diabetes 1991; 40: 1418-1422. [CrossRef]

Turk J Surg 2018; 34(4): 286-289
DOI: 10.5152/turkjsurg.2018.3988

Original Article

Could local antibiotics be included in the treatment of acute anal fissure?

Banu Karapolat

ABSTRACT

Objective: Acute anal fissure is a very common disorder of the anorectal region. Its most widely used treatment method is the medications given in addition to conservative therapies. The objective of the present study was to investigate the effects of local metronidazole use in the treatment of acute anal fissure on the symptoms and remission processes of the patients.

Material and Methods: This was a prospective, randomized, controlled clinical study conducted on 100 consecutive patients who presented to our clinic between March 2016 and March 2017 and who were diagnosed with acute anal fissure. Patients were randomly divided into two groups of 50 persons. Patients in Group 1 were given only 5% lidocaine pomade as a local anesthesia, and those in Group 2 were given 5% lidocaine pomade and metronidazole cream. Patients applied the medications topically to the anal margin 3 times per day for 4 weeks. Patients' demographic characteristics, such as age and gender, were recorded. All patients were invited for check-up at the end of weeks 1, 2, and 4 of treatment. The Visual Analogue Scale scores for pain and the healing status of their fissure by visual inspection, as well as any adverse effects of the drugs, were recorded. The results were compared statistically. A p-value <0.05 was considered significant.

Results: The mean ages of the patients were 34.2±4.1 years in Group 1 and 36.6±3.8 years in Group 2. As a result of the statistical comparison of the Visual Analogue Scale scores, there was a statistically significant difference between the two groups at the end of weeks 2 and 4 (p=0.004 and p<0.001, respectively). In Group 1, 28 (56%) patients recovered, but no recovery was observed in 22 (44%) patients. In Group 2, 43 (86%) patients recovered, whereas 7 (14%) patients had no recovery (p=0.004).

Conclusion: The topical antimicrobial treatment with metronidazole as an addition to the classical medical treatments in acute anal fissure is an effective and safe practice resulting in further reduction in pain and increased healing rate.

Keywords: Acute anal fissure, antibacterial agents, metronidazole, therapeutics

INTRODUCTION

Anal fissure is one of the most common diseases of the anorectal region that is frequently encountered in surgical practice (1). It is a longitudinal rupture of the stratified squamous epithelial tissue formed in the anoderm distal to the dentate line and is generally located on the middle line posterior to the anus (2, 3). Although the exact etiology is not clearly known, the factors affecting the physiopathology of anal fissure are thought to include disadvantageous anatomic structure such as tight anal sphincter and multifactorial origin, such as internal anal sphincter spasms, ischemia, infectious conditions, and local traumas due to hard stool passage, long-lasting constipation, or diarrhea.

In the treatment of acute anal fissure where a speedy and effective treatment is preferred, nitroglycerin and calcium channel blockers, such as diltiazem, are also used as first-line agents in addition to conservative treatments, such as fiber-rich diet and warm sitz baths. These reduce the internal anal sphincter tone. Local anesthesia and steroid containing pomades are also used to eliminate pain and laxatives to prevent any anal canal trauma (3, 4). In patients who do not respond to these medical treatments, a surgical lateral internal sphincterotomy is required as a gold standard of treatment (3, 5, 6). Anal fissure is often accompanied by infections in many patients as the rupture is in a region with a bacterial concentration and due to personal hygiene problems. In such cases, antibiotherapy that can be used against infection in addition to the classical treatment of anal fissure may facilitate recovery of patients.

Metronidazole is a 5-nitroimidazole derivative antibiotic of a lipophilic character with a bactericidal effect particularly on anaerobic pathogen bacteria. It is widely used in clinical practice against protozoon infections as well as for the treatment of ailments where mixed pathogen microorganisms are active.
The purpose of the present study was to investigate whether it is effective and safe to use a metronidazole-containing local antibiotic in reducing the symptoms and improving the recovery process when treating patients for acute anal fissure.

ORCID ID of the author:
B.K. 0000-0001-5132-8266.

Cite this paper as:
Karapolat B. Could local antibiotics be included in the treatment of acute anal fissure?. Turk J Surg 2018; 34(4): 286-289.

Department of General Surgery, Kanuni Training and Research Hospital, Trabzon, Turkey

Corresponding Author
Banu Karapolat
e-mail:banukarapolat@hotmail.com

Received: 15.08.2017
Accepted: 06.12.2017
Available Online Date: 11.09.2018

MATERIAL AND METHODS

This was a prospective, randomized, controlled clinical study conducted on 100 consecutive patients who presented to the general surgery outpatient clinic of Trabzon Kanuni Training and Research Hospital between March 2016 and March 2017 were diagnosed with acute anal fissure. The major complaints of the patients were painful defecation, bleeding, constipation, diarrhea, and itching. The diagnosis of acute anal fissure was made based solely on clinical examination. The study included patients aged between 18 and 70 years who had their complaints for <6 weeks, whose lesions were limited to the epithelium, and who had pain in the anal region together with ulcers in the posterior anoderm without any skin tags. Patients with perianal fistula, perianal abscess, accompanying inflammatory bowel disease, and immune deficiency; receiving oral immunosuppressive drugs or steroids; with a history of hemorrhoid or hemorrhoidectomy; with a chronic disease, such as ischemic heart disease, hypertension, chronic obstructive pulmonary disease, and diabetes mellitus; who were pregnant; and with lateral or anterior localized fissures were excluded from the study.

Patients were randomly divided into two groups of 50 persons by choosing a color-coded card in thick white envelopes. Patients received the medication from an assistant staff who saw the color of the cards. The researcher was blinded to the medicine administered to each patient. Patients in Group 1 were given only 5% lidocaine pomade (Anestol 5% pomade; Sandoz İlaç San. ve Tic. A.Ş., Istanbul, Turkey) as a local anesthesia, and those in Group 2 were given 5% lidocaine pomade (Anestol 5% pomade) and metronidazole cream (Roza cream; ORVA İlaç San. ve Tic A.Ş., Izmir, Turkey). All patients underwent detailed anamnesis and physical examination before treatment was commenced. All patients were instructed to apply a pea-sized amount of each drug topically to their anal margins 3 times per day for 4 weeks. They were also advised to follow a fiber-rich diet, take the laxatives, and have a 15-minute warm bath 3 times per day. Patients' demographic characteristics, such as age and gender, were recorded. All patients were physically examined at the end of weeks 1, 2, and 4 of treatment. Complaints of pain during defecation were assessed using the Visual Analogue Scale (VAS). Clinical healing was considered as complete reepithelialization of the anal canal mucosa and closure of the fissure with no erythema or inflammation and elimination of patient complaints. The VAS score was used to measure pain. The scale was divided into 10 equal parts, with 0 to denote no pain and 10 to denote unbearable pain. All patients' VAS scores for pain and healing of fissure by visual inspection, as well as any adverse effects of the drugs, were recorded and statistically compared.

The study protocol was approved by the local ethics committee. All patients were provided with adequate verbal information about the study. Written informed consent was obtained from all patients. All patient data were kept confidential. The study was conducted according to the Declaration of Helsinki as revised in 2000.

Sample size

The sample size was determined post hoc. At the end of the study, the healing rate was found to be 56% in Group 1 and 86% in Group 2. Considering the healing rate prevalence as 86%, the sample size was calculated as 47 for one group at 95% confidence interval with 10% deviation, presuming type 1 error as 0.05. Calculation of the sample size was performed by the OpenEpi version 3 (http://www.openepi.com/SampleSize/SSPropor.htm).

Statistical Analyses

All statistical data analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 15.0 for Windows software (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used for comparisons. Student's t test, Mann–Whitney U test, and chi-square test were used to assess independent samples. A p-value <0.05 was accepted as statistically significant.

RESULTS

There were 40 (80%) female and 10 (20%) male patients in Group 1 and 38 (76%) female and 12 (24%) male patients in Group 2. The mean ages of the patients were 34.2±4.1 years in Group 1 and 36.6±3.8 years in Group 2. No statistically significant difference was found between the two groups with respect to gender distributions and mean ages (p=0.412 and p=0.510, respectively). An assessment of the patient complaints revealed that the most common complaint was pain and bleeding during defecation. Table 1 shows the frequencies and percentages of patient complaints in the groups. Table 2 shows the median duration of symptoms of patients. All patients completed the treatment period without any problems. No side effects or complications associated with the medications used occurred in any of the patients.

The mean VAS scores of the patients at the time of presentation to the hospital (pretreatment) were 7.8±0.9 in Group 1 and 7.9±0.7 in Group 2 (p=0.417). The mean VAS scores of the patients at the end of week 1 were 4.6±1.0 in Group 1 and 4.3±0.9 in Group 2 (p=0.151). The mean VAS scores of the patients at the end of week 2 were 3.3±1.3 in Group 1 and 2.6±1.1

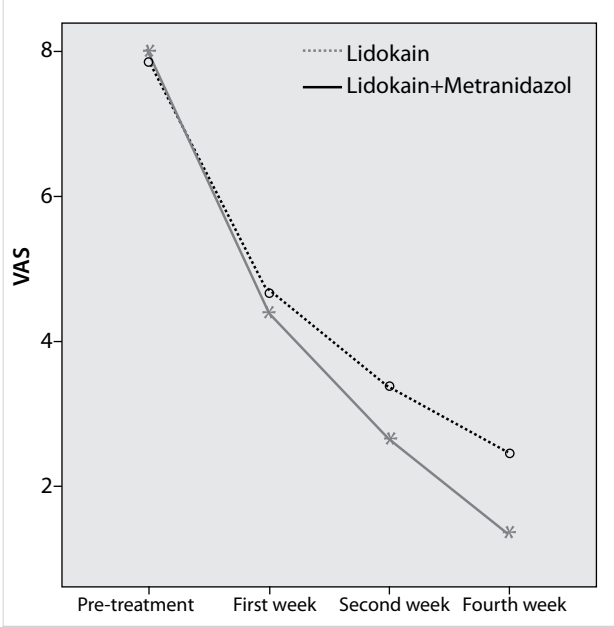


Figure 1. Reduction rates of the VAS scores of Group 1 and Group 2 during the study

Table 1. Frequencies and percentages of patient complaints in the groups

	Group 1 (n=50)	Group 2 (n=50)
Pain during defecation (days)	50 (100)	50 (100)
Bleeding (days)	40 (80)	37 (74)
Constipation (days)	33 (66)	35 (70)
Diarrhea (days)	7 (14)	8 (16)
Itching (days)	18 (36)	20 (40)

Datas are presented as n (%)

Table 2. Median duration of symptoms of patients

	Group 1 mean (range)	Group 2 mean (range)
Pain during defecation (days)	21 (9–41)	16 (5–38)
Bleeding (days)	11 (1–27)	9 (3–19)
Constipation (days)	29 (14–38)	32 (11–40)
Diarrhea (days)	8 (7–16)	5 (3–9)
Itching (days)	12 (5–26)	18 (5–32)

in Group 2 (p=0.004). The mean VAS scores of the patients at the end of week 4 were 2.47 in Group 1 and 1.36 in Group 2 with a median of 1 (interquartile range (IQR): 1–4) in Group 1 and a median of 1 (IQR: 1–1) in Group 2 (p<0.001).

A statistical comparison of the VAS scores showed that there was a statistically significant difference between the two groups at the end of weeks 2 and 4 (Figure 1).

In Group 1, 5 (10%) patients had recovery at week 2 and 23 (46%) patients at week 4 with no recovery seen in 22 (44%) patients. In Group 2, 9 (18%) patients had recovery at week 2 and 34 (68%) patients at week 4 with no recovery seen in 7 (14%) patients. There was a statistically significant difference between these data (p=0.004).

DISCUSSION

Acute anal fissure involves high prevalence and great discomfort and equally affects both women and men. We think that the reason why there were more female than male patients in the present study was because the surgeon who performed the anal examinations and treatments of the patients was a woman. The sociocultural characteristics of female patients in our country and particularly in our region call for conservative attitude and embarrassment associated with physical examination for perianal disorders, urging women to prefer a female surgeon. Acute anal fissure is mostly seen in individuals aged between 20 and 40 years. We found that the majority of the patients in our study were 30–40 years old, which is compatible with the literature (1, 2).

The typical symptoms of presentation in acute anal fissure are proctalgia and bleeding (7). Pain is usually sharp and intensifies during defecation. Bleeding may accompany painful defecation. Rectal bleeding is bright red in color and generally occurs in minor amounts (8). The initial complaints of our patients included mostly pain during and after defecation, bleeding, and constipation. These data are compatible with those in the literature (3, 7).

In the present study, we found that the use of local metronidazole in combination with local anesthesia drugs prescribed as a first-line therapy for acute anal fissure resulted in a marked reduction of pain symptoms especially after week 2 of treatment. The rupture occurring at the anoderm causes spasm at the internal sphincter located right under the fissure tissue and increases resting pressures of the anal canal, leading to pain and decrease regional blood flow. As a result, pain, spasm, and ischemia cycles turn the rupture into a difficult-to-cure wound, resulting in chronic anal fissure (3). In view of this information, the idea that eliminating pain effectively during the initial treatment will break the vicious cycle mentioned above and result in healing has led to the widespread use of local anesthesia drugs first in the medical treatment. A previous study showed that 40%–60% healing occurs with the use of local lidocaine in patients with acute anal fissure (9). Our results were similar to these except that the healing rate was 56% in the group where lidocaine was used alone. Considering that approximately half of the patients have not recovered using this treatment, it is obvious that elimination of other factors that may be effective in the physiopathology of acute anal fissure will increase the healing rate. We think that one of these important factors is local inflammation and infection as we consider the current flora of the region and the microorganisms in stool (Gram-positive/Gram-negative anaerobic bacteria or Gram-negative aerobic bacteria). In fact, a previous study stated that the infections in this region may be one of the main causes of acute anal fissure (10). Occasionally, even an infection localized in the subcutaneous area at the anal fissure region that progresses subclinically may cause the fissure symptoms to become chronic (11). As general information, if any wound is accompanied by ischemia and infection, healing of the wound is delayed. Owing to all these reasons, we included metronidazole, which has an effective spectrum on the above-mentioned microorganisms, in the first-line treatment of acute anal fissure in the present study. What happened here was that decreasing the bacterial load with topical antibacterial treatment accelerated fissure healing. Owing to this, the healing rate increased to 86% in Group 2. Keeping the local infection under control led to a decrease in pain that was associated with sphincter spasm aggravated by inflammation. This was demonstrated by decreases in the VAS scores at the end of weeks 2 and 4 of treatment. A review of the literature revealed that there was improvement in the symptoms in a pilot study involving local application of povidone-iodine solution in chronic anal fissure (12). Moreover, with oral ciprofloxacin and ornidazole that were used for a period of only 5 days, significant symptomatic relief was achieved in >90% of cases with chronic anal fissure (13). The same authors reported in 2014 that the local application of ornidazole cream for 3 months in addition to the above regimen sustained the symptomatic benefits achieved and helped cure chronic anal fissure in up to 90% of patients (14). Grekova et al. (10) found that patients with chronic anal fissure and anaerobic bacteria in their swabs who received topical metronidazole treatment experience rapid relief of pain and anal sphincter spasm along with enhanced fissure healing (healing rate: 95.6%). To our knowledge, this is the first study on the use of local antibiotics in acute anal fissure. All these results show that infection has a major role in the etiopathogenesis of anal fissure. For this reason, we think that local antibiotic use before

the condition becomes chronic will shorten the recovery time and increase the healing rates in cases with acute anal fissure.

The limitations of the present study include short follow-up time, small sample sizes of the two groups, and the study having been conducted in a single site. Therefore, the long-term recurrence rates of the patients remain unknown. Nevertheless, we think that our study adds useful data to the treatment of acute anal fissure. Further multicenter clinical studies involving broad patient populations, longer follow-up times, and recurrence rates will aid to understand the efficacy and safety of metronidazole in the treatment of acute anal fissure.

CONCLUSION

Although various non-surgical and surgical treatment methods have been used, an ideal treatment method for acute anal fissure is still debatable. The topical antimicrobial treatment with metronidazole in addition to conventional medical treatments is an effective, easy-to-use, safe, fast and comfortable practice that enables further reduction of anal fissure pain and increases the healing rate. With this promising treatment, cases with acute anal fissure can be prevented from becoming chronic, and patients can be saved from being subject to future surgical interventions that involve high complication rates.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Kanuni Training and Research Hospital.

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

Peer-review: Externally peer-reviewed.

Conflict of Interest: The author has no conflicts of interest to declare.

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

REFERENCES

1. Vaithianathan R, Panneerselvam S. Randomised Prospective Controlled Trial of Topical 2% Diltiazem Versus Lateral Internal Sphincterotomy for the Treatment of Chronic Fissure in Ano. Indian J Surg 2015; 77(Suppl 3): 1484-1487. [CrossRef]
2. Motie MR, Hashemi P. Chronic Anal Fissure: A Comparative Study of Medical Treatment Versus Surgical Sphincterotomy. Acta Med Iran 2016; 54: 437-440.
3. Coskun A, Uzunkoy A, Akinci F. The treatment efficacy of medical sphincterotomy with glycerol trinitrate on acute and chronic anal fissures. Ulus Cerrahi Derg 2000; 16: 176-181.
4. Uluutku H, Akin ML, Erenoglu C, Yildiz M, Urkaya N, Celenk T. Efficacy of nifedipine, glyceryl trinitrate and botulinum toxin in treatment of chronic anal fissure. Ulus Cerrahi Derg 2001; 17: 343-350.
5. Colak T, Ipek T, Kanik A, Aydin S. A randomized trial of botulinum toxin vs lidocain pomade for chronic anal fissure. Acta Gastroenterol Belg 2002; 65: 187-190.
6. Yakoot M, Abdel Salaam M. Study of efficacy and safety of a new local cream ('healer') in the treatment of chronic anal fissure: a prospective, randomized, single-blind, comparative study. Arq Gastroenterol 2009; 46: 179-182. [CrossRef]
7. Sánchez Romero A, Arroyo Sebastián A, Pérez Vicente F, Serrano Paz P, Candela Polo F, Tomás Gómez A, et al. Open lateral internal anal sphincterotomy under local anesthesia as the gold standard in the treatment of chronic anal fissures. A prospective clinical and manometric study. Rev Esp Enferm Dig 2004; 96: 856-863. [CrossRef]
8. Khaledifar B, Mahmoudi MY, Mobasheri M. A Double-Blind Randomized Trial Comparing the Effectiveness and Safety of Nifedipine and Isosorbide Dinitrate in Chronic Anal Fissure. Malays J Med Sci 2015; 22: 42-49.
9. Higuero T. Update on the management of anal fissure. J Visc Surg 2015; 152(2 Suppl): S37-S43. [CrossRef]
10. Grekova NM, Maleva EA, Lebedeva Y, Bordunovsky VN, Telesheva LF, Bychkovskikh VA. The effects of topical application of metronidazole for treatment of chronic anal fissure: A randomized, controlled pilot study. Indian J Gastroenterol 2015; 34: 152-157. [CrossRef]
11. Garg P. Local and Oral Antibiotics with Avoidance of Constipation (LOABAC) Treatment for Anal Fissure: a New Concept in Conservative Management. Indian J Surg 2016; 78: 80. [CrossRef]
12. Durai R, Razvi A, Hin PN. Novel use of povidone iodine in fissure-in-ano. Singapore Med J 2010; 51: 837-838.
13. Garg P, Lakhtaria P, Nalamati S, Gupta V, Thakur J. Chronic anal fissure: is it an infection in a physically deformed lesion?—a new insight into an old plight. In Annual conference of American Society of Colon Rectum Surgeons (ASCRS). San Antonio 2012.
14. Garg P, Lakhtaria P. Non-surgical management of chronic fissure-in-ano with high success rate: a simple novel concept in the treatment of chronic fissure-in-ano. In Annual conference of American Society of Colon Rectum Surgeons (ASCRS). Fort Laurderdale 2014.

Turk J Surg 2018; 34(4): 290-294
DOI: 10.5152/turkjsurg.2018.4025

Original Article

Cosmetic outcomes of infraumbilical, supraumbilical, and transumbilical entry routes in laparoscopic surgery

Mehmet Baki Şentürk[1], Ozan Doğan[2], Mesut Polat[1], Çetin Kılıççı[3], Çiğdem Pulatoğlu[4], Ahter Tanay Tayyar[3]

ABSTRACT

Objective: The aim of the present study was to determine which of the umbilical entry routes for intraperitoneal access has a better cosmetic result.

Material and Methods: This was a prospective study (Canadian Task Force classification II-1). In total, 105 patients who underwent laparoscopic surgery were included. A vertical or transverse umbilical incision is appropriately made for the trocar to be inserted, and an infraumbilical, supraumbilical, or transumbilical route was preferred for initial intraperitoneal access. Demographic data of patients, body mass indices, entry point of the trocars (infraumbilical–transumbilical–supraumbilical), type of incision (vertical–transverse), duration of the operation, and scar properties at postoperative week 12 were prospectively collected and analyzed. The Vancouver scar scale was used to evaluate the cosmetic results.

Results: Cosmetic results did not differ statistically between the transumbilical–infraumbilical–supraumbilical groups. The variables, such as vascularity, height, and total score, of the Vancouver scar scale were significantly higher in patients who had transverse incisions. There was no statistically significant effect of using a Veress needle with the cosmetic results. There was no statistically significant correlation between age, gravida, body mass indices, skin thickness, time of entry, duration of the operation, and cosmetic results in terms of vascularity, height, and total score.

Conclusion: During laparoscopic surgery, each patient should be assessed individually for the satisfaction of the patient and, thereby, of the surgeon in terms of cosmetic outcomes. Vertical incision offers superior cosmetic effects than transverse incision. Further research is required to define long-term scar-related outcomes of the laparoscopic intraperitoneal access techniques.

Keywords: Cosmetic outcome, laparoscopic surgery, umbilical incision, scarless surgery

ORCID IDs of the authors:
M.B.Ş. 0000-0002-1915-163X;
O.D. 0000-0002-0016-8749;
M.P. 0000-0003-0618-742X;
Ç.K. 0000-0002-9674-2505;
Ç.P. 0000-0002-7595-3629;
A.T.T. 0000-0001-9491-9998.

Cite this paper as:
Şentürk MB, Doğan O, Polat M, Kılıççı Ç, Pulatoğlu Ç, Tanar AT. Cosmetic outcomes of infraumbilical, supraumbilical, and transumbilical entry routes ın laparoscopic surgery. Turk J Surg 2018; 34(4): 290-294.

[1]Department of Obstetrics and Gynecology, İstanbul Medeniyet University School Of Medicine, İstanbul, Turkey

[2]Department of Obstetrics and Gynecology, Şişli Hamidiye Etfal Training and Research Hospital, İstanbul, Turkey

[3]Department of Obstetrics and Gynecology, Zeynep Kamil Training and Research Hospital, İstanbul, Turkey

[4]Department of Obstetrics and Gynecology, Bayburt Government Hospital, İstanbul, Turkey

Corresponding Author
Ozan Doğan
e-mail: ozandogan02@hotmail.com

Received: 03.11.2016
Accepted: 20.03.2017
Available Online Date: 28.08.2018

INTRODUCTION

Laparoscopic surgery is now a well-established alternative to open surgery for many gynecological disorders owing to its faster wound healing, shorter hospital stay, less postoperative pain, and better cosmetic results (1). Postoperative scar cosmesis is a critical issue for women, especially for young women. These scars may have negative impacts, such as psychological consequences. The symptoms associated with the wound, such as pain, tenderness, and itching, can be induced by the scars (2, 3). Recently, there has been an increased surge of interest in laparoscopy for scarless surgery with the development of surgical instruments and advancement of techniques. Surgeons are concerned about how to restore the natural appearance of the umbilicus as it is an important aesthetic component of the abdomen (4). In a review of laparoscopic practice, approximately half of the laparoscopists preferred the infraumbilical route and 35.7% the supraumbilical area for entry (5). To our knowledge, there are no studies in the literature describing cosmetic outcomes specific to the umbilical port insertion techniques.

The aim of the present study was to determine which method of infra–trans–supraumbilical entry techniques in laparoscopic surgery should be preferred in terms of cosmetic results.

Anatomy

The umbilicus is a cone-shaped tract with its apex pointing toward the surface. Its vertex, formed by the fusion of the skin, fascia, and peritoneum, is devoid of preperitoneal and subcutaneous fat no matter how obese the patient is. It is discernible on the surface as a tiny but clearly circumscribed punctum with a diameter of approximately 1 to 3 mm. The fascia, peritoneum, and skin are fused at the punctum. From the peripheral to the umbilical punctum, the fascia is separated from the overlying skin and the underlying peritoneum by variable amounts of fat even within the confines of the umbilical ring, and more laterally still, the fascia splits to cover the rectus muscles. At the umbilical ring, the circumferential confluence of the abdominal wall fascia and the skin results in a shallow region, allowing easy access to the abdominal cavity. The absence of the subcutaneous fat and muscle at the umbilicus suggests that

the dissection plane remains bloodless to the peritoneum if the midline is adhered to (6).

MATERIAL AND METHODS

This was a prospective study conducted between January and June 2016 at a single tertiary center. A total of 105 patients who underwent laparoscopic surgery were included in the study. The local ethics committee approved the study (clinical trial no: NCT02672956, approval no: 129). Written informed consent was obtained from all participants prior to enrollment in the study.

Patients with previous abdominal surgery and scar, umbilical hernia, burns in the umbilical region; who are in the postmenopausal period; and who have hyperpigmented skins were excluded from the study. Demographic data of patients, body mass indices (BMIs), entry point of the trocars (infra–trans–supraumbilical), type of incision (vertical–transverse), duration of the operation, and scar properties at follow-ups were prospectively collected and analyzed.

Patients were assigned to one of the groups by random allocation. The assigned entry points (infra–trans–supraumbilical) and incision types were sealed in secure opaque envelopes. The allocated envelope was opened before surgery. Under general anesthesia, the umbilicus was prepared by removing all debris using gauze, cotton swabs. A vertical or transverse umbilical incision was appropriately widened enough (1.0–1.5 cm) for the trocar to be inserted without undue resistance from the skin so that the trocar passed through the fascia and the peritoneum with ease. Infraumbilical, supraumbilical, or transumbilical incision was performed for initial intraperitoneal access. Access to the abdominal cavity was performed by direct trocar in some of the patients, whereas a Veress needle was inserted before the entry of the trocar in others. No clamps were used to elevate the abdominal wall in both methods. The trocar entry sites for intraperitoneal access and incision type were randomized, whereas the choice of using a Veress needle was left to the experience and preference of the surgeon. A 10-millimeter trocar was inserted, and the pneumoperitoneum was achieved by carbon dioxide insufflation, up to a pressure of 12 mm Hg. Surgical procedures were performed using conventional laparoscopic instruments under vision with a rigid 0-degree, 10-millimeter EndoEYE laparoscope (Laparoscope; Olympus Surgical Technologies America, Ohio, United States of America). The type of suture and technique for closing the skin and the fascia after the operation was the same for all cases. The fascia layer of the umbilical incision was closed with a number 0 absorbable monofilament suture material. The skin incision was closed with a number 2/0 rapid absorbable vicryl suture using a simple interrupted suture technique. Neither additional incisions nor laparotomic conversion was required in any cases. In the present case series, no major surgical complications were experienced. All of the operations were performed by two surgeons who were educated and experienced in laparoscopic operations.

Scar assessment was performed at postoperative week 12 by another surgeon other than the operator. The Vancouver scar scale was used to evaluate the healing of the port entry site in the umbilical region, and cosmesis analysis was performed. All patients were divided into groups according to the site of trocar insertion and incision type then compared in terms of cosmetic outcome.

All statistical analyses were performed using the Statistical Package for the Social Sciences version 22.0 for Windows (SPSS Inc., Chicago, IL, USA). Data were expressed by mean, median, standard deviation, percentage, and minimum and maximum values. The comparisons were conducted using the chi-square test, Spearman rank correlation analysis, and Kruskal–Wallis one-way ANOVA test, with post hoc analysis performed using the Mann–Whitney U test, as needed, for categorical and continuous variables. A p-value <0.05 was considered as statistically significant.

RESULTS

A total of 105 patients who underwent laparoscopic surgery for various gynecological disorders were evaluated. All patients were females. The mean age of the patients was 39.79±11.99 years. The BMI of the patients was 24.5±4.37 kg/m^2. The mean laparoscopic surgery duration was 94.90±42.88 min, and the mean time of trocar insertion was 2 (1–5) min. Transumbilical incisions were performed in 35 (33.3%) patients, infraumbilical incision in 36 (34.3%), and supraumbilical incision in 34 (32.4%). In addition, 53 (50.4%) patients had vertical incision, and 52 (49.5%) had transverse incision. A Veress needle was not used in 17 (16.2%) patients, and intraperitoneal access was provided by direct trocar entry. Table 1 shows the demographic data of the patients. The transverse incision was the most preferred incision in the supraumbilical group,

Table 1. Patient characteristics (n=105)

Age* (year)	39.79±11.99
Gravida (median (minimum–maximum))	2 (0–9)
BMI* (kg/m^2)	24.55±4.37
Skin thickness*	1.56±0.64
Site of entry#	
Infraumbilical	35 (33.3)
Supraumbilical	36 (34.3)
Transumbilical	34 (32.4)
Incision#	
Vertical	53 (50.4)
Transverse	52 (49.5)
Trocar entry time (min) (median (minimum–maximum))	2 (1–5)
Veress needle#	
Not used	17 (16.2)
Used	88 (83.8)
Duration of the operation* (min)	94.90±42.88
Vascularity*	1.21±0.50
Pigmentation*	1.54±0.57
Pliability*	1.28±0.70
Height*	0.89±0.66
Total*	4.94±1.58

*; mean±SD, #; n (%); BMI; body mass index

Table 2. Patient characteristics versus entry routes

	Infraumbilical (n=35) Mean±SD	Supraumbilical (n=36) Mean±SD	Transumbilical (n=34) Mean±SD	p
Age*** (year)	37.03±11.93	40.14±12.17	42.26±11.61	0.190*
BMI*** (kg/m^2)	24.66±3.40	24.68±4.76	24.32±4.91	0.932*
Duration of the entry*** (min)	2.23±1.03	2.47±1.25	2.09±1.26	0.394*
Skin thickness***	1.65±0.67	1.50±0.60	1.54±0.66	0.598*
Gravida median (IQR)	2 (3)	2 (1.75)	2 (3)	0.246**
Incision#				
Vertical	23 (65.7)	10 (27.7)	20 (58.8)	0.001**
Transverse	12 (34.2)	26 (72.2)	14 (41.1)	
Veres needle#	35 (100.0)	34 (94.4)	19 (55.9)	0.001**

*Spearman rank correlation analysis **Kruskal–Wallis one-way ANOVA test ***; mean±SD, #; n (%)
BMI; body mass index

Table 3. Cosmetic results according to the site of trocar entry

	Infraumbilical (n=35) Mean±SD	Supraumbilical (n=6) Mean±SD	Transumbilical (n=34) Mean±SD	p
Vascularity	1.23±0.55	1.25±0.55	1.18±0.39	0.744
Pigmentation	1.54±0.51	1.53±0.61	1.56±0.61	0.924
Pliability	1.17±0.71	1.33±0.63	1.32±0.77	0.557
Height	0.89±0.58	1.00±0.68	0.79±0.73	0.412
Total	4.83±1.54	5.11±1.75	4.88±1.45	0.631

Kruskal–Wallis one-way ANOVA test

Table 4. Cosmetic results according to the type of incision

	Vertical (n=53) Mean±SD	Transverse (n=52) Mean±SD	p
Vascularity	1.18±0.49	1.44±0.51	0.040
Pigmentation	1.51±0.59	1.75±0.45	0.122
Pliability	1.22±0.70	1.56±0.63	0.076
Height	0.82±0.63	1.31±0.70	0.008
Total	4.74±1.49	6.06±1.61	0.004

Mann–Whitney U test

Table 5. Cosmetic results according to the use of a Veress needle

	Not used (n=17) Mean±SD	Used (n=88) Mean±SD	p
Vascularity	1.29±0.47	1.20±0.51	0.460
Pigmentation	1.53±0.62	1.55±0.57	0.988
Pliability	1.29±0.77	1.27±0.69	0.950
Height	0.94±0.75	0.89±0.65	0.786
Total	5.12±1.76	4.91±1.55	0.915

Mann–Whitney U test

and a Veress needle was used more frequently in the infra–supraumbilical group than in the transumbilical group (Table 2).

Cosmetic results did not differ statistically between the trans–infra–supraumbilical groups (p>0.05) (Table 3). Vascularity, height, and total score were significantly higher in patients who had transverse incision (p=0.040, p=0.008, and p=0.004, respectively) (Table 4). There was no statistically significant effect of using a Veress needle on the cosmetic results (Table 5). There was no statistically significant correlation between age, gravida, BMI, skin thickness, time of entry, duration of the operation, and cosmetic results in terms of vascularity, height, and total score. As BMI increased, pigmentation also increased (p=0.015). The increase in gravida increased pliability (p=0.029). These relationships were found to be statistically significant (Table 6).

DISCUSSION

Laparoscopically, at the entrance to the abdominal cavity, an umbilical incision is often the first choice. This can be an infraumbilical, transumbilical, or supraumbilical incision. In the literature, there is a scarcity of data in terms of the cosmetic outcome on all three routes for laparoscopic port insertion (infra–trans–supraumbilical). Our study addresses this important need.

In the present study, it was shown that there were no differences between infra–trans–supraumbilical routes of entry to the peritoneal cavity in terms of cosmetic results, whereas it was found that cosmetic results were better in the vertical incision. It was suggested that the patient should be evaluated individually at admission, and vertical incision should be used with the technique that may have better cosmetic results.

Table 6. Correlation of cosmetic results and age, gravida, BMI, skin thickness, duration of the trocar entry, and operation

	Vascularity		Pigmentation		Pliability		Height		Total	
	r	p	r	p	r	p	r	p	r	p
Age (year)	–0.150	0.128	0.053	0.593	0.083	0.402	0.006	0.955	0.046	0.640
Gravida	0.019	0.850	0.010	0.923	0.214	0.029	0.024	0.809	0.091	0.355
BMI (kg/m^2)	0.053	0.588	0.237	0.015	–0.159	0.106	–0.069	0.483	0.001	0.991
Skin thickness	–0.10	0.325	–0.048	0.627	–0.015	0.877	–0.099	0.314	–0.061	0.538
Duration of the trocar entry (min)	0.052	0.600	0.070	0.477	–0.160	0.102	0.133	0.175	0.001	0.994
Duration of the operation (min)	0.103	0.295	–0.166	0.112	0.029	0.770	0.098	0.319	–0.025	0.798

Spearman rank correlation analysis
BMI; body mass index

Nozaki et al. (4) showed that a U-shaped infraumbilical incision that is made traditionally along the umbilical ring and the standardized site for access to the abdominal cavity for laparoscopy are well known; however, this type of incision leaves a more postoperative scar or umbilical deformity. Therefore, the umbilical depression had been everted, and the longitudinal skin incision of the umbilicus was made at the midline. The incision length was within the depression of the umbilicus. The scar receded into the umbilicus and was hardly visible (4). If the umbilicus has been previously used to gain access to the abdomen, one may access the abdomen through alternative incisions, such as infraumbilical incision (7). From our study, since there was no difference among cosmetic results of all three infra–trans–supraumbilical techniques, the umbilical entrance route may be selected, which has not been used during previous surgeries, to access the abdominal cavity easier and end up with better cosmetic results. The results of the present study showed no umbilical deformity on postoperative evaluation.

Kim et al. (8) preferred entry to the peritoneal cavity with supraumbilical incision, which they thought had better cosmetic results, based on the complaints of postoperative scars of female patients. The scar at the supraumbilical incision was found to be barely visible. Both patients and surgeons were satisfied with the cosmetic results of the supraumbilical entry, and the scar was integrated into the natural umbilical fold 3 months after surgery (8). In our study, the patients had postoperative follow-up in 12 weeks, and there was no difference in cosmetic results between all three infra–trans–supraumbilical techniques. Wang et al. (9) found that the cosmetic results of the transumbilical incision are remarkably well. However, the present study had no data on infra–supraumbilical incision (9).

Sinha used all three techniques and found that the transumbilical incision, rather than a supra- or infraumbilical incision, has a better cosmetic scar and a nearly normal-looking umbilicus (10). Transumbilical camera port insertion leaves no scar, but it has higher complication rates. Many pediatric surgeons use supraumbilical or infraumbilical port incision owing to complications following transumbilical insertion, such as wound site infection or trocar site hernia (11). According to our study, the cosmetic results of transumbilical port insertion appear to have no difference from other techniques. Therefore, it would be more advantageous to use other entry techniques instead of transumbilical entry that has more complication rates.

In a review that assessed the practice of general surgeons in Canada, it was shown that surgeons mostly prefer the transumbilical route in patients with no previous abdominal surgery. Half of the laparoscopists preferred infraumbilical port insertion, and 35.7% preferred suprapubic insertion. In the presence of suspected adhesions, the most preferred entry sites were the supraumbilical and infraumbilical regions with a frequency of 41.9% and 36.6%, respectively (12). Since patients with existing scar tissue due to previous surgery or burn were excluded in our study, intraoperative complications of the umbilical port insertion routes could not be evaluated. No data were found with regard to adhesions. These issues may be the limitations of our study.

The depth and length of the incision should depend on the size and diameter of the trocar to be inserted further. Sasmal et al. (13) suggested that vertical incision has better postoperative cosmetic results than transverse incision. Similar to our study, vertical incision had more satisfactory postoperative cosmetic results than transverse incision. On the contrary, Mowat et al. (14) reported that transverse incision is advantageous over longitudinal incision with regard to postoperative pain, mobility, and cosmetic effects.

In 1978, Dingfelder et al. (15) described direct trocar entry into the abdominal cavity and argued that the complications associated with a Veress needle do not occur at the entrance with direct trocars. In the literature, there are many studies that compare the entrance to the abdominal cavity with the aid of a Veress needle or with a direct trocar (16, 17). However, to our knowledge, there were no studies on the effect of a Veress needle on wound healing and cosmetic results. The use of a Veress needle had no statistically significant effect on the cosmetic results of the present study.

Studies have shown that as the BMI increases, the distance between the port insertion area and the abdominal organs increases, making it difficult to enter the abdominal cavity (18). Cosmetic healing can be negatively affected by micro and macro tissue damages during trocar entry. Although the Vancouver scar scale computes the total score rating, the scar height is the decisive factor (19, 20). In our study, no statistically significant relationship was found between vascularity, height, and total score with regard to the Vancouver scar scale of BMI.

The positive effect of estrogen on skin collagen and wound healing has been proven. Estrogen increases collagen content, skin thickness, and pliability (21). As gravida increases, the amount of exposed estrogen increases, hence pliability of the skin increases. In our study, the increase in gravida increases the pliability of the skin. However, as mentioned previously, the increase in pliability alone does not cause a clinically significant change in terms of cosmetic results. Estrogen also causes an increase in pigmentation; however, in our study, no significant difference was found between gravida increase and pigmentation. Since none of our patients were in the menopausal period, no estrogen deficiency was considered.

