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AIMS AND SCOPE

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

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

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

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

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

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

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INSTRUCTIONS TO AUTHORS

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

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

In addition to being accountable for the parts of the work he/she has done, an author should be able to identify which co-authors are responsible for other specific parts of the work. In addition, authors should have confidence in the integrity of the contributions of their co-authors.

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

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 responsibility for authorship during the submission and review stages of the manuscript.

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

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

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

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Authors are required to submit the following:

- Copyright Transfer Form,

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- 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, which should include:

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

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

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

Manuscript Types

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

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

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

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

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

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

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

Human Subjects Research

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

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

Animal Research

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

Table 1. Limitations for each manuscript type

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

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

Tables

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

Figures and Figure Legends

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

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

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

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

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

References

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

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

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

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

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

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

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

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

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

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

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

REVISIONS

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

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

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FROM THE EDITOR'S DESK
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In Memorium: Prof. Dr. Cemalettin Topuzlu

With deep regret and sadness, we report the death of Professor Cemalettin Topuzlu, founder of the Turkish Journal of Surgery (priorly Ulusal Cerrahi Dergisi), who served as the Editor-in-Chief between 1985-2005 (Figure 1). First, I would like to express my sincere condolences to the Topuzlu Family.

Dr. Cemalettin Topuzlu was born in 1939 in İstanbul. His grandfather, Dr. Cemil Topuzlu was a prominent figure in Turkish medicine as well as politics. Dr. Cemil Topuzlu was among the pioneers in the history of Turkish surgery and performed the world's first intraoperative arterial suturing (1). Just like his grandfather, Dr. Cemalettin Topuzlu had pursued a long professional and academic career with very remarkable achievements.

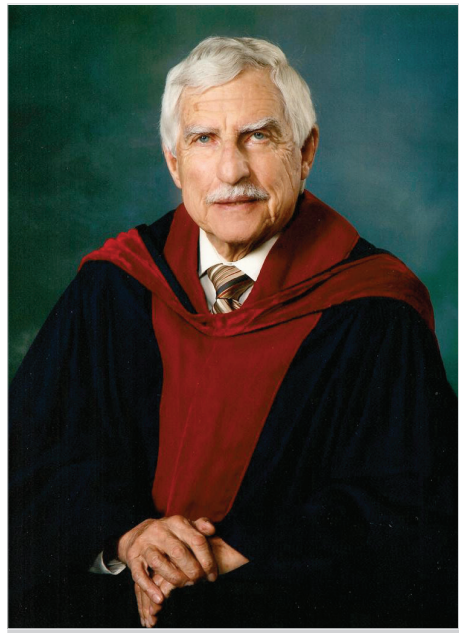


Figure 1. Prof. Dr. Cemalettin Topuzlu (1939-2022).

He graduated from İstanbul University, Faculty of Medicine in 1962 (the first prize-Yaman Egeli award). He completed his surgical residency in University of Vermont, Department of Surgery, U.S.A in 1967. Subsequently, he was appointed as Instructor and later as Assistant Professor of surgery and co-chairman of the surgical research laboratory in the same institution.

Throughout those years, he was closely involved with experimental surgical research principally in "renal function in obstructive jaundice", "functional aspects of lymph nodes", "physiology of blunt chest trauma" and "micro-surgical repair of peripheral nerves". He published several landmarking articles in leading surgical and medical journals (2-6). He was the recipient of some prizes from American Cancer Society (1967), South East Surgical Congress New Orleans (gold paper award, 1969) and the Eczacıbaşı Foundation (1971) (7).

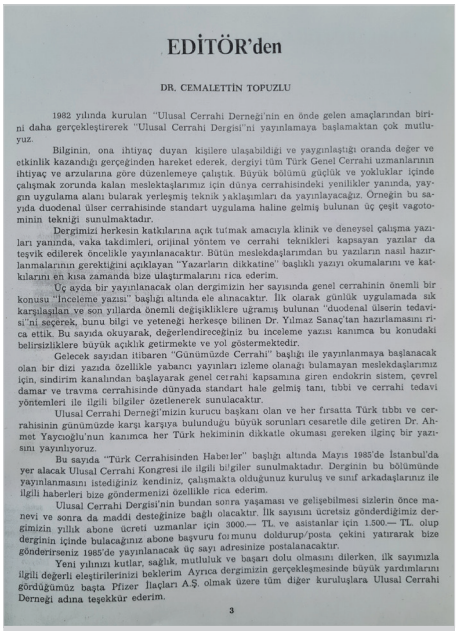
Dr. Topuzlu was not only a very good surgeon but also the founder and an active member of several academic organizations. He was one of the Founders and past Vice President of the Turkish Surgical Society and the Founder of the American College of Surgeons Turkish Chapter (2004). Between 1971-2006, he served in different academic and administrative positions in Ege, Marmara and Istanbul Universities. His main interests were breast surgery and medical student teaching.

Among these great achievements, I would like to stress once again his important role, as the Founder and Chief Editor of the "Turkish Journal of Surgery" between 1985-2005. Dr. Topuzlu was greatly passionate of medical publishing. His first editorial for Turkish Journal of Surgery -37 years ago- is a great example of his precise work that he performed before launching a whole new journal (Figures 2 and 3).

I had the privilege to take part of a session about medical publishing that Dr. Topuzlu co-chaired during the 22th Turkish National Congress (23th-27th March 2022). All the audience and I were absolutely amazed about his high experience and passion about medical publishing. As the current editor of Turkish Journal of Surgery, I can only promise to give my best to improve this -already 37 year-old- journal with my great respect to our founder editor Dr. Cemalettin Topuzlu.

As you all know, Turkish Journal of Surgery is being published in English but I would like to bid farewell to Dr. Topuzlu with a few last words in our native language Turkish.

Figure 2. Ulusal Cerrahi Dergisi (Turkish Journal of Surgery): The cover of the first issue (January 1985).



EDİTÖR'den

DR. CEMALETTİN TOPUZLU

1982 yılında kurulan "Ulusal Cerrahi Derneği"nin en önde gelen amaçlarından birini daha gerçekleştirerek "Ulusal Cerrahi Dergisi"ni yayınlamaya başlamaktan çok mutluyuz.

Bilginin, ona ihtiyaç duyan kişilere ulaşabildiği ve yaygınlaştığı oranda değer ve etkinlik kazandığı gerçeğinden hareket ederek, dergiyi tüm Türk Genel Cerrahi uzmanlarının ihtiyaç ve arzularına göre düzenlemeye çalıştık. Büyük bölümü güçlük ve yokluklar içinde çalışmak zorunda kalan meslektaşlarımız için dünya cerrahisindeki yenilikler yanında, yaygın uygulama alanı bularak yerleşmiş teknik yaklaşımları da yayınlayacağız. Örneğin bu sayıda duodenal ülser cerrahisinde standart uygulama haline gelmiş bulunan üç çeşit vagotominin tekniği sunulmaktadır.

Dergimizi herkesin katkılarına açık tutmak amacıyla klinik ve deneysel çalışma yazıları yanında, vaka takdimleri, orijinal yöntem ve cerrahi teknikleri kapsayan yazılar da teşvik edilerek öncelikle yayınlanacaktır. Bütün meslekdaşlarımdan bu yazıların nasıl hazırlanmalarının gerektiğini açıklayan "Yazarların dikkatine" başlıklı yazıyı okumalarını ve katkılarını en kısa zamanda bize ulaştırmalarını rica ederim.

Üç ayda bir yayınlanacak olan dergimizin her sayısında genel cerrahinin önemli bir konusu "İnceleme yazısı" başlığı altında ele alınacaktır. İlk olarak günlük uygulamada sık karşılaşılan ve son yıllarda önemli değişikliklere uğramış bulunan "duodenal ülserin tedavisi"ni seçerek, bunu bilgi ve yeteneği herkesçe bilinen Dr. Yılmaz Sanaç'tan hazırlamasını rica ettik. Bu sayıda okuyarak, değerlendireceğiniz bu inceleme yazısı kanımca bu konudaki belirsizliklere büyük açıklık getirmekte ve yol göstermektedir.

Gelecek sayıdan itibaren "Günümüzde Cerrahi" başlığı ile yayınlanmaya başlanacak olan bir dizi yazıda özellikle yabancı yayınları izleme olanağı bulamayan meslekdaşlarımız için, sindirim kanalından başlayarak genel cerrahi kapsamına giren endokrin sistem, çevrel damar ve travma cerrahisinde dünyada standart hale gelmiş tanı, tıbbi ve cerrahi tedavi yöntemleri ile ilgili bilgiler özetlenerek sunulacaktır.