CONCLUSION

During laparoscopic surgery, each patient should be assessed individually for the satisfaction of the patient and, thereby, of the surgeon in terms of cosmetic outcomes. Vertical incision offers superior cosmetic effects than transverse incision. Further research is required to define long-term scar-related outcomes of the laparoscopic intraperitoneal access techniques (infra–supra–transumbilical).

Ethics Committee Approval: The local ethics committee approved the study (NCT02672956/129).

Informed Consent: Written informed consent was obtained from all patients who participated in this study.

Author Contributions: Concept - M.B.Ş., O.D., Ç.K.; Design - M.B.Ş., O.D., Ç.P.; Supervision - M.P., AT.T., O.D.; Resource - M.P., Ç.P., A.T.T.; Materials - M.B.Ş., O.D., M.P.; Data Collection and/or Processing - O.D., Ç.P., M.P.; Analysis and/or Interpretation - A.T.T., O.D., M.B.Ş.; Literature Search - O.D., Ç.P. ; Writing Manuscript - O.D., Ç.P., M.B.Ş.; Critical Reviews - Ç.K., O.D., M.B.Ş.

Conflict of Interest: The authors declare no conflict of interest.

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

REFERENCES

1. Pitkin RM, Parker WH. Operative laparoscopy: a second look after 18 years. Obstet Gynecol 2010; 115: 890-891. [CrossRef]
2. Vercelli S, Ferriero G, Sartorio F, Stissi V, Franchignoni F. How to assess postsurgical scars: a review of outcome measures. Disabil Rehabil 2009; 31: 2055-2063. [CrossRef]
3. Gangl O, Hofer W, Tomaselli F, Sautner T, Fugger R. Single incision laparoscopic cholecystectomy (SILC) versus laparoscopic cholecystectomy (LC)-a matched pair analysis. Langenbecks Arch Surg 2011; 396: 819-824. [CrossRef]
4. Nozaki T, Ichimatsu K, Watanabe A, Komiya A, Fuse H. Longitudinal Incision of the Umbilicus for Laparoendoscopic Single Site Adrenalectomy: A Particular Intraumbilical Technique. Surg Laparosc Endosc Percutan Tech 2010; 20: e185-e188. [CrossRef]
5. Compeau C, McLeod NT, Ternamian A. Laparoscopic entry: a review of Canadian general surgical practice. Can J Surg 2011; 54: 315-320. [CrossRef]
6. Kadar N. A new technique of primary trocar insertion for laparoscopy. J Am Assoc Gynecol Laparosc 1997; 4: 485-489. [CrossRef]
7. Danielle S. Walsh Todd A. Ponsky Nicholas E. Bruns Editors The SAGES Manual of Pediatric Minimally Invasive Surgery.
8. Kim E, Kim D, Lee S, Lee H. Minimal-Scar Laparoscopic Adjustable Gastric Banding (LAGB). Obes Surg 2009; 19: 500-503. [CrossRef]
9. Wang L, Cai C, Liu B, Yang Q, Wu Z, Xiao L, et al. Perioperative Outcomes and Cosmesis Analysis of Patients Undergoing Laparoendoscopic Single-site Adrenalectomy: A Comparison of Transumbilical, Transperitoneal Subcostal, and Retroperitoneal Subcostal Approaches . Urology 2013; 82: 358-364. [CrossRef]
10. Sinha R. Single-Incision Laparoscopic Transabdominal Preperitoneal Inguinal Hernia Repair Using Only Conventional Instruments: An Initial Report. J Laparoendosc Adv Surg Tech A 2011; 21: 335-340. [CrossRef]
11. Tsang T. The Scarless Umbilical Port Insertion (SUPI) Technique for Laparoscopic Surgery in Children Caroline Mary Smith. Available from: https://www.researchgate.net/publication/322096533_The_Scarless_Umbilical_Port_Insertion_SUPI_Technique_for_Laparoscopic_Surgery_in_Children
12. Compeau C, McLeod NT, Ternamian A. Laparoscopic entry: a review of Canadian general surgical practice. Can J Surg 2011; 54: 315-320. [CrossRef]
13. Sasmal PK, Tantia O, Jain M, Khanna S, Sen B. Primary access-related complications in laparoscopic cholecystectomy via the closed technique: experience of a single surgical team over more than 15 years. Surg Endosc 2009; 23: 2407-2415. [CrossRef]
14. Mowat J, Bonnar J. Abdominal wound dehiscence after caesarean section. Br Med J 1971; 2: 256-257. [CrossRef]
15. Dingfelder JR. Direct laparoscope trocar insertion without prior pneumoperitoneum. J Reprod Med 1978; 21: 45-47.
16. Catarci M, Carlini M, Gentileschi P, Santoro E. Major and minor injuries during the creation of pneumoperitoneum. A multicenter study on 12,919 cases. Surg Endos 2001; 15: 566-569. [CrossRef]
17. Molloy D, Kaloo PD, Cooper M, Nguyen TV. Laparoscopic entry: a literature review and analysis of techniques and complications of primary port entry. Aust NZJ Obstet Gynaecol 2002; 42: 246-254. [CrossRef]
18. Tulikangas PK, Nicklas A, Falcone T, Price LL. Anatomy of the left upper quadrant for cannula insertion. J Am Assoc Gynecol Laparosc 2000; 7: 211-214. [CrossRef]
19. Atiyeh BS, Costagliola M, Hayek SN. Keloid or hypertrophic scar: the controversy: review of the literature. Ann Plast Surg 2005; 54: 676-680. [CrossRef]
20. Thompson CM, Sood RF, Honari S, Carrougher GJ, Gibran NS. What score on the Vancouver Scar Scale constitutes a hypertrophic scar? Results from a survey of North American burn-care providers. Burns 2015; 41: 1442-1448. [CrossRef]
21. Calleja-Agius J, Brincat M, Borg M. Skin connective tissue and ageing. Best Pract Res Clin Obstet Gynaecol 2013; 27: 727-740. [CrossRef]

Turk J Surg 2018; 34(4): 295-299
DOI: 10.5152/turkjsurg.2017.3973

Original Article

Evaluation of the readability of informed consent forms used in urology: Is there a difference between open, endoscopic, and laparoscopic surgery?

Mehmet Giray Sönmez[1], Betül Kozanhan[2], Mehmet Serkan Özkent[1], Gökhan Ecer[1], Mehmet Salih Boğa[3], Erhan Demirelli[4], Ahmet Öztürk[1]

ABSTRACT

Objective: The aim of this study is to evaluate the readability levels of informed consent forms used in Turkey before urological surgery and to compare the readability levels of open, endoscopic, and laparoscopic surgical informed consent forms.

Material and Methods: A total of 529 informed consent forms used for urological open, endoscopic, and laparoscopic surgical procedures were collected from different hospitals in Turkey. Evaluating informed consent forms that have exactly the same text only once, a total of 69 consent forms were evaluated. The Gunning Fog Index and Flesch–Kincaid test measuring the general readability level were used to calculate the readability level of informed consent forms in addition to the Ateşman and Bezirci–Yılmaz formulas defined to determine the readability level of Turkish texts. Informed consent forms were evaluated and divided into three groups as open, endoscopic, and laparoscopic surgery forms, depending on their content.

Results: Among 69 informed consent forms evaluated, 35 were open, 19 were endoscopic, and 15 were laparoscopic surgery consent forms. The readability level of all informed consent forms was detected as average according to the Ateşman formula, very difficult according to the Flesch–Kincaid test, difficult according to the Gunning Fog Index, and at the high school education level according to the Bezirci–Yılmaz formula. A statistical evaluation of the three groups did not show a significant difference in the readability level.

Conclusion: In this study, it was detected that the informed consent form readability levels used for urological surgical procedures in our country were rather low. We think that the cooperation of the concerned institutions is required for the revision of the consent information texts available and the improvement of the texts according to the strategies recommended.

Keywords: Informed consent forms, readability, understandability, urological surgery

ORCID IDs of the authors:
M.G.S. 0000-0003-4615-7348;
B.K. 0000-0002-5097-9291;
M.S.Ö. 0000-0002-6613-0671;
G.E. 0000-0002-2805-8664;
M.S.B. 0000-0001-7979-8075;
E.D. 0000-0002-0187-2156;
A.Ö. 0000-0002-8491-3346.

Cite this paper as:
Sönmez MG, Kozanhan B, Özkent MS, Ecer G, Boğa MS, Demirelli E, et al. Evaluation of the readability of informed consent forms used in urology: Is there a difference between open, endoscopic, and laparoscopic surgery?. Turk J Surg 2018; 34(4): 295-299.

[1]Department of Urology, Necmettin Erbakan University Meram School of Medicine, Konya, Turkey

[2]Department of Anesthesiology and Reanimation, University of Health Sciences Konya Training and Research Hospital, Konya, Turkey

[3]Department of Urology, Kağıthane State Hospital, İstanbul, Turkey

[4]Department of Urology, Giresun University School of Medicine, Giresun, Turkey

This study was presented at the 26th National Urology Congress, 12-15 October 2017, Girne, Cyprus.

Corresponding Author
Mehmet Giray Sönmez
e-mail: drgiraysonmez@gmail.com

Received: 24.08.2017
Accepted: 01.11.2017
Available Online Date: 28.08.2018

INTRODUCTION

Informed consent means the authorization given to the health professional for the diagnosis or treatment interventions planned with the patient's consent. Informed consent forms (ICF), being an inseparable constituent of the consent phase, are used to help the patients during the treatment phase by explaining the indications, advantages, and possible risks of medical applications (1). It was also shown that these texts may be effective in solving problems in the treatment phase with advantages such as providing the patient–doctor communication and making the agreement of the patient to treatment easier (2, 3). But as the value of information is limited with the comprehension ability of the patients, the "readability" and "understandability" of information are as important as its reliability and currency.

Presenting some quantitative data on texts, readability provides information on whether the text is easily understandable by the reader at a certain level through the characteristics of the syllables, words, and sentences in that language. Factors influencing readability are the average word length, word frequency, multisyllabic words, average sentence length, ambiguous word number, and average syllable number. The sentence readability of decreases as the number of words in a sentence increase. Readability formulas were developed using criteria such as the length of words and sentences and the word syllable number in readability evaluation. There are many formulas developed for readability analysis (4-9).

The Ateşman and Bezirci–Yılmaz formulas (6, 7) defined to determine the readability level of Turkish texts and Gunning Fog Index and Flesh–Kincaid test measuring the general readability level are the most common readability formulas used (8, 9). In a research conducted in Turkey, it was found that 64.6% of the public had inadequate health literacy (5).

The aim of this study is to evaluate the readability levels of ICFs used in our country before urological surgery and to compare the readability levels of ICF specifically prepared for open, endoscopic, and laparoscopic surgery.

MATERIAL AND METHODS

This research was conducted according to the principles of the World Medical Association's Declaration of Helsinki. Since there were no human participants in this study, it was not necessary to obtain ICF.

A total of 529 ICFs used for urological open, endoscopic, and laparoscopic surgical procedures were collected from different hospitals in Turkey. Evaluating ICFs that have exactly same text only once, a total of 69 consent forms were evaluated for the sentence number, word number, letter number, character number, syllable number, and words with an average syllable number of four and above.

The informative text available in these consent forms was copied and transferred to Microsoft Word (Microsoft, Redmond, WA) program and was calculated manually with Microsoft Excel (Microsoft, Redmond, WA) program. The Ateşman and Bezirci–Yılmaz formulas (6, 7) for determining the readability level of Turkish texts and the Gunning Fog Index and Flesch–Kincaid (8, 9) test for measuring the general readability level were used for calculating the readability level of ICF.

Ateşman readability formula (Ateşman readability formula, Ankara, Turkey)

The Ateşman readability formula is a formula based on the length of words and sentences.

The readability score is formulated as 198.825−40.175× (total syllables/total words)−2.610×(total words/total sentences). It is understood that the readability level of a text is considered easier when it is closer to100 and harder when it is closer to 0, according to the Ateşman formula.

Table 1. Readability intervals of the readability formulas used in the study

Ateşman Value	**Readability Interval**
90–100	Very easy
70–89	Easy
50–69	Average difficulty
30–49	Difficult
1–29	Very difficult
Bezirci–Yılmaz Value	**Readability Interval According to the Education Level**
1–8	Elementary school
9–12	High school
12–16	Bachelor's degree
>16	Academic
Gunning Fog Index Value	**Readability Interval**
8–10	Easy
>11	Difficult
Flesch–Kincaid Grade Level	**Numeric Level of the Text**	**Readability Interval**
5	90–100	Very easy
6	80–90	Easy
7	70–80	Quite easy
8–9	60–70	Standard
10–11	50–60	Rather difficult
13–16	30–50	Difficult
Adults	0–30	Very difficult

Bezirci–Yılmaz readability formula (Bezirci–Yılmaz readability formula, Ankara, Turkey)

The Bezirci–Yılmaz readability formula was developed based on the sentence length and syllable number in words, characteristics of different formulas developed until today, and the statistical characteristics of the Turkish language. According to this formula, the readability difficulty of the text increases when the sentences in the text are longer. Similarly, an increase of the syllable number in a word makes the readability of that word and the sentences harder most of the time.

$$\sqrt{\mathbf{AWNx}\left((\mathbf{S3x0.84}) + (\mathbf{S4x1.5}) + (\mathbf{S5x3.5}) + (\mathbf{S6x6.26.25})\right)}$$

AWN: Average word number; S3: Number of words with an average of three syllables; S4: Number of words with an average of four syllables; S5: Number of words with an average of five syllables; S6: Number of words with an average of six or more syllables

The result acquired from this formula explains which class level a text addresses to according to the education system in our country. The education system shows the elementary school education level for Grades 1–8, secondary (high) school education for Grades 9–12, bachelor's degree for Grades 12–16, and academic education level for Grades 16 and above.

Flesch–Kincaid test (Flesch–Kincaid test, Columbia, USA)

The length of the words and sentences is determined.

Readability=(0.39×sentence length)+(1.18×word length)−15.59

World length=syllable number/word number

Sentence length=word number/sentence number

The syllable number is divided with the word number for the word length, and the word number is divided with the sentence number for sentence length. The text is evaluated as easy when the syllable number of each word is closer to 1 and as difficult when the syllable number rises up to 10. The same operation is valid for the sentence. The text is evaluated as easy when the word number decreases to 1 and as difficult when it is more than 10.

Gunning Fog Index (Gunning Fog Index formula, New York, USA)

There are two important aspects of the Gunning Fog Index. These are words containing three or more syllables and the average number of words used in sentences.

Fog Index=0.4×(word rate with three syllables+average number of words)

Word rate with three syllables=(number of words with three or more syllables/remaining number of words)×100

Average number of words=word number/sentence number.

It is an easy text if the result is between 8 and 10 and a difficult text if the result is above 11.

The readability intervals of the readability formulas used in the study are available in Table 1.

Informed consent forms were separated into three groups as open (Group 1), laparoscopic (Group 2), and endoscopic (Group 3) surgery according to their content. The readability levels were compared with the Ateşman, Bezirci–Yılmaz, Gunning Fog, and Flesch–Kincaid formulas and the sentence number, word number, letter number, character number, syllable number, and average number of words with four and more syllables.

Statistical Analysis

The SPSS 20.0 (IBM Corp.; Armonk, NY, USA) program was used for statistical evaluation. For the comparison of the groups, T-test and Mann–Whitney U test were used for binary group analyses, and the Kruskal–Wallis test was used for triple groups analyses. $p<0.05$ was regarded as significant for all examinations.

RESULTS

Among 69 ICFs evaluated, 35 were open (Group 1), 15 were laparoscopic (Group 2), and 19 were endoscopic surgery (Group 3) consent forms. No significant difference was observed in the sentence number, word number, letter number, character number, syllable number, and words with an average syllable number of four and above among the consent forms. Among the three groups and among the groups in binary statistical evaluation, no significant difference was detected in readability level among the groups.

Readability level of all consent forms was detected as average according to the Ateşman formula, very difficult according to Flesch–Kincaid test, difficult according to the Gunning Fog Index, and at high school education level according to the Bezirci–Yılmaz formula. Numeric and statistical values among the groups are available in Table 2.

DISCUSSION

Informed consent is one of the most important aspects of ethical medical practice. In legal terms, making an intervention without informed consent may mean negligence or malpractice and may lead to a legal action, maltreatment, and even an attack against the doctor. Informed consent allows the patient to understand the risks and benefits of all interventions and provides the voluntary consent of patients to be able to continue the procedure. A consent form through which the patients can completely understand the process to be made can be called the ideal informed consent. Ethically, to be able to make a conscious decision, it is very important for the patient to understand the recommended procedure (10, 11). Also, the increasing tendency of health insurance costs and malpractice cases, especially for the surgeons and doctors making invasive interventions, makes the readability and understandability of ICFs even more important (11-13).

It is estimated that the patient level of understanding during the informed consent phase is better than it is actuallly reported (14). But Crepeau et al. (15) found the understanding and recalling of the patients for surgical consent form to be unexpectedly low. As the average readability level of adults in the United States is at the eighth-grade level, the National Institutes of Health and the American Medical Association suggest that the readability of patient materials should be lower than or at the sixth-grade reading level (16-18).

While the average education level of the whole population over 15 years of age is reported as 7.18 years in Turkey according to 2010 data, the average education level of only the females over 15 years of age is reported as 6.33 years (19). Also, according to a research made in 2014, it was found that two-thirds of the population in Turkey has an inadequate level of health literacy (5). So, it is considered that easy readability of ICFs in Turkey would increase the clarity of the procedure to be applied.

Readability levels of ICFs were measured in different countries for different medical branches before. According to Mariscal-Crespo et al. (20) ICFs used in public hospitals were analyzed globally in Spain, and it was shown that 62.4% had "somewhat difficult," 23.4% had "normal," and 13.4% had "very difficult" readability. The ICF readability values among the branches were compared in another study, and it was reported that

Table 2. Numeric and statistical values among the groups

	Total	Group 1 Open	Group 2 Laparoscopic	Group 3 Endoscopic	Group 1, 2, 3 p*	Group 1–2 p+	Group 1–3 p+	Group 2–3 p+
Informed consent form number	69	35	15	19				
Sentence number	121.9±34.2	119.9±33	133±39.1	117±31	0.24	0.39	0.4	0.86
Word number	1093±272	1033.2±215	1251.3±333.9	1078.3±278	0.07	0.06	0.33	0.36
Letter number	7445.3±1951	7129.1±1608	8313.1±2603	7342.6±1843	0.25	0.054	0.61	0.22
Character number	9294±2293	8870.6±1901	10397±2900	9202.3±2321	0.14	0.064	0.45	0.35
Syllables number	3245.7±844	3101.4±704	3643±1096	3197.9±803	0.23	0.06	0.6	0.24
Words with an average syllable number of four and above	364.9±113	350.1±97	410.2±162	356.4±88.7	0.26	0.059	0.7	0.07
Flesch–Kincaid	23.1±2	23.18±1.6	22.9±3.3	23.12±1.3	0.35	0.06	0.82	0.08
Gunning Fog	17.05±1.7	16.9±1.6	17.2±2.3	17±1.5	0.4	0.13	0.11	0.24
Ateşman	55.1±7.3	55.5±7	54.5±9.7	55±6.1	0.47	0.2	0.16	0.22
Bezirci–Yılmaz	9.68±1.8	9.43±1.8	9.9±2.2	9.91±1.6	0.17	0.31	0.31	0.39

*Kruskal–Wallis test; +Mann–Whitney U test
Datas are presented as mean ± SD

urology ICFs were at a "very and somewhat difficult" interval (21). We think that this situation may be related to the fact that urological operations especially include endoscopic and laparoscopic surgeries, and ICFs containing the details of different special techniques used in these cases cannot be prepared at a level understandable by the patients. So, we compared the readability levels of open, endoscopic, and laparoscopic consent forms in our study. Although no significant difference was detected between the readability levels of all three surgery groups, we detected that the average of sentence, word, syllable, and number of words with four and more syllables was higher for laparoscopic surgeries.

Gargoum and Keeffe (22) evaluated the information forms used for endoscopic interventions in Ireland and reported that only 62% of the forms were easy to ready, and 57% were at the reading level of 13–15 years of age. In a study made in the United States, it was reported that the invasive operation ICFs were written at an average of 15th grade level (i.e., third year of college) (23). Boztaş et al. evaluated the ICFs used before anesthesia in Turkey and reported that these had low-to-very low readability levels (4). Şahin et al. reported that 41.5% of the patients who underwent orthopedic surgery after taking ICF in Turkey did not remember potential complications, and only 29.6% of the patients completely read the ICFs (24).

Difficult readability level can be one of the reasons for not reading ICFs completely. In our study, it was detected that the urological ICFs had a different readability level and were understandable at the high school education level. This condition is in line with studies made in different branches in many countries. So, the things to be done so that ICFs can be more readable and understandable should be discussed.

Borello et al. (1) prepared ICFs that were made easier to comprehend with marked texts and diagrams for laparoscopic cholecystectomy and reported that these forms are easier to understand and remember. Shukla et al. (25) reported that the cataract surgery ICFs at the second-grade reading level and video support are easier to understand.

To increase the readability level of ICFs, we recommend decreasing the number of multisyllabic worlds, sentences, and words, to form the document by words in a an understandable level for the patient, to minimize the words with a medical content that cannot be understood by the patient, and to enrich them with visual information such as videos and diagrams. Also, the patients may have acquired information on the subjects on the surgical procedure themselves (especially through the internet), which may not actually be correct, and patients with a low educational level may feel ashamed to ask the questions for explanation. Thus, the doctor has to be open in the evaluation phase of ICFs, give opportunity to the patients to ask questions, and should spare adequate time for the patient. Additionally, giving permission to an individual such as a relative or friend whom the patient trusts during the informed consent phase may help the patient to understand the ICFs readability and the procedure to be applied, and it may provide emotional support. We think that the application of all these strategies would let the patients understand the procedure and increase the recall rates of the procedure risks.

CONCLUSION

A readability level of the urology ICFs used in our country was detected to be low and difficult in this study. Also, a significant difference was not detected in the readability among the open, endoscopic, and laparoscopic surgery ICFs. We think that attention should be paid to this subject, which is both medically and legally binding for the doctors, and verbal and visual support should be provided in addition to ICFs during patient informing. Presenting proof-based information at a clear, understandable, and appropriate reading level in consent texts would contribute the improvement of communication between urologists and patients in the preoperative and postoperative process, and would cause a better informing of the patients, especially on post-surgery results. We think that the cooperation of the concerned institutions is required for the revision of the ICFs available and the improvement of the texts according to the strategies recommended.

Ethics Committee Approval: Authors declared that the research was conducted according to the principles of the World Medical Association eclaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects" (amended in October 2013).

Informed Consent: Not required in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - M.G.S., B.K.; Design - M.G.S., B.K., M.S.Ö.; Supervision - M.G.S., B.K., A.Ö.; Resource - M.G.S., B.K., M.S.Ö., G.E., M.S.B., E.D., A.Ö.; Materials - M.G.S., B.K., M.S.Ö., G.E., M.S.B., E.D., A.Ö.; Data Collection and/or Processing -M.G.S., B.K.; Analysis and/or Interpretation - M.G.S., B.K., A.Ö.; Literature Search - M.G.S., B.K.; Writing Manuscript - M.G.S., B.K.; Critical Reviews - M.G.S., B.K., A.Ö.

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

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

REFERENCES

1. Borello A, Ferrarese A, Passera R, Surace A, Marola S, Buccelli C, et al. Use of a simplified consent form to facilitate patient understanding of informed consent for laparoscopic cholecystectomy. Open Med (Wars) 2016; 11: 564-573. [CrossRef]
2. Ritterband LM, Thorndike FP, Cox DJ, Kovatchev BP, Gonder-Frederick LA. A behavior change model for internet interventions. Ann Behav Med 2009; 38: 18-27. [CrossRef]
3. Kozanhan B, Tuta MS. Readability of Patient Education Texts Presented on the Internet in the Field of Anesthesiology. Turkiye Klinikleri J Anest Reanim 2017; 15: 63-70. [CrossRef]
4. Boztaş N, Özbilgin Ş, Öçmen E, Altuntaş G, Özkardeşler S, Hancı V, et al. Evaluating the Readibility of Informed Consent Forms Available Before Anaesthesia: A Comparative Study. Turk J Anaesth Reanim 2014; 42: 140-144. [CrossRef]
5. Tanrıöver MD, Yıldırım HH, Ready FND, Çakır B, Akalın HE. Sağlık Okuryazarlığı Araştırması. 2014.
6. Ateşman E. Measuring readability in Turkish. A.U. Tömer Language Journal 1997; 58: 171-174.
7. Bezirci B, Yılmaz AE. A software library for measurement of readability of texts and a new readability metric for turkish. DEÜ FMD 2010; 12: 49-62.
8. Flesch R. A new readability yardstick. J Appl Phycol 1948; 32: 221. [CrossRef]

9. Gunning R. "The Technique of Clear Writing", McGraw-Hill International Book Co, New York. 1952.
10. The Metaphysics Resaerch Lab. In The Stanford Encyclopedia of Philosophy. "Informed Con-sent," 2011. Available from URL: http://plato.stanford.edu/entries/informed-consent (Accessed July 15, 2015).
11. Eltorai AE, Naqvi SS, Ghanian S, Eberson CP, Weiss AP, Born CT, et al. Readability of Invasive Procedure Consent Forms. Clin Transl Sci 2015; 8: 830-833. [CrossRef]
12. Mello MM, Studdert DM, DesRoches CM, Peugh J, Zapert K, Brennan TA, Sage WM. Effects of a malpractice crisis on specialist supply and patient access to care. Ann Surg 2005; 242: 621-628. [CrossRef]
13. Paasche-Orlow MK, Taylor HA, Brancati FL. Readability standards for informed-consent forms as compared with actual readability. N Engl J Med 2003; 348: 721-726. [CrossRef]
14. Sugarman J, McCrory DC, Powell D, Krasny A, Adams B, Ball E, et al. Empirical research on informed consent: an annotated bibliography. Hastings Cent Rep 1999; 29: 1-42. [CrossRef]
15. Crepeau AE, McKinney BI, Fox-Ryvicker M, Castelli J, Penna J, Wang ED. Prospective evaluation of patient comprehension of informed consent. J Bone Joint Surg Am 2011; 93: e114 (1-7).
16. Eltorai AE, Sharma P, Wang J, Daniels AH. Most American academy of orthopaedic surgeons' online patient education material exceeds average patient reading level. Clin Orthop Relat Res 2015; 473: 1181-1186. [CrossRef]
17. Eltorai AE, Han A, Truntzer J, Daniels AH. Readability of patient education materials on the American Orthopaedic Society for Sports Medicine website. Phys Sports Med 2014; 42: 125-130. [CrossRef]
18. Eltorai AE, Ghanian S, Adams CA Jr, Born CT, Daniels AH. Readability of patient education materials on the American association for surgery of trauma website. Arch Trauma Res 2014; 3: e18161. [CrossRef]
19. Barro R, Lee JW. Educational Attainment Dataset. [Online] Available from URL: http://www.barrolee.com/ 2011.
20. Mariscal-Crespo MI, Coronado-Vázquez MV, Ramirez-Durán MV. Global analysis of the readability of the informed consent forms used in public hospitals of Spain. Rev Calid Asist 2017; 32: 200-208. [CrossRef]
21. San Norberto EM, Gómez-Alonso D, Trigueros JM, Quiroga J, Gualis J, Vaquero C. Readability of surgical informed consent in Spain. Cir Esp 2014; 92: 201-207. [CrossRef]
22. Gargoum FS, O'Keeffe ST. Readability and content of patient information leaflets for endoscopic procedures. Ir J Med Sci 2014; 183: 429-432. [CrossRef]
23. Eltorai AE, Naqvi SS, Ghanian S, Eberson CP, Weiss AP, Born CT et al. Readability of Invasive Procedure Consent Forms. Clin Transl Sci 2015; 8: 830-833. [CrossRef]
24. Sahin N, Oztürk A, Ozkan Y, Demirhan Erdemir A. What do patients recall from informed consent given before orthopedic surgery? Acta Orthop Traumatol Turc 2010; 44: 469-475. [CrossRef]
25. Shukla AN, Daly MK, Legutko P. Informed consent for cataract surgery: patient understanding of verbal, written, and videotapedinformation. J Cataract Refract Surg 2012; 38: 80-84. [CrossRef]

Turk J Surg 2018; 34(4): 300-305
DOI: .5152/turkjsurg.2018.3992

Original Article

Investigation of inadvertent hypothermia incidence and risk factors

Fatma Vural, Buket Çelik, Zeynep Deveci, Kübra Yasak

ABSTRACT

Objective: This study was conducted to determine the incidence of inadvertent hypothermia in operative patients and the risk factors that are involved in the development of hypothermia.

Material and Methods: This prospective, descriptive, cross-sectional study was conducted from January 2016to August 2016 with 144 patients who over the age of 18 years, underwent general surgery, orthopedic surgery, urologic surgery, neurosurgery, and plastic and reconstructive surgery. Data was collected with the "Hypothermia Data Collection Form." Body temperature was measured by the tympanic membrane in the waiting room, operating room, and PACU.

Results: Overall, 89% of the patients (n=129) were normothermic in the preoperative phase; 74.30% of the patients (n=107) in intraoperative phase and 75.70% of the patients (n=109) in postoperative phase were hypothermic. American Society of Anesthesiologist (ASA) score, preoperative body temperature, operating room temperature, and using heating method at operation were found to be effective in the development of inadvertent hypothermia during the operating period. It was determined that premedication, preoperative and postoperative body temperature, and the operating room temperature were effective for inadvertent hypothermia in the postoperative period.

Conclusion: As a result of the study, it was determined the rate of inadvertent hypothermia was high during and after surgery. Preoperative and intraoperative patient body temperature and operating room temperature were found to be effective in preventing inadvertent hypothermia.

Keywords: Inadvertent hypothermia, Incidence, Risk factors, Operating room

INTRODUCTION

Providing and maintaining normothermia in the preoperative, intraoperative, and postoperative periods is highly important in terms of patient safety, positive surgical results, and patient satisfaction (1, 2). Inadvertent hypothermia can cause complications such as postoperative myocardial events, surgical site infections, and prolonged durations of hospitalization and recovery (3-6). It has been reported that the maintenance of normothermia decreases the length of hospitalization by approximately 40% and the risk of surgical site infection by 64% (7). Every year, about 24%–90% of surgical patients suffer from inadvertent hypothermia (8). Hypothermia is defined as the decrease in patient's core body temperature below 36.0°C (9, 10). In the guideline for the management of inadvertent hypothermia in adults published by the National Institute for Health and Care Excellence (NICE), inadvertent hypothermia is examined in three phases: (1) *the preoperative phase*, which is defined as the hour before induction of anesthesia when patient is prepared for surgery; (2) *the intraoperative phase,* which covers the administration of anesthesia; and (3) *the postoperative phase*, which is defined as the 24 hours beginning with the entry into the recovery unit (9).

Surgery and general anesthesia affect the normal balance between heat production and heat loss. Anesthetic agents, opioids, and sedatives suppress behavioral and autonomic responses by influencing patient's thermoregulation feature that can change depending on the environmental temperature (7). Inadvertent hypothermia results from anesthesia, temperature of the operating room, and the use of cold intravenous solutions and cold blood products (7, 10). When anesthesia is administered, the factors increasing the risk of hypothermia are the application of a large and moderate-degree surgical intervention, inclusion in the American Society of Anesthesiologist (ASA) II-IV group, female gender, preoperative body temperature below 36°C, administration of sedation and premedication, the presence of coexisting cardiac and vascular diseases, application of combined regional and general anesthesia, age over 70 years, and systolic blood pressure above 140 mmHg (11).

This study aimed to determine the incidence of inadvertent hypothermia and the risk factors affecting the development of hypothermia in patients undergoing a surgery.

Cite this paper as:
Vural F, Çelik B, Deveci Z, Yasak K. Investigation of inadvertent hypothermia incidence and risk factors in operating on patients. Turk J Surg 2018; 34(4): 300-305.

Department of Surgical Nursing, Dokuz Eylül University School of Nursing, İzmir, Turkey

This study was presented at the 15th Congress of Surgery Nursing, 13-17 April 2016, Antalya, Turkey.

Corresponding Author
Zeynep Deveci
e-mail: devecizeynepzd@gmail.com

Received: 27.09.2017
Accepted: 14.12.2017

MATERIAL AND METHODS

This prospective, descriptive, and cross-sectional study was conducted in the surgical clinics and operating unit of a university hospital. The study included all patients who were operated in the departments of general surgery, orthopedics, urology, neurosurgery, and plastic and reconstructive surgery in our hospital between January and August 2016. The patients who were planned for emergency surgery needed to be applied therapeutic hypothermia, and they were followed in the intensive care unit after operation. The patients whose body temperature could not be tympanically measured during operation were not included in this study. The study consisted of 144 patients who met these inclusion criteria. The patients whose body temperature was below 36°C were accepted to be hypothermic. Data were collected by measuring patients' body temperatures three times: in waiting unit before surgery, during operation, and in the recovery room after surgery. The power of the study was calculated over its own sampling through GPower 3.1, and it was found to be 0.94.

The data were collected by the researchers through face-to-face interviews with the patients. Their body temperatures were measured using a calibrated Genius 2 Infrared Tympanic Electronic Thermometer (Covidien, Mansfield, America) by the researchers in the waiting unit, operating room (before giving anesthesia and during operation), and in the recovery room. After surgery, the first measurements of patients' body temperatures were recorded in the clinic. The data of the study were collected between January and August 2016. This study was approved by the non-interventional ethics committee of the Dokuz Eylül University with the decision number 2015/28-26, dated 01.17.2015, and protocol number 2351-GOA. Necessary institutional permissions were obtained from the hospital where the study was conducted. Verbal and written informed consents were received from the patients who confirmed their participation in this study.

Data collection instruments

The data were collected using a "Hypothermia data collection form" that was developed by the researchers in accordance with literature (4, 7, 9-11). This form, which consisted of two parts within itself, included "Form for Patient Characteristics" in the first part and "Form for the Identification of Hypothermia" in the second part.

Part 1. Form for Patient Characteristics: This form was designed by the researchers in accordance with literature, and it consisted of seven items including patient's sociodemographic features: age, gender, height, weight, and clinical features: planned surgery, the department where the patient was hospitalized, and the drugs that the patient used.

Part 2. Form for the Identification of Hypothermia: This form, which was developed in accordance with literature, consisted of three parts. The first part included six items on patient-related risk factors for undesired hypothermia, age, body mass index (BMI), chronic diseases, ASA level, systolic blood pressure, and preoperative body temperature. The second part included 12 items on surgery-related risk factors for undesired hypothermia, application of premedication, type of anesthesia, type of surgery, duration of surgery, temperature of the operating room, amount of fluid given in the operating room, application and amount of blood transfusion, heating method used intraoperatively, application of a heating technique in the recovery room, room temperature of the recovery unit, room temperature in the clinic, and application of a heating method in the clinic. The third part consisted of the measurements of patients' body temperatures in the clinic and waiting room where the patients stayed before operation, just before the induction of anesthesia and during the operation in the operating room, and in the recovery room and clinic after operation.

Statistical Analysis

The collected data were analyzed using the Statistical Package for the Social Sciences Version 20,0 (SPSS) (SPSS, Inc., New York, USA). Number, percentage, and mean were used to analyze the sociodemographic features, clinical features, and the frequency of hypothermia. Univariate and multivariate linear regression analysis methods were employed to compare hypothermia risk factors and body temperature measurements, which were the independent variables of the research.

RESULTS

The descriptive features of the patients participating in the study are presented in Table 1. Of the patients, 62.50% (n: 90) were male, and 37.50% (n: 54) were female. The mean age of the patients was 53.59±15.88 years. Among the patients, 49.30% had a chronic disease, and 52.80% were evaluated to be at ASA II level. It was found that 89% of the patients (n: 129) (36.37±0.51°C) were normothermic in the waiting unit and on the operating table before the induction of anesthesia in the preoperative phase (1), in one hour when they prepared for the surgery. Inadvertent hypothermia developed in 74.30% of the patients (n: 107) (35.52±0.69°C) in the intraoperative phase (2) after the induction of anesthesia, and in 75.70% of the patients (n: 109) (35.43±0.73°C) in the 24-hour postoperative phase (3) beginning with the entry into the recovery unit.

For the predicted risk factors for inadvertent hypothermia developing preoperatively, intraoperatively, and postoperatively, the results of univariate linear regression analysis and multivariate linear regression analysis are shown in Table 2 and Table 3, respectively.

According to the results of univariate and multivariate analyses, age, gender, BMI, systolic blood pressure, and application of premedication had no effect on the preoperative development of inadvertent hypothermia ($p>0.05$).

It was found that body temperature in the waiting room, ASA level, temperature of the operating room, and the intraoperative application of a heating method positively affected the intraoperative body temperature, and this finding was statistically significant ($p<0.05$). Also in the multivariate analysis, the effects of body temperatures of the patients in the waiting room and temperature of the operating room on the intraoperative body temperature were detected to be positive and statistically significant ($p<0.05$). It was revealed that body temperatures of the patients in the waiting unit and temperature of the operating room affected the intraoperative development of inadvertent hypothermia at the rates of 60% and

37.80%, respectively (B: 0.604 95% CI: 0.375—0.833; B:0.378 95% CI: 0.237–0.552, respectively).

In the univariate analysis, the effects of preoperative body temperature, intraoperative body temperature, the application of premedication, and temperature of the operating room on the postoperative body temperature were found to be positive and statistically significant ($p<0.05$). On the other hand, in the multivariate analysis, only intraoperative body temperature and temperature of the operating room were observed to have a positive effect on the postoperative body temperature, and this finding was statistically significant ($p<0.05$). It was found that temperature of the operating room and intraoperative body temperature affected the postoperative development of inadvertent hypothermia at the rates of 19.80% and 48.30%, respectively (B: 0.198 95% CI: 0.048-0.347; B: 0.483 95% CI: 0.294-0.672, respectively).

Table 1. Characteristics of the patients

Characteristics	**n: 144**	
Age*	53.59±15.88	
Body mass index*	27.16±4.57	
	n	%
Gender		
Female	54	37.50
Male	90	62.50
Department where the patient was operated		
Urology	47	32.60
General Surgery	44	30.60
Orthopedics and Traumatology	26	18.10
Brain and Nerve Surgery	14	9.70
Plastic and Reconstructive Surgery	13	9.10
Chronic disease		
Yes	71	49.30
No	73	50.70
¥ASA state		
I	56	38.90
II	76	52.80
III	12	8.30
	mean±SD (min-max)	
Body temperature in the waiting unit (n: 144) (preoperative phase)	36.46±0.46 (min: 35.00-max: 37.60)	
Body temperature before the induction of anesthesia (n: 144) (Preoperative phase)	36.37±0.51 (min: 34.60-max: 37.70)	
Intraoperative body temperature (n: 144) (intraoperative phase)	35.52±0.69 (min: 33.10-max: 37.00)	
Body temperature in the recovery unit (n:144) (postoperative phase)	35.43±0.73 (min: 33.80-max: 37.50)	
The first body temperature measured in the clinic (n: 144) (postoperative phase)	35.92±0.44 (min: 35.00-max: 37.40)	

*: mean± standard deviation
¥ASA: American Society of Anesthesiology Classification

DISCUSSION

Providing and maintaining normothermia in the preoperative, intraoperative, and postoperative periods is very important for patient safety and satisfaction (2, 12). The data obtained in our study were discussed under three headings as the preoperative, intraoperative, and postoperative phases, in accordance with the definition of inadvertent hypothermia by NICE. In many studies examining risk factors affecting the development of inadvertent hypothermia (13-21), risk factors were evaluated perioperatively, and they were not examined separately in the preoperative, intraoperative, and postoperative periods.

Preoperative period

In our study, the incidence of hypothermia in the preoperative period was found to be 11% (n= 15). The incidence of preoperative hypothermia was reported to be 4% in the study of Horn et al. (13) and 2.40% in the study of Aksu et al. (14). Compared to these two studies, the higher incidence in our study might have resulted from non-application of any heating method preoperatively and taking the patients into the operating room without checking their body temperatures.

It was found that age, gender, BMI, systolic blood pressure, and ASA level did not have any effect on preoperative inadvertent hypothermia. This result is considered to be associated with the fact that the development of hypothermia has a multifactorial etiology.

Intraoperative period

In our study, the incidence of intraoperative hypothermia was found to be 74.30% (n=107). Similar to our results, the incidence of intraoperative hypothermia was reported as 74% in a study conducted in Australia (22). Different from the results of our study, it was detected to be 39.90% in a study performed in China (15) and 28% in another study performed in the Netherlands (16). The difference between the incidences of inadvertent hypothermia in the studies might have resulted from the differences in the interventions performed for providing normothermia in the institutions where the studies were conducted. In literature, the preoperative use of a heating method and taking patient into operation after having provided normothermia are known to be important for the prevention of inadvertent hypothermia development (12). The higher incidence in our study might have been due to non-application of preoperative heating to the patients and intraoperative application of a heating method at a low rate as 27.80% (n=40) (Table 2).

The results of univariate and multivariate linear regression analyses revealed that temperature of the operating room and preoperative body temperature affected the development of inadvertent hypothermia (Table 3). The results of our study are consistent with those in literature. In the studies conducted to determine the incidence of postoperative hypothermia and risk factors, temperature of the operating room and preoperative body temperature were reported to be associated with the development of inadvertent hypothermia (14, 23).

In the studies of Belayneh et al. (24) and Monzón et al. (25), ASA level was found to affect the development of hypothermia. On the other hand, in some studies, no effect of ASA level

was reported on the development of hypothermia (17, 26). In our study, although ASA score was found to be an effective risk factor in the univariate analysis, it was found to have no effect in the multivariate analysis (Table 2).

According to the results of our study, intraoperative heating affected the intraoperative development of inadvertent hypothermia (Table 2). Our result is consistent with that in literature (8, 13, 14). In the study performed by Horn et al. (13) to deter-

Table 2. Univariate linear regression analysis of risk factors and body temperature values

	Preoperative				Intraoperative				Postoperative			
Parameters	**B**	**95% CI**		**p**	**B**	**95% CI**		**p**	**B**	**95% CI**		**p**
Age	-0.002	-0.007	0.003	0.352	-0.001	-0.008	0.006	0.761	0.000	-0.008	0.008	0.991
Gender	-0.116	-0.273	0.041	0.146	-0.166	-0.403	0.070	0.166	-0.093	-0.345	0.159	0.467
Body mass index	0.009	-0.008	0.026	0.289	0.017	-0.008	0.042	0.181	-0.005	-0.032	0.021	0.690
ASA	-0.057	-0.182	0.068	0.367	0.186	0.001	0.371	0.049*	0.141	-0.055	0.337	0.157
Systolic blood pressure	-0.056	-0.185	0.073	0.390	0.087	-0.106	0.280	0.374	0.063	-0.140	0.266	0.541
Application of premedication	-0.114	-0.533	0.305	0.591	0.384	-0.242	1.009	0.228	0.728	0.078	1.378	0.028*
Preoperative body temperature					0.686	0.464	0.908	0.000*	0.511	0.260	0.761	0.000*
Type of anesthesia					0.112	-0.102	0.326	0.303	0.085	-0.141	0.310	0.460
Type of surgery					0.024	-0.128	0.176	0.753	-0.061	-0.220	0.099	0.454
Duration of surgery					0.012	-0.026	0.051	0.534	-0.008	-0.048	0.033	0.716
Temperature of the operating room					0.367	0.243	0.491	0.000*	0.392	0.261	0.523	0.000*
Amount of fluid given during operation					0.095	-0.119	0.309	0.381	0.002	-0.223	0.228	0.984
Application of a heating method in the operating room					0.355	0.104	0.605	0.006*	0.128	-0.144	0.400	0.354
Intraoperative body temperature									0.630	0.488	0.771	0.000*
Application of a heating method during recovery									0.098	-0.263	0.459	0.591

R^2: 0.071; Corrected R^2: 0.022 R^2: 0.286; Corrected R^2: 0.212 R^2: 0.437; Corrected R^2: 0.363
ASA: American Society of Anesthesiology Classification
CI: Confidence interval
*p<0.05

Table 3. Multivariate linear regression analysis of risk factors and body temperature values

	Preoperative				Intraoperative				Postoperative			
Parameters	**B**	**95% CI**		**p**	**B**	**95% CI**		**p**	**B**	**95% CI**		**p**
Age	-0.001	-0.006	0.005	0.864	-0.003	-0.011	0.006	0.499	0.000	-0.008	0.008	0.957
Gender	-0.130	-0.295	0.036	0.124	-0.195	-0.403	0.041	0.104	0.020	-0.207	0.246	0.864
Body mass index	0.009	-0.008	0.026	0.318	0.022	-0.003	0.046	0.078	-0.015	-0.038	0.009	0.212
ASA	-0.042	-0.188	0.105	0.573	0.003	-0.223	0.229	981	0.070	-0.147	0.286	0.526
Systolic blood pressure	-0.016	-0.158	0.126	0.820	0.025	-0.193	0.243	0.823	-0.046	-0.252	0.161	0.664
Application of premedication	-0.108	-0.528	0.312	0.611	0.248	-0.349	0.844	0.413	0.519	-0.052	1.090	0.074
Preoperative body temperature					0.604	0.375	0.833	0.000*	0.179	-0.085	0.443	0.182
Type of anesthesia					0.086	-0.118	0.289	0.407	-0.015	-0.209	0.178	0.875
Type of surgery					0.012	-0.178	0.202	0.901	0.001	-0.179	0.180	0.992
Duration of surgery					0.016	-0.028	0.060	0.471	-0.003	-0.045	0.039	0.887
Temperature of the operating room					0.378	0.237	0.520	0.000*	0.198	0.048	0.347	0.010*
Amount of fluid given during operation					0.077	-0.179	0.333	0.554	-0.019	-0.264	0.225	0.876
Application of a heating method in the operating room					0.196	-0.073	466	0.152	-0.183	-0.442	0.077	0.167
Intraoperative body temperature									0.483	0.294	0.672	0.000*
Application of a heating method during recovery									0.101	-0.212	0.415	0.523

R^2: 0.071; Corrected R^2: 0.022 R^2: 0.286; Corrected R^2: 0.212 R^2: 0.437; Corrected R^2: 0.363
ASA: American Society of Anesthesiology Classification
CI: Confidence interval
*p<0.05

mine the effect of heating on the prevention of the occurrence of inadvertent hypothermia, it was reported that the rate of hypothermia development was lower in patients undergoing intraoperative active heating. In a study conducted by Aksu et al. (14), less hypothermia was reported in patients undergoing heating during operation. As recommended in the guidelines for the prevention of inadvertent hypothermia, intraoperative heating prevents the development of inadvertent hypothermia (2, 9, 12, 27).

In various studies in literature, no statistically significant difference was found between the development of intraoperative inadvertent hypothermia and some parameters such as age, gender, BMI, ASA score, systolic blood pressure, preoperative body temperature in the clinic, type of surgery, duration of surgery, and temperature of the operating room (15, 17, 19, 28). On the other hand, in some studies, age, gender, ASA level, type of surgery, and duration of surgery were found to have an effect on the development of intraoperative hypothermia (19-21). The risk factors affecting the occurrence of intraoperative hypothermia vary. In our study, the results of univariate and multivariate regression analyses demonstrated that the variables of age, gender, BMI, systolic blood pressure, premedication, type of anesthesia, type of surgery, duration of surgery, and amount of fluid given during operation did not affect the intraoperative development of inadvertent hypothermia.

Postoperative period

In our study, the incidence of postoperative inadvertent hypothermia was detected to be 75.70% (n= 109). The incidence rates differ in the studies on hypothermia. The incidence was reported to be 13.50% in a study performed in Australia (29), 32% in a study conducted in Portugal (17), and 47.50% in a study performed in Turkey (14). It is thought that the differences among the incidence rates of inadvertent hypothermia are associated with the variations in the applications.

Preoperative body temperature affects postoperative body temperature (11, 15). Our study revealed that preoperative body temperature affected the development of inadvertent hypothermia (Table 2). In a study performed to determine the incidence of inadvertent hypothermia and risk factors, it was found that the risk of hypothermia was lower in patients having high body temperature before surgery (15). Mehta and Barclay conducted a study on patients undergoing colorectal surgery, and they reported that the development of hypothermia was 20 times higher in patients with low body temperature before surgery (22). Therefore, it is important to provide normothermia in patients before surgery and to use heating methods when needed.

It was found that the application of premedication had an effect on the development of inadvertent hypothermia (Table 2). The results of studies conducted by D'AngeloVanni et al. (30) and Matsukawa et al. (31) are consistent with ours. With other risk factors causing hypothermia, premedication leads to vasodilatation and inhibits patients to preserve their body temperatures (32).

In our study, the results of multivariate analysis showed that temperature of the operating room affected the occurrence of postoperative inadvertent hypothermia (Table 2, 3). Similar to these results, Yi et al. found a statistically significant difference between the temperature of the operating room and inadvertent hypothermia (15). In the study of Poveda et al., temperature of the operating room was reported to be associated with the development of hypothermia (33). Different from the results of our study, another study demonstrated no statistically significant difference between the temperature of the operating room and inadvertent hypothermia in patients undergoing emergency operation (34).

According to the results of univariate and multivariate regression analyses, intraoperative body temperature was found to be effective in the development of postoperative inadvertent hypothermia (Table 2, 3). In the studies that were conducted to determine the risk factors for the development of postoperative undesired hypothermia, the rate of postoperative inadvertent hypothermia was reported to be higher in patients having low body temperature during surgery (15, 24, 28). In our study, age, gender, BMI, ASA score, premedication, type of surgery, duration of surgery, amount of fluid given during operation, and the application of a heating method in the operating room and in the recovery room were found to have an effect on the development of postoperative inadvertent hypothermia.

A limitation of this study is that the body temperatures of the patients were not measured before taking them into the operating room and in the clinic after operation.

CONCLUSION

In our study, in which the incidence of inadvertent hypothermia and risk factors were examined, the incidence of hypothermia was found to be quite high. It was detected that preoperative body temperature, temperature of the operating room, and the intraoperative application of a heating method affected the development of inadvertent hypothermia.

Health staff has great responsibilities toward patients undergoing surgery in the preoperative period, in the operating room, and in the postoperative period to protect them from inadvertent hypothermia and its effects. The body temperature of patient should be checked and evaluated preoperatively, intraoperatively, and postoperatively.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Dokuz Eylül University School of Medicine (2015/28-26 - 01.17.2015).

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - F.V., Z.D.; Design - F.V., Z.D., B.Ç.; Supervision - F.V.; Resource - Z.D., B.Ç, K.Y.; Materials - Z.D., K.Y..; Data Collection and/or Processing - Z.D., B.Ç, K.Y.; Analysis and/or Interpretation - Z.D., K.Y.; Literature Search - B.Ç., Z.D.; Writing Manuscript - F.V., Z.D., B.Ç, K.Y.; Critical Reviews - F.V.

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

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

REFERENCES

1. American Society of PeriAnesthesia Nurses-ASPAN. Clinical guideline for the prevention of unplanned perioperative hypothermia. J Perianesth Nurs 2001; 16: 305-314. [CrossRef]
2. Association of Surgical Technologists-AST. AST Guidline statement for the maintenance of normothermia in the perioperative patient. 2005. Avilable from URL: https://static1.squarespace.com/static/579770cd197aea84455d6908/t/57fd36f9ff7c508da3feb38f/1476212473146/Guideline_Normothermia.pdf (access date: 17.08.2015)
3. Forbes SS, Eskicioglu C, Nathens AB, Fenech DS, Laflamme C, McLean RF, et al. Evidence based guidelines for prevention of perioperative hypotermia. J Am Coll Surg 2009; 209: 492-504. [CrossRef]
4. Diaz M. Hypothermia and temperature regulation considerations during anesthesia. Avilable from URL: http://www.sld.cu/galerias/pdf/sitios/anestesiologia/hypothermia.pdf (access date: 17.08.2015)
5. Görges M, Ansermino JM, Whyte SD. A retrospektive audit to examine the effectiveness of preoperative warming on hypotermia in spine deformity surgery patient. Paediatr Anaesth 2013; 23: 1054-1061. [CrossRef]
6. Leaper DJ, Tanner J, Kiernan M, Assadian O, Edmiston CE Jr. Surgical site infection: poor compliance with guidlines and care bundles. Int Wound J 2015; 12: 357-362. [CrossRef]
7. Burns SM, Wojnakowski M, Piotrowski K, Caraffa G. Unintentional hypotermia: implications for perianesthesia nurses. J Perianesth Nurs 2009; 24: 167-176. [CrossRef]
8. Torossian A, Brauer A, Hocker J, Bein B, Wulff H, Horn EP. Preventing inadvertent perioperative hypotermia. Dtsch Arztebl Int 2015; 112: 166-172.
9. NICE-National Institute for Health and Care Excellence. The Management of inadvertent perioperative hypotemia in adults. 2008. Updated 2016. Avilable from URL: https://www.nice.org.uk/guidance/cg65/chapter/Recommendations (access date: 17.08.2015)
10. Journeaux M. Peri-operative hypotermia: implications for practice. Nurs Stand 2013; 27: 33-38. [CrossRef]
11. Türk Anesteziyoloji ve Reanimasyon Derneği. İstenmeyen perioperatif hipoterminin önlenmesi rehberi. Turk J Anaesth Reanim. 2013; 41: 188-190.
12. AORN. Guideline for prevention of unplanned patient hypothermia. In: Guidelines for Perioperative Practice. Denver, CO: AORN 2016: 531-554.
13. Horn EP, Bein B, Böhm R, Steinfath M, Sahili N, Höcker J. The effect of short time periods of pre-operative warming in the prevention of peri-operative hypothermia. Anaesthesia 2012; 67: 612-617. [CrossRef]
14. Aksu C, Kuş A, Gürkan Y, Solak M, Toker K. Survey on Postoperative Hypothermia Incidence In Operating Theatres of Kocaeli University. Turk J Anesth Reanim 2014; 42: 66-70. [CrossRef]
15. Yi J, Xiang Z, Deng X, Fan T, Fu R, Geng W, et all. Incidence of inadvertent intraoperative hypothermia and its risk factors in patients undergoing general anesthesia in beijing: a prospective regional survey. Plos One 2015; 10: 1-12. [CrossRef]
16. Leijtens B, Koëter M, Kremers K, Koëter S. High incidence of postoperative hypothermia in total knee and total hip arthroplasty A Prospective Observational Study. J Arthroplasty 2013; 28: 895-898. [CrossRef]
17. Luís C, Moreno C, Silva A, Páscoa R, Abelha F. Inadvertent postoperative hypothermia at post-anesthesia care unit: incidence, predictors and outcome. Open J Anesthesiol 2012; 2: 205-213. [CrossRef]
18. Andrzejowski JC, Turnbull D, Nandakumar A, Gowthaman S, Eapen G. A randomised single blinded study of the administration of pre-warmed fluid vs active fluid warming on the incidence of peri-operative hypothermia in short surgical procedures. Anaesthesia 2010; 65: 942-945. [CrossRef]
19. Fernandes LA, Braz LG, Koga FA, Kakuda CM, Mo´dolo NSP, Carvalho LR, et al. Comparison of peri-operative core temperature in obese and non-obese patients. Anaesthesia 2012; 67: 1364-1369. [CrossRef]
20. Karalapillai D, Story D, Hart GK, Bailey M, Pilcher D, Schneider A, et al. Postoperative hypothermia and patient outcomes after majör elective non-cardiac surgery. Anaesthesia 2013; 68: 605-611. [CrossRef]
21. Yang L, Huang CY, Zhou ZB, Wen ZS, Zhang GR, Liu KX, et al. Risk factors for hypothermia in patients under general anesthesia: Is there a drawback of laminar airflow operating rooms? A prospective cohort study. Int J Surg 2015; 21: 14-17. [CrossRef]
22. Mehta OH, Barclay KL. Perioperative hypothermia in patients undergoing major colorectal surgery. ANZ J Surg 2014; 84: 550-555. [CrossRef]
23. Yi J, Zhan L, Lei Y, Xu S, Si Y, Li S, et al. Establishment and validation of a prediction equation to estimate risk of intraoperative hypothermia in patients receiving general anesthesia. Sci Rep 2017; 7: 13927. [CrossRef]
24. Belayneh T, Gebeyehu A, Abdissa Z. Post-operative hypothermia in surgical patients at University of Gondar Hospital, Ethiopia. J Anesth Clin Res 2014; 5: 1-4. [CrossRef]
25. Monzón CGC, Arana CAC, Valz HAM, Rodríguez FA, Mejía JJB, Gómez JAA. Temperature management during the perioperative period and frequency of inadvertent hypothermia in a general hospital. Rev Colomb Anestesiol 2013; 41: 97-103. [CrossRef]
26. Adriani MB, Moriber N. Preoperative forced-air warming combined with ıntraoperative warming versus ıntraoperative warming alone in the prevention of hypothermia during gynecologic surgery. AANA J 2013; 81: 446-451.
27. Card R, Sawyer M, Degnan B, Harder K, Kemper J, Marshall M, et al. Institute for clinical systems improvement. Perioperative protocol. 2014. Avilable From URL: https://www.icsi.org/guidelines__more/catalog_guidelines_and_more/catalog_guidelines/catalog_patient_safetyreliability_guidelines/perioperative/ (access date: 15.08.2016)
28. Frisch NB, Pepper AM, Jildeh TR, Shaw J, Guthrie T, Silverton C. Intraoperative hypothermia during surgical fixation of hip fractures. Orthopedics 2016; 39: 1170-1177. [CrossRef]
29. Ireland S, Endacott R, Cameron P, Fitzgerald M, Paul E. The incidence and significance of accidental hypothermia in major trauma- a prospective observational study. Resuscitation 2011; 82: 300-306. [CrossRef]
30. D'Angelo Vanni SM, Castiglia YM, Ganem EM, Rodrigues Júnior GR, Amorim RB, Ferrari F, et al. Preoperative warming combined with intraoperative skin-surface warming does not avoid hypothermia caused by spinal anesthesia in patients with midazolam premedication. Sao Paulo Med J 2007; 125: 144-149. [CrossRef]
31. Matsukawa T, Ozaki M, Nishiyama T, Makoto I, Iwamoto R, Iijima T, Kumazawa T. Atropine prevents midazolam-induced core hypothermia in elderly patients. J Clin Anesth 2001; 13: 504-508. [CrossRef]
32. Yüksel S, Altun Uğraş G. The role of nurses in preventing hypothermia in surgical patients. Mersin Univ Saglık Bilim Derg 2016; 9: 113-121.
33. de Brito Poveda V, Galvão CM, dos Santos CB. Factors associated to the development of hypothermia in the intraoperative period. Rev Lat AM Enfermagem 2009; 17: 228-233. [CrossRef]
34. Inaba K, Berg R, Barmparas G, Rhee P, Jurkovich GJ, Recinos G, Teixeira PG, Demetriades D. Prospective evaluation of ambient operating room temperature on the core temperature of injured patients undergoing emergent surgery. J Trauma Acute Care Surg 2012; 73: 1478-1483. [CrossRef]

Turk J Surg 2018; 34(4): 306-310
DOI: 10.5152/turkjsurg.2017.3808

Endoscopic retrograde cholangiopancreatography for biliary system parasites

Sezgin Yılmaz[1], Murat Akıcı[1], Merih Şimşek[2], Nazan Okur[3], Ogün Erşen[1], Ahmet Ali Tuncer[4]

ABSTRACT

Objective: Endoscopic retrograde cholangiopancreatography may be useful in the diagnosis and management of biliary system parasites.

Material and Methods: Investigators retrospectively evaluated patients with biliary system parasites who underwent endoscopic retrograde cholangiopancreatography procedures over an eight-year period. We collected data regarding patient demographics, clinical features, and parasite type. We aimed to determine the utility of endoscopic retrograde cholangiopancreatography as a diagnostic and therapeutic intervention in patients with biliary system parasites.

Results: We identified 22 patients with biliary system parasites from a total of 3,450 endoscopic retrograde cholangiopancreatography procedures performed during an eight-year period. Parasite types included *Echinococcus granulosus* (n=19), *Fasciola hepatica* (n=2), and *Ascaris lumbricoides* (n=1). Fifteen patients with liver hydatid cysts underwent endoscopic retrograde cholangiopancreatography prior to surgery due to obstructive jaundice. The endoscopic retrograde cholangiopancreatography procedure enabled definitive treatment without the need for surgery in the remaining two patients. Two patients with fascioliasis underwent endoscopic retrograde cholangiopancreatography due to clinical presentation of cholangitis, cholecystitis, and obstructive jaundice, leading to presumptive diagnosis of cholangiocarcinoma. However, the final diagnosis was made using endoscopic retrograde cholangiopancreatography following inspection of flat, leaf-shaped, motile flukes extracted from the bile duct. In one patient with ascariasis, a longitudinal tubular structure was identified in the bile duct; emergency surgery was required.

Conclusion: The diagnosis of parasitic diseases is clinically challenging, and definitive diagnosis requires endoscopic retrograde cholangiopancreatography in some cases. Moreover, endoscopic retrograde cholangiopancreatography provides a therapeutic option for ascariasis, fascioliasis, and some forms of hydatidosis. Accordingly, the use of endoscopic retrograde cholangiopancreatography may change preoperative management and treatment strategies for biliary system parasite infections.

Keywords: Echinococcosis, endoscopic retrograde cholangiopancreatography, Fasciola hepatica, biliary system

Cite this paper as:
Yılmaz S, Akıcı M, Şimşek M, Okur N, Erşen O, Tuncer AA. Endoscopic retrograde cholangiopancreatography for biliary system parasites. Turk J Surg 2018; 34(4): 306-310.

[1]Department of General Surgery, Afyon Kocatepe University School of Medicine, Afyonkarahisar, Turkey
[2]Department of Microbiology, Afyon Kocatepe University School of Medicine, Afyonkarahisar, Turkey
[3]Clinic of Radiology, Afyon State Hospital, Afyonkarahisar, Turkey
[4]Department of Pediatric Surgery, Afyon Kocatepe University School of Medicine, Afyonkarahisar, Turkey

Corresponding Author
Ahmet Ali Tuncer
e-mail: drtaali@yahoo.com

Received: 10.01.2017
Accepted: 18.04.2017
Available Online Date: 03.01.2018

Available online at
www.turkjsurg.com

INTRODUCTION

Parasites are endemic in various regions of the world and are associated with severe health problems in these areas. Poor sanitation, overpopulation, intercontinental migration, and the international food trade contribute to the increasing prevalence of parasite infestations. As a result, parasitic infections are increasingly being recognized as a clinical problem, even in non-endemic countries. The involvement of the biliary system in parasitic infections may cause severe morbidity and, rarely, mortality due directly to the parasites or to related complications, even in childhood (1, 2). The clinical presentation of parasite infection varies depending on the type and location of infestation within the biliary tree. Hepato-biliary problems arise from compression of the biliary system by parasites or infestation of the bile ducts (3-5). Biliary infestation occurs due to the rupture of parasites into the biliary tree or direct transmission of parasites through the papillary orifice. These complications may result in obstructive jaundice or acute cholangitis, necessitating urgent decompression by surgical, radiological, or endoscopic techniques.

The diagnosis of biliary system parasites is challenging with conventional radiological methods. Although computed tomography and ultrasonography can successfully demonstrate the location of cysts within the liver, these techniques typically fail to demonstrate biliary tree involvement. Additionally, some parasite species (e.g., *Fasciola hepatica*) may mimic radiological features of cholangiocarcinoma. Accordingly, endoscopic retrograde cholangiopancreatography (ERCP) may play a role in the differential diagnosis and subsequent surgical treatment of suspected cases. ERCP provides a wide range of clinical benefits for biliary complications during both the pre- and postoperative periods (6). Although ERCP is commonly used for in patients with bile duct injury following hepatobiliary surgery, patients with parasite-related cholangitis or obstructive jaundice may also benefit from decompression of parasitic obstruction by ERCP (7, 8). Moreover, endoscopic sphincterotomy (ES) may be useful in the clearance

of parasites from the bile duct and associated structures. ERCP may also aid in the closure of biliary fistulae during the postoperative period by decreasing intraluminal pressure within the biliary system (9).

The utility of ERCP in the treatment of biliary system parasites differs according to parasite type and intervention timing. For example, parasite extraction provides a therapeutic option for *F. hepatica* if antimicrobial therapy fails to completely eradicate biliary system parasites (10-14). Moreover, ERCP provides a bridge to safe surgery for *Echinococcus granulosus* by extracting vesicles from the biliary channel preoperatively. Additionally, ERCP and sphincterotomy have clinical benefits by decreasing the postoperative output of biliary fistulae occurring after surgery for *E. granulosus*.

Investigators performed 3,450 ERCP procedures over an eight-year period and encountered 22 cases of biliary system parasites (n=19 for *E. granulosus*, n=2 for *F. hepatica*, and n=1 for *Ascaris lumbricoides*). The aim of the present study was to determine clinical and radiological differences between biliary system parasite types. The role of ERCP in the diagnosis and management of biliary system parasites was also examined.

MATERIAL AND METHODS

The present retrospective study includes 22 patients with biliary system parasite infections identified from a total of 3,450 ERCP procedures performed during an eight-year period. Of these, *E. granulosus* infection was observed in 19 cases, *F. hepatica* in two cases, and *A. lumbricoides* in one case. The demographic and clinical features of the patients are depicted in Table 1. For patients with hepatic hydatid disease, the necessity of the ERCP procedure was determined according to the following criteria:

a. Preoperative ERCP was performed in cases of obstructive jaundice resulting from occlusion of the bile duct with hydatid membranes/fragments and/or daughter cysts in cases of hydatid cysts confirmed by radiological, serological, and blood tests.

b. Postoperative ERCP was performed in patients with external biliary fistulae following cyst surgery, new onset cholangitis, obstructive jaundice, or postoperative biloma (after percutaneous catheterization with a permanent fistula).

As the presentations of *F. hepatica* and *A. lumbricoides* infections have vague clinical and imaging findings, the decision to perform ERCP was made according to standard indications for ERCP. Endoscopic and additional surgical procedures were performed by S.Y. and M.A. using video duodenoscopy (EPX-4400 HD Video GI Endoscopy System; Fujinon GmbH, Willich, Germany) with patients in the prone position. During ERCP procedures, all patients received fentanyl and midazolam intravenously, with additional doses provided as required to maintain sedation. Antibiotic prophylaxis was provided via intravenous administration of 1 g cefazolin. Duodenal peristalsis was reduced by intravenous hyoscine-N-butylbromide injection. For patients in the 1/a group, appropriate surgical procedures were performed according to ERCP and radiological findings. ERCP procedures are diagnostic only in patients with *A. lumbricoides* due to the inability to extract the parasites; therefore, open surgery, including choledochotomy and parasite extraction, is performed in such cases. Statistical Package for the Social Sciences 16.0 software for Windows (SPSS Inc; Chicago, IL, USA) was used to statistically evaluate the data. Numerical values were expressed as average or median values. Ethics committee approval was received according to the Declaration of Helsinki and Good Clinical Practice Guidelines. Written informed consent was obtained from the patients for the publication of this report and the accompanying images.

RESULTS

Investigators performed 3450 ERCP procedures between 2008 and 2016 at our center. Of these, 22 patients were found to have biliary system parasite infections during the ERCP procedure, with 19 cases of *E. granulosus,* two cases of *F. hepatica*, and one case of *A. lumbricoides.*

E. granulosus

Fifteen patients with liver hydatid cysts underwent ERCP preoperatively due to obstructive jaundice and cholangitis resulting from bile duct occlusion (Figure 1). Germinative membrane fragments, daughter cysts, and accompanying biliary sludge were causative factors extracted from the choledochus (Figure 2). Patients were scheduled for surgery after their liver function tests had returned to normal. Ten patients were referred to the original referring centers, whereas five patients underwent surgical interventions at our center; three patients underwent surgery via a laparoscopic approach, and the other two patients underwent surgery via laparotomy. No cases of postoperative mortality were observed, and patients were discharged with prescriptions for albendazole and annual control.

Four patients underwent ERCP following surgery performed 7 to 20 days previously at other centers due to persistently high output from biliary fistulae. Causative factors were germina-

Table 1. Demographic and clinical features of patients who underwent endoscopic retrograde cholangiopancreatography for the treatment of biliary system parasites

Parasite	Age	Gender (F/M)	Timing†	Surgery after ERCP	Definitive treatment‡
Hydatidosis (19)	52.6	7/12	15/4	13	2
Fascioliasis (2)	71.0	1/1	2/0	1	1
Ascariasis (1)	79.0	0/1	1/0	1	0

ERCP: endoscopic retrograde cholangiopancreatography

†Timing: whether ERCP was performed preoperatively or postoperatively (preoperative/postoperative)

‡Definitive treatment: whether ERCP provided definitive treatment, obviating the need for further surgery

tive membrane fragments; an accompanying bile duct stone was observed in one patient. Two patients received temporary biliary stents in addition to sphincterotomy.

F. hepatica

Two patients with fascioliasis underwent ERCP due to the presence of cholangitis, cholecystitis, and obstructive jaundice informing a presumptive diagnosis of cholangiocarcinoma (Figure 3). However, the final diagnosis was made by ERCP following inspection of flat, leaf-shaped, motile flukes extracted from the bile duct (Figure 4). Indirect hemagglutination tests for fascioliasis were high, with a measured titre of 1/320. As both patients had cholelitiasis, open cholecystectomy was performed, and both patients were discharged with prescriptions for triclabendazole.

A. lumbricoides

One patient was found to be infected with *A. lumbricoides*. He was referred to our center for ERCP with a diagnosis of suppurative cholangitis. As radiological and laboratory findings were strongly suggestive of suppurative cholangitis, the patient was scheduled to undergo ERCP. Although a longitudinal tubular structure was found in the bile duct, extraction through the papillary orifice was not possible for technical reasons. Emergency surgery was accordingly planned. Intraoperatively, severely infected bile, pus formation, and a 30-cm-long worm located in the lumen were observed (Figure 5). The procedure was completed with placement of a T-tube; however, the patient subsequently died despite intense supportive treatment.

Figure 1. Cyst pouch of *Echinococcus granulosus* on cholangiography

Figure 2. Germinative membrane extraction using a basket catheter

DISCUSSION

Endoscopic retrograde cholangiopancreatography is an effective and reliable method for the treatment and differential diagnosis of various parasitic diseases involving the biliary system. Of these, the daughter vesicles and/or germinative membranes of *E. granulosus* are the most frequent cause of

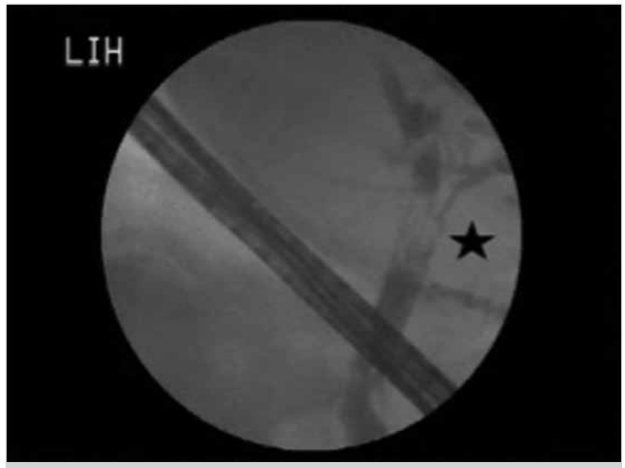


Figure 3. Irregular filling defect mimicking cholangiocarcinoma on cholangiography

Figure 4. Extraction of Fasciola hepatica using a balloon catheter

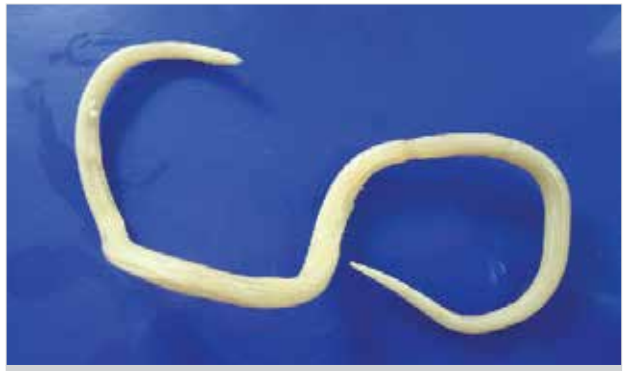


Figure 5. Ascaris lumbricoides extraction from the bile duct during emergency laparotomy

biliary system conditions, such as jaundice, cholangitis, and biliary fistulae. Intrabiliary rupture is the most common and serious complication in patients with hydatid cysts (6). In particular, open and wide communication between the cyst wall and the biliary system may present as biliary colic, jaundice, cholangitis, or an abscess; it also rarely presents as anaphylaxis or pancreatitis (5). These patients may require ERCP during the preoperative period due to the aforementioned complications or during the postoperative period due to sustained biliary fistulae. In certain cases, wide communication between the cyst and biliary channel allows the germinative membrane and cyst contents to be completely evacuated during ERCP; further surgery may not be required.

In the present study, 15 patients underwent ERCP prior to surgery. Of these, further surgery was not required in two patients following cyst extraction and clearance of the biliary channel of daughter cysts and vesicles. Several previous studies have reported that up to 25% of patients can be cured without the need for further surgical intervention after preoperative ERCP (6). The postoperative complications observed after surgery for hydatid disease are persistent biliary fistulae, obstructive jaundice, and related biochemical abnormalities. ERCP plays a principal role in the management of these complications. Although daily fistula output, progression, and accompanying abscess formation determine the indications for ERCP, Adas et al. (15) recommended that the ERCP procedure should be performed at an early period. ES and/or stent placement are useful in the treatment of these complications. Four patients in the present study underwent ERCP due to persistent biliary fistulae; ES was successfully performed in two patients, and ES plus stent placement was successfully performed in the other two patients.

Fascioliasis is a parasitic disease that has acute (hepatic) and chronic (biliary) phases. Although it is a substantial clinical issue in developing countries, the incidence of fascioliasis is gradually increasing worldwide (13). The natural environment of the parasite is the duodenal lumen; it is transmitted to the liver parenchyma and biliary channel by an ascending route through the peritoneal cavity. The diagnosis of fascioliasis is often delayed due to non-specific radiological and clinical findings. Patients infected with *F. hepatica* are typically admitted with symptoms of biliary colic, liver abscess, choledocholithiasis, pancreatitis, and compressive symptoms mimicking cholangiocarcinoma (11, 12, 14). ERCP can be performed for the differential diagnosis and definitive treatment of *F. hepatica*, thus avoiding further surgery (16). Two patients in the present study were admitted to our center with presumptive diagnoses of cholangitis and cholangiocarcinoma. Therefore, we performed diagnostic ERCP on these patients; final diagnosis and eventual treatment were enabled by the procedure. A single dose of triclabendazole was also administered to these patients.

The adult forms of *A. lumbricoides* inhabit the duodenal lumen and are rarely transmitted to the biliary channel by penetrating the papillary orifice. Once it has entered into the choledochus, *A. lumbricoides* causes severe cholangitis, obstructive jaundice, acalculous cholecystitis, and, rarely, pancreatitis. Because albendazole treatment is ineffective in the treatment of biliary ascariasis, parasites should be directly removed from the bile duct (17). Endoscopic procedures should be initially attempted to remove parasites, as laparotomy may increase mortality and aggravate sepsis in patients with cholangitis (18). However, it may be impossible to extract parasites due to their size; in these cases, laparotomy is necessary. In the present case, although we performed ERCP as the initial procedure, it was impossible to remove the parasite for technical reasons; therefore, choledochotomy, parasite removal, and T-tube placement were performed.

CONCLUSION

Although parasites are a rare cause of cholangitis, they may cause severe morbidity and even death in certain cases. The diagnosis of parasitic disease is challenging with standard imaging modalities if the parasite is located within the biliary system. Accordingly, definitive diagnosis may only be possible with ERCP in some cases. Moreover, ERCP provides a therapeutic option for ascariasis, fascioliasis, and some forms of hydatidosis. Accordingly, the use of ERCP may change the preoperative management and treatment of biliary system parasites.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of of Afyon Kocatepe University.

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - S.Y., M.A., A.A.T., O.E.; Design - S.Y., M.A., M.Ş.; Supervision - S.Y., M.A., A.A.T., N.O.; Resource - S.Y., M.A., M.Ş. N.O.; Materials - O.E., M.A., M.Ş.; Data Collection and/or Processing - N.O., S.Y., O.E.; Analysis and/or Interpretation - M.A., S.Y., O.E.; Literature Search - A.A.T., N.O., S.Y.; Writing Manuscript - A.A.T., M.A., S.Y.; Critical Reviews - A.A.T., M.A., S.Y., O.E., N.O., M.Ş.

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

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

REFERENCES

1. Tuncer AA, Embleton DB, Yilmaz S, Okur N, Kacar E, Bayraktaroglu A. ERCP treatment for intrabiliary rupture of hepatic hydatid cyst in a child. J Exp Clin Med 2016; 33: 37-39.
2. Miman O, Okur N, Cufali D, Yilmaz S. Suppurative cholangitis caused by ascaris lumbricoides: Report of a fatal case. Kafkas Univ Vet Fak Derg 2012; 18: 235-237.
3. Akaydin M, Erozgen F, Ersoy YE, Birol S, Kaplan R. Treatment of hepatic hydatid disease complications using endoscopic retrograde cholangiopancreatography procedures. Can J Surg 2012; 55: 244-248. [CrossRef]
4. Yücesoy AN, Poçan S. Secondary gallbladder hydatidosis and nonfragmanted germinative membrane sourced obstructive jaundice caused by intrabiliary ruptured hepatic hydatid cyst (a case report): two rare complication of the intrabiliary ruptured hepatic hydatid cyst. Hepatobiliary Surg Nutr 2014; 3: 209-211.
5. Bayhan Z, Yilmaz S, Tiryaki C, Kargi E, Ucar BI. Acute Pancreatitis due to rupture of the hydatid cyst into the biliary tract: a case report. Natl J Med Res 2014; 4: 92-94.