Ulusal Cerrahi Derneği'mizin kurucu başkanı olan ve her fırsatta Türk tıbbı ve cerrahisinin günümüzde karşı karşıya bulunduğu büyük sorunları cesaretle dile getiren Dr. Ahmet Yaycıoğlu'nun kanımca her Türk hekiminin dikkatle okuması gereken ilginç bir yazısını yayınlıyoruz.

Bu sayıda "Türk Cerrahisinden Haberler" başlığı altında Mayıs 1985'de İstanbul'da yer alacak Ulusal Cerrahi Kongresi ile ilgili bilgiler sunulmaktadır. Derginin bu bölümünde yayınlanmasını istediğiniz kendiniz, çalışmakta olduğunuz kuruluş ve sınıf arkadaşlarınız ile ilgili haberleri bize göndermenizi özellikle rica ederim.

Ulusal Cerrahi Dergisi'nin bundan sonra yaşaması ve gelişebilmesi sizlerin önce manevi ve sonra da maddi desteğinize bağlı olacaktır. İlk sayısını ücretsiz gönderdiğimiz dergimizin yıllık abone ücreti uzmanlar için 3000.— TL ve asistanlar için 1.500.— TL olup derginin içinde bulacağınız abone başvuru formunu doldurup posta çekini yatırarak bize gönderirseniz 1985'de yayınlanacak üç sayı adresinize postalanacaktır.

Yeni yılınızı kutlar, sağlık, mutluluk ve başarı dolu olmasını dilerken, ilk sayımızla ilgili değerli eleştirilerinizi beklerim. Ayrıca dergimizin gerçekleşmesinde büyük yardımlarını gördüğümüz başta Pfizer İlaçları A.Ş. olmak üzere tüm diğer kuruluşlara Ulusal Cerrahi Derneği adına teşekkür ederim.

3

Figure 3. The first editorial of Dr. Topuzlu in the issue January 1985.

"Sevgili Cemalettin Hocam,

Sizin tam 37 yıl önce kurmuş olduğunuz Ulusal Cerrahi Dergisi'ni yaşatmak, geliştirmek ve uluslararası alanda daha da ileri noktalarda taşımak her zaman en büyük hedefimiz. Koltuğunuzda oturuyor olmanın hem onurunu hem de büyük sorumluluğunu hissediyorum. Umarım bu görevi genç meslektaşlarınız olarak layıkıyla başarabiliriz.

Nurlar içinde yatın!"

Kindest regards,

Kaya SARIBEYOĞLU

Editor-in-Chief
Turkish Journal of Surgery

P.S. I wish to express my sincere gratitude to the Topuzlu Family for providing the documents and images.

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ORIGINAL ARTICLE
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Turkish HPB Surgery Association consensus report on hepatic cystic *Echinococcosis* (HCE)

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ABSTRACT

Objective: Cystic *Echinococcosis* (CE) is one of the important problems of the Eurasian region. We aimed to prepare a consensus report in order to update the treatment approaches of this disease. This study was conducted by Turkish HPB Surgery Association.

Material and Methods: This study was conducted with the modified Delphi model. For this purpose, we conducted a three-stage consensus-building approach.

Results: Six topics, including diagnosis, medical treatment, percutaneous treatment, surgical treatment, management of complications and posttreatment follow-up and recurrences in HCE were discussed.

Conclusion: The expert panel made recommendations for every topic.

Keywords: Liver, cystic echinoncoccus, expert consensus

INTRODUCTION

Cystic *Echinococcosis* (CE) is one of the important problems of the Eurasian region that has been waiting for a solution for years. It is basically a public health issue. There has been an increase in the number of clinical cases in recent years. Despite the expansion of the health system in Turkey in recent years and the provision of health services to more people and the improvement of sanitation services, there is an increase in CE cases. This increase in the number of cases is attributed to the early detection of most asymptomatic cases. One other important reason of the increase of CE cases is that Turkey hosts too many immigrants from neighboring countries. While CE of the liver (Hepatic CE-HCE) was treated only in some centers where advanced surgical treatment was performed years ago, it can now be treated in many centers in Turkey thanks to developing facilities, medical technologies and trained personnel. Many centers have renewed their infrastructure to treat this disease with the most up-to-date approaches. Therefore, we decided to prepare a consensus report in order to update the treatment approaches of these centers and to assist in the standardization between centers. This study was conducted by Turkish HPB Surgery Association.