6. Dolay K, Akbulut S. Role of endoscopic retrograde cholangiopancreatography in the management of hepatic hydatid disease. World J Gastroenterol 2014; 20: 15253-15261. [CrossRef]
7. Yilmaz S, Ersen O, Ozkececi T, Turel KS, Kokulu S, Kacar E, et al. Results of the open surgery after endoscopic basket impaction during ERCP procedure. World J Gastrointest Surg 2015; 7: 15-20. [CrossRef]
8. Yilmaz S, Akici M, Okur N, Türel S, Erşen O, Şahin E. Spontaneous postoperative choledochoduodenal fistula due to bile duct injury following laparoscopic cholecystectomy. Int J Surg Case Rep 2016; 25: 199-202. [CrossRef]
9. Ambregna S, Koch S, Sulz MC, Grüner B, Öztürk S, Chevaux JB, et al. A European survey of perendoscopic treatment of biliary complications in patients with alveolar echinococcosis. Expert Rev Anti Infect Ther 2017; 15: 79-88. [CrossRef]
10. Ozer B, Serin E, Gümürdülü Y, Gür G, Yilmaz U, Boyacioğlu S. Endoscopic extraction of living fasciola hepatica: case report and literature review. Turk J Gastroenterol 2003; 14: 74-77.
11. Jha AK, Goenka MK, Goenka U, Chakrabarti A. Hepatobiliary fascioliasis in non-endemic zones: a surprise diagnosis. Arab J Gastroenterol 2013; 14: 29-30. [CrossRef]
12. Kang BK, Jung BK, Lee YS, Hwang IK, Lim H, Cho J, et al. A case of Fasciola hepatica infection mimicking cholangiocarcinoma and ITS-1 sequencing of the worm. Korean J Parasitol 2014; 52: 193-196. [CrossRef]
13. Yilmaz S, Celep B, Altindis M, Arikan Y. A stranger in the main bile duct. Fasciola hepatica, the extraction by ERCP. Selcuk Tıp Derg 2014; 30: 172-174.
14. Sezgin O, Altintaş E, Tombak A, Uçbılek E. Fasciola hepatica-induced acute pancreatitis: report of two cases and review of the literature. Turk J Gastroenterol 2010; 21: 183-187. [CrossRef]
15. Adas G, Arikan S, Gurbuz E, Karahan S, Eryasar B, Karatepe O, et al. Comparison of endoscopic therapeutic modalities for postoperative biliary fistula of liver hydatid cyst: a retrospective multicentric study. Surg Laparosc Endosc Percutan Tech 2010; 20: 223-237. [CrossRef]
16. Okudan M, Egeli T, Taşkesen F, Yılmaz Ş. A rare cause of obstructive jaundice: Fasciola hepatica. Turk J Surg 2011; 27: 164-166. [CrossRef]
17. Mitoro A, Yoshikawa M, Yamao J, Yoshida M, Kojima K, Sawai M, et al. Endoscopic extraction of biliary ascariasis by using a wire-guided basket, without a sphincterotomy. Gastrointest Endosc 2007; 65: 327. [CrossRef]
18. Lee YS, Kim DK, Choi YH, Kim DJ, Shim MS, Shim CS, et al. Biliary ascariasis as a cause of acute cholangitis: a case report. Pancreatology 2013; 13: 23-24. [CrossRef]

Turk J Surg 2018; 34(4): 311-314
DOI: 10.5152/turkjsurg.2018.3972

Original Article

Comparison of limberg flap and oval flap techniques in sacrococcygeal pilonidal sinus disease surgery

Banu Karapolat[1], Sercan Büyükakıncak[2], Eray Kurnaz[1], Üzer Küçüktülü[1]

ABSTRACT

Objective: Although many surgical techniques have been described for treatment of pilonidal sinus disease (PSD), the ideal treatment method remains controversial. The purpose of this study was to compare Limberg flap and oval flap techniques in patients with PSD.

Material and Methods: Patients diagnosed with PSD who underwent surgery using either the Limberg flap or oval flap technique between January 2012 and January 2016 at the general surgery outpatient clinic were retrospectively reviewed from the database of our hospital; 142 patients (124 males and 18 females) were invited for examination. The demographic characteristics of the patients such as age and gender, hospital stays, seroma occurrence, surgical site infections, wound dehiscence, flap necrosis, loss of sensation, and recurrences were evaluated based on the information obtained from the database and from physical examinations as well as questioning of the patients. The results were statistically compared, and a p value of <0.05 was considered significant.

Results: The mean age of the patients was 27.5±7.8 years in the Limberg flap group and 26.5±7.2 years in the oval flap group. No significant difference was found between the two groups regarding patients' mean age; gender distribution; postoperative hospital stay; recurrence; and complications, such as seroma, infection, wound dehiscence, and loss of sensation. Flap necrosis was not observed in any of the patients.

Conclusion: The Limberg flap and oval flap procedures both involve minimum morbidity and short hospital stay because they were not superior to one another regarding treatment effectiveness, complications, and recurrence in the pilonidal sinus surgery.

Keywords: Pilonidal sinus, surgical flaps, postoperative complications, recurrence

ORCID IDs of the authors:
B.K. 0000-0001-5132-8266;
S.B. 0000-0002-1262-9936;
E.K. 0000-0002-9043-558X;
Ü.K. 0000-0003-4481-9176.

Cite this paper as:
Karapolat B, Büyükakıncak S, Kurnaz E, Küçüktülü Ü. Comparison of limberg flap and oval flap techniques in sacrococcygeal pilonidal sinus disease surgery. Turk J Surg 2018; 34(4): 311-314.

[1]Department of General Surgery, Kanuni Training and Research Hospital, Trabzon, Turkey

[2]Department of General Surgery, Akcaabat State Hospital, Trabzon, Turkey

Corresponding Author
Banu Karapolat
e-mail: banukarapolat@hotmail.com

Received: 23.08.2017
Accepted: 13.10.2017
Available Online Date: 28.08.2018

INTRODUCTION

Many conservative and surgical methods have been described for the treatment of sacrococcygeal pilonidal sinus disease (PSD), but the standard and optimal surgical method remains controversial (1-3). The main principle in the treatment of PSD is to enable patients to return to their normal life at the earliest after a complication-free surgical procedure as well as to prevent recurrence. The medical treatments include local curettage, phenol injection, silver nitrate applications, and electrocauterization of the cavity. The most frequently used surgical methods include excision–primary repair, excision–marsupialization, excision–leaving open, Bascom's operation, Karydakis operation, VYZ plasty, and Limberg flap and oval flap techniques. In recent years, various flap techniques have become popular worldwide, particularly because of low complication and recurrence rates and early wound healing associated with them (2).

In the present study, we compared the Limberg flap and oval flap techniques used in the surgical treatment of PSD with respect to the demographic characteristics of the patients as well as associated complications and recurrence; furthermore, we have discussed the results by referring to the available data.

MATERIAL AND METHODS

In this study, we included 213 patients who had visited the general surgery outpatient clinic of the Trabzon Kanuni Training and Research Hospital between January 2012 and January 2016 and who had undergone surgery using either the Limberg flap or oval flap technique after being diagnosed with PSD. All the patients were retrospectively reviewed from the database of our hospital, and 142 patients (124 males and 18 females) who could be contacted were invited for examination. The study included patients aged >18 years who were diagnosed with chronic PSD, were symptomatic, had not benefited from medical treatment, and did not have any comorbid medical conditions. The exclusion criteria included age <18 years, presence of concurrent abscess formation or active infections, recurrent PSD, more complex PSD (orifices of the sinus extending laterally or near the anus), collagen tissue disease, and insufficient medical records. The time elapsed from the surgery to the date of the invitation ranged between 1.5 years and 5 years. The patients were divided into two groups according to the surgical method: Limberg flap and oval flap groups. There were 60 male and 10 female patients in the Limberg flap group and 64 male and 8 female patients in the oval flap group. The mean follow-up period was 31.4 months (range, 18–54 months) in the Limberg flap group and 34.6 months (range 22–60 months) in the oval flap group. The demographic characteristics of the patients such as age and gender, hospital stay, seroma occurrence, surgical site in-

fections, wound dehiscence, flap necrosis, loss of sensation, and recurrences were evaluated based on the information obtained from the database as well as from physical examinations and questioning of the patients.

The protocol of this study was approved by the local ethics committee, and all the participants provided written informed consent for participation after adequate verbal information was provided to them about the study. The study was conducted in accordance with the principles of the Helsinki Declaration revised in 2000.

Surgical technique

All the patients were admitted to the hospital the night before their surgery and treated with two enemas: one at night and the other 2 h preoperatively. The gluteal and sacral regions of the patients were shaved on the surgery day. All the patients were prophylactically administered 1 g of ampicillin–sulbactam during anesthesia induction. Under spinal anesthesia, the patients were placed in the prone jackknife position and their gluteus muscles were separated from each other, with a plaster revealing the intergluteal sulcus. To reveal the pilonidal sinus cavity, each patient was injected 2 mL of methylene blue through the sinus using a 5 mL hypodermic needle. Marking of healthy tissues was avoided by ensuring that methylene blue was not injected in a pressurized manner. All surgical interventions were performed by the same team. First, the pilonidal cyst was completely excised up to the presacral fascia 2 cm lateral to the middle line with an elliptic- or rhombus-shaped incision without injuring the pilonidal sinus and without leaving any sinus residue. In the patients who were treated using a Limberg flap, the skin was deepened on the gluteus muscle where the flap was to be raised in the form of a continuation of the rhombus in lengths equal to the sides of the rhombus to encompass the subcutaneous tissue and gluteal muscle fascia for preparing a Limberg flap (Figure 1). In the patients who were treated using an oval flap, an oval-shaped was prepared to encompass the same tissue layers from the right and left gluteal regions (Figure 2). After controlling the bleeding, the plasters that maintained the gluteus muscles in traction were opened to ease the wound closure; the flaps were positioned properly and were sutured using a 2-0 polyglactin suture to encompass the fascia–subcutaneous tissues. In all the patients, a vacuum hemovac drain was placed underneath the flap and onto the fascia with its end taken out from another hole and fixed onto the skin ensuring negative pressure drainage. The skin was closed using 3-0 polypropylene sutures. After cleaning the site with physiological saline solution, the dressing was completed using povidone iodine and sterile gauze bandages. There were no major complications or mortality. Postoperatively, the removed pilonidal sinus was sent for pathological examination without opening.

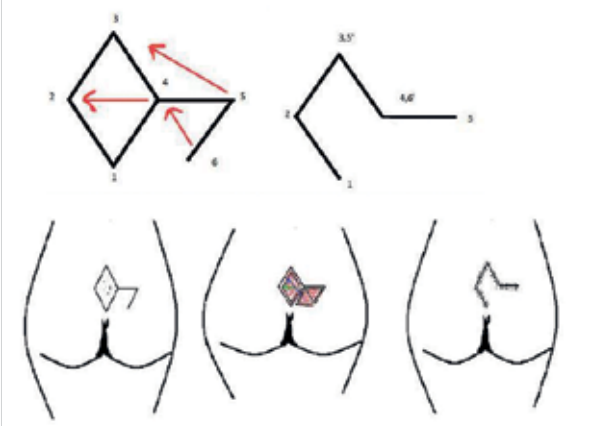


Figure 1. Illustration of Limberg flap preparation

Figure 2. Illustration of oval flap preparation

Table 1. Postoperative complications and recurrence rates

	Limberg flap	Oval flap	p
Seroma	5 (7.1)	2 (2.8)	0.230
Infection	5 (7.1)	2 (2.8)	0.230
Wound dehiscence	7 (10)	2 (2.8)	0.077
Flap necrosis	0 (0)	0 (0)	-
Loss of sensation	5 (7.1)	5 (6.9)	0.594
Recurrence	3 (4.3)	0 (0)	0.129

Datas are presented as n (%)

Postoperative period

The patients were mobilized on postoperative day 1, and their physical examinations were performed on postoperative days 1 and 5. All the patients were given ampicillin–sulbactam 375 mg 2×1 PO as antibiotics for postoperative 5 days. When the drainage dropped below 20 mL, the drains were withdrawn. The sutures were removed on postoperative day 10. All the patients were trained at the time of their discharge in maintaining hygiene in the perianal and gluteal regions.

Sample size

The sample size was determined post hoc. At the end of the study, the early postoperative complication rate was found to be 24.3% in the Limberg flap group and 8.3% in the oval flap group. Considering the early postoperative complication prevalence as 24.3%, the sample size was calculated to be 71 for one group at 95% confidence with 10% deviation, presuming the type 1 error as 0.05. The sample size calculation was performed using OpenEpi Version 3 (http://www.openepi.com/SampleSize/SSPropor.htm) software.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for Social Sciences version 15.0 for Windows package program (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used. For comparisons, independent samples t-test and χ^2 test were used. The significance level was set at $p<0.05$.

RESULTS

The mean age of the patients was 27.5±7.8 years in the Limberg flap group and 26.5±7.2 years in the oval flap group. There were 60 males (85.7%) and 10 females (14.3%) in the Limberg flap group and 64 males (88.9%) and 8 females (11.1%) in the oval flap group. No significant difference was observed between the two groups regarding patients' mean age and gender distribution (p=0.438 and p=0.570, respectively).

Postoperative hospital stay was 2.0±0.9 days in the Limberg flap group and 1.9±0.9 days in the oval flap group. No significant difference was found between the two groups regarding patients' hospital stays (p=0.649). Regarding complications, seroma developed in five (7.1%) patients of the Limberg flap group and two (2.8%) patients of the oval flap group (p=0.230). Infection was noted in five (7.1%) patients of the Limberg flap group and two (2.8%) patients of the oval flap group (p=0.230). There was no significant difference between the two groups regarding seroma accumulation and infection.

Wound dehiscence occurred in seven (10%) patients in the Limberg flap group and two (2.8%) patients in the oval flap group (p=0.077). Flap necrosis was not seen in any of the patients. Loss of sensation was present in five (7.1%) patients in the Limberg flap group and five (6.9%) patients in the oval flap group (p=0.594). Recurrence occurred in three (4.3%) patients in the Limberg flap group; no recurrence was seen in the oval flap group (p=0.129). The median time of recurrences was 8 (range, 3–12) months. No significant difference was found between the groups regarding wound dehiscence, flap necrosis, loss of sensation, and recurrence (Table 1).

However, overall early postoperative complications occurred in the Limberg flap group at a rate of 24.3% (five seroma, five infection, and seven wound dehiscence cases in 17 patients out of 70) and at a rate of 8.3% in the oval flap group (two seroma, two infection, and two wound dehiscence cases in 6 patients out of 72). A significant difference was found regarding these between the two groups ($p<0.05$).

DISCUSSION

Pilonidal sinus disease is an inflammatory disease mostly observed in young males and manifests as an acute painful or chronic form in the intergluteal region (1, 2). The incidence is 0.7%, and it is seen mostly in the 15–30-year age group (2-4). Although PSD has been known for many years and frequently encountered in clinics, there is no consensus on the choice of the ideal surgical technique for its treatment, and various surgical methods are available. Often it becomes necessary to reconstruct the cavity using flaps, especially in complicated pilonidal sinuses requiring wide excision. In this study, we compared the Limberg flap and oval flap techniques that are commonly preferred among a large variety of flap procedures found in literature.

The facts that majority of the patients who were operated for PSD in this study were males and the mean age was within the second and third decades indicate the natural characteristics of PSD that have been known for years (2-5).

One of the major factors that determine the quality of life in patients operated for PSD is length of hospital stay and the other is time taken for patient to resume routine activities. Generally, these periods are significantly shorter in patients who are treated with flaps than in those who are left for primary closing or secondary healing. The patients who were treated with the Limberg and oval flaps in this study were hospitalized for an average of 2 days and then discharged. This finding is similar to that reported in literature (1, 6, 7).

Seroma occurrence was higher in patients treated using Limberg flaps; however, the difference in seroma occurrence was not significant between the two groups. The flaps used in PSD surgery are physiologically fed through macro- and microcirculations. The anatomy of macrocirculation is used in the definition and design of flaps. The arteriolar, capillary, venule, and arteriovenous anastomoses at the microcirculation level are the places where cellular metabolism occurs and where perfusion is often controlled (8). This circulation mechanism is partly disturbed in Limberg flaps as the edges of the flap end in sharp angles, leading to a local blood circulation deficit. Because there are no edges in oval flaps, microcirculation is maintained and a homogenous feeding is secured in the whole flap. The information that seroma accumulation will generally be less in flaps that are fed better can explain our finding of less seroma occurrence in patients treated using oval flaps.

Wound infection is a complication that can be seen in PSD patients in the postoperative period and may involve serious consequences. The infection-causing factors include increased bacterial colonization, wound site being close to the anal channel, obesity, hygiene difficulties due to localization of the lesion, and humidity (5). Additionally, the dead space at the surgical site and in the subcutaneous tissue as well as the tension occurring in the skin may be the cause of many complications, including seroma, hematoma, dehiscence, and infection (9). Infections can endanger flap vitality, adversely affect quality of life in patients, and lead to reoperations and sometimes to long-term painful dressings when the patients are left for secondary healing. In the present study, wound infections developed in five patients in the Limberg flap group and in two patients in the oval flap group. Although there was no significant difference between the two groups regarding wound site infection, the occurrence of 2.5 times more infections in the Limberg flap group than in the oval flap group can be explained by the abovementioned microcirculation-related problems associated with Limberg flaps, particularly the contamination occurring due to the flap edges being closer to the anal channel compared with oval flaps.

The postoperative wound site dehiscence that can be seen in PSD patients occurs because the region is a humid and narrow area and the wound sides that are brought together in a strained way during the surgery may split again after the sutures are removed while performing daily activities, such as sitting down and using the toilet. In fact, one of the main reasons for preferring flap techniques in PSD surgery is that they cause far less strain at the wound sides than primary closing. Despite this, wound dehiscence occurred in seven (10%) patients treated with Limberg flaps in this study. When these patients were questioned, nearly all of them stated that they performed improper exercises that may have caused excessive strain in the region in the early postoperative period and that they overlooked their local hygiene. Wound dehiscence was seen in only two (2.8%) patients treated with oval flaps. This may be associated with the oval preparation of the distal free end of the flap instead of it being sharp corner. In fact, the suturing of the sharp distal edges may lead to ischemia and necrosis in Limberg flaps due to decreased circulation at the thin corner. The flap vitality can be better, particularly in the distal corners, in the oval flap reconstruction (10). This can explain the occurrence of wound dehiscence more in the patients treated with Limberg flaps in our study.

When the overall early postoperative complications including seroma, infection, and wound dehiscence were assessed, such complications were seen approximately 3 times more in the Limberg flap group than in the oval flap group. This finding, which

showed a significant difference between the groups, indicates that there were less perioperative complications in the oval flap group. Nevertheless, a large majority of these complications were treated using minimally invasive methods, such as simple aspiration, drainage–antibiotic therapy, and wound dressings.

Flap necrosis that can occur regardless of the flap technique used in a PSD surgery is known to be an important complication requiring reoperation. In essence, flap necrosis is often a preventable complication if the tissue is handled gently when preparing the flap and care is taken to not impair the pedicular structure of the flap. When preparing flaps, we take care not to damage the vascular structures by avoiding excessive dissection, particularly in the pedicular region. We believe that this careful approach is the reason for the absence of flap necrosis in our study.

Postoperative regional loss of sensation was seen in five patients in both the groups but to the extent not causing any distress that would impair the quality of life in the patients. We believe that the loss of sensation occurred at similar rates in the two groups because the pilonidal sinus tissues removed surgically had approximately the same width.

The term "recurrence" is defined as disease symptoms re-emerging a while after full recovery of the wound. In addition to a well-applied surgical intervention, small changes that patients should make in their lifestyles ensuring maintenance of intergluteal region hygiene will prevent recurrence. In this study, recurrence was seen in three (4.3%) patients in the Limberg flap group and in none in the oval flap group. Being the main problem encountered after a PSD surgery, recurrence has been reported at rates between 3% and 46% in literature depending on the technique used (2). With the Limberg flap technique, which is increasingly being preferred at many surgical clinics, recurrence rate ranges between 0% and 5% and infection rate ranges between 1.2% and 4.8% (4, 6). Our results are compatible with those reported in literature (2, 4, 6). The reasons for recurrence generally include the region being humid and in deep localization, the vacuum effect due to hip movements, obesity, and excessive bacterial colonization due to poor hygiene. The criticized points of the Limberg flap technique are undesired cosmetic appearance, necrosis of the flap vertex, and maceration occurring in the skin at the incision site (2). We believe that the Limberg flap technique used by us involves difficulty in maintaining hygiene because the inferior part of the incision and the lower pole of the flap remain in the intergluteal sulcus and the incision area remains humid and is close to the anal channel; this in turn increases the risk of infection, leading to wound site dehiscence and recurrence. Many studies have reported that the defect occurring after the surgery performed using the Limberg flap technique can be closed fully and without straining; thus, wound site infections at an early stage and recurrences at a later stage are seen less, and with a quick healing time, the time required by the patients to return to their routine life is shorter (4, 6). We believe that the reason for the absence of recurrence in patients treated with oval flaps is that the inferior part of the incision remains on the lateral side not entering the intergluteal sulcus; thus, it poses no difficulty of hygiene even in obese people.

The limitations of this study include its retrospective design, single-center nature, and a small sample size. After all, this study was a pilot study showing mid-term results in PSD patients who were surgically treated using two different flap techniques. We believe that the results obtained here will be more meaningful when further prospective, randomized, multicenter studies are conducted with larger patient populations.

CONCLUSION

The Limberg flap and oval flap techniques used in a PSD surgery are not superior to each other regarding treatment effectiveness, complications, and recurrence. Both are highly effective procedures that can be easily applied and enable complete and unstrained closure of the defect that occurs upon the removal of the affected tissue as a whole; both are associated with minimum morbidity and short hospital stay and are tolerated well by the patients.

Ethics Committee Approval: Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects" (amended in October 2013).

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - B.K., S.B., U.K.; Design - B.K., E.K., U.K.; Supervision - B.K., S.B., E.K., U.K.; Resource - B.K., S.B., E.K.; Materials - B.K., S.B., E.K., U.K.; Data Collection and/or Processing - B.K., E.K.; Analysis and/or Interpretation - B.K., S.B., E.K., U.K.; Literature Search - B.K., S.B., E.K.; Writing Manuscript - B.K., S.B., U.K.; Critical Reviews - B.K., S.B., U.K.

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

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

REFERENCES

1. Kucukkartallar T, Tekin A, Vatansev C, Aksoy F, Erenoglu B. The comparison of the results of different operation techniques for pilonidal sinus disease. Genel Tıp Der 2007; 17: 95-97.
2. Sabuncuoglu MZ, Sabuncuoglu A, Dandin O, Benzin MF, Celik G, Sozen I, et al. Eyedrop-shaped, modified Limberg transposition flap in the treatment of pilonidal sinus disease. Asian J Surg 2015; 38: 161-167. [CrossRef]
3. Tardu A, Haslak A, Ozcınar B, Basak F. Comparison of Limberg and Dufourmentel flap in surgical treatment of pilonidal sinus disease. Ulus Cerrahi Derg 2011; 27: 35-40. [CrossRef]
4. Aren A, Sagban AD, Gokce AH. Comparison of Limberg flap and modified Limberg flap in the surgical treatment of Pilonidal sinus. Istanbul Med J 2010; 11: 149-153.
5. Duman K, Gırgın M, Harlak A. Prevalence of sacrococcygeal pilonidal disease in Turkey. Asian J Surg 2017; 40: 434-437. [CrossRef]
6. Mentes O, Bagci M, Bilgin T, Ozgul O, Ozdemir M. Limberg flap procedure for pilonidal sinus disease: results of 353 patients. Langenbecks Arch Surg 2008; 393: 185-189. [CrossRef]
7. Uçar AD, Cartı EB, Oymacı E, Sarı E, Yakan S, Yıldırım M, et al. Recurrent pilonidal disease surgery: Is it second primary or reoperative surgery? Ulus Cerrahi Derg 2015; 32: 162-167.
8. Vedder N.B. Flap physiology. Mathes Plastic Surgery, 2nd edition. Philadelphia: Saunders Elsevier Inc, Vol: 1; 483-506, 2006.
9. Arslan S, Karadeniz E, Ozturk G, Aydinli B, Bayraktutan MC, Atamanalp SS. Modified Primary Closure Method for the Treatment of Pilonidal Sinus. Eurasian J Med 2016 ; 48: 84-89. [CrossRef]
10. Polat C, Gungor B, Karagul S, Buyukakincak S, Topgul K, Erzurumlu K. Is oval flap reconstruction a good modification for treating pilonidal sinuses? Am J Surg 2011; 201: 192-196. [CrossRef]

Turk J Surg 2018; 34(4): 315-318
DOI: 10.5152/UCD.2017.3437

Case Report

Robot-assisted endoscopic mediastinal parathyroidectomy

Özer Makay[1], Said F. Durmaz[2], Murat Özdemir[1], Ilgın Şimşir[3], Gökhan İçöz[1], Mahir Akyıldız[1]

ABSTRACT

Ectopic parathyroid glands can be located at any anatomical location from the base of the tongue to the mediastinum. One-third of these glands migrate deep into the mediastinum, which are not accessible with a low cervical incision. In this article, we described the robotic approach to an ectopic mediastinal parathyroid gland. This management method of mediastinal adenomas has significant advantages when compared to conventional surgery.
Keywords: Robotic surgery, thoracoscopic surgery, parathyroid adenoma, parathyroidectomy

INTRODUCTION

The parathyroid glands are generally located in the cervical region, just behind the thyroid gland. These glands are involved in the production of parathyroid hormone (PTH), which is important for the concentration of calcium and phosphate in the blood. In some cases, there is an excess of PTH in the bloodstream due to over activity of one or more parathyroid glands, also called primary hyperparathyroidism. In addition, 15-20 percent of patients with abnormally functioning parathyroid glands have ectopic parathyroid glands due to abnormal migration during embryogenesis (1). These glands can be located at any anatomical location from the base of the tongue to the mediastinum. Removal of these ectopic parathyroid glands depends on their size and location. In most cases, these glands are found in the superior mediastinum which can be successfully removed by a cervical approach (2). Unfortunately, one-third of ectopic parathyroid glands migrate deep into the mediastinum and thus are not accessible with a low cervical incision (3). The ectopic parathyroid glands used to be removed by performing a sternotomy or thoracotomy (4). However, these open procedures were correlated with a higher morbidity risk, high complication rate, longer post-operative recovery, and poor cosmetic results (4). In the past decades, video-assisted thoracoscopic surgery (VATS) was described to be a more safe, less invasive, effective, and feasible procedure for resection of the deep mediastinal parathyroid lesions (5). However, randomized controlled trials should be carried out to support these findings.

Recently, another alternative minimally invasive technique was introduced to the surgical treatment of ectopic mediastinal parathyroid, namely, the da Vinci® robotic system. In a similar context, this technique has already made a significant contribution to, among others, thymectomies (6). This technology revolutionized the field of minimally invasive surgery. In this article, we report a case of robot-assisted endoscopic mediastinal parathyroidectomy, which to our knowledge, is the first case in Turkey.

CASE PRESENTATION

Preoperative Work-Up

A 45-year-old man with a body mass index of 22 presented to a hospital with a history of nephrolithiasis, diffuse joint pain, and problems with walking for 1 year. His serum calcium, PTA and alkaline phosphatase (ALP) levels were increased. A thoracic computed tomography (CT) scan showed a lesion that was interpreted as a lymphadenopathy. Also, a bone scintigraphy was performed and the findings confirmed a metabolic bone disease. The patient was then referred to our institution for further evaluation.

The patient had normal findings on physical examination. However, blood tests revealed an elevated serum calcium (12.9 mg/dL; normal value: 8.5 to 10.2 mg/dL), elevated ALP (2540 U/L; normal value: 20 to 120 IU/L), decreased phosphate (1.7 mg/dL; normal value: 2.4-4.1 mg/dL), and an elevated PTH level (1529.2 pg/mL; normal value: 13 to 54 pg/mL). With regard to these findings, a neck ultrasound showed no evidence of a parathyroid adenoma. Subsequently, a CT scan of the thorax and abdomen showed a 2 cm, hyper-vascular, solitary nodule at the anterior mediastinum, at the level of the anterior aspect of the ascending aorta (Figure 1). This was confirmed by a ^{99m}Tc methoxyisobutylisonitrile

Cite this paper as:
Makay Ö, Durmaz SF, Özdemir M, Şimşir I, İçöz G, Akyıldız M. Robot-assisted endoscopic mediastinal parathyroidectomy. Turk J Surg 2018; 34(4): 315-318.

[1]Division Endocrine Surgery, Department of General Surgery, Ege University School of Medicine Hospital, İzmir, Turkey
[2]Department of Surgery, University Medical Center Rotterdam, Erasmus MC, Rotterdam, Nederlands
[3]Division Endocrinology and Metabolic Diseases, Department of Internal Medicine, Ege University School of Medicine Hospital, İzmir, Turkey

Corresponding Author
Özer Makay
e-mail: ozer.makay@ege.edu.tr

Received: 30.10.2015
Accepted: 17.06.2016
Available Online Date: 03.01.2018

Available online at
www.turkjsurg.com

(MIBI) scintigraphy (Figure 2). In addition, the CT-scan identified diffuse heterogeneous density of the bone structures and a well-defined lytic bone lesion of 2.2 cm at the level of the left femoral head, which could be associated with a Brown tumor. With regard to this, a bone scintigraphy was performed that showed diffuse increased bone activity. This finding could be consistent with the ectopic parathyroid adenoma. Primary hyperparathyroidism may occur as a part of Multiple Endocrine Neoplasia (MEN) type 1 or type 2A. Multiple endocrine neoplasia type 2A (MEN-2A) is a hereditary condition associated with three primary types of tumors: medullary thyroid cancer, parathyroid tumors, and pheochromocytoma. Multiple Endocrine Neoplasia (MEN-1) was originally known as Wermer syndrome. The most common tumors seen in MEN-1 involve the parathyroid gland, islet cells of the pancreas, and pituitary gland. Therefore, a magnetic resonance imaging (MRI) of the pituitary gland was performed to exclude this option. The MRI scan showed no abnormalities and therefore MEN-1 was not considered as part of differential diagnosis. During the pre-operative period, serum calcium level was determined daily due to hypercalcemia. The elevated serum calcium level was tried to be lowered with intravenous saline hydration, furosemide, and pamidronate treatment. Nevertheless, the serum calcium level remained high (>15.0 mg/dL). Therefore, hemodialysis was carried out two times prior to surgery.

Figure 1. Mediastinal parathyroid adenoma CT image

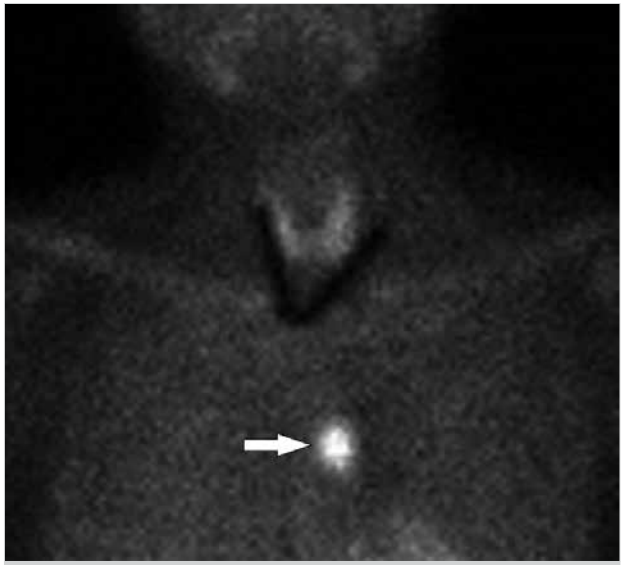


Figure 2. Mediastinal parathyroid adenoma MIBI scintigraphy image

Operative Approach

This patient was evaluated by the Multidisciplinary Endocrine Consultation Team. The team proposed to perform thoracic resection of the MIBI-positive mediastinal solitary nodule using a robotic assisted approach. An informed consent was obtained from the patient, and the operation was performed totally thoracoscopically via the da Vinci Si robot system® (Intuitive Surgical Sarl, Aubonne, Switzerland) with intraoperative intact PTH guidance.

The da Vinci robot consists of a manipulator unit with three arms (two instrument arms and a central arm to guide the endoscope), and a remote master console (optical control with 3-dimensional vision and tele manipulators of the arms). A right-sided approach was chosen due to the location of the solitary ectopic gland. The patient was positioned in a supine position at the edge of the operating table by placing silicone gel behind his right shoulder/upper back. The patient was somewhat tilted to the left side. The right arm was positioned below the table level with flexion at the elbow. The procedure was performed under general anesthesia with double-lumen endotracheal intubation for left single-lung ventilation. The right parietal pleura was incised, and the right chest cavity was entered. A 12-mm port for the 30-degree upward stereo endoscope was placed in the 5th intercostal space at the mid-axillary line, where the incision was made previously for entering the right cavity. Subsequently, two 8-mm robotic operating ports were positioned, both at the anterior axillary line, in the 3rd and 6th intercostal spaces. The three robotic arms of the da Vinci system were attached to these three ports. An accessory additional port was placed in the midclavicular line, just below the nipple (Figure 3). The procedure was performed by two surgeons, one at the console and one surgeon assisting at the operating table using the additional port. The right lung was deflated, and CO2 insufflation was set at 10mm Hg through the camera port with careful hemodynamic monitoring. With this, an improvement of the visualization of the operative field is achieved by washing out diathermy smoke. Fenestrated bipolar forceps and electrocautery hook with EndoWrist® action were used for dissection of the ectopic gland. Dissection was started towards the ectopic gland, skin marking has been previously performed. The mediastinal pleura was opened until the left parietal pleura was visible. Dissection was proceeded towards the ascending aorta and the ectopic gland was identified adjacent to this major blood vessel. The ectopic gland was manipulated and finally removed using the instruments

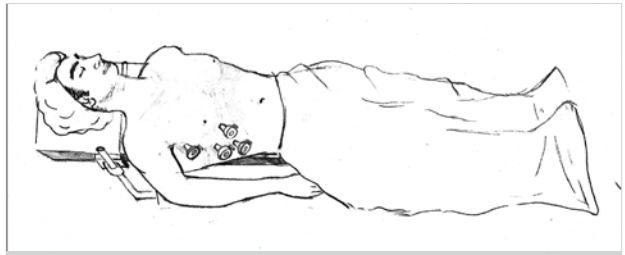


Figure 3. Patient and port positioning

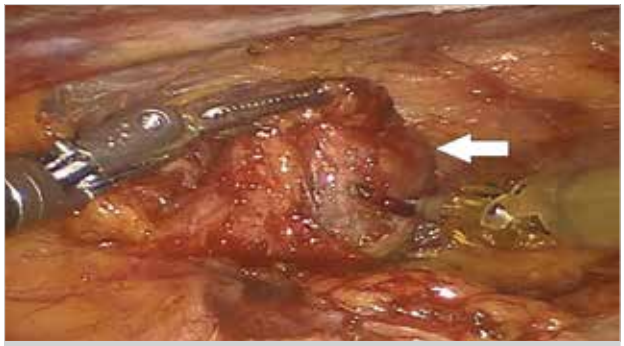


Figure 4. Operative image (Dissection of parathyroid adenoma)

(Figure 4). The right phrenic nerve and the esophagus were identified and preserved. After completion of the dissection, the ectopic gland was removed from the thoracic cavity using an Endo Catch™ bag. At the end of the operation, a chest tube was placed and directed toward the apex of the right hemithorax.

The total operative time was 119 minutes, while the robotic process took 35 minutes and the docking time lasted only 5 minutes. Intraoperative blood loss was minimal and no complications occurred during the operation. There was no bleeding. Serum PTH and calcium levels were determined 20 minutes post-excision. Both PTH and calcium levels showed an appropriate decrease after removal of the ectopic gland (31.6 pg/mL and 9.1 mg/dL, respectively). The patient recovered in the post anesthesia unit and was transferred to the regular nursing unit on the same day. A chest x-ray was performed that did not showed any signs of pneumothorax. The chest tube was removed on postoperative day 1.

With regard to hungry bone syndrome, serum PTH and calcium levels were assessed daily during the postoperative period. During the early postoperative period, calcium levels dropped slightly below normal levels. Hereby, the patient received calcium and vitamin D3 supplements. There were no postoperative complications. The patient was discharged with calcium and vitamin D3 supplements, and the tissue was histopathologically confirmed as a parathyroid adenoma.

DISCUSSION

Parathyroid glands are rarely located in the mediastinum, which are often removed through sternotomy or thoracotomy (<1% - 3%) (3). In this article, we described the robotic approach to the ectopic mediastinal parathyroid gland. This management method of mediastinal adenomas has significant advantages when compared to conventional surgery and maybe even the VATS procedure. Compared with the conventional open approach, the robotic technique seems to have significant benefits in quality of life and morbidity (7). Likewise, in the current literature, multiple case reports have described the robotic technique with similar promising results like the VATS procedure (8, 9). In addition, the da Vinci® robotic system gives the opportunity for a more comfortable approach of the tissue in contrast to the disadvantages of the VATS procedure (e.g. two-dimensional view, unstable camera platform and poor ergonomic position of the surgeon). The robotic technique provides excellent visualization with three-dimensional view, better color resolution, better contrast, precision, and enhanced skills in order to ensure an effective, safe, and accurate operation (8, 9). These potential advantages ensure the possibility for the differentiation of the ectopic parathyroid gland from surrounding tissue (e.g. adipose tissue and thymus). That is why, the technique is very useful to access small and remote surgical fields.

In the current literature, the robotic technique is being increasingly used by other medical specialties. There are promising results in cardiac, gynecologic, urologic, transplantation, and general surgery. As mentioned above, several reports presenting promising outcomes of the robot-assisted mediastinal parathyroidectomy have been published (8, 9). However, to date there is a lack of studies with larger cohorts and randomized control trails to confirm these outcomes. Furthermore, almost all studies that described robot-assisted mediastinal parathyroidectomy have several limitations such as small sample size, being a single-center experience, or mostly being case-reports.

With the introduction of high sensitive radiographic modalities (e.g. MIBI scan, CT, MRI, and venous blood sampling), more ectopic parathyroid glands can be detected in patients with hyperparathyroidism symptoms (10). The advances in preoperative screening enable accurate localization of the ectopic parathyroid gland(s). This is one of the key concepts of endocrine and robotic surgery, which makes targeted minimally invasive approaches feasible. Inadequate diagnostic imaging could lead to waste of time and a failed surgical procedure for an hyperactive ectopic parathyroid gland (9). At our center, localization studies begin with ultrasound and a MIBI scan, involving the chest along with the neck.

Despite the potential advantages and promising results of the robotic technique, there are some obstacles. First of all, there is a need for a specially trained surgical team to perform the robotic technique. All participants are closely involved with the operation, including the surgeon(s), assistants, anesthesiologist, and other personnel. The surgeons also have to undergo training to achieve the robotic surgery skills. These aspects are very important for a successful robotic procedure. Besides, the robotic technique has a high cost due to the additional expenditure of the da Vinci® robotic system and the robotic instruments.

CONCLUSION

Based on our results, we concluded that resection of anterior mediastinal parathyroid gland with the da Vinci® robotic system is feasible. Accurate localization of the ectopic parathyroid gland(s) via preoperative screening is essential for the robotic approach. This technique has already been described in several reports with promising results. This report validates previous results and is another contribution to the literature. Therefore, the robotic approach is our preferred method for mediastinal located parathyroid glands.

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

Peer-review: Externally peer-reviewed

Author Contributions: Concept - Ö.M., M.A.; Design - Ö.M., M.Ö., I.Ş.; Supervision - Ö.M., G.İ., M.A.; Resource - M.Ö., I.Ş.; Materials - S.F.D., I.Ş., M.Ö.; Data Collection and/or Processing - M.Ö., I.Ş., S.F.D.; Analysis and/or Interpretation - Ö.M., M.Ö., S.F.D.; Literature Search - S.F.D., M.Ö., I.Ş.; Writing Manuscript - M.A., I.Ş., S.F.D.; Critical Reviews - M.A., G.İ., Ö.M.

Acknowledgements: The authors thank Tayfun Yoldaş for his wonderful drawing.

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

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

REFERENCES

1. Kaplan EL, Yashiro T, Salti G. Primary hyperparathyroidism in the 1990s. Choice of surgical procedures for this disease. Ann Surg 1992; 215: 300-317. [CrossRef]
2. Freeman JB, Sherman BM, Mason EE. Transcervical thymectomy: an integral part of neck exploration for hyperparathyroidism. Arch Surg 1976; 111: 359-364. [CrossRef]
3. Alesina PF, Moka D, Mahlstedt J, Walz MK. Thoracoscopic removal of mediastinal hyperfunctioning parathyroid glands: personal experience and review of the literature. World J Surg 2008; 32: 224-231. [CrossRef]
4. Russell CF, Edis AJ, Scholz DA, Sheedy PF, van Heerden JA. Mediastinal parathyroid tumors: experience with 38 tumors requiring mediastinotomy for removal. Ann Surg 1981; 193: 805-809.[CrossRef]
5. Iihara M, Suzuki R, Kawamata A, Horiuchi K, Okamoto T. Thoracoscopic removal of mediastinal parathyroid lesions: selection of surgical approach and pitfalls of preoperative and intraoperative localization. World J Surg 2012; 36: 1327-1334. [CrossRef]
6. Rea F, Schiavon M, Di Chiara F, Marulli G. Single-institution experience on robot-assisted thoracoscopic operations for mediastinal diseases. Innovations (Phila) 2011; 6: 316-322. [CrossRef]
7. Balduyck B, Hendriks JM, Lauwers P, Mercelis R, Ten Broecke P, Van Schil P. Quality of life after anterior mediastinal mass resection: a prospective study comparing open with robotic-assisted thoracoscopic resection. Eur J Cardiothorac Surg 2011; 39: 543-548. [CrossRef]
8. Ismail M, Maza S, Swierzy M, Tsilimparis N, Rogalla P, Sandrock D, et al. Resection of ectopic mediastinal parathyroid glands with the da Vinci robotic system. Br J Surg 2010; 97: 337-343. [CrossRef]
9. Chan AP, Wan IY, Wong RH, Hsin MK, Underwood MJ. Robot-assisted excision of ectopic mediastinal parathyroid adenoma. Asian Cardiovasc Thorac Ann 2010; 18: 65-67. [CrossRef]
10. Johnson NA, Tublin ME, Ogilvie JB. Parathyroid imaging: technique and role in the preoperative evaluation of primary hyperparathyroidism. AJR Am J Roentgenol 2007; 188: 1706-1715. [CrossRef]

Turk J Surg 2018; 34(4): 319-322
DOI: 10.5152/turkjsurg.2017.3383

Case Report

Minimally invasive thyroid anaplastic carcinoma with long survival

Mustafa Ümit Uğurlu[1], İpek Erbarut Seven[2], Funda Eren[2], Cumhur Yeğen[1], Bahadır Mahmut Güllüoğlu[1]

ABSTRACT

Anaplastic thyroid carcinoma is a highly lethal malignancy. Previously, only five cases of a noninvasive form of anaplastic thyroid carcinoma with excellent prognosis were reported. We report a case of a 68-year-old man who presented with a 3.8 cm thyroid nodule diagnosed by fine needle aspiration biopsy as poorly differentiated spindled and epithelial malignant cells. Lobectomy and isthmusectomy were performed, and the final diagnosis was microinvasive anaplastic thyroid carcinoma arising in a poorly differentiated carcinoma. The patient remains disease-free after six years, even after hemithyroidectomy and radiation treatment. Noninvasive/microinvasive anaplastic thyroid carcinoma appears to be a different disease entity from classical anaplastic thyroid carcinoma, with favorable prognosis and long disease-free survival.

Keywords: Thyroid, anaplastic thyroid carcinoma, microinvasion

INTRODUCTION

Anaplastic (undifferentiated) thyroid carcinoma (ATC) comprises 1% to 3% of all thyroid carcinomas. It is one of the most aggressive malignancies and is characterized by extensive local invasion and rapid progression with a median survival of five months (1). According to the American Joint Committee on Cancer, all ATC patients are classified as stage IV: the primary lesion is restricted to the thyroid gland in stage IVA; involvement of the locoregional lymph nodes is observed in stage IVA/IVB; and stage IVC disease is defined by distant metastases (2). The usual course of ATC is a rapidly growing fixed neck mass that is often seen with metastatic local lymph nodes on physical examination, and 40% of patients develop multiple organ failure as cause of death (3).

A few fortunate patients with encapsulated ATC with no invasion or minimal invasion have been described in the literature (4-7). These patients have favorable outcomes and long-term survival rates compared to classical ATC patients. As noninvasive/minimal invasive anaplastic thyroid carcinoma (ATC) is a rare disease entity, we wish to share our case, who is disease-free after six years even after hemithyroidectomy and radiation treatment.

CASE PRESENTATION

A 68-year-old male was admitted for foreign body sensation in the neck. Patient had a remote history of smoking for 35 years; however, the patient had quit 15 years previously. Medical histoy of the patient consisted of coronary artery disease and chronic obstructive pulmonary disease. There was no history of radiation to the neck or thoracic region. Upon physical examination, patient had two bilateral palpable thyroid nodules. The patient was euthyroid at admission. Ultrasound (US) examination showed heterogeneous thyroid parenchyma with a 3.8 cm hypoechoic solid nodule on the left lobe which had fine calcification. A 2-cm isoechoic solid nodule was observed on the right lobe with coarse calcifications. There were no cervical or thoracic radiologically significant lymph nodes. US-guided fine needle aspiration (US-FNAB) biopsy of the left thyroid nodule revealed "poorly differentiated spindled and epithelial malignant cells," and US-FNAB of the right nodule revealed a "benign colloidal nodule." No further radiological evaluation was performed. Fiber-optic laryngoscopy prior to the operation showed normal bilateral vocal cords. Total thyroidectomy was planned.

The procedure started with exploration of the left thyroid lobe, which was reported as malignant. The left thyroid lobe was mobilized with difficulty due to adhesions to the adjacent structures. A single solid nodule was palpated in that lobe. The operation was terminated with left hemithyroidectomy and isthmusectomy. The reason for terminating the operation was operative difficulties, such as adhesion to surrounding structures and concomitant bleeding. We postponed the right hemithyroidectomy and decided to wait for definitive pathological analysis of the left lobe. Postoperatively, the patient recovered without incident.

ORCID ID of the author:
M.Ü.U. 0000-0002-4757-5560.

Cite this paper as:
Uğurlu MÜ, Erbarut Seven İ, Eren F, Yeğen C, Güllüoğlu BM. Minimally invasive thyroid anaplastic carcinoma with long survival. Turk J Surg 2018; 34(4): 319-322.

[1]Department of General Surgery, Marmara University School of Medicine, İstanbul, Turkey
[2]Department of Pathology, Marmara University School of Medicine, İstanbul, Turkey

Corresponding Author
Mustafa Ümit Uğurlu
e-mail: umitugurlu@gmail.com

Received: 16.09.2015
Accepted: 25.12.2015

Available online at
turkjsurg.com

On gross pathology, the specimen weighed 41 grams and the left lobe was 6.5 cm×5.5 cm×2.5 cm in diameter. On the left lobe, there was a 4 cm×2.2 cm×2 cm solid nodule with indistinct borders; a yellow to tan color protruded from the cut surface upon sectioning. At low magnification, the neoplasm was an encapsulated tumor showing focal follicular and insular patterns (Figure 1a, b) along with solid and trabecular patterns (Figure 1c). Focal comedo-type necrosis and mitosis were found in this poorly differentiated component. In addition, there were anaplastic areas (Figure 1a, d) composed of plump spindle cells and pleomorphic cells with vesicular chromatin and prominent nucleoli, constituting approximately 50% of the lesion. The entire tumor was submitted for histological evaluation; capsular microinvasion and vascular invasive foci (Figure 1e) were associated with this anaplastic component, although no evidence of extrathyroidal extension was obtained. The adjacent parenchyma was seen as a rim with features of mass effects of the tumor. The poorly differentiated/insular component showed positivity for cytokeratin, thyroglobulin (Figure 1f), thyroid transcription factor-1 (TTF-1) (Figure 1g), and B-cell lymphoma-2 (BCL-2) stains (Figure 1h); however, it was negative for anti-mesothelioma antibody (HBME1) stain. The anaplastic component was negative for cytokeratin, thyroglobulin (Figure 1f), TTF-1 (Figure 1g), and HBME-1. Increased staining with p53 (Figure 1ı) and decreased staining with BCL-2 (Figure 1j) were noted. Also, the Ki-67 (MIB-1) proliferation index was low (Figure 1k). Based on the light microscopy and immunohistochemical findings, a diagnosis of undifferentiated (anaplastic) thyroid carcinoma arising in a poorly differentiated carcinoma was reported.

During a multidisciplinary meeting, a team composed of physicians from surgery, medical oncology, radiation oncology, nuclear medicine, radiology, and pathology decided to complete the surgery as a total or near-total thyroidectomy and to administer further systemic chemotherapy and radiation therapy. The patient refused to undergo re-surgery and also refused chemotherapy; he only agreed to undergo radiation treatment. Before radiation therapy, whole body computed tomography was performed, and no evidence was found of any distant metastatic foci. At postoperative two weeks, a radiation dose of 60 Gray on a once-daily schedule was administered. The follow-up involved physical examination every three months for the first postoperative year and biannually for the following years. US examination of the neck was performed biannually. Distant metastatic screening was performed yearly with computed tomography (brain, chest, neck, and pelvis). We observed no local or distant metastasis during follow-up. The patient is disease-free 72 months after diagnosis. Recently, a positron emission tomography/computed tomography (PET/CT) scan was performed. No significant hypermetabolic lesion was observed by PET/CT imaging; only the right thyroid lobe was visible (Figure 2). The ultrasound examination of the neck confirmed the presence of a 2 cm isoechoic single nodule in the right lobe without changes in size or structure.

Written consent was taken from the patient to present the case report.

DISCUSSION

Anaplastic thyroid carcinoma is an extremely aggressive tumor with a disease-specific high mortality approaching 100%. Due to its poor prognosis, ATC is classified as TNM stage IV regard-

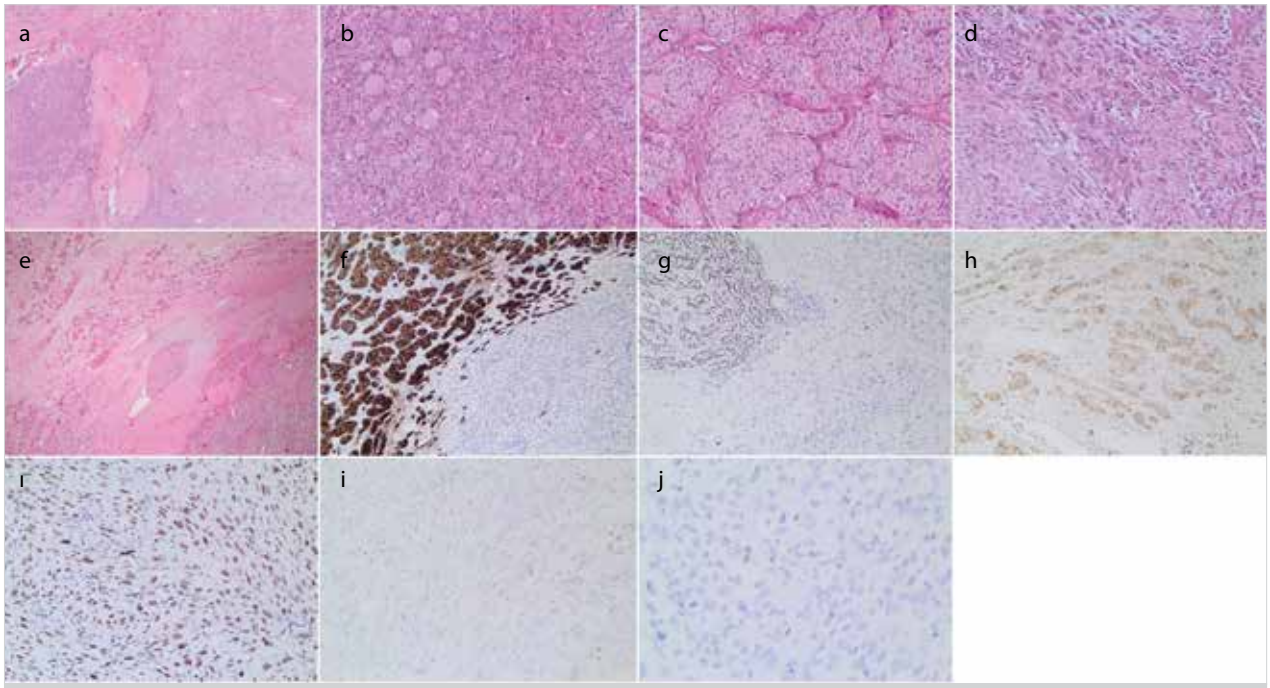


Figure 1. a-k. (a) Poorly differentiated carcinoma component (left side) and anaplastic carcinoma component (right side) (H&E, 100x). (b) Focal follicular pattern (H&E, 400x). (c) Trabecular pattern (H&E, 100x). (d) Anaplastic area (H&E, 400x). (e) Capsular and vascular invasion with anaplastic component (H&E, 100x). (f) The follicular and trabecular component showed positivity for cytokeratins and thyroglobulin. (g) The follicular and trabecular components showed positivity for thyroid transcription factor-1 (TTF-1). (h) The follicular and trabecular components showed positivity for BCL-2. (ı) Increased staining for p53 antibody. (j) Decreased staining of the anaplastic area for BCL-2. (k) Low Ki-67 (MIB-1) proliferation index

less of tumor burden (2). Prompt initiation of treatment is essential, and management plans, mostly for comfort care measures, should be undertaken early in the course of the disease (8).

Our case had a tumor with an ATC component; however, surprisingly, he showed an exceptional long-term disease-free survival of six years. The patient had a microinvasive anaplastic carcinoma as confirmed by conventional histology and immunohistochemistry. According to our pathologic findings, the microinvasive ATC component of the tumor demonstrated negative staining for cytokeratin, thyroglobulin TTF-1 and HBME-1, and BCL-2 and increased staining with p53; it also showed typical ATC characteristics, with high cell-proliferating activity and a disrupted mechanism of apoptosis. The improved prognosis in our patient can be explained by encapsulation of the tumor. Encapsulation in ATC was previously described in a few case reports. Voutilainen et al. (5) reported a retrospective case series of ATC patients; 1 of their 33 patients had microscopic focus of ATC within follicular carcinoma and survived for 156 months. Guimaraes et al. (4) reported a 74-year-old patient with ATC who had two foci (0.8 mm and 2.5 mm) of capsular invasion. Their patient remained disease-free for 35 months after total thyroidectomy. Another case from Japan, reported by Ito et al. (6) involved a 77-year old patient with a 7.5 cm encapsulated ATC with excellent survival. Recently, Dibelius et al. (7) reported a case of an 81-year-old man with a 3.5 cm encapsulated ATC. He was treated with total thyroidectomy. Even though no further adjuvant therapy was administered, the patient was disease-free 14 months after diagnosis.

Multimodal interventions involving surgery, chemotherapy, and radiation treatment are supported in current recommendations to improve both locoregional and metastatic disease outcomes (9). The decision to use these options in order or in combination must be made separately for each patient, primarily to increase the quality of life and to reduce disease-specific mortality.

Surgery remains the cornerstone for prolonged survival in ATC when feasible. The surgical approach to ATC depends on the resectability (R0 or R1) of the tumor; hence, surgical resection is recommended if it is possible and if excessive morbidity can be avoided. According to the American Thyroid Association (ATA) ATC treatment guidelines, in patients without extrathyroidal extension, total lobectomy or total/near-total thyroidectomy with therapeutic central and lateral lymph node dissection is recommended. In contrast, in patients with extrathyroidal extension, if R1 resection is possible, en bloc resection is recommended (10). Sugitani et al. (11) reported the data of an ATC Research Consortium of Japan (ATCCJ) cohort study of 677 patients. According to the ATCCJ, four clinical types of ATC were defined: common ATC, anaplastic change at the neck, incidental ATC, and anaplastic change at the distant site. Incidental ATC was found to have more favorable outcomes, and surgery was considered to be the main factor improving the survival. However, controversy remains regarding the effects of the extent of the surgical procedure. Venkatesh et al. (12) found that total thyroidectomy does not have any survival advantage over ipsilateral lobectomy for anaplastic tumors confined entirely to the thyroid; they also found that total thyroidectomy is associated with a higher complication rate. In a study of 134 ATC cases, neither the extent of operation nor the completeness of resection affected survival (13).

In our case, total thyroidectomy could not be technically achieved, and a probably benign thyroid lobe was left *in situ*. After the multidisciplinary meeting, a candid meeting was scheduled with the patient to disclose the risks and benefits of the treatment options. The options were combination treatment with completion of total/near-total thyroidectomy, adjuvant chemotherapy, and adjuvant radiation therapy. The patient refused to have completion surgery or undergo chemotherapy; his treatment was finalized with external beam radiation therapy (EBRT).

External beam radiation therapy has been suggested to reduce morbidity and mortality in adjuvant settings. After complete resection, prolonged survival (>2 years) was reported in conjunction with postoperative adjuvant chemotherapy (14). High dose EBRT of >45-50 Gy was found to be associated with improved one-year survival; however, its toxic effects are of great concern (15). The optimal timing and the selection of the chemotherapy regimen are uncertain for classic-type ATC. Non-randomized studies have evaluated different regimens concurrently with EBRT. Mostly doxorubicin-based regimens were used, and the median survival ranged from 6 months to 1 year (16, 17). Also, chemotherapy with a combination of taxane, anthracyclines, and cysplatin was proposed to have considerable palliative effects (18). Although combination chemotherapy was shown to improve the effects of radiation treatment in locoregional and distant disease control

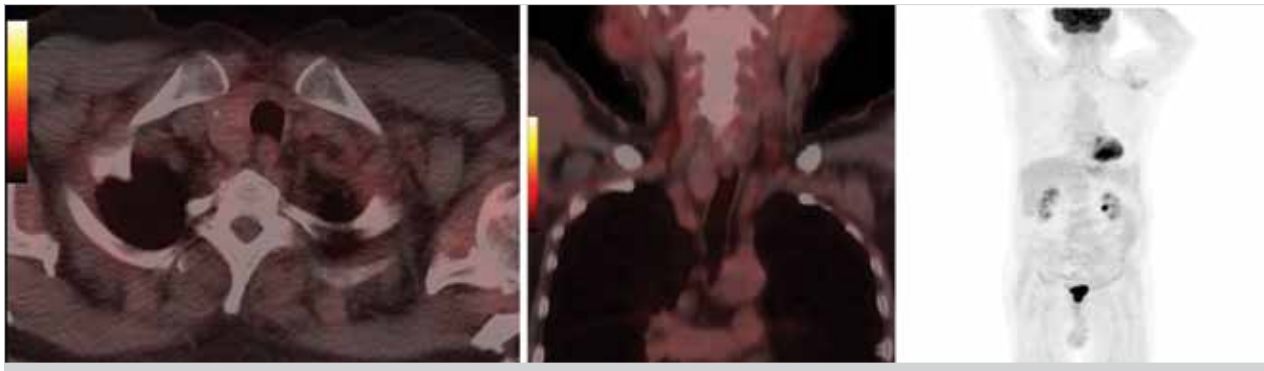


Figure 2. a-c. Positron emission tomography/computed tomography (PET/CT) imaging showing the remnant right lobe (a, b) without any area of local or distant hypermetabolic activity (c)

in a retrospective series (19), randomized controlled trials are not available to demonstrate the benefits of combined chemotherapy. Thus, there is no standard regimen for classic-type ATC in an adjuvant setting.

CONCLUSION

Despite the overall poor outcome of classical ATC, microinvasive/noninvasive ATC may be considered to be curable. The previous five reports on this entity showed improved survival in these patients. In our case, although the histopathology revealed an encapsulated tumor with microscopic capsular and vascular invasion of anaplastic cells, the patient is a long-term survivor. There is still insufficient data regarding optimal treatment of minimally invasive or noninvasive ATC. We suggest considering reclassification of noninvasive/microinvasive ATC as a separate disease entity.

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - M.U.U.; Design - M.U.U.; Supervision - F.E., C.Y., B.M.G.; Analysis and/or Interpretation - M.Ü.U., İ.E.S.; Literature Search - M.Ü.U., İ.E.S.; Writing Manuscript - M.Ü.U., İ.E.S.; Critical Reviews - F.E., C.Y., B.M.G.

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

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

REFERENCES

1. Brignardello E, Palestini N, Felicetti F, Castiglione A, Piovesan A, Gallo M, et al. Early surgery and survival of patients with anaplastic thyroid carcinoma: analysis of a case series referred to a single institution between 1999 and 2012. Thyroid 2014; 24: 1600-1606. [CrossRef]
2. Edge SB, American Joint Committee on C, American Cancer S. AJCC cancer staging handbook : from the AJCC cancer staging manual. New York: Springer; 2010.
3. Kitamura Y, Shimizu K, Nagahama M, Sugino K, Ozaki O, Mimura T, et al. Immediate causes of death in thyroid carcinoma: clinicopathological analysis of 161 fatal cases. J Clin Endocrinol Metab 1999; 84: 4043-4049. [CrossRef]
4. Guimaraes L, Meneses A, Carrara W, Kefalas A. Encapsulated anaplastic thyroid carcinoma with three-year disease-free survival. Pathol Res Pract 2000; 196 : 867-870. [CrossRef]
5. Voutilainen PE, Multanen M, Haapiainen RK, Leppaniemi AK, Sivula AH. Anaplastic thyroid carcinoma survival. World J Surg 1999; 23: 975-998. [CrossRef]
6. Ito Y, Matsuzuka F, Yoshida H, Morita S, Nakano K, Kobayashi K, et al. Encapsulated anaplastic thyroid carcinoma without invasive phenotype with favorable prognosis: report of a case. Surg Today 2003; 33: 277-281. [CrossRef]
7. Dibelius G, Mehra S, Clain JB, Urken ML, Wenig BM. Noninvasive anaplastic thyroid carcinoma: report of a case and literature review. Thyroid 2014; 24: 1319-1324. [CrossRef]
8. Neff RL, Farrar WB, Kloos RT, Burman KD. Anaplastic thyroid cancer. Endocrinol Metab Clin North Am 2008; 37: 525-538. [CrossRef]
9. Haddad RI, Lydiatt WM, Ball DW, Busaidy NL, Byrd D, Callender G, et al. Anaplastic Thyroid Carcinoma, Version 2.2015. J Natl Compr Canc Netw 2015; 13: 1140-1150. [CrossRef]
10. Smallridge RC, Ain KB, Asa SL, Bible KC, Brierley JD, Burman KD, et al. American Thyroid Association guidelines for management of patients with anaplastic thyroid cancer. Thyroid 2012; 22: 1104-1139. [CrossRef]
11. Sugitani I, Miyauchi A, Sugino K, Okamoto T, Yoshida A, Suzuki S. Prognostic factors and treatment outcomes for anaplastic thyroid carcinoma: ATC Research Consortium of Japan cohort study of 677 patients. World J Surg 2012; 36: 1247-1254. [CrossRef]
12. Venkatesh YS, Ordonez NG, Schultz PN, Hickey RC, Goepfert H, Samaan NA. Anaplastic carcinoma of the thyroid. A clinicopathologic study of 121 cases. Cancer 1990; 66 :321-330. [CrossRef]
13. McIver B, Hay ID, Giuffrida DF, Dvorak CE, Grant CS, Thompson GB, et al. Anaplastic thyroid carcinoma: a 50-year experience at a single institution. Surgery 2001; 130: 1028-1034. [CrossRef]
14. Haigh PI, Ituarte PH, Wu HS, Treseler PA, Posner MD, Quivey JM, et al. Completely resected anaplastic thyroid carcinoma combined with adjuvant chemotherapy and irradiation is associated with prolonged survival. Cancer 2001; 91: 2335-2342. [CrossRef]
15. Bhatia A, Rao A, Ang KK, Garden AS, Morrison WH, Rosenthal DI, et al. Anaplastic thyroid cancer: Clinical outcomes with conformal radiotherapy. Head Neck. 2010;32:829-836.
16. De Crevoisier R, Baudin E, Bachelot A, Leboulleux S, Travagli JP, Caillou B, et al. Combined treatment of anaplastic thyroid carcinoma with surgery, chemotherapy, and hyperfractionated accelerated external radiotherapy. Int J Radiat Oncol Biol Phys 2004; 60: 1137-1143. [CrossRef]
17. Sherman EJ, Lim SH, Ho AL, Ghossein RA, Fury MG, Shaha AR, et al. Concurrent doxorubicin and radiotherapy for anaplastic thyroid cancer: a critical re-evaluation including uniform pathologic review. Radiother Oncol 2011; 101: 425-430. [CrossRef]
18. Foote RL, Molina JR, Kasperbauer JL, Lloyd RV, McIver B, Morris JC, et al. Enhanced survival in locoregionally confined anaplastic thyroid carcinoma: a single-institution experience using aggressive multimodal therapy. Thyroid 2011; 21: 25-30. [CrossRef]
19. Brignardello E, Gallo M, Baldi I, Palestini N, Piovesan A, Grossi E, et al. Anaplastic thyroid carcinoma: clinical outcome of 30 consecutive patients referred to a single institution in the past 5 years. Eur J Endocrinol 2007; 156: 425-430. [CrossRef]

Turk J Surg 2018; 34(4): 323-326
DOI: 10.5152/UCD.2017.3514

Laparoscopic pancreaticoduodenectomy in pancreatic cancer: Our initial experience

Hüseyin Ayhan Kayaoğlu, Hacı Murat Çaycı, Umut Eren Erdoğdu, Evren Dilektaşlı, Mehmet Emrah Bayam, Hasan Çantay

ABSTRACT

Pancreas cancer is an important cause of mortality worldwide. It has no particular symptoms, and may cause different complaints according to tumor diameter and localization. Local invasion may develop in the short term and distant metastasis may occur in vascular structures in its neighborhood. That's why, resectability rates are low at the time of diagnosis with a negative effect on survival rates. Minimally invasive surgery is being increasingly implemented in pancreas lesions owing to the positive short-term oncologic results of the technique in many other procedures. Traditionally, conventional open surgery is performed in pancreatic head tumors. As laparoscopic resection of pancreatic head cancer has serious technical difficulties and requires advanced laparoscopic experience, minimal invasive attempts in this field have not yet reached sufficient acceptance worldwide. Besides the fact that laparoscopic pancreaticoduodenectomy may provide sufficient short-term oncologic results that are comparative with open surgery, it can be implemented in selected patients in centers with advanced laparoscopic resection capacity. In this case series, we aimed to present our experience of laparoscopic pancreaticoduodenectomy in pancreatic head cancer patients.

Keywords: Minimal invasive, pancreas, laparoscopy, cancer

INTRODUCTION

Pancreas cancer displays an aggressive character with a tendency to rapid invasion of vascular structures around itself, early distant metastasis, and rapid local recurrence. The five-year survival rate in pancreas ductal adenocarcinomas is reported as 6-10% (1). Effective oncologic resection offers the only potentially curative treatment option for this disease (2). However, only 15-20% of patients with pancreas cancer have resectable disease at the time of admission (2).

Minimal invasive surgery is being applied more frequently than conventional surgical operations due to achievement of satisfactory oncologic results, and decreases in postoperative pain, narcotic analgesic usage, and length of hospital stay (3). Initially, application of laparoscopy in pancreas surgery was limited to benign or premalignant lesions such as cyst drainage or enucleation. This was followed by radical resections on selected patients with malignant diseases, and the first laparoscopic pancreaticoduodenectomy was defined in 1994 (4). Difficulty in detecting pancreas cancer patients in the resectable period, rapid invasion of major vascular structures, challenges in pancreatic resection and anastomosis restrict the use of laparoscopic operations in this field. Experience in advanced laparoscopic techniques is essential for radical pancreatic resections. The effectiveness of minimally invasive surgery in pancreatic cancer will be shown with the detection of local recurrence and survival rates in long-term follow-ups. Discussions about the utility of laparoscopic approaches or that they produce better results than open surgery still continue because the studies are still limited to case series or few randomized controlled and short-term follow-up studies. In this report, we aimed to present five patients with pancreas head cancer who underwent laparoscopic pancreaticoduodenectomy in our clinics and to review the literature.

CASE PRESENTATION

Data of 5 patients who underwent laparoscopic pancreaticoduodenectomy in Bursa Yüksek İhtisas Training and Research Hospital between January 1St to December 31St, 2015 due to pancreatic head tumor were evaluated retrospectively. All patients were informed about the laparoscopic operation, and their informed consents were taken. Demographic data of the patients, presence of comorbidity, ASA scores (American Society of Anesthesiologists), preoperative bilirubin and tumor marker levels, diameters of the common bile duct and pancreatic duct, duration of the operations, tumor diameter, presence of lymph node metastasis, morbidity and mortality rates were evaluated.

The presence of regional or distant metastasis, possible invasion to the portal vein, superior mesenteric vein (SMV), and superior mesenteric artery (SMA) and diameter of the tumor were evaluated with multi-

Cite this paper as:
Kayaoğlu HA, Çaycı HM, Erdoğdu UE, Dilektaşlı E, Bayam ME, Çantay H. Laparoscopic pancreaticoduodenectomy in pancreatic cancer: Our initial experience. Turk J Surg 2018; 34(4): 323-326.

Clinic of General Surgery, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey

Corresponding Author
Hacı Murat Çaycı
e-mail: hmurat.cayci@gmail.com

Received: 14.01.2016
Accepted: 16.03.2016
Available Online Date: 03.01.2018

Available online at
www.turkjsurg.com

slice computed tomography (CT) in the preoperative period in all patients. Routine blood tests and carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) levels were studied preoperatively. Preoperative biliary drainage (percutaneous or surgical) was not performed in any patient with high levels of total and direct bilirubin levels. Enteral supplement and liquid diet were given in preoperative period.

Laparoscopic pancreaticoduodenectomy operations were performed by the same surgeon. The patient was operated in reverse Trendelenburg and Lloyd-Davis positions. A 10-12 mm telescope trocar was placed in the abdomen below the umbilicus following pneumoperitoneum. Then, one 10-12 mm trocar was inserted at the right midclavicular line and three 5 mm trocars at the left midclavicular line, right and left anterior axillary lines under direct vision. A 30 ° telescope was used in the operations. At the beginning of the process, the duodenum was mobilized with a Kocher maneuver. First the inferior vena cava and aorta, then the pancreatic head was revealed by opening the gastrocolic ligament. It was seen that the lesion was resectable by mobilization of the pancreatic neck from the SMV and middle colic vein. Antrectomy was made with an endoscopic linear stapler (EchelonFlex™; Ethicon, USA). Following cholecystectomy, the common bile duct was suspended and then cut. High energy instruments (Harmonic scissors, Ethicon, USA) were used in the division of pancreatic neck. The ligament of Treitz was mobilized, and the fourth part of the duodenum and jejunum were transected with an endoscopic linear stapler (EchelonFlex™; Ethicon, USA). Resection was completed with standard lymphadenectomy. Following Pfannenstiel mini-incision, the resection specimen was taken out of the abdomen within a container (Endobag™; Covidien, USA). The Wirsung duct was found in the remnant pancreas and a stent was placed, then retro-colic Wirsung-jejunostomy, hepaticojejunostomy, and gastrojejunostomy anastomoses were made intra-corporeally (Figure 1, 2). Two drains were used, and they were placed next to the pancreas and bile duct anastomosis from the right and left. Intraoperative ultrasound was not used during the operation. AJCC (American Joint Committee on Cancer) and TNM (T tumor, N node, and M metastasis) criteria were used for postoperative histopathologic and clinical evaluations.

The series consisted of three (60%) female and two (40%) male patients. The average age of our patients was 62.8 years (range 51-77). ASA scores were 1 in 2 patients and 2 in 3 patients. All five patients underwent total laparoscopic pancreaticoduodenectomy and intracorporeal anastomosis. Conversion laparotomy was not made during the operations. The stent was placed in the Wirsung duct of all patients and an end to side Wirsung-jejunostomy was perfromed. No intraoperative complication developed during the procedure. The average Wirsung duct diameter was 6 mm (5 mm- 8 mm), and that of the bile duct was 17 mm (15 mm -20 mm). The operation lasted approximately 264 minutes (240-300 minutes). There was no pancreatic anastomosis leakage in the patients. Biliary leakage was detected in 2 (40%) patients in the postoperative period. The biliary leakages closed spontaneously on the 7th day in the first patient and the 10th day in the second patient. One mortality occurred (20%) in a patient following sudden bleeding on the sixth postoperative day. The surgical exploration of this patient revealed that the clips on the gastroduodenal artery were opened, and caused the bleeding. The adenocarcinoma differentiation degree was reported as good in 3 patients and as moderate in 2 patients. Surgical margins were negative in all patients. Patient characteristics, tumor localization, comorbidity presence, total and direct bilirubin values, CEA and CA 19-9 values, surgical tumor diameter, bile duct and Wirsung duct diameters are presented in Table 1. The blood loss during operation, operation duration, tumor characteristics, lymph node metastasis, length of hospital stay, morbidity and mortality rates are also presented.

DISCUSSION

Minimal invasive surgical procedures were initially used for staging and palliation in pancreas surgery followed by radical resections (4). Retroperitoneal localization of the pancreas gland and its close relationships with the duodenum and mesenteric-portal vascular structures restrict minimal invasive attempts due to technical difficulties in intracorporeal anastomosis (two-dimensional camera, hand tools with limited mobility and independent mobility of the devices – fulcrum effect) and critical postoperative complications.

Patient selection is critical for a successful procedure. Laparoscopic resection is recommended for small, benign or low-grade pancreas head, duodenal ampulla, and distal biliary duct tumors as long as there is no vascular and extra-biliary spread (3, 5). Especially, lesions without major artery and vein involvement, those localized in the pancreatic uncinate and neck part or ampullary lesions, mucinous cystic neoplasms and intra-papillary mucinous neoplasms (IPMNs) are ideal for laparoscopic resection.

Laparoscopic intracorporeal anastomosis, mini-laparotomy or hand-port techniques have been used in laparoscopic resec-

Figure 1. The Wirsung duct was found and placed a stent

Figure 2. Retro-colic Wirsung-jejunostomy

tion and reconstruction (6). A review of the literature showed that after the first laparoscopic pancreaticoduodenectomy in 1994, resection was perfromed in 746 cases; complete laparoscopic resection and anastomosis in 386 (51.7%) patients, robotic resection and anastomosis in 234 (31.3%) patients, laparoscopic resection and anastomosis with mini-laparotomy in 121 (16.2%) patients, hand-assisted resection and anastomosis in 5 (0.6%) patients (7).

In patients who underwent complete laparoscopic resection it was detected that; biliary leakage rate was 2.4-7%, average blood loss was 65-240 cc, the rates of delay in gastric emptying was reported as 7-9.1%, bowel obstruction as 6.2%, intraabdominal bleeding as 5.3%, intraabdominal abscess development as 2.4%-19.9%, wound infection as 11.3%, and pulmonary complications and deep vein thrombosis (DVT) as 2.4%-14.3% (3). The start of bowel movements was determined as about 4 days and the average length of hospital stay was between 8-18 days (8). Similar operative time (268 minutes and 286 minutes), blood loss (75 cc or 83 cc), complication rate (33% and 25%) and length of hospital stay (13.4 days and 14 days) were detected in laparoscopic and hybrid methods (9). After laparoscopic resections, a lower rate of delay in gastric emptying and surgical site infection were seen as compared to open surgery (10). Conversion rate from laparoscopy to open surgery changes between 0% and 31.6% (11). Operation times were longer than 7 hours in the initial laparoscopic surgeries. On the other hand, with experience, operation and hospitalization times became shorter and blood loss was reduced during the operation (5). There was no delay in gastric emptying, any pulmonary complications, or DVT in our patients. Although biliary leakage was detected in two patients, they closed spontaneously. Bleeding occurred in one patient that resulted in mortality.

It is shown that laparoscopic minimal invasive procedures provide equivalent short-term oncologic results to open surgeries. R0 resection and sufficient lymph node dissection can be achieved via laparoscopic pancreaticoduodenectomy; 15 lymph nodes on average (minimum 7, maximum 36) are reported to be extracted after resection, and the positive margin was 0.4% (3, 10). In studies on laparoscopic pancreaticoduodenectomy, usually low grade (2.1-3 cm) patients without major vascular involvement are selected. Negative surgical limits are achieved in 100% of laparoscopic procedure while R0 resection could be obtained in 70-80% in open surgery. This difference is attributed to patient selection criteria in laparoscopic attempts (12). The two-year survival rate is found as 36% after open surgery, and 43% after laparoscopic surgery (13).

Postoperative morbidity rate is reported as 25-48% for laparoscopic resections, and 31% for open resections (12). Pancreas fistula is a significant problem in the postoperative period. ISGPF (International Study Group of Pancreatic Fistula) specifies grade B pancreatic fistula rate between 2.4-18%, which is similar to open surgery (3-13%) (5, 8). In addition to the anastomosis technique, the consistency of the remnant pancreas tissue is quite critical. A soft remnant pancreas tissue is an important risk factor for fistula development (14). There was no pancreatic anastomotic leakage in our patients. This was probably related to the low patient number in the series and to the anastomotic technique of Wirsung duct to jejunum mucosa anastomosis over a stent that has been used. The mortality rate varies between 1.9-5.7% in the first postoperative month (8). Pulmonary complications, difficulties in early mobilization, deep venous thrombosis, intraabdominal abscess and bleeding, anastomotic problems and vascular injury were the reasons of post-operative mortality (15). In our study, one patient died due to gastro-duodenal artery bleeding on the 6th post-operative day.

Although the number of patients is low and the follow-up period is short in our study, we think that radical pancreas surgery with laparoscopic method contains similar risks with

Table 1. Patient demographic, clinical and histopathologic data

	1st Patient	2nd Patient	3rd Patient	4th Patient	5th Patient
Age (year)	77	74	51	59	53
Sex	F	F	M	M	M
Comorbidity	HT	HT	-	DM	-
Total-Direct Bilirubin (mg/dL)	3.7-3.03	0.68-0.28	3.07-2.43	9.12-7.19	9.27-6.51
CEA-CA 19.9 (ng/mL)	0.87-313	2.7-41	9.56-4142	10.48-700	1.28-288
Tumor Diameter (mm)	30	25	20	36	30
Common bile duct Diameter (mm)	15	15	20	15	20
Wirsung duct Diameter (mm)	5	5	8	7	5
Operation Time (minute)	240	240	300	240	300
Blood loss during operation (cc)	120	150	210	600	200
Length of hospital stay (day)	8	8	10	6	16
Lymph Node Metastasis	1/12	0/12	0/11	0/13	0/12
Morbidity	-	-	Bile leakage	-	Bile leakage
Mortality	-	-	-	+	-

F: female; M: male; HT: hypertension; DM: diabetes mellitus

the conventional method. Despite the technical difficulties of laparoscopic pancreaticoduodenectomy and its requirement of a learning curve, it may be applied to selected patients as an alternative to open surgical procedures, in centers with necessary equipment and experience in laparoscopic resections, due to its less blood loss, the improvement in gastric emptying, early discharge from hospital, and return to work advantages. Well-planned studies with a high number of patients are needed to evaluate long-term oncologic results.

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - H.A.K.; Design - H.M.Ç.; Supervision - U.E.E.; Resource - H.M.Ç.; Materials - H.M.Ç.; Data Collection and/or Processing - H.M.Ç., E.D., M.E.B.; Analysis and/or Interpretation - H.A.K., H.M.Ç., E.D.; Literature Search - H.M.Ç., U.E.E., E.D., M.E.B.; Writer Manuscript - H.A.K., H.M.Ç., E.D.; Critical Review U.E.E., M.E.B.

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

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

REFERENCES

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. CA Cancer J Clin 2013; 63: 11-30. [CrossRef]
2. Bilimoria KY, Bentrem DJ, Ko CY, Stewart AK, Winchester DP, Talamonti MS. National failure to operate on early stage pancreatic cancer. Ann Surg 2007; 246: 173-180. [CrossRef]
3. Ammori BJ, Ayiomamitis GD. Laparoscopic pancreaticoduodenectomy and distal pancreatectomy: a UK experience and a systematic review of the literature. Surg Endosc 2011; 25: 2084-2099. [CrossRef]
4. Gagner M, Palermo M. Laparoscopic Wipple procedure: review of the literature. J Hepatobiliary Pancreat Surg 2009; 16: 726-730. [CrossRef]
5. Kendrick ML, Cusati D. Total laparoscopic pancreaticoduodenectomy: feasibility and outcome in an early experience. Arch Surg 2010; 145: 19-23. [CrossRef]
6. Lee JS, Han JH, Na GH, Choi HJ, Hong TH, You YK, Kim DG. Laparoscopic pancreaticoduodenectomy assisted by mini-laparotomy. Surg Laparosc Endosc Percutan Tech 2013; 23: 98-102. [CrossRef]
7. Boggi U, Amorese G, Vistoli F, Caniglia F, De Lio N, Perrone V, et al. Laparoscopic pancreaticoduodenectomy: a systematic literature review. Surg Endosc 2015; 29: 9-23. [CrossRef]
8. Asbun HJ, Stauffer JA. Laparoscopic vs open pancreaticoduodenectomy: overall outcomes and severity of complications using the Accordion Severity Grading System. J Am Coll Surg 2012; 215: 10-819. [CrossRef]
9. Dulucq JL, Wintringer P, Stabilini C, Feryn T, Perissat J, Mahajna A. Are major laparoscopic pancreatic resections worthwhile? A prospective study of 32 patients in a single institution. Surg Endosc 2005; 19: 1028-1034. [CrossRef]
10. Gumbs AA, Rodriguez Rivera AM, Milone L, Hoffman JP. Laparoscopic pancreatoduodenectomy: a review of 285 published cases. Ann Surg Oncol 2011; 18: 1335-1341. [CrossRef]
11. Kuroki T, Adachi T, Okamoto T, Kanematsu T. A nonrandomized comparative study of laparoscopy-assisted pancreaticoduodenectomy and open pancreaticoduodenectomy. Hepatogastroenterology 2012; 59: 570-573. [CrossRef]
12. Sohn TA, Yeo CJ, Cameron JL, Koniaris L, Kaushal S, Abrams RA, et al. Resected adenocarcinoma of the pancreas-616 patients: results, outcomes, and prognostic indicators. J Gastrointest Surg 2000; 4: 567-579. [CrossRef]
13. Kendrick ML. Laparoscopic and robotic resection for pancreatic cancer. Cancer J 2012; 18: 571-576. [CrossRef]
14. Berger AC, Howard TJ, Kennedy EP, Sauter PK, Bower-Cherry M, Dutkevitch S, et al. Does type of pancreaticojejunostomy after pancreaticoduodenectomy decrease rate of pancreatic fistula? A randomized, prospective, dualinstitution trial. J Am Coll Surg 2009; 208: 738-747. [CrossRef]
15. Çakır M, Küçükkartallar T, Tekin A, Tuncer FB, Kartal A. Bile duct ischemia developing after reconstruction of the hepatic artery during the Whipple operation. Ulus Cerrahi Derg 2015; 31: 235-237.

Turk J Surg 2018; 34(4): 327-330
DOI: 10.5152/turkjsurg.2017.3507

Case Report

Portal vein ligation and in situ liver splitting in metastatic liver cancer

Afag Aghayeva[1], Bilgi Baca[1], Deniz Atasoy[1], Sina Ferahman[2], Sezgin Uludağ[2], İsmail Ahmet Bilgin[3], Sonay Beyatlı[4], İsmail Mihmanlı[5], İsmail Hamzaoğlu[3]

ABSTRACT

The most serious complication after major liver resection is liver failure. Depending on preoperative liver function, a future liver remnant of 25%-40% is considered sufficient to avoid postoperative liver failure. A new technique known as portal vein ligation combined with in situ splitting has been developed to obtain rapid liver hypertrophy. Herein, we present a case where we performed portal vein ligation combined with in situ splitting. A 37-year-old male patient with a diagnosis of sigmoid adenocarcinoma and liver metastasis underwent anterior resection because of an obstructing sigmoid tumor and received palliative chemotherapy. After chemotherapy, abdominal computed tomography revealed a lesion, 50 mm in diameter, localized between segments 5-8 of the liver on the bifurcation of the anteroposterior segmental branch of the right portal vein. Computed tomography volumetric assessments of the liver were performed in the preoperative period, and it was found that the remnant left liver volume was less than 25%. In the first stage, portal vein ligation and in situ splitting of the liver parenchyma were performed. On the second and sixth postoperative days, computed tomography revealed hypertrophy of the left liver lobe. On the sixth day, a right hepatectomy was performed. Portal vein ligation combined with in situ splitting has been used by surgeons worldwide to obtain rapid and adequate liver hypertrophy. This new approach yields hope for patients with locally advanced liver tumors and may increase the number of curative resections for primary or metastatic liver tumors.

Keywords: Portal vein ligation, in situ liver splitting, metastatic liver cancer

ORCID ID of the author:
D.A. 0000-0002-5703-4549.

Cite this paper as:
Aghayeva A, Baca B, Atasoy D, Ferahman S, Uludağ S, Bilgin İA, et al. Portal vein ligation and in situ liver splitting in metastatic liver cancer. Turk J Surg 2018; 34(4): 327-330.

[1]Department of General Surgery, Acıbadem University School of Medicine Atakent Hospital, İstanbul, Turkey

[2]Department of General Surgery, İstanbul University Cerrahpaşa School of Medicine, İstanbul, Turkey

[3]Department of General Surgery, Acıbadem University School of Medicine Maslak Hospital, İstanbul, Turkey

[4]Student of Acıbadem University School of Medicine, İstanbul, Turkey

[5]Department of Radiology, İstanbul University Cerrahpaşa School of Medicine, İstanbul, Turkey

This study was presented at the 19th National Surgical Congress, 16-20 April 2014, Antalya, Turkey.

Corresponding Author
Afag Aghayeva
e-mail: aghayevaa@gmail.com

Received: 31.01.2016
Accepted: 19.04.2016

Available online at
turkjsurg.com

INTRODUCTION

One of the most important limiting factors for major liver resection is insufficient remnant liver volume. Depending on preoperative liver function, a liver remnant of 25%-40% is considered sufficient to avoid postoperative liver failure (1, 2). Portal vein embolization (PVE), chemotherapy, local ablation, and surgical portal vein ligation have been developed to induce liver tissue hypertrophy before major liver resection. *In situ* liver splitting and portal vein ligation (PVL) have been developed to induce rapid and effective hepatic hypertrophy as an alternative to these methods (3). In this approach, at the first stage, the hepatic vein, artery, and hepatic canal are preserved while PVL is performed; then, the liver parenchyma is split. At the second stage, the hepatic artery, vein, and hepatic canals are tied and the approach is completed with hepatectomy. This technique has been well accepted and used with good outcomes worldwide. Herein, we present a case where we performed PVL combined with *in situ* liver splitting.

CASE PRESENTATION

A 37-year-old male patient with a diagnosis of sigmoid adenocarcinoma and liver metastasis ($cT_4N_1M_1$) underwent anterior resection in December 2012 because of an obstructing sigmoid tumor; he also underwent palliative chemotherapy. After the chemotherapy, abdominal computed tomography (CT) revealed that there was no regression over the metastatic lesions localized in the right lobe of the liver; thus, a right hepatectomy procedure was planned. A written informed consent was obtained from the patient. Abdominal CT revealed a lesion, 50 mm in diameter, localized between segments 5 to 8 of liver on the bifurcation of the anteroposterior segmental branch of the right portal vein (Figure 1). According to abdominal CT volumetric evaluation during the preoperative period, the volume of the left liver remnant was less than 25% and would not be sufficient for liver function.

In the first stage, perioperative ultrasound was performed to evaluate the left lobe. Only a subcapsular millimetric nodule was detected. The right portal vein was transected with a vascular staple; the right hepatic artery, vein, and right hepatic canal were saved (Figure 2, 3), and the parenchymal dissection of the right liver lobe was performed with an ultrasonic dissector and isolated with a sterile plastic bag (Figure 4). Additionally, the subcapsular millimetric nodule localized to the left lobe was excised. At the end of the first stage of this approach, a drain was placed in the subhepatic region before closure of the abdomen. The total operation time was 210 minutes and the total amount of blood loss was 1000 ml.

On postoperative days (PODs) 2 and 6 of the first operation, it was revealed by abdominal CT that the volume of the left lobe was hypertrophied by more than 25% (Figure 5). It was seen that the left lobe passed the midline, extending toward the spleen (Figure 6). For the second stage, the right hepatic vein was transected with a vascular staple, and the right hepatic artery and right hepatic canal, which had been saved during the first stage, were tied with 2/0 silk sutures. Right hepatectomy was completed with removal of the previously split right liver parenchyma. The total operation time was 60 minutes, and the total blood loss was 50 mL. After the second stage of surgery, the patient's INR, total bilirubin, and direct bilirubin levels were 1.61, 3.7 mg/dl, and 2.82 mg/dL, respectively. His AST and ALT levels were two times higher than the normal range. However, before his discharge from the hospital, the patient's liver func-

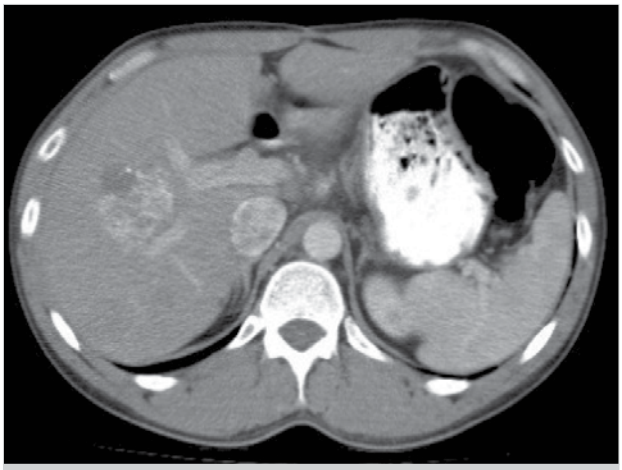


Figure 1. Preoperative image: lesion localized between segments 5 to 8 of the liver on the bifurcation of the anteroposterior segmental branch of the right portal vein

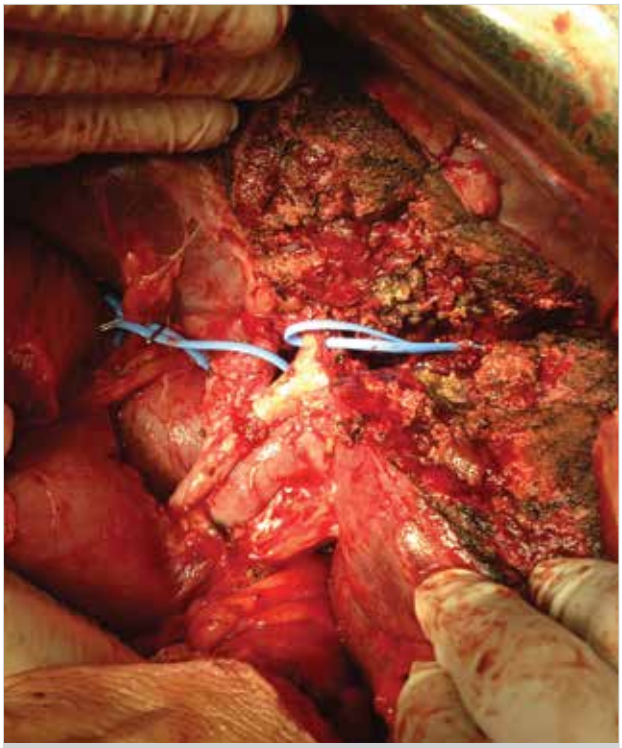


Figure 2. Right hepatic artery and right hepatic duct

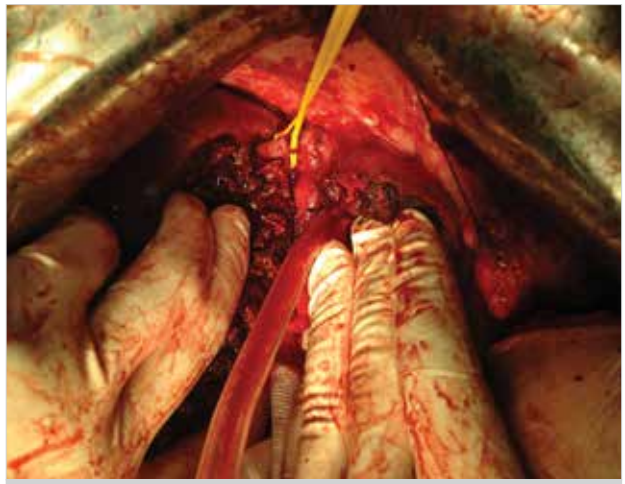


Figure 3. Right hepatic vein

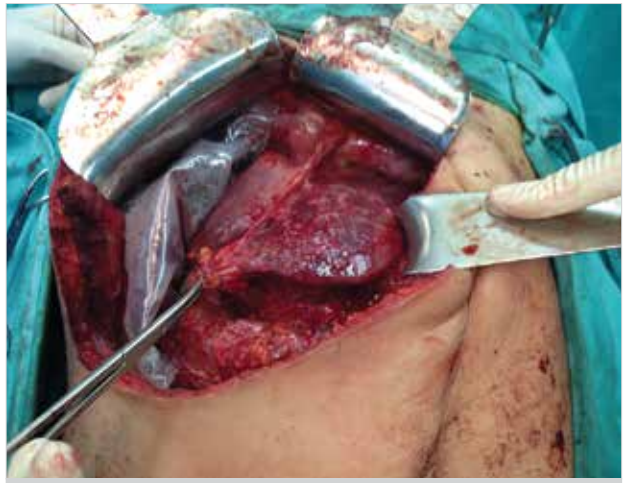


Figure 4. Isolation of split right liver lobe with a sterile plastic bag

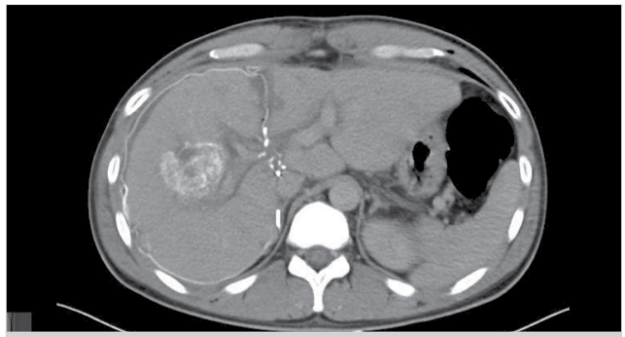


Figure 5. CT image of postoperative day 2

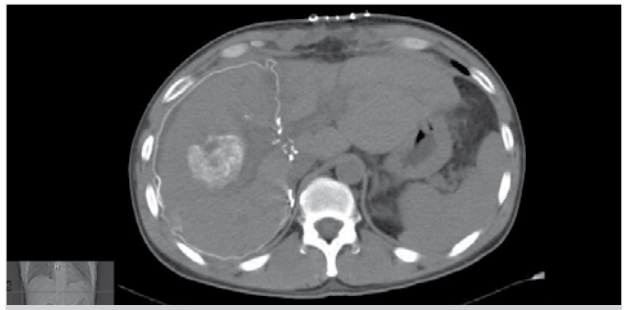


Figure 6. CT image of postoperative day 6

tion tests were normal. The patient was discharged on POD 11 uneventfully. On POD 20, abdominal CT revealed that the left lobe was hypertrophied by passing through the midline up to the midclavicular line (Figure 7). Histopathological examination revealed a colonic-type metastatic adenocarcinoma on the right lobe of the liver at segment four. After a follow-up of two years, the patient has no recurrence. A recent PET-CT scan is shown in Figure 8.

DISCUSSION

The only curative treatment option for primary or metastatic liver cancers is surgical excision. However, in some patients with large tumors or with small tumors close to central main structures, the functional remnant liver volume after radical resection may be too small to maintain normal liver function. At least 25%-40% of the liver volume should be left after surgery to maintain normal liver function (3). Schnitzbauer et al. (3) described a two-stage technique that enhanced liver hypertrophy in a short period of time. This technique is known as associating liver partition and portal vein ligation (ALPPS).

Figure 7. CT image of POD 20

Portal vein ligation, chemotherapy, local ablation, and surgical PVL are other methods used to increase the volume of the liver before resection. In an article published by Liu and Zhu (4), it was demonstrated that the liver underwent hypertrophy by about 10%-46% within 2-8 weeks after PVE. In another study, it was shown that the liver was hypertrophied by 38% within eight weeks after PVL (5). However, tumor progression, insufficient hypertrophy, and invasions of tumors to the right portal vein and precluding PVE are some disadvantages of these techniques. Additionally, in the case of small metastatic lesions on the left liver lobe, the blood supply to these lesions also increases with radiologic right PVE. The ALPPS approach induces a median hypertrophy of 74% within nine days (3). One of the benefits of ALPPS is the ability to remove tumors earlier than radiologic PVE. According to some authors, a disadvantage of ALPPS is the persistence of the right liver parenchyma within the plastic bag; if, for some reason, the second stage of this procedure cannot be performed, further surgery is required to remove this plastic bag.

In our case, it was seen that the liver was hypertrophied on the 6th day after the first stage; right hepatectomy was then performed for the second stage. Liver function tests were slightly elevated in the early days of postoperative evaluation, but no liver failure occurred. It was observed that starting on the 10th day after the first operation, the patient's liver function tests were normal.

The morbidity after major liver resections is 20%-50%, depending on the general status of the patient during the op-

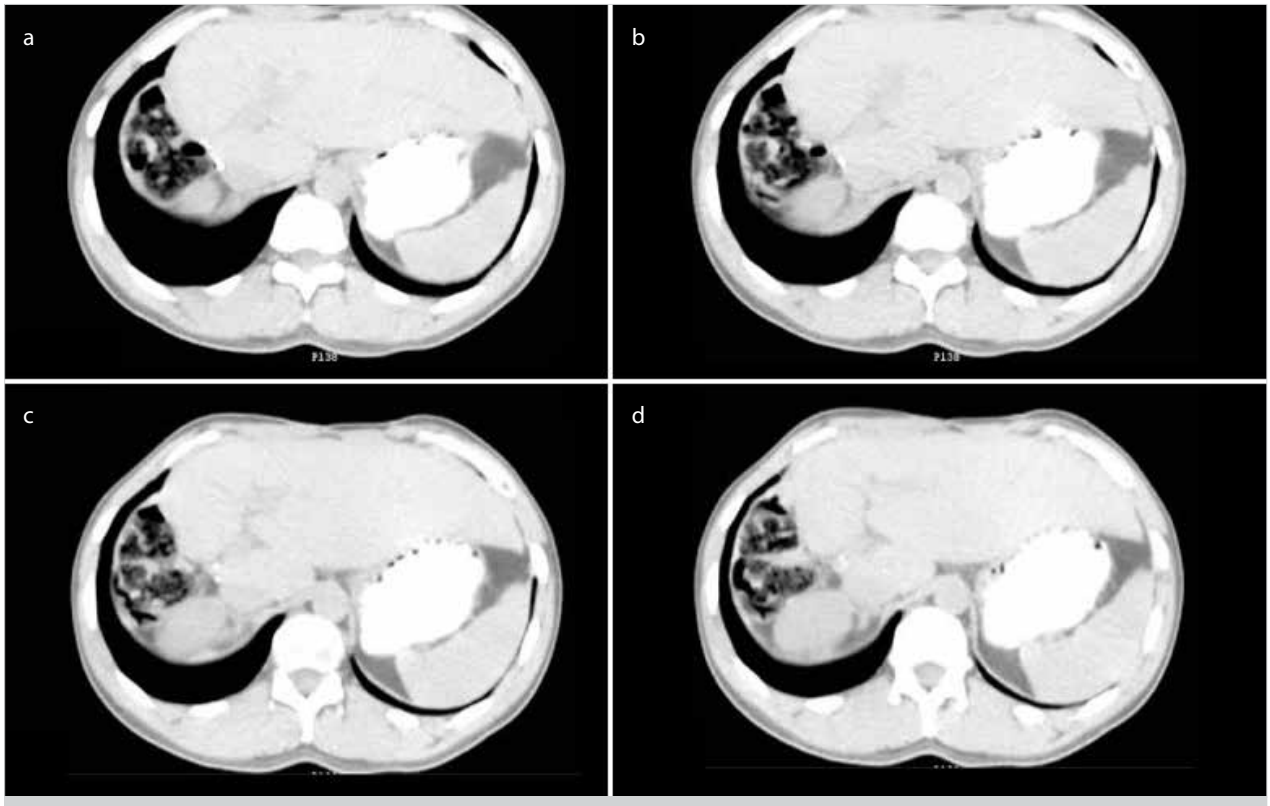


Figure 8. a-d. PET-CT images of second-year follow-up. Consecutive axial sections are presented

eration, the presence of an underlying disease, and the size of the resection (6, 7). In the literature, biliary fistula, sepsis, and infection have been described as the major complications of ALPPS during the postoperative period (3).

Between 2011 and 2014, 320 ALPPS operations have been performed in 55 different centers worldwide (8). The age of the patient, type of tumor, timing of the operation during the first stage, and intraoperative blood transfusion are factors affecting the mortality. Patients over 60 years of age who are treated with ALPPS and those who undergo operations due to gallbladder carcinoma or cholangiocarcinoma show higher mortality rates (8).

The disadvantage of ALPPS that we encountered in our case was higher intraoperative blood loss compared to standard right hepatectomy.

CONCLUSION

Portal vein ligation combined with in situ splitting has been used to obtain rapid and adequate liver hypertrophy. This new approach could increase the number of curative resections in patients with locally advanced and primary or metastatic liver tumors.

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - B.B., İ.H., İ.M.; Design - A.A., B.B., D.A.; Supervision - İ.H., B.B., A.A.; Resource - S.F., S.U., İ.A.B.; Materials - A.A., B.B., S.B.; Data Collection and/or Processing - A.A., S.B., İ.A.B.; Analysis and/or Interpretation - D.A., A.A., B.B.; Literature Search - S.F., S.U., A.A.; Writing Manuscript - A.A., D.A., B.B.; Critical Reviews - B.B., İ.H., İ.M.

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

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

REFERENCES

1. Tucker ON, Heaton N. The 'small for size' liver syndrome. Curr Opin Crit Care 2005; 11: 150-155. [CrossRef]
2. Tanaka K, Shimada H, Matsuo K, Ueda M, Endo I, Togo S. Remnant liver regeneration after two-stage hepatectomy for multiple bilobar colorectal metastases. Eur J Surg Oncol 2007; 33: 329-335. [CrossRef]
3. Schnitzbauer AA, Lang SA, Goessmann H, Nadalin S, Baumgart J, Farkas SA, et al. Right portal vein ligation combined with in situ splitting induces rapid left lateral liver lobe hypertrophy enabling 2-staged extended right hepatic resection in small-for-size settings. Ann Surg 2012; 255: 405-414. [CrossRef]
4. H. Liu, S. Zhu. Present status and future perspectives of preoperative portal vein embolization. Am J Surg 2009; 197: 686-690. [CrossRef]
5. Aussilhou B, Lesurtel M, Sauvanet A, Farges O, Dokmak S, Goasguenet N, et al. Right portal vein ligation is as efficient as portal vein embolization to induce hypertrophy of the left liver remnant. J Gastrointest Surg 2008; 12: 297-303. [CrossRef]
6. Sgourakis G, Sotiropoulos GC, Bockhorn M, Fuzas I, Radtke A, Molmenti EP, et al. Major liver resections for primary liver malignancies in the elderly. Acta Chir Belg 2009; 109: 340-344. [CrossRef]
7. Lang H, Sotiropoulos GC, Fruhauf NR, Dömland M, Paul A, Kind EM, et al. Extended hepatectomy for intrahepatic cholangiocellular carcinoma (ICC): when is it worthwhile? Single center experience with 27 resections in 50 patients over a 5-year period. Ann Surg 2005; 241: 134-143.
8. Schadde E, Raptis DA, Schnitzbauer AA, Ardiles V, Tschuor C, Lesurtel M, et al. Prediction of mortality after ALPPS stage-1: an analysis of 320 patients from the international ALPPS Registry. Ann Surg 2015; 262: 780-786. [CrossRef]

Turk J Surg 2018; 34(4): 331-333
DOI: 10.5152/turkjsurg.2017.3115

Case Report

Primary small bowel lymphoma presenting as invagination

Nidal İflazoğlu[1], Aslı Mengeloğlu[2], Nilay Şen Korkmaz[3], Bilgin Karaalioğlu[4], Murat Yülüklü[5]

ABSTRACT

One of the causes of invagination in adults is primary small bowel lymphoma. Primary small bowel lymphomas are rare, present themselves with complications due to diagnostic difficulties, and are diagnosed only after surgical intervention. In case of invagination, one of the complications of these tumors, namely primary small bowel lymphoma, should also be considered as a cause in the diagnosis. In this paper, the diagnosis and therapy of a rare case of primary polypoid-type small intestinal lymphoma demonstrating findings of obstruction due to invagination have been presented and discussed in the light of the literature.

Keywords: Lymphoma, invagination, small bowel

INTRODUCTION

An invagination is a condition in which the proximal part of the intestine folds into the distal part of the intestine, similar to the way the parts of a collapsible telescope slide into one another. One of the causes of invagination in adults is small bowel lymphoma (1, 2). Obstruction, perforation, bleeding, and invagination are the well-defined complications of small bowel lymphoma (2).

In this paper, the diagnosis of and therapy for a rare case of primary polypoid-type small bowel lymphoma demonstrating findings of obstruction due to invagination are presented and discussed in the light of the literature.

CASE PRESENTATION

A 34-year-old male patient presented to the General Surgery Outpatient Clinic with complaints of weakness, weight loss (10 kg), and abdominal pain in the last 3 months and abdominal swelling and vomiting in the last 10 days. The patient looked pale, anergic, and anemic. The patient's life history and family history presented no significance. On physical examination, his blood pressure was 90/60 mm Hg, his pulse was 102/min, and his body temperature was 36.5°C. The thorax was found to be normal. Abdominal examination with deep palpation yielded a suspect mass in the right lower quadrant. The result of rectal examination was normal. His blood count showed the following: white blood cells, 4.2 K/mm^3; hemoglobin, 8.5 g/dL; hematocrit, 27.2%; and platelets, 140,000 /µL. The results of his renal and hepatic function tests were within normal limits. Blood tumor markers (such as CEA and CA 19-9) and the results of a complete urine test were found to be normal. Abdominal computed tomography (CT) showed a mass in the right side of the abdomen (Figure 1). The subsequent colonoscopy identified an atypical mass lesion in the hepatic flexura, obstructing the lumen almost completely (Figure 2). Multiple biopsy specimens were obtained from the mass. The pathology report of the specimens was malignancy of an unknown nature. Upon findings of obstruction and determination of malignancy, the patient underwent conventional surgery. The exploration showed the ileum (with a palpable mass in the lumen) to have been invaginated into the right colon; moreover, it also showed palpable enlarged lymph nodes in the ileocolic mesothelium. The liver and spleen were evaluated and found to be normal. Subsequently, in accordance with the cancer surgery principles (total mesocolic excision+proper surgical boundaries), right hemicolectomy, partial ileum resection, and ileotransversostomy were performed.

In the following histopathological examination of the ileum specimen, invaginating from the ileocecal valve into the colon, that is, in the resected 18-cm long small intestinal and 25-cm long large intestinal material, macroscopically, there was a tumoral mass localized in the terminal ileum. The mass was 4×3×2.5 cm in size, had a smooth surface, was of fish-meat consistency in the sectional surface, and showed invasion to the serosa and the surrounding fatty tissue. Tumoral cells were observed in the microscopic examination of the material. The cells showed a diffuse distribution pattern; were round and of medium size; and had narrow basophilic cytoplasm, markedly hyperchromatic nuclei, and apparent multiple nucleoli (Figure 3). In the immunohistochemical examination of the material, CD45, CD20, CD79a, bcl-6, and CD10 were found to be positive, but CD3, CD5, CyclinD1, and bcl2 were determined

Cite this paper as:
İflazoğlu N, Mengeloğlu A, Şen Korkmaz N, Karaalioğlu B, Yülüklü M. Primary small bowel lymphoma presenting as invagination Turk J Surg 2018; 34(4): 331-333.

[1]Department of General Surgery, Kilis State Hospital, Kilis, Turkey
[2]Department of Pathology, Kilis State Hospital, Kilis, Turkey
[3]Department of Pathology, Afyon State Hospital, Afyon, Turkey
[4]Department of Intarnal Medicine, Şanlıurfa Mehmet Akif İnan Training and Research Hospital, Şanlıurfa, Turkey
[5]Department of General Surgery, Afyon State Hospital, Afyon, Turkey

Corresponding Author
Nidal İflazoğlu
e-mail: nidal1933@yahoo.com

Received: 16.02.2015
Accepted: 10.06.2015

Available online at
turkjsurg.com

to be negative (Figure 4, 5). The Ki-67 proliferation index was 99%. Thus, the diagnosis was reported as Burkitt's lymphoma.

After establishing the diagnosis of small bowel lymphoma, systemic involvement according to Dawson's criteria was checked, and no peripheral lmyphadenopathy was found (3). A thorax CT revealed no lymph node of pathological size. The examination results of a peripheral blood smear and bone marrow aspiration biopsy were also normal. Following all of these examinations, the patient received the final diagnosis of primary small bowel lymphoma. According to Musshoff's staging system, the patient was placed in Stage 2E1 because he had serosal involvement and regional lymph node positivity (4). In the postoperative stage, the patient developed no complications and was discharged with no problems from the hospital on the sixth postoperative day. The patient gave consent for this publication when he visited the hospital for controls.

DISCUSSION

Invagination occurs often and idiopathically in childhood (5). In adults, invagination is seldom seen and is due to an underlying pathology in up to 80% of the cases. Of the pathologies underlying invagination, about 40% are either primary or secondary malignant diseases. Polyps, lipomas, malignant masses, and adhesions due to past surgery are the causes or starting points of well-defined invaginations (1, 6, 7). In the present study, compatible with the literature, our patient had primary small bowel lymphoma as the starting point of his invagination.

Figure 1. Computed tomographic examination showed mass image in the right abdomen

Figure 2. Atypical mass lesion in the hepatic flexura of the colon, a colonoscopy figure

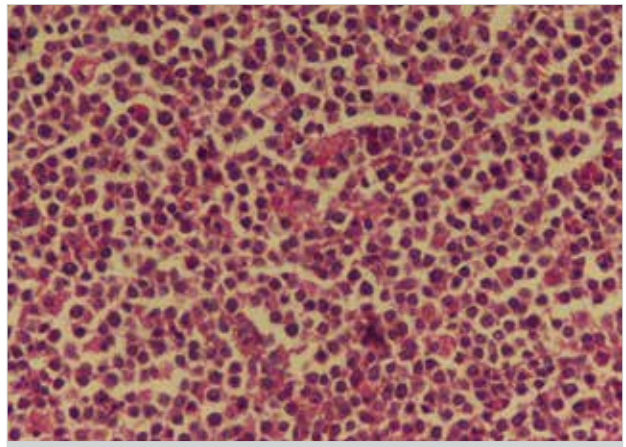


Figure 3. Microscopic examination of the material (H&E, 200×)

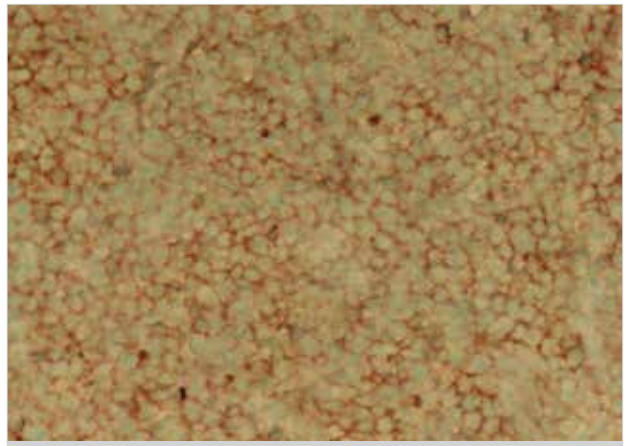


Figure 4. Immunohistochemical examination of the material (CD20, 400×)

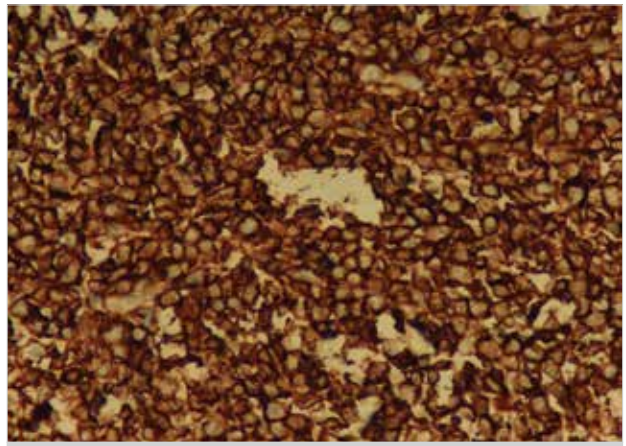


Figure 5. Immunohistochemical examination of the material (CD45, 400×)

Primary lymphomas make up about 1%-4% of all gastrointestinal system tumors. Of these, about 20%-30% are primary small bowel lymphomas (8). According to Barakat's endoscopic classification, primary small bowel lymphomas are described as granulopapular, nodulopolypoid, ulcerative, infiltrative, and mixed (9). Retrospectively, it can be said that our patient had the nodulopolypoid type of lymphoma.

Small bowel lymphomas can have different clinical courses; generally, however, they present with nonspecific findings and cause difficulty in endoscopic or radiological diagnosis due to their localization and consequently are diagnosed when complicated or by histopathological examination following surgery. Many presented cases in the literature have been diagnosed months after the symptoms start (10). The fact that our patient was also diagnosed months after the symptoms had begun as a complicated case points to the diagnostic difficulty of the disease.

Histopathologically, about 90% of small bowel lymphomas are B-cell non-Hodgkin lymphoma, and the next most common types are T-cell non-Hodgkin lymphoma and Hodgkin lymphoma (6). Our patient was diagnosed with Burkitt's lymphoma, which is one of B-cell non-Hodgkin lymphomas.

In recent years, primary small bowel lymphomas are increasingly seen, particularly in immunocompromised patients, and frequently cause co-morbidity in cases with transplantation history, inflammatory intestinal diseases, and some immunodeficiency syndromes (11, 12). Our patient had no such comorbidity based on his anamnesis and clinical findings.

The treatment of primary small bowel lymphomas is still controversial and lacks a clear optimum strategy. This situation may be due to the limited number of cases and the lack of high-quality prospective studies. Various combinations of surgery, chemotherapy (CT), and radiotherapy (RT) are the options for treatment. Although surgery and RT are thought to provide local control of the tumor, these two therapeutic approaches are being increasingly displaced by alternatives of combined chemotherapy. Surgery is recommended for complicated cases during the process of diagnosis/therapy or for post-therapy residual disease. It has been reported that chemotherapy alone is equivalent to surgery in uncomplicated cases in the early stage (13, 14). Since our patient was a complicated case, we performed surgery and planned to initiate chemotherapy.

CONCLUSION

Primary small bowel lymphomas are rare, present themselves with complications due to diagnostic difficulties, and are diagnosed only after surgical intervention. In case of invagination, one of the complications of these tumors, namely, primary small bowel lymphoma, should also be considered as a cause in the diagnosis. We are of the opinion that with the advances in diagnostic methods and technical facilities, primary small bowel lymphomas can be diagnosed early and treated before complications develop.

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - N.İ., A.M.; Design - N.İ., A.M., N.Ş.K.; Supervision - N.İ., B.K., M.Y.; Resource - A.M., N.Ş.K.; Materials - N.İ., B.K., M.Y.; Data Collection and/or Processing - N.İ., N.Ş.K.; Analysis and/or Interpretation - B.K., M.Y.; Literature Search - N.İ., B.K., M.Y.; Writing Manuscript - N.İ., B.K., M.Y.; Critical Reviews - N.İ., A.M., N.Ş.K.

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

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

REFERENCES

1. Nestorovic M, Stanojevic G, Brzacki V, Milojkovic V, Brankovic B, Pecic V, et al. Ileocolic intussusception as a presenting sign of primary lymphoma of the colon. Srp Arh Celok Lek 2011; 139: 673-676. [CrossRef]
2. Minrui LM, Zhang S, Gu F, Xiao W, Yao J, Chao K, et al. Clinicopathological characteristics and prognostic factors of primary gastrointestinal lymphoma: a 22-year experience from South China. Int J Clin Exp Pathol 2014; 7: 2718-2728.
3. Dawson IM, Cornes JS, Morson BC. Primary malignant lymphoid tumours of the intestinal tract. Report of 37 cases with a study of factors influencing prognosis. Br J Surg 1961; 49: 80-89. [CrossRef]
4. Musshoff K. Prognostic and therapeutic implications of staging in extranodal Hodgkin's disease. Cancer Res 1971; 31: 1814-1827.
5. Wei CH, Fu YW, Wang NL, Du YC, Sheu JC. Laparoscopy versus open surgery for idiopathic intussusception in children. Surg Endosc 2015; 29: 668-672. [CrossRef]
6. Akbulut S. Unusual cause of adult intussusception: diffuse large B-cell non-Hodgkin's lymphoma: a case report and review. Eur Rev Med Pharmacol Sci 2012; 16: 1938-1946.
7. Honjo H, Mike M, Kusanagi H, Kano N. Adult intussusception: a retrospective review. World J Surg. 2015; 39: 134-138. [CrossRef]
8. Howell JM, Auer-Grzesiak I, Zhang J, Andrews CN, Stewart D, Urbanski SJ. Increasing incidence rates, distribution and histological characteristics of primary gastrointestinal non-Hodgkin lymphoma in a North American population. Can J Gastroenterol 2012; 26: 452-456. [CrossRef]
9. Barakat MH. Endoscopic features of primary small bowel lymphoma: a proposed endoscopic classification. Gut 1982; 23: 36-41. [CrossRef]
10. Albayrak D, Ibis AC, Hatipoglu AR, Polat N, Hoscoskun Z. Perforated primary small bowel lymphoma: a case report. Balkan Med J 2008; 25: 60-64.
11. Bende RJ, Smit LA, Bossenbroek JG, Aarts WM, Spaargaren M, de Leval L, et al. Primary follicular lymphoma of the small intestine: alpha4beta7 expression and immunoglobulin configuration suggest an origin from local antigen-experienced B cells. Am J Pathol 2003; 162: 105-113. [CrossRef]
12. Loftus EV Jr, Tremaine WJ, Habermann TM, Harmsen WS, Zinsmeister AR, Sandborn WJ. Risk of lymphoma in inflammatory bowel disease. Am J Gastroenterol 2000; 95: 2308-2312. [CrossRef]
13. Yin L, Chen CQ, Peng CH, Chen GM, Zhou HJ, Han BS, et al. Primary small-bowel non-Hodgkin's lymphoma: a study of clinical features, pathology, management and prognosis. J Int Med Res 2007; 35: 406-415. [CrossRef]
14. Jayabackthan L, Murgi SB, Graham S, Kini RG. A rare case of primary lymphoma of the caecum presenting as intussusception. J Lab Physicians 2013; 5: 118-120. [CrossRef]

Turk J Surg 2018; 34(4): 334-336
DOI: 10.5152/turkjsurg.2017.3406

Case Report

A rare cause of obstructive defecation in a 29-year-old woman: Ileo-colo-colonic intussusception treated by subtotal colectomy with posterior rectopexy

Enver Kunduz[1], Fatma Ümit Malya[1], Elnur Mehdi[2], Mustafa Hasbahçeci[1]

ABSTRACT

Adult intussusception is a rare clinical condition. In majority of adult cases, there is an underlying cause such as polyps or colon cancers. In the present study, a 29-year-old woman with intermittent and colicky abdominal pain, constipation, and painful defecation, accompanied with distention and sense of rectal fullness, was evaluated with computed tomography. Ileo-colo-colic intussusception was determined. Subtotal colectomy with posterior rectopexy was performed. After the surgery, she was doing well at 13-month follow-up.

Keywords: Obstructive defecation, intussusception, subtotal colectomy

INTRODUCTION

Intussusception is the invagination of an intestinal segment to the continuing part of the intestine. Usually, it is a pediatric diagnosis due to benign pathologies (1, 2). Intussusception as the most common cause of intestinal obstruction occurs most frequently in infants (3, 4). However, less than 5% of the intussusception cases are seen in adults (5). Majority of the cases in children are idiopathic, but an organic cause, such as a polyp or colonic malignancy, is usually detected as the underlying cause of intussusception in adults (6, 7). Intussusception in adults most commonly appears as enteroenteric (limited to small intestine). It has been known that colo-colonic intussusception (limited in colon and rectum, without anal protrusion) is the least common type (8). In these circumstances, colonic tumors have been regarded to be the main cause (9). However, intussusception starting from the distal ileal segments to the rectum without proven gastrointestinal malignancy can be a very rare event in adults.

In this paper, we present a young female patient with obstructive defecation caused by ileo-colo-colonic intussusception.

CASE PRESENTATION

A 29-year-old woman with intermittent and colicky abdominal pain, constipation, and painful defecation, accompanied with distention and a sense of rectal fullness was hospitalized. Similar symptomatology was present for last three months. The patient was described fecal incontinence with a mass protruding from her anus during maximal discomfort. Physical examination revealed distended abdomen with mild tenderness. Patulous anus with a bulky mass protruding through the rectum mimicking prolapse was detected on rectal examination. Coronal curved multiplanar reconstruction of contrast-enhanced computed tomography (CT) (Figure 1) showed bowel-within-bowel appearance of ileo-colo-colic intussusception elongated from the cecum to the splenic flexure. Surgical intervention had been decided and informed consent had been received. At diagnostic laparoscopy, a dilated and partially invaginated bowel was observed. On conversion to laparotomy, ileo-colo-colic intussusception including terminal ileum and right, transverse, left, and sigmoid colon was determined. Subtotal colectomy had been initiated because all colonic segments invaginated each other down till recto-sigmoidal junction. Subtotal colectomy with ileorectal anastomosis and posterior rectopexy was performed (Figure 2). Pathological examination revealed a benign cecal ulcer causing colo-colic intussusception. After an unremarkable postoperative course, she was doing well at the 13-month follow-up.

DISCUSSION

Although intussusception is one of the most common leading causes of intestinal obstruction in children, it is very rare in adults (10, 11). Enteroenteric intussusception has been reported as the most common type in adults, followed by ileocecal and colo-colonic types. Clinical presentation and the underlying pathology of these patients shows great variability based on these localizations (11). It has been reported that non-specific symptoms including abdominal pain, hematochezia, abdominal mass, and altered bowel habits can be seen in adults (12). In accordance with these findings, intermittent and colicky abdominal pain accompanied with sense of a mass protruding from her anus during maximal discomfort and fecal incontinence was present in our patient. Therefore, it should be kept in mind that

ORCID IDs of the authors:
E.K. 0000-0002-7686-2809;
F.Ü.M. 0000-0002-6593-6112;
E.M. 0000-0001-6281-1026;
M.H. 0000-0002-5468-5338.

Cite this paper as:
Kunduz E, Ümit Malya F, Mehdi E, Hasbahçeci M. A rare cause of obstructive defecation in a 29-year-old woman: Ileo-colo-colonic Intussusception treated by subtotal colectomy with posterior rectopexy. Turk J Surg 2018; 34(4): 334-336.

[1]Department of General Surgery, Bezmialem Vakif University School of Medicine, İstanbul, Turkey

[2]Department of Radiology, Bezmialem Vakif University School of Medicine, İstanbul, Turkey

Corresponding Author
Enver Kunduz
e-mail: drkunduz@yahoo.com

Received: 04.10.2015
Accepted: 17.01.2016

Available online at
turkjsurg.com

atypical presentation of intussusception can be seen in adult patients.

A malignant tumor has been reported as the common cause of colo-colonic intussusception in adults; however, benign tumors including lipomas are the main causes of enteroenteric ones. Although it could not be possible to detect a tumor lesion at the cecum and show a photographic and radiological extent of this intussusception down to the anus in the present case, obstructed defecation caused by benign cecal ulceration may be regarded as a rare event. However, a finding of patulous anus with a bulky mass protruding through the rectum should warn physicians to think of such rare pathologies in adult patients.

The extension of intussusception has not been studied in detail in previous studies (11). In the presence of a leading point causing the proximal intestinal segments to be invaginated, it may be thought that the extent of that segment may be directly related with severity of symptoms. Therefore, recurrent partial obstruction with the leading point at the cecum may cause an intussusception from the distal ileal segments down to almost descending colon. In literature, there has been very limited number of cases with ileo-rectal or ileo-anal intusussusception (See comment in PubMed Commons below13-16). A failure in the embryologic development of the mesenteries of the ascending and descending colon to blend with the posterior abdominal wall may be regarded as the underlying cause for such a rare event (11). By that way, it can be possible to see migration of the colon to long distances freely without obstruction. In these cases, limited resection of the intussuscepted segments from the distal ileum to the proximal colon should be performed. However, it could be possible to resect all intussuscepted segments via subtotal colectomy in the present case. Additionally, suture rectopexy was added to the surgical treatment for the prevention of future prolapse. Therefore, the extent of the pathology in our case might be greater than that in previously reported cases.

Although preoperative diagnosis of intussusception is difficult due to the atypical and non-specific presentation in adults and it is generally determined at laparotomy, it may also be diagnosed by CT, especially in colo-colonic types caused by tumor lesions (17-19). It has been reported that CT is the most sensitive diagnostic test for the confirmation of intussusception with a diagnostic accuracy of 58%-100% (5, 20). Target or sausage shaped lesions as a concentric hyperdense double-ring or bowel-within-bowel appearance are the characteristic signs suggesting intussusception during CT scan, as in our case. Therefore, early radiological investigation should be conducted for differential diagnosis of intestinal obstruction in adults, even in emergent cases suspicious for intussusception. There have been different approaches for the treatment of intussusception in children (21). Pre- or intraoperative reduction or surgical resection depending on the underlying pathology, which should be confirmed as benign, and on clinical presentation can be performed in these patients. However, laparotomy and bowel resection en-bloc without reduction has been advocated as the management strategy in adults due to the

Figure 1. Bowel-within-bowel appearance of colo-colic intussusception (stars) elongating from cecum (arrowhead) to splenic flexure (arrow)

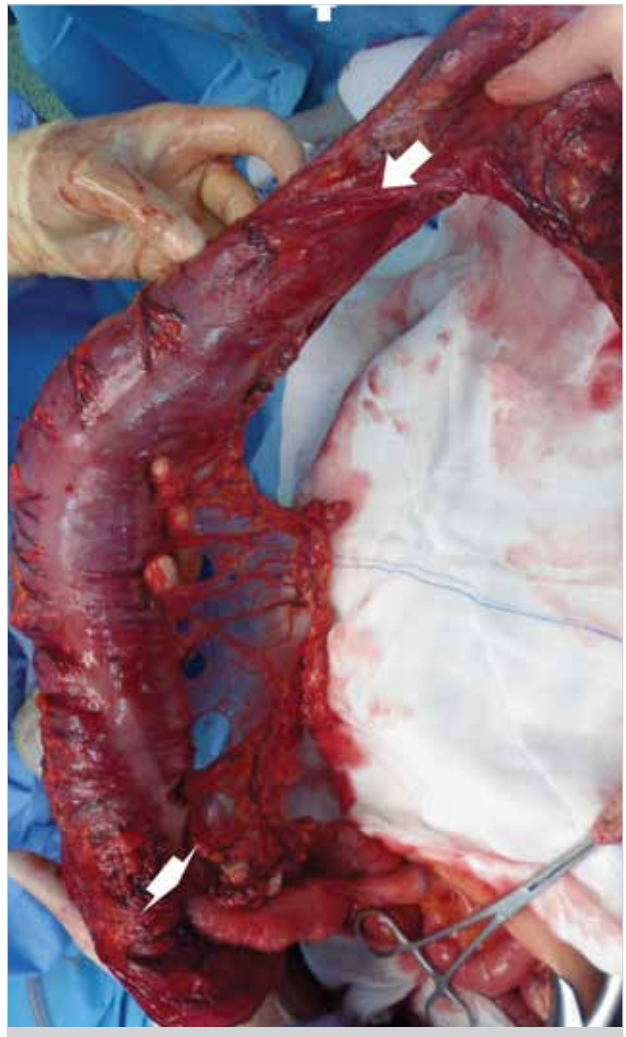


Figure 2. Cecum (arrowhead) to splenic flexure (arrow)

high rate of malignant causes, although the necessity and extent of the resection in each patient has been controversial (18). Intraoperative reduction has also often been discouraged for the fear of causing tumor rupture and potentially upstaging the cancer (8, 17, 22).

CONCLUSION

Although it is a very rare event in adult population, intussusception can be seen in the presence of an underlying pathology including a polyp or malignancy. Enteroenteric small intestinal intussusception is the most common type in adults; however, ileo-colo-colonic intussusception with anal protrusion may occur in the absence of an organic cause. Bowel resection en-bloc without reduction should be offered as the management strategy in adults due to the suspicious malignant causes.

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

Peer-review: Externally peer-reviewed.

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

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

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

REFERENCES

1. Huang BY, Warshauer DM. Adult Intusseption: diagnosis and clinical revelance. Radiol Clin North Am 2003; 41: 1137-1151. [CrossRef]
2. Haas EM, Etter EL, Ellis S, Taylor TV. Adult intussepti on caused by blunt abdominal trauma. J Trauma 1999; 47: 156-157. [CrossRef]
3. Applegate KE. Intussception in children: evidence-based diagnosis and treatment. Pediatr Radiol 2009; 39 (Suppl 2): S140-143. [CrossRef]
4. Lloyd DA, Kenny SE. The surgical abdomen. In: Walker WA, Goulet O, Kleinman RE, et al. editors. Pediatric Gastrointestinal Disease: Pathopsychology, Diagnosis, Management. 4th ed, BC Decker, Ontario; 2004. p. 604-615.
5. Marinis A, Yiallourou A, Samanides L, Dafnios N, Anastasopoulos G, Vassiliou I, et al. Intussusception of the bowel in adults:a review. World J Gastroenterol 2009; 15: 407-411. [CrossRef]
6. Erkan N, Haciyanli M, Yildirim M, Sayhan H, Vardar E, Polat AF. Intussusception in adults: an unusual and challenging condition for surgeons. Int J Colorectal Dis 2005; 20: 452-456. [CrossRef]
7. Ongom PA, Opio CK, Kijjambu SC. Presentation, aetiology and treatment of adult intussusception in a tertiary Sub-Saharan Hospital: a 10-year retrospective study. BMC Gastroenterology 2014, 14: 86. [CrossRef]
8. H Honjo, M Mike, H Kusanagi, N Kano. Adult Intussusception: A Retrospective Review. World J Surg 2015; 39: 134-138. [CrossRef]
9. Sarr MG, Nagorney DM, McIlrath DC. Postoperative intussusception in the adult: a previously unrecognized entity? Arch Surg 1981; 116: 114-148. [CrossRef]
10. Kouladouros K, Gärtner D, Münch S, Paul M, Schön MR. Recurrent intussusception as initial manifestation of primary intestinal melanoma: Case report and literature review. World J Gastroenterol 2015; 21: 3114-3120. [CrossRef]
11. Robertson CG, Due SL, Shimokawa K, Yeow M. Caecal tumor biopsy with a rigid sigmoidoscope - Ileorectal intussusception. Int J Surg Case Rep 2015; 12: 1-3. [CrossRef]
12. Barussaud M., Regenet N., Briennon X. Clinical spectrum and surgical approach of adult intussusceptions: a multicentric study. Int J Colorectal Dis 2006; 21: 834-839. [CrossRef]
13. Siddiqui AA, Glynn C, Harford WV, Lopez J. Cecoanal intussusception in an adult caused by cecal polyp. South Med J 2009; 102: 446-447. [CrossRef]
14. Shinoda M, Hatano S, Kawakubo H, Kakefuda T, Omori T, Ishii S. Adult cecoanal intussusception caused by cecum cancer: report of a case. Surg Today 2007; 37: 802-805. [CrossRef]
15. Redkar RG, Sathe SS, Dalvi AN, Kulkarni BA, Supe AN, Chandrashekhar, et al. Ileo-caeco-colic intussusception due to extensive benign lymphoid hyperplasia of the ileo-caecal region (a case report). J Postgrad Med 1991; 37: 177-178.
16. Kuzmich S, Connelly JP, Howlett DC, Kuzmich T, Basit R, Doctor C. Ileocolocolic intussusception secondary to a submucosal lipoma: an unusual cause of intermittent abdominal pain in a 62-year-old woman. J Clin Ultrasound. 2010; 38: 48-51.
17. Stewardson RH, Bomberk CT, Nyhus LM. Critical operative management of small bowel obstruction. Ann Surg 1978; 187: 189-193. [CrossRef]
18. Mrak K. Uncommon conditions in surgical oncology: acute abdomen caused by ileocolic intussusception. J Gastrointest Oncol. 2014; 5: E75-79.
19. Iko BO, Teal JS, Siram SM, Chinwuba CE, Roux VJ, Scott VF. Computed tomography of adult colonic intussusception: clinical and experimental studies. AJR Am J Roentgenol 1984; 143: 769-772. [CrossRef]
20. Ibrahim D, Patel NP, Gupta M, Fox JC, Lotfipour S. Ileocecal intussusception in the adult population: case series of two patients. West J Emerg Med 2010; 11: 197-200.
21. Pierro A, Donnell SC, Paraskevopoulou C, Carty H, Lloyd DA. Indications for laparotomy after hydrostatic reduction for intussusception. J Pediatr Surg 1993; 28: 1154-1157. [CrossRef]
22. Weilbaecher D, bolin JA, Hearn D, Ogden W 2nd. Intussusception in adults: review of 160 patients. Am J Surg 1971; 121: 531-535. [CrossRef]

Turk J Surg 2018; 34(4): 337-339
DOI: 10.5152/turkjsurg.2017.3468

Case Report

Incidental intestinal malrotation in an adult: Midgut volvulus

Mehmet Tolga Kafadar[1], Aysun Yakut Cengiz[2], Tuğba Çaviş[3], İsmail Bilgiç[4], Işılay Nadir[5]

ABSTRACT

Intestinal malrotation is a developmental anomaly characterized by a midgut fixation disorder and failure to complete its normal fetal rotation around the superior mesenteric artery inside the peritoneal cavity. Malrotation is a rare cause of mechanical intestinal obstruction in adults. It may manifest as an emergency condition or with chronic abdominal symptoms. Although its diagnosis remains difficult, early diagnosis and treatment usually yield favorable outcomes. Intestinal malrotation rarely has an asymptomatic course, in which the diagnosis is usually made incidentally. Multislice computed tomography is quite helpful for making a correct diagnosis. In this study, we reported a 56-year-old patient incidentally who was detected to have intestinal malrotation and was managed symptomatically after presenting at our clinic with signs and symptoms of intestinal obstruction; we also provided a discussion of the relevant literature.

Keywords: Midgut malrotation, volvulus, adult

ORCID ID of the author:
M.T.K. 0000-0002-9178-7843.

Cite this paper as:
Kafadar MT, Cengiz AY, Çaviş T, Bilgiç İ, Nadir I. Incidental intestinal malrotation in an adult: Midgut volvulus. Turk J Surg 2018; 34(4): 337-339

[1]Clinic of General Surgery, Health Sciences University Mehmet Akif İnan Training and Research Hospital, Şanlıurfa, Turkey
[2]Clinic of Radiology, Medical Park Sivas Hospital, Sivas, Turkey
[3]Clinic of Radiology, Atatürk Training and Research Hospital, Ankara, Turkey
[4]Clinic of General Surgery, Ankara Umut Hospital, Ankara, Turkey
[5]Clinic of Gastroenterology, Medical Park Ankara Hospital, Ankara, Turkey

This study was presented at the 13th National Hepatogastroenterology Congress, 27 April-1 May 2016, Antalya, Turkey

Corresponding Author
Mehmet Tolga Kafadar
e-mail: drtolgakafadar@hotmail.com

Received: 26.11.2015
Accepted: 29.12.2015

Available online at
turkjsurg.com

INTRODUCTION

Midgut volvulus is a rare type of malrotation that develops as a result of the rotation of the mesenteric root around the superior mesenteric artery (1). Although it is more common in infants, it can also be encountered in adults. Midgut volvulus possible signs include the whirlpool sign in omphalomesenteric vessels, atypical location of the superior mesenteric artery and vein, and signs of intestinal malrotation. Its incidence has been reported to be one per 500 births in epidemiological studies (2). Herein, we report a 56-year-old patient with an incidental finding of intestinal malrotation presenting with signs of small intestinal obstruction.

CASE PRESENTATION

A 56-year-old man presented with the complaints of abdominal pain, nausea, vomiting, bloating, and inability to pass gas and feces for 3 days. History of patient was remarkable for intermittent abdominal pain. Hemoglobin, white blood cell count, and basic biochemistry panel were all within normal limits. He was administered an oral contrast agent to obtain a whole abdomen computed tomography (CT) scan, which showed a distended stomach filled with the orally administered contrast agent (Figure 1a). The vascular structures and mesentery twisted clockwise (whirlpool sign) at the abdominal midline, and superior mesenteric vein was located to the left of superior mesenteric artery (Figure 1b, c). No sign of necrosis was apparent in intestinal segments. The patient was hospitalized with an initial diagnosis of ileus; his oral intake was stopped and symptomatic treatment was initiated. He began to pass gas and feces 2 days after admission. Having an overall favorable general status, the patient was discharged on day 5. He returned for a follow-up appointment 15 days later when he had no clinical problem. A Magnetic Resonance (MR) enterography was performed, which again showed the whirlpool sign (Figure 2). Informed consent was obtained from the patient who participated in this case.

DISCUSSION

Midgut volvulus is a serious anomaly that develops as a result of narrow attachment of midgut mesentery due to a rotation anomaly, resulting in clockwise twisting of intestinal segments on the superior mesenteric artery axis; it may end up with ischemia and necrosis (1). Normal rotation and fixation events in an embryo occur between the 5th and 12th weeks of gestation. Starting from the 5th week, intestinal development shifts to the interior of the umbilical cord as a result of insufficient space inside the primitive coelomic space. Ultimately, at the 10th embryonic week, intestines return to abdominal cavity and complete their rotation, with the duodenojejunal loop being in the first place. Intestinal malrotation develops as a result of a deficient rotation and fixation of the midgut segment after its passage through the umbilicus and return to coelomic space. Midgut volvulus becomes symptomatic within 1 month after birth in 80% of cases (2).

Figure 1. a-c. (a) Stomach appears distended by filling of its lumen by the orally administered contrast agent. (b) Duodenojejunal junction is located to the right of the midline; the whirlpool sign formed by the proximal jejunal segment and the surrounding mesenteric fat tissue around SMA is seen. (c) SMA (filled arrow) is visualized to the right of SMV (empty arrow)

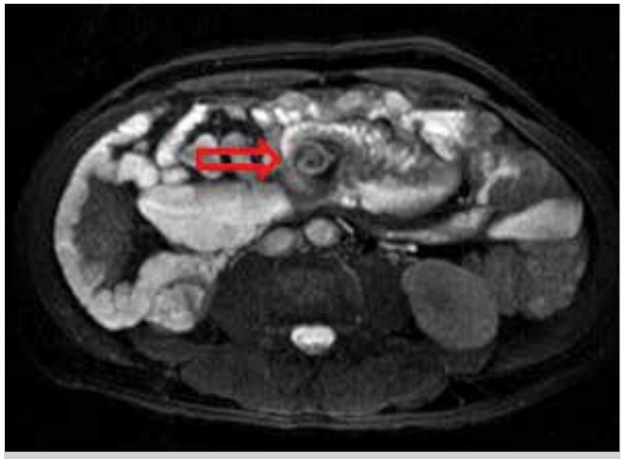


Figure 2. MR Enterography shows the typical whirlpool sign (Axial fat-suppressed T2A sequence)

Midgut volvulus is an extremely rare anomaly in adults. Patients with malrotation may be asymptomatic at an early stage. Some patients may present with chronic, unexplained abdominal discomfort or, more rarely, with acute abdominal pain. These symptoms may be secondary to Ladd's bands causing acute or chronic intestinal obstruction or volvulus (3). History, physical examination, and laboratory examinations are integral to the diagnosis of midgut volvulus. CT, ultrasonography, small intestinal passage films, and MR enterography may reveal the typical signs of midgut volvulus. Edema-induced mural thickening in the duodenum and the location of superior mesenteric vein to the left and anterior to superior mesenteric artery are diagnostic signs (4). Even in our patient, the location of the duodenojejunal junction to the right of the vertebral column, the clockwise malrotation of the mesenteric root (whirlpool sign), and the location of the vascular structures on BT were demonstrated in detail. Our case was interesting with respect to the age of the patient, rotation of mesenteric meso, and the absence of signs of ischemia.

Hanna et al. (5) reported that they initially considered diverticulitis in a patient with signs of acute abdomen due to malrotation; the authors later diagnosed midgut volvulus and a left-sided appendicitis upon the intensification of patient's symptoms, but they could not avoid a delay in diagnosis and management. Our patient also had intermittent symptoms; however, he did not care about these symptoms too much and did not seek for any medical attention owing to the mild nature of symptoms. His diagnosis was thus delayed.

Although many adult patients are symptomatic, the diagnosis may still be delayed owing to the lack of specific symptoms. Many patients with malrotation may suffer incorrect diagnoses and wrong procedures due to these atypical symptoms (6). Patients may also be entirely asymptomatic. Most patients are diagnosed accidentally during an operation or at autopsy. Malrotation cases operated for ileus or acute appendicitis with left lower quadrant pain have been reported (7).

Midgut volvulus can be managed symptomatically or, sometimes, surgically. Patients with this condition are typically considered to be candidates for intestinal obstruction and are associated intestinal necrosis. Thus, some authors have recommended elective laparotomy and Ladd's procedure (6). The aim of the latter, which is the most common intervention performed in malrotation, is to cut Ladd's bands compressing the duodenum and jejunum to relieve small intestine. Other surgical procedures include duodenopexy, cecopexy, and adhesiolysis (8). Complicated volvulus may become fatal unless treated. Liao et al. (9) detected an adult patient with midgut volvulus due to delayed posttraumatic hemorrhagic mesenteric pseudocyst that was treated by urgent surgery. Önder et al. (10) on the other hand, treated a 61-year-old patient with midgut volvulus symptomatically and did not perform surgery. We also did not undertake any surgical intervention, and our patient was relieved by symptomatic treatment and was followed without any problem for 1 month.

CONCLUSION

Intestinal malrotation is a quite rare anomaly in adults, although it is highly important with respect to its potential complications. The possibility of malrotation should not be omitted in patients with non-specific abdominal complaints. Although mostly difficult, diagnosis of malrotation in adults can be possible by considering it in the differential diagnosis of small intestinal obstruction.

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - M.T.K., T.Ç., İ.B.; Design - M.T.K., A.Y.C.; Supervision- M.T.K., İ.B.; Resource - M.T.K., I.N.; Materials - M.T.K., A.Y.C., T.Ç., I.N.; Data Collection and/or Processing - M.T.K., A.Y.C., T.Ç.; Analysis and/or Interpretation - M.T.K.; Literature Search - M.T.K., T.Ç.; Writing Manuscript - M.T.K.; Critical Reviews - M.T.K., İ.B., I.N.

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

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

REFERENCES

1. Papadimitriou G, Marinis A, Papakonstantinou A. Primary midgut volvulus in adults: report of two cases and review of the literature. J Gastrointest Surg 2011; 15: 1889-1892. [CrossRef]
2. Kamal IM. Defusing the intra-abdominal ticking bomb: intestinal malrotation in children. CMAJ 2000; 162: 1315-1317.
3. Gamblin TC, Stephens RE Jr, Johnson RK, Rothwell M. Adult Malrotation: A case report and review of the literature. Curr Surg 2003; 60: 517-520. [CrossRef]
4. Wanjari AK, Deshmukh AJ, Tayde PS, Lonkar Y. Midgut malrotation with chronic abdominal pain. N Am J Med Sci 2012; 4: 196-198. [CrossRef]
5. Hanna T, Akoh JA. Acute presentation of intestinal malrotation in adults: a report of two cases. Ann R Coll Surg Engl 2010; 92: 15-18. [CrossRef]
6. Cohen Z, Kleiner O, Finaly R, Mordehai J. How much of a misnomer is 'asymptomatic' intestinal malrotation? Isr Med Assoc J 2003; 5: 172-174.
7. Goicochea Mancilla C, Diaz Plasencia J, Balmaceda Fraselle T. Intestinal obstruction for malrotation in an adult patient. Report of a case. Rev Gastroenterol Peru 2001; 21: 60-63.
8. Dietz DW, Walsh RM, Grundfest-Broniatowski S, Lavery IC, Fazio VW, Vogt DP. Intestinal malrotation: a rare but important cause of bowel obstruction in adults. Dis Colon Rectum 2002; 45: 1381-1386. [CrossRef]
9. Liao WI, LinYY, Ko KH, Chu SJ, Tsai SH. Midgut volvulus as a delayed consequence of posttraumatic mesenteric pseudocyst. Am J Emerg Med 2009; 27: 1025. [CrossRef]
10. Önder H, Özmen CA, Gümüş M, Ekici F, Bükte Y. Midgut volvulus in an adult patient due to intestinal malrotation. Sakarya Med J 2012; 2: 102-104. [CrossRef]

Turk J Surg 2018; 34(4): 340-341
DOI: 10.5152/turkjsurg.2017.3458

Case Report

An unusual cause of acute abdomen: Post-colonoscopy appendicitis

Mehmet Tolga Kafadar[1], İsmail Bilgiç[2], Seyfi Kartal[3], Sefa Güliter[4]

ABSTRACT

Colonoscopy is commonly performed for diagnostic and therapeutic purposes and has a relatively low morbidity rate. Nevertheless, it is necessary for operators to be aware of the rare complications of colonoscopy due to a large number of procedures performed in daily practice. Acute appendicitis is an unusually rare occurrence after colonoscopy, with no clear association being found between the colonoscopy and acute appendicitis. A rapid diagnosis of this complication is possible by widespread awareness in surgeons regarding this condition. Acute appendicitis cannot be reliably resulted in as the cause of acute abdominal pain due to relatively subtle signs, symptoms, and studies performed for bowel perforation. The diagnosis of postcolonoscopy appendicitis is difficult, and strategies for its treatment show significant variation. This report presents a patient having undergone urgent laparotomy within 12 h after colonoscopy on having signs and symptoms of acute appendicitis-induced peritonitis.

Keywords: Appendicitis, colonoscopy, fecalith

ORCID ID of the author:
M.T.K. 0000-0002-9178-7843.

Cite this paper as:
Kafadar MT, Bilgiç İ, Kartal S, Güliter S. An unusual cause of acute abdomen: Post-colonoscopy appendicitis. Turk J Surg 2018; 34(4): 340-341.

[1]Clinic of General Surgery, Health Sciences University Mehmet Akif İnan Training and Research Hospital, Şanlıurfa, Turkey
[2]Clinic of General Surgery, Ankara Umut Hospital, Ankara, Turkey
[3]Clinic of Anaesthesiology and Reanimation, Health Sciences University Kanuni Training and Research Hospital, Trabzon, Turkey
[4]Clinic of Gastroenterology, Minasera Aldan Hospital, Ankara, Turkey

This study was presented at the 13th National Hepatogastroenterology Congress, 27 April-1 May 2016, Antalya, Turkey.

Corresponding Author
Mehmet Tolga Kafadar
e-mail: drtolgakafadar@hotmail.com

Received: 18.11.2015
Accepted: 19.02.2016

Available online at
turkjsurg.com

INTRODUCTION

The aim of performing colonoscopy is to detect and treat any lesion or pathology in the colon or distal small intestine; its use in clinical practice has witnessed a recent dramatic increase. Colonoscopy is well known to cause intestinal perforation and hemorrhage in some patients, albeit at a very low rate (1). Appendicitis, on the other hand, is much rarer after colonoscopy. Fortunately, a timely and effective intervention is possible when this condition is promptly identified (2). Here we present a 34-year-old man who developed acute abdomen after colonoscopy.

CASE PRESENTATION

A 34-year-old man underwent screening colonoscopy for investigation of iron-deficiency anemia. The patient had an unremarkable bowel preparation and denied any abdominal pain, vomiting, or nausea before the procedure. Colonoscopy was performed according to the standard protocol using a video colonoscope. The endoscope was advanced to the cecum, and the appendix orifice was visualized. No abnormality was found during the colonoscopy, and he underwent colonoscopy without complication. He was observed for 2 h. Over the 2 h, marked abdominal pain developed acutely. Physical examination revealed right lower quadrant tenderness and rebound pain. Blood pressure was 110/70 mmHg, pulse rate was 92/min, and body temperature was 38°C. Laboratory data showed a white cell count of 19.600/mm^3 and CRP of 30.8 mg/L. No free intraabdominal air was identified on erect chest X-ray. There were no signs or symptoms of appendicitis before colonoscopy. Abdominal ultrasonography performed after the patient complained of right lower abdominal pain showed an inflamed appendix. A computed tomography (CT) scan was promptly obtained to investigate other causes of his abdominal pain and an appendix containing fecalith, which distended to 15 mm, was identified (Figure 1). The patient was brought to the surgery room due to presence of acute peritonitis and was found to have a swollen and inflamed appendix (Figure 2) requiring open appendectomy with no additional surgical intervention and drain placement. The surgery was initiated by laparoscopy but converted to open surgery because of retrocecal localization of appendix and difficulty experienced during dissection. The cecum and right colon were inspected and found to be uninjured. The patient was discharged with full recovery 2 days later. Histopathological examination confirmed the diagnosis of acute appendicitis. His postoperative course was unremarkable. Informed consent was obtained from the patient who participated in this case.

DISCUSSION

Colonoscopy offers an effective diagnostic and therapeutic management opportunity for colorectal disorders. Although it is relatively safe, it is not entirely immune to risks. Rare major complications include hemorrhage, colonic perforation, and postpolypectomy syndrome. Minor complications may occur more commonly and include abdominal pain, vomiting, nausea, intestinal spasm, and mucosal tears in the lining of the colon (1).

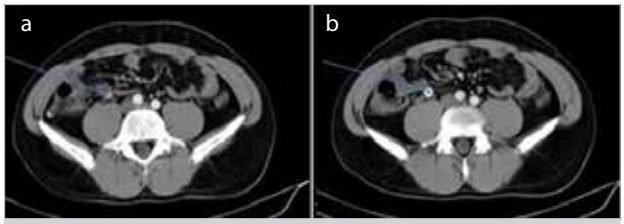


Figure 1. a, b. Axial abdominal CT scan image showing a distended appendix (a) and an intraluminal fecalith (b)

Figure 2. The intraoperative findings revealed acute appendicitis; lumen of the appendix was filled with fecal material

Acute appendicitis postcolonoscopy is an extremely rare occurrence. Appendicitis after colonoscopy was first reported by Houghton and Aston; there are only 12 such cases reported in the medical literature so far (2). Three cases were reported by Vender et al. (3) from two centers with a total volume of 8000 colonoscopies, thus indicating an appendicitis incidence of around 0.038%. This figure is well below that of other complications of colonoscopy, including hemorrhage (0.21%), colonic perforation (0.1%), or abdominal pain (0.09%). However, unfortunately, acute appendicitis is mostly missed because abdominal pain is a common finding after colonoscopy, mostly due to retained gas or colonic spasm after the procedure (1).

Although acute appendicitis after colonoscopy may simply be a coincidence having nothing to do with colonoscopy, Occam's razor may suggest otherwise. Our patient did not have concurrent coincidental appendicitis, as the appendiceal orifice visualized at colonoscopy was normal along with the caecum and terminal ileum, indicating no evidence of inflammatory bowel disease. The pathophysiology of this condition is not completely understood. Based on certain endoscopic features and the timing of occurrence, several theories have been put forward, including barotrauma induced by overinsufflation, direct trauma of appendiceal lumen caused by accidental luminal entry, and pushing feces into the lumen, thereby obstructing the orifice and worsening a previously silent disease or inflammation (4).

Although acute appendicitis is well known for producing abdominal pain, its detection and management are often delayed when it occurs after colonoscopy. This may derive from a symptom set shared with some more common colonoscopy complications such as colonic perforation and postpolypectomy syndrome (5). Therefore, radiological imaging is important for making the correct diagnosis. Another reason may be the unawareness of such a complication after colonoscopy.

Sometimes, multiple mechanisms may be operational in the development of this complication; this holds especially true when patients have some anatomical or immunological abnormalities creating a tendency for inflammation, which is further corroborated by the preparatory phase of the procedure or the procedure itself. Our patient had no previous disorder creating any tendency for an appendiceal disease, and the clinical presentation was consistent with a newly occurring appendicitis 2 h after the colonoscopy procedure; we therefore suggest that our procedure cause the complication by forcing a fecalith into the appendiceal lumen. Our theory was confirmed by a preoperative CT scan that showed appendicoliths as well as the postoperative pathology report stating the same finding. While CT is helpful to diagnosis, lack of inflammatory alterations in the appendiceal lumen in the early stages of the condition often preclude the optimal use of this modality (6).

Most patients affected by postcolonoscopy appendicitis are treated by open appendectomy, and the laparoscopic approach is another alternative. Laparotomy may be preferred to avoid colonoscopic bowel perforation and intraabdominal sepsis. Considering appendicitis as a potential complication may have allowed a laparoscopic approach in the beginning. Delayed identification of this condition may prevent early appendectomy from being performed with an associated increase in the complication rate (7).

CONCLUSION

Appendicitis is an important, albeit fairly rare, complication of colonoscopy, and it can easily lead to diagnostic confusion with other potential complications. While a rapid diagnosis allows timely intervention and improved outcomes, delays in detection may result in serious adverse events. It is therefore vital for clinicians to keep in mind that appendicitis is a potential cause of abdominal pain after colonoscopy.

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - M.T.K., İ.B.; Design - M.T.K., S.K.; Supervision - M.T.K., İ.B., S.G.; Resource - M.T.K., S.K.; Materials - M.T.K., İ.B.; Data Collection and/or Processing - M.T.K., S.G.; Analysis and/or Interpretation - M.T.K., İ.B.; Literature Search - M.T.K., S.K.; Writing Manuscript - M.T.K.; Critical Reviews - M.T.K., İ.B., S.G.

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

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

REFERENCES

1. Viiala C, Zimmerman M, Cullen DJ, Hoffman NE. Complication rates of colonoscopy in an Australian teaching hospital environment. Intern Med J 2003; 33: 355-359. [CrossRef]
2. Houghton A, Aston N. Appendicitis complicating colonoscopy. Gastrointest Endosc 1988; 34: 489. [CrossRef]
3. Vender R, Larson J, Garcia J, Topazian M, Ephraim P. Appendicitis is a rare complication of colonoscopy. Gastrointest Endosc 1995; 41: 514-516. [CrossRef]
4. Shaw D, Gallardo G, Basson MD. Post-colonoscopy appendicitis: A case report and systematic review. World J Gastrointest Surg 2013; 5: 259-263. [CrossRef]
5. Takagi Y, Abe T. Appendicitis following endoscopic polypectomy. Endoscopy 2000; 32: S49.
6. Bildzukewicz NA, Weinstein MS. Appendicitis following virtual colonoscopy: a case report. J Gastrointest Surg 2012; 16: 2291-2293. [CrossRef]
7. Mason RJ, Moazzez A, Sohn H, Katkhouda N. Meta-analysis of randomized trials comparing antibiotic therapy with appendectomy for acute uncomplicated (no abscess or phlegmon) appendicitis. Surg Infect (Larchmt) 2012; 13: 74-84. [CrossRef]

Turk J Surg 2018; 34(4): 342-345
DOI: 10.5152/turkjsurg.2017.3203

Case Report

Spontaneous perforation of pyometra: A rare cause of acute abdomen and sepsis

Şener Balas[1], Kerim Bora Yılmaz[1], Seray Akçalar Yıldırım[2], Bilgihan Açıkgöz[3], İdil Güneş Tatar[2], Bahattin Bayar[1], Melih Akıncı[1], Oskay Kaya[1]

ABSTRACT

Pyometra, the accumulation of purulent material in the uterine cavity, is a rare gynecological condition whose etiology is impaired drainage of the uterine cavity. It is uncommon in premenopausal age and occurs mainly in older and postmenopausal women. Clinical signs of pyometra are vaginal discharge, postmenopausal bleeding, and lower abdominal pain. An 87-year-old woman was admitted to our emergency department with abdominal pain, fever, and vomiting. The results of physical examination revealed rebound tenderness and muscular rigidity in the lower abdomen. Ultrasonography demonstrated free fluid in the abdomen, and percutaneous aspiration revealed that this fluid was purulent. A computed tomography scan showed a large amount of free fluid in the abdominal cavity and a uterine myoma. The patient underwent emergency laparotomy due to acute abdomen. During the laparotomy, a 2x1 cm perforation was seen at the fundus of the uterus. The patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy. A culture of the pus grew Escherichia coli. Histopathological examination revealed degenerative uterine myoma with no evidence of malignancy. Pathological results indicated myometrial suppurative inflammation along with neutrophilia and necrosis. Pyometra is a rare event; however, it must be considered when investigating acute abdomen etiology. Because pyometra involves abscess formation, drainage and evacuation of the uterine cavity while leaving a drain in the cavity and dilating the cervical canal is the main treatment protocol. In cases of perforation, hysterectomy is the treatment choice; however, with concomitant diseases in older patients, immediate surgery is related to important morbidity and mortality risks.

Keywords: Acute abdomen, pyometra, sepsis, uterine perforation

ORCID IDs of the authors:
K.B.Y. 0000-0002-5514-4103;
M.A. 0000-0001-8719-6584;
O.K. 0000-0002-1864-896X;
B.A. 0000-0003-4837-8187;
İ.G.T. 0000-0003-2499-4532.

Cite this paper as:
Balas Ş, Yılmaz KB, Akçalar Yıldırım S, Açıkgöz B, Güneş Tatar İ, Bayar B, et al. Spontaneous perforation of pyometra: A rare cause of acute abdomen and sepsis. Turk J Surg 2018; 34(4): 342-345.

[1]Clinic of General Surgery, Health Science University Dışkapı Yıldırım Beyazıt Research and Training Hospital, Ankara, Turkey
[2]Clinic of Radiology, Health Science University Dışkapı Yıldırım Beyazıt Research and Training Hospital, Ankara, Turkey
[3]Clinic of Pathology, Health Science University Dışkapı Yıldırım Beyazıt Research and Training Hospital, Ankara, Turkey

This study presented at the 20th National Surgical Congress, 13-17 April 2016, Antalya, Turkey.

Corresponding Author
Kerim Bora Yılmaz
e-mail: borakerim@yahoo.com

Received: 13.02.2016
Accepted: 06.05.2016

Available online at
turkjsurg.com

INTRODUCTION

Pyometra, the accumulation of purulent material in the uterine cavity, represents 0.038% of gynecologic admissions; its etiology is impaired drainage of the uterine cavity (1). It is uncommon in premenopausal age and occurs mainly in older and postmenopausal women. The classical clinical signs of pyometra are vaginal discharge, postmenopausal bleeding, and lower abdominal pain (2). The etiology of the uterus perforation is blockage of natural drainage due to stenotic cervix, which results in a degenerative or necrotic change in the pyometra (3, 4). This perforation is related to diffuse peritonitis and causes acute surgical abdomen with free intra-abdominal air.

Herein, we report an a patient presenting with abdominal pain and generalized peritonitis caused by perforation of pyometra without malignancy.

CASE PRESENTATION

An 87-year-old woman was admitted to our emergency department with abdominal pain, fever, and vomiting lasting approximately two days. The patient had a history of diabetes and hypertension, and the patient was immobilized and permanently bedridden for two years due to pelvic trauma and poor general condition. Her gynecological history was unremarkable, and she had no vaginal bleeding or increased discharge. The results of a physical examination revealed rebound tenderness, muscular rigidity in the lower abdomen, and distention. Her body temperature was 38.4 °C, her pulse rate was 112 beats/min, and her blood pressure was 140/70. Laboratory studies on admission demonstrated a white cell count of 5000/mm^3 with 83.6% neutrophilia and hemoglobin 11.3. A plain chest x-ray showed no free air under the diaphragm and no intestinal obstruction sign. Ultrasonography demonstrated free fluid at the iliac fossa/pelvis; percutaneous aspiration revealed that this fluid was purulent, with no relationship to gastrointestinal tract perforation or bile fistula.

A computed tomography (CT) scan of the abdomen with intravenous contrast showed a large amount of free fluid in the abdominal cavity and a uterine myoma with a diameter of 77x58 mm (Figure 1a). Computed tomography (CT) with an intravenous injection of contrast material showed an enlarged and distended uterus with a breach at the uterine fundus. A dilated endometrial cavity with hypodense fluid collection was suggestive of pyometra. Due to perforated pyometra, multiple pelvic and intra-abdominal fluid collec-

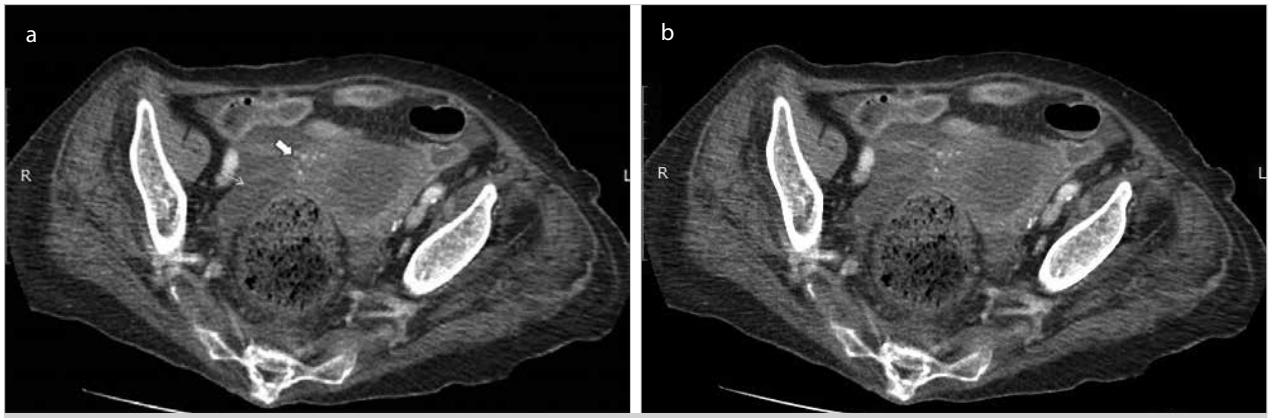


Figure 1. a, b. Axial (solid arrow) (a) and arrow (b) show contrast-enhanced CT images obtained through the midportion of the uterus showing a distended endometrial cavity with perforation at the fundus in the right side (solid arrow), presence of collected fluid within the pelvic cavity (arrow)

Figure 2. Uterus with perforation on the anterior wall

tions were observed in the CT scan (Figure 1b). The patient underwent emergency laparotomy due to acute abdomen. During the laparotomy, a 2x1 cm perforation was seen at the fundus of the uterus (Figure 2). There was one liter of purulent material in the abdomen. The patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy. A culture of the pus grew *Escherichia coli*. Histopathological examination revealed degenerative uterine myoma with no evidence of malignancy. Pathological results indicated myometrial suppurative inflammation with neutrophilia and necrosis (Figure 3). Postoperatively, the patient was monitored in the surgical intensive care unit, as septic shock required inotropic support for five days. The patient had wound problems that required vacuum-assisted closure; after that, she recovered and was discharged at the 28th postoperative day after providing informed consent.

DISCUSSION

Pyometra is a rare event; however, it must be considered when investigating acute abdomen etiology, and emergency physicians must be aware of ruptured pyometra. Although it is a rare condition, it carries morbidity and mortality risks. In the English literature between 1985 and 2015, only 68 cases of pyometra perforation were reported; 38 of these cases did not originate from a malignancy, similar to our report (5). Because of canal stenosis, the uterus enlarges progressively with degenerative changes until the uterine contents finally spill into the abdominal cavity with perforation (6). Pyometra is related to a general etiology of benign or malignant gynecologic tumors, radiation cervicitis, atrophic cervicitis, congenital anomalies, intrauterine devices, and traumatic damage to the cervix (7). If the pyometra is related to malignancy and perforation of the uterus, the prognosis is very poor and bears significant morbidity and mortality risks (8).

In the literature, the median age of ruptured pyometra was 73.8; in geriatric women with concomitant diseases, the mortality rate is 25% to 40% (5, 6, 9). For these septic geriatric patients, emergency conditions and surgery require resuscitation and management of respiration as well as circulation in the intensive care unit and long hospital stays, as in the case of the patient reported in this study. Immunocompromised state has been documented as a high risk for perforation; these patients also have a higher mortality risk (6).

The clinical signs and emergency department admission of pyometra patients are due to acute abdomen. However, a significant percentage of patients with unruptured pyometra are asymptomatic (10). Additionally, due to the nonspecific symptoms associated with rupture, early and accurate diagnosis of perforation is limited. Accurate preoperative diagnoses were obtained for only 21% of ruptured pyometra patients (5). Acute abdomen symptoms such as abdominal pain, vomiting, and fever predominate at admission, while gynecological symptoms such as vaginal bleeding or discharge occur in fewer than 10% of cases (11, 12). The initial diagnosis of the disease can be mistaken as gastrointestinal perforation because of the pneumoperitoneum; however, definitive diagnosis of the disease is sometimes obtained intra-operatively (13). Radiological findings of contrast-enhanced CT are important in diagnosis, along with findings of the presence of fluids in

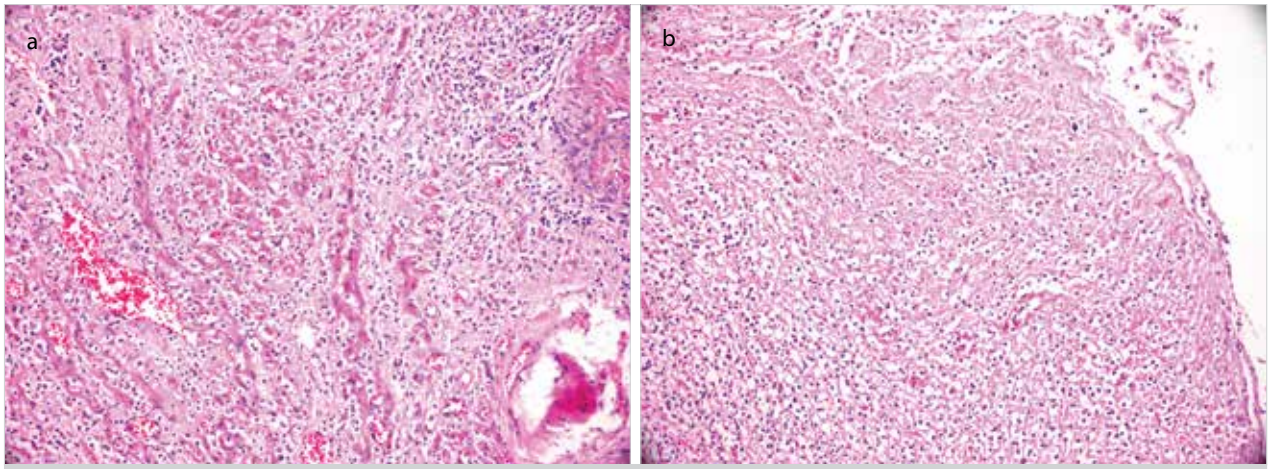


Figure 3. a, b. Pathological results showing myometrial suppurative inflammation with neutrophilia and necrosis

the uterus, defects of the uterine wall, and intraperitoneal fluid collection (14). Free air in the peritoneal cavity and the uterine cavity due to gas-forming organisms are reasons to suspect ruptured pyometra (5). Some reporters illustrate the importance of transvaginal ultrasound to accurate preoperative diagnosis (5, 11). In the absence of gynecological symptoms in most cases, sonography may be adequate to illustrate fluid accumulation in the cavity (11).

Pyometra involves abscess formation; drainage and evacuation of the uterine cavity is the main treatment protocol, along with placing a drain in the cavity and dilating the cervical canal (8, 15). Persistent pyometra requires repeated drainage and dilatation. In cases of perforation, hysterectomy is the treatment choice, with peritoneal lavage and abscess drainage (2). In some reports, the authors suggest management by total abdominal hysterectomy with bilateral salpingo-oophorectomy; however, subtotal or supravaginal hysterectomy, drainage alone, and surgical closure of the perforated uterine wall have been reported in different cases (6, 11).

The pathological results of pyometra are related to the etiology of the disease. Benign tumors, spread of malignance from the endocervix, and endometrial cancer are usually associated with pyometra, and xanthogranulomatous inflammation is also reported in surgical specimens (16, 17). The necrotic nature of the uterine tissue with pyometra sometimes requires frozen section examination.

Treatment of pyometra includes broad spectrum antibiotics against aerobic and anaerobic bacteria. Occasionally, upon microbiological examination, *Escherichia coli*, *Bacteroides fragilis*, *Streptococcus* spp. and *Pseudomonas aeruginosa* are isolated (18, 19). Similar to published reports, in our case, culture of the pus grew *Escherichia coli*; this is the most common infectious agent. Source control with surgery is important in the resuscitation of septic conditions due to peritonitis.

CONCLUSION

Pyometra perforation is a rare cause of acute abdomen. In older patients with concomitant diseases, immediate laparotomy, peritoneal lavage, and hysterectomy are associated with important morbidity and mortality risks. Sepsis, septic shock, and multiple organ failure may be encountered in clinical presentation due to bacteremia. These acute conditions require intensive care. Accurate and early diagnosis with proper treatment can reduce the mortality and morbidity of pyometra.

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - Ş.B., K.B.Y., M.A.; Design - O.K., İ.G.T., Ş.B.; Supervision - B.B., O.K., B.A.; Resource - B.B., İ.G.T., B.A.; Materials - K.B.Y., Ş.B., M.A.; Data Collection and/or Processing - B.B., S.A.Y., İ.G.T., B.A.; Analysis and/or Interpretation - Ş.B., O.K., M.A.; Literature Search -K.B.Y., B.B., Ş.B., S.A.Y.; Writing Manuscript - Ş.B., K.B.Y., M.A.; Critical Reviews - O.K., İ.G.T., S.A.Y.

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

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

REFERENCES

1. Chan LY, Lau TK, Wong SF, Yuen PM. Pyometra. What is its clinical significance? J Reprod Med 2001; 46: 952-956.
2. Yildizhan B, Uyar E, Sişmanoğlu A, Güllüoğlu G, Kavak ZN. Spontaneous perforation of pyometra. Infect Dis Obstet Gynecol 2006; 2006: 1-3. [CrossRef]
3. Sujatha VV, Babu GS. Spontaneous perforation of uterine pyometra -A case report and review of literature. Apollo Medicine 2013; 10: 248-250. [CrossRef]
4. Chan LY, Yu VS, Ho LC, Lok YH, Hui SK. Spontaneous uterine perforation of pyometra. A report of three cases. J Reprod Med 2000; 45: 857-860.
5. Uno K, Tano S, Yoshihara M, Mayama M, Ukai M, Kishigami Y, et al. A Case Report and Literature Review of Spontaneous Perforation of Pyometra. J Emerg Med 2016; 16: S0736-4679(16)00036-6.
6. Kitai T, Okuno K, Ugaki H, Komoto Y, Fujimi S, Takemura M. Spontaneous uterine perforation of pyometra presenting as acute abdomen. Case Rep Obstet Gynecol 2014; 2014: 738568. [CrossRef]
7. Lien WC, Ong AW, Sun JT, Tsai MT, Lai TI, Liu YP, et al. Pyometra: a potentially lethal differential diagnosis in older women. Am J Emerg Med 2010; 28: 103-105. [CrossRef]
8. Lim SF, Lee SL, Chiow AK, Foo CS, Wong AS, Tan SM. Rare cause of acute surgical abdomen with free intraperitoneal air: Spontaneous perforated pyometra. A report of 2 cases. Am J Case Rep. 2012; 13: 55-57. [CrossRef]

9. Ikeda M, Takahashi T, Kurachi H. Spontaneous perforation of pyometra: a report of seven cases and review of the literature. Gynecol Obstet Invest 2013; 75: 243-249. [CrossRef]
10. Nuamah NM, Hamaloglu E, Konan A. Spontaneous uterine perforation due to pyometra presenting as acute abdomen. Int J Gynaecol Obstet 2006; 92: 145- 146. [CrossRef]
11. Yamada T, Ando N, Shibata N, Suitou M, Takagi H, Matsunami K, et al. Spontaneous perforation of pyometra presenting as acute abdomen and pneumoperitoneum mimicking those of gastrointestinal origin. Case Rep Surg 2015; 2015: 548481. [CrossRef]
12. Shapey IM, Nasser T, Dickens P, Haldar M, Solkar MH. Spontaneously perforated pyometra: an unusual cause of acute abdomen and pneumoperitoneum. Ann R Coll Surg Engl 2012; 94: 246-248. [CrossRef]
13. Ou YC, Lan KC, Lin H, Tsai CC, Chang Chien CC. Clinical characteristics of perforated pyometra and impending perforation: specific issues in gynecological emergency. J Obstet Gynaecol Res. 2010; 36: 661-666. [CrossRef]
14. Izumi J, Hirano H, Yoshioka H, Takisawa J. Computed tomography findings of spontaneous perforation of pyometra. Jpn J Radiol 2010; 28: 247-249. [CrossRef]
15. Chuang CJ, Hung YC, Hsieh MC, Hsu CS. Huge asymptomatic pyometra with an intrauterine device. Taiwan J Obstet Gynecol 2013; 52: 426- 427. [CrossRef]
16. Liao CY, Chiu CH, Luo FJ. Xanthogranulomatous inflammation of myometrium with uterine perforation. Taiwan J Obstet Gynecol 2013; 52: 428- 430. [CrossRef]
17. Babarinsa IA, Campbell OB, Adewole IF. Pyometra complicating cancer of the cervix. Int J Gynaecol Obstet 1999; 64: 75-76. [CrossRef]
18. Chao A, Wang AM, Wang TH, Wu TI, Chao AS. An atypical and fatal case of pyometra accompanied by the superficial spread of squamous cell carcinoma of the endometrium and the fallopian tubes. Taiwan J Obstet Gynecol. 2013; 52: 440-442. [CrossRef]
19. Tai CC, Lien WC, Wang HP, Liu KL. Early diagnosis of gas-forming pyometra in an aged patient can prevent mortality. Am J Emerg Med. 2007; 25: 126-127. [CrossRef]

Turk J Surg 2018; 34(4): 346-348
DOI: 10.5152/UCD.2016.3151

Case Report

Primary paraspinal lumbar hydatid disease: A known diagnosis in an unusual localization

Fatma Ceren Sarıoğlu[1], Yeliz Pekçevik[1], Hilal Şahin[1], Eyüp Kebapçı[2], Emel Ebru Pala[3]

ABSTRACT

Hydatid disease is a parasitic infection caused by Echinococcus granulosus. Although the liver and lung are the most common sites of hydatid disease, it can also be seen in other organs due to migration via systemic circulation. Paraspinal lumbar hydatid disease without the involvement of other organs is extremely rare. We aimed to present the imaging and histopathological findings of a case with painful lumbar swelling that was later diagnosed as primary lumbar paraspinal hydatid disease. Hydatid disease should be considered as the differential diagnosis in patients with a lumbar paraspinal mass, particularly that containing multiple well-defined, round, small cysts, and in patients living in or traveling to endemic regions.

Keywords: Hydatid disease, intramuscular, paraspinal muscles, magnetic resonance imaging

ORCID IDs of the authors:
F.C.S. 0000-0002-6714-2367;
Y.P. 0000-0003-1421-3376;
H.Ş.0000-0001-8726-8998;
E.K. 0000-0003-1967-2789;
E.E.P. 0000-0001-7262-1867.

Cite this paper as:
Sarıoğlu FC, Pekçevik Y, Şahin H, Kebapçı E, Pala E. Primary paraspinal lumbar hydatid disease: a known diagnosis in an unusual localization. Turk J Surg 2018; 34(4): 346-348.

[1]Department of Radiology, İzmir Tepecik Training and Research Hospital, İzmir, Turkey
[2]Department of General Surgery, İzmir Tepecik Training and Research Hospital, İzmir, Turkey
[3]Department of Pathology, İzmir Tepecik Training and Research Hospital, İzmir, Turkey

This study was presented at the TMRD (Turkish Society of Magnetic Resonance) 20th Congress, 21-23 May 2015, Ankara, Turkey.

Corresponding Author
Yeliz Pekcevik
e-mail: yelizpekcevik@yahoo.com

Received: 25.03.2015
Accepted: 07.06.2015

Available online at
turkjsurg.com

INTRODUCTION

Hydatid disease (HD) is a parasitic infection caused by *Echinococcus granulosus*. Although the liver (50%-70%) and lung (20%-30%) are the most common sites of HD, it can also be seen in other organs (e.g., the brain, heart, orbital, kidney, urinary bladder, and thyroid gland) due to migration via systemic circulation (1). Paraspinal HD without the involvement of other organs is extremely rare (0.5%-3%) because muscles produce lactic acid, which results in an unsuitable environment for hydatid cysts that need oxygen for growing (1, 2). The psoas muscle and lumbar paraspinal muscles are the most common locations of paraspinal HD (3-5).

We aimed to present imaging and histopathological findings of a case with painful lumbar swelling that was later diagnosed as primary lumbar paraspinal HD.

CASE PRESENTATION

A 51-year-old woman presented with swelling in the left lumbar region. The patient complained of slowly growing swelling in the lumbar region and noticed pain and tenderness since the last 1 week. Patient's medical history and physical examination and laboratory test findings were unremarkable. Ultrasonography of the patient demonstrated a mass with cystic and solid portions. Magnetic resonance (MR) imaging of the lesion (1.5 T, Achieva; Philips Medical Systems, Best, the Netherlands) showed a well-defined mass that was located in the lumbar paraspinal muscles. The mass was hypointense on T1-weighted images (Figure 1a), was hyperintense on T2-weighted images (Figure 1b), and showed only peripheral enhancement after the injection of gadolinium contrast media (Figure 1c). There was no spinal or intraspinal extension. Although the lumbar paraspinal muscle is not a common location of HD, because of imaging findings, particularly multiple well-circumscribed small cysts resembling daughter cysts, the differential diagnosis was suggested to be HD. A serological test was performed and was found to be negative for HD. The negative serology did not exclude the diagnosis, and therefore, surgical excision was considered. After complete resection of the soft tissue mass, macroscopic evaluation of the intramuscular mass with round vesicles was indicative of HD (Figure 2). Microscopic examination showed the cuticular membranes of the hydatid cysts and the outer fibrous capsule (Figure 3).

DISCUSSION

We present a case with primary lumbar paraspinal HD that had some diagnostic findings. Although the liver and lung (20%-30%) are the most common sites of HD, it can also be seen in other organs due to migration via systemic circulation (1). Paraspinal HD without the involvement of other organs is extremely rare (0.5%-3%), and the psoas muscle and lumbar paraspinal muscles are the most common locations of paraspinal HD (2, 4, 6).

Ultrasonography can be the first modality to be chosen in the diagnosis of HD. The sensitivity of ultrasonography is 95%, and if vesicular membranes are present, the sensitivity can be up to 100%. However, in the paraspinal region, it cannot evaluate the extent of the disease and relationship between

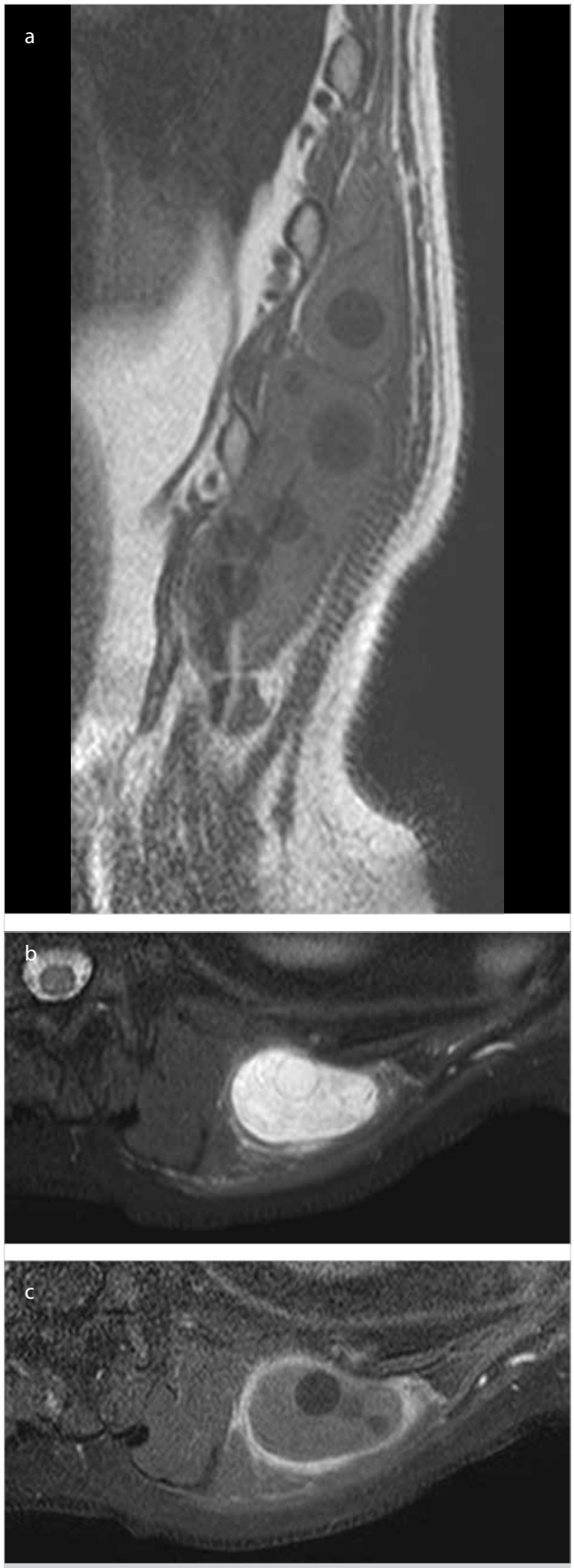


Figure 1. a-c. (a) Sagittal T1-weighted and (b) axial T2-weighted fat-suppressed images show a well-defined paraspinal mass in the left lumbar region with small, well-circumscribed, round cysts. (c) On axial post-contrast fat-suppressed T1-weighted image, the lesion shows peripheral enhancement

Figure 2. Macroscopic evaluation demonstrates intramuscular mass with round vesicles

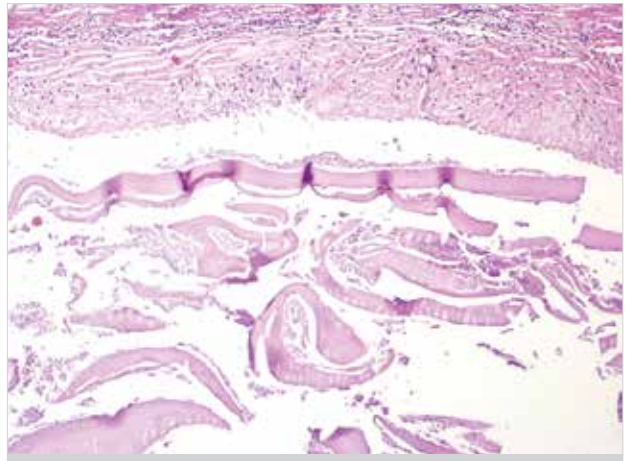


Figure 3. Photomicrograph of microscopic examination of the lesion after surgical resection (H&E×100) shows cuticular membranes of the hydatid cysts and outer fibrous capsule

the mass and the spine. Computed tomography may be performed in suspicious cases to demonstrate the presence of HD or the relationship with adjacent organs before surgery. Its sensitivity has been reported to be 85% (3, 4).

Magnetic resonance imaging can reveal most imaging findings of HD, with the exception of calcifications. Paraspinal HD is usually hypointense on T1-weighted images and hyperintense on T2-weighted images. It shows peripheral enhancement of the pseudocapsule after the intravenous injection of gadolinium contrast media (4). The most striking

finding that helps to differentiate HD from other soft tissue tumors in the paraspinal region is the presence of multiple well-defined, round cysts in the lesion (1-4). This finding was also suggestive of the presence of HD in our patient. The diagnosis can be supported by serological tests. Specific immunoglobulin G (IgG), complement fixation, and indirect fluorescent tests as well as enzyme-linked immunosorbent assay (ELISA) can be used. These tests are more sensitive in the detection of liver cysts than in the detection of cysts located in other organs (5). It is important to know that although positive serological test results are suggestive of the presence of HD, negative test results do not exclude the diagnosis (5, 6). Paraspinal HD may be treated surgically and with anti-infective drug treatment (5).

CONCLUSION

Our findings demonstrate that HD should be considered in the differential diagnosis of lumbar paraspinal masses. HD should be considered in patients with a lumbar paraspinal mass, particularly that containing multiple well-defined, round, small cysts, and in patients living in or traveling to endemic regions.

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - F.C.S., Y.P., H.Ş., E.K., E.E.P.; Design - F.C.S., Y.P., H.Ş., E.K., E.E.P.; Supervision - F.C.S., Y.P., H.Ş.; Resource - F.C.S., Y.P., H.Ş., E.K., E.E.P.; Materials - F.C.S., Y.P., H.Ş., E.K., E.E.P.; Data Collection and/or Processing - F.C.S., Y.P., H.Ş.; Analysis and/or Interpretation - F.C.S., Y.P., H.Ş.; Literature Search - F.C.S., Y.P., H.Ş.; Writing Manuscript - F.C.S., Y.P.; Critical Reviews - F.C.S., Y.P., H.Ş., E.K., E.E.P.

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

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

REFERENCES

1. Arkun R, Mete BD. Musculoskeletal hydatid disease. Semin Musculoskelet Radiol 2011; 15: 527-540.[CrossRef]
2. Brunetti E, Kern P, Vuitton DA. Expert consensus for the diagnosis and treatment of cystic and alveolar echinococcosis in humans. Acta Trop 2010; 114: 1-16. [CrossRef]
3. Merkle EM, Schulte M, Vogel J, Tomczak R, Rieber A, Kern P, et al. Musculoskeletal involvement in cystic echinococcosis: report of eight cases and review of the literature. AJR Am J Roentgenol 1997; 168: 1531-1534. [CrossRef]
4. Pedrosa I, Saiz A, Arrazola J, Ferreiros J, Pedrosa CS. Hydatid disease: radiologic and pathologic features and complications. Radiographics 2000; 20: 795-817. [CrossRef]
5. Sakamoto FA, Winalski CS, Golden KL, Ready JE. Painful left thigh mass. Skeletal Radiol 2014; 43: 61-62. [CrossRef]
6. Tatari H, Baran O, Sanlidağ T, Göre O, Ak D, Manisali M, Havitçioğlu H. Primary intramuscular hydatidosis of supraspinatus muscle. Arch Orthop Trauma Surg 2001; 121: 93-94. [CrossRef]

Turk J Surg 2018; 34(4): 349-350
DOI: 10.5152/turkjsurg.2018.4319

Editorial Comment on "Could local antibiotics be included in the treatment of acute anal fissure?"

Pankaj Garg

I read the article by Karapolat (1) with great interest and congratulate the author for conducting a randomized controlled trial on such a relevant topic. Because we have conducted extensive and pioneering work in the conservative treatment of fissure-in-ano [Local and Oral Antibiotics with Avoidance of Constipation (LOABAC)](2, 3), we would like to add few points and share our experience.

There is a reason that antibiotics are effective in providing relief in patients with fissure-in-ano. The deepening of the fissure mostly due to persistent trauma of hard stools leads to the formation of a subcutaneous tract in which indolent sub-clinical infection gets superimposed (2-4). This is much more likely to happen in patients with chronic fissure-in-ano. Therefore, although the authors used the LOABAC concept in acute fissure-in-ano, it is even more effective in chronic fissure-in-ano (2, 3).

Like several other chronic diseases, fissure-in-ano has also been categorized into three types (2): acute (spasm present, duration <6 weeks), chronic (spasm absent, duration >6 weeks), and acute-on-chronic (spasm present, duration >6 weeks)(2). This classification explains the pathophysiology of fissure-in-ano in a simpler manner. Acute fissure-in-ano is abrupt in onset and occurs most commonly due to trauma by a hard fecalith. Marked spasm due to severe pain is usually the main complaint. Chronic fissure-in-ano is a long-developing illness with lesser intense pain and minimal spasm. The main symptoms (mild to moderate pain, burning, and itching) in chronic fissure-in-ano are due to low-grade infection. Any superimposed insult to the anoderm by a hard fecalith in a patient with chronic fissure-in-ano leads to the development of acute-on-chronic fissure-in-ano (2).

This classification simplifies the treatment. For the acute component (main issue: hypertonicity/spasm), the primary treatment is sphincter relaxation (sitz bath plus diltiazem cream)(2, 3). For the chronic component (main issue: low-grade infection), the primary treatment is antibiotics (local plus oral). For acute-on-chronic fissure-in-ano, both sphincter relaxation and antibiotics are very effective (2, 3).

Lateral internal sphincterotomy (LIS) is considered a safe and gold-standard surgery for the treatment of fissure-in-ano. However, a recent meta-analysis of LIS with long-term follow-up (>2 years) showed an incontinence rate of 14% (5). Therefore, the importance and necessity of the non-surgical management of fissure-in-ano cannot be undermined.

In our experience with 505 patients over the last 6 years, LOABAC (local antibiotic cream-metronidazole + povidine-iodine locally for 1 month, oral course of antibiotics-Ciprofloxacin 500 mg + Ornidazole 500 mg twice a day for 5 days, and avoidance of constipation) cured >90% of patients with chronic fissure-in-ano (2, 3). Topical nifedipine/diatiazem and sitz bath were prescribed when there was associated spasm in patients with acute or acute-on-chronic fissure-in-ano (2, 3). Botulinum toxin was needed in only two patients in whom the spasm did not get relieved after LOABAC treatment. The only patients who required surgery were the ones in whom the fissure had deepened into a small intersphincteric fistula. Once a deep tract had formed, conservative treatment was not effective.

To conclude, a vast majority of all patients with fissure-in-ano can perhaps be treated without surgical intervention. Like any other surgery, surgery for fissure-in-ano (LIS) has its side effects. Therefore, surgery should be reserved for a minority of patients with fissure-in-ano who do not respond to medical management.

Peer-review: Externally peer-reviewed.

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

ORCID ID of the author:
P.G. 0000-0002-0800-3578.

Cite this paper as:
Garg P. Editorial Comment on "Could local antibiotics be included in the treatment of acute anal fissure?". Turk J Surg 2018; 34(4): 349-350.

Department of Colorectal Surgery, Garg Fistula Research Institute, Panchkula, India

Corresponding Author
Pankaj Garg
e-mail: drgargpankaj@yahoo.com

Received: 25.09.2018
Accepted: 12.10.2018

Available online at
turkjsurg.com

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

REFERENCES

1. Karapolat B. Could local antibiotics be included in the treatment of acute anal fissure? Turk J Surg 2018: 1-4.
2. Garg P, Lakhtaria P, Gupta V. Oral Plus Local Antibiotics Significantly Reduce the Need for Operative Intervention in Chronic Anal Fissure: a Novel Finding. Indian J Surg 2018; 80: 415-20. [CrossRef]
3. Garg P. Local and Oral Antibiotics with Avoidance of Constipation (LOABAC) Treatment for Anal Fissure: a New Concept in Conservative Management. Indian J Surg 2016; 78: 80. [CrossRef]
4. Pelta AE, Davis KG, Armstrong DN. Subcutaneous fissurotomy: a novel procedure for chronic fissure-in-ano. a review of 109 cases. Dis Colon Rectum 2007; 50: 1662-7. [CrossRef]
5. Garg P, Garg M, Menon GR. Long-term continence disturbance after lateral internal sphincterotomy for chronic anal fissure: a systematic review and meta-analysis. Colorectal Dis 2013; 15: e104-17. [CrossRef]

Retraction Notice

DOI: 10.5152/turkjsurg.2018.151118

Retraction Notice

The following article is retracted from publication in the Turkish Journal of Surgery by decision of editors of the journal since it is a duplicate publication, which has been previously published in Clin Surg 2017; 2: 1677.

Duplicate publication

Effect of postoperative ischemia on steroid hormone receptors and c-erbB-2 levels in breast cancer tissue.

Mehmet Saydam, İbrahim Yılmaz

Department of General Surgery, Dıskapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey

Turk J Surg 2018

DOI: 10.5152/turkjsurg.2018.4001

Original publication

The Effect of Postoperative Ischemia on Steroid Receptors and C-Erbb-2 Levels in Breast Cancer Tissue

Mehmet Saydam* and Ibrahim Yilmaz

Department of General Surgery, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara/Turkey

Clin Surg 2017; 2: 1677

Reviewer List

Acar Aren
Ahmet Çınar Yastı
Ahmet Tekin
Ali İlker Filiz
Bekir Kuru
Betül Bozkurt
Beyza Özçınar
Cumhur Yeğen
Cüneyt Kayaalp
Ersin Öztürk
Ethem Alhan
Gökhan İçöz
Gürsel Soybir
Hasan Karanlık
Hüsnü Alptekin
Koray Topgül
Levent Yeniay
Levent Avtan
Levhi Akın
Mehmet Eryılmaz
Mehmet Kurtoğlu
Nuri Gönüllü
Ömer Alabaz
Ömer Yerci
Öner Menteş
Özer Makay
Serap Erel
Tamer Akça
Tevfik Küçükkartallar
Turgut İpek
Uğur Bengisun
Zeki Yılmaz