MATERIAL and METHODS

This study was conducted with the modified Delphi model. For this purpose, we conducted a three-stage consensus-building approach:(1) identifying the list of topics for inclusion based on literature review and the study team's experience; (2) a two-round modified Delphi exercise with a panel of experts to establish consensus

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on the importance of these features; and (3) a small in-person consensus group meeting to create options-recommendations about every topic included to the study.

Panel Selection

Turkish Association of HPB Surgery executive committee selected 34 specialists as committee members for the development of this consensus report. These specialists were selected according to their literature reports, number of ongoing cases, and clinical and surgical experience about HCE. Twelve of them were selected as authors. Authors addressed six topics, including diagnosis, medical treatment, percutaneous treatment, surgical treatment, management of complications and posttreatment follow-up and recurrences in HCE. These topics were selected according to the literature. An ongoing debate was the key point for selection of the topics. Two experts for every topic were assigned and they have performed a literature review and recommendations.

The remaining 22 specialists were assigned as expert panel members for the development of further Delphi processes. The literature review and recommendations created by the authors were evaluated and criticized by this expert panel. After the first and second Delphi rounds, a third in-person meeting was performed and the final options for every topic were created. Levels of recommendations given in this document follow the "Guide to Practice Guidelines" of the Infectious Diseases Society of America (1) (Table 1).

Exclusion/Inclusion Criteria

A literature search for every topic covering the same dates was made. For this purpose, a search was performed including the Pubmed database for English publications and the TR Index-Ulakbim database for Turkish publications. Keywords for Pubmed search were "*Echinococcal cysts, hydatid cysts, hydatid disease, cystic Echinococcosis, hydatidosis, hydatid*" and for Turkish literature search in the TR Index-Ulakbim database "kist hidatik" (hydatid cyst). Additional keywords were used for every single topic according the choices of the authors. Preliminary search results were filtered for human studies, original reports, reviews and meta-analyses and studies reporting liver involvement. Animal studies, case reports and articles reporting only extra-hepatic involvement were excluded.

RESULTS

All authors created their own search for their topic. After they performed their review, they set recommendations for each topic. These reviews and recommendations were sent to the expert panel. The expert panel reviewed every recommendation and sent the results back to the authors. This was the first round of the modified Delphi procedure. The authors revised the recommendations according to the reviews and votes of the panel and sent them to the expert panel for a second round. After the second-round results were collected, an in-person meeting was performed for the establishment of final recommendations. Expert panel voted every recommendation in every round. Recommendations that were accepted below 50% of the expert panel were withdrawn. Recommendations that were accepted between 50-80% of the expert panel were revised. Recommendations that were accepted by over 80% of the panel were assigned as recommendation.

The reviews and recommendations for every topic are summarized below;

Chapter 1. Diagnosis of HCE

A literature search on the subject, covering the dates 01.01.1900-09.12.2018, was carried out using the Pubmed database for English publications and the TR Index-Ulakbim database for Turkish publications. Pubmed search with the keywords "*Echinococcal* cysts, hydatid cysts, hydatid disease, cystic *Echinococcosis*, hydatidosis, hydatid, classification, diagnosis" revealed a total of 6599 articles. Of these, 5466 were in English, and 3697 were on humans. After excluding 1858 case reports, 1839 articles were included in the preliminary evaluation. Of these 1839 articles, 53 were clinical

Table 1. Infectious Diseases Society of America grading system (strength of recommendation and quality of evidence)

Strength of recommendation	
A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Poor evidence to support a recommendation
D	Moderate evidence to support a recommendation against use
E	Good evidence to support recommendation against use
Quality of evidence	
I	Evidence from ≥1 properly randomized, controlled trial
II	Evidence from ≥1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies; from multiple time series; or from dramatic results from uncontrolled experiments
III	Evidence from recommendations of respected authorities, based on clinical experience, descriptive studies, or reports of committees

trials (20 controlled, 16 randomized controlled) and 394 were Reviews. After excluding articles that did not contain liver involvement, did not relate to the diagnosis of cystic *Echinococcosis* or were not adequately included in the diagnosis, the study evaluated 15 clinical trial articles and 61 reviews.

A total of 503 articles were found in the Turkish literature search using the keyword "kist hidatik" (hydatid cyst) in the TR Index-Ulakbim database. Of these, 477 were related to medicine. After excluding the articles that did not include liver involvement, were not related to the diagnosis of cystic *Echinococcosis*, or insufficiently related to the diagnosis, a total of 26 Turkish articles were evaluated within the scope of the study.

1.1. Clinical findings

The diagnosis of CE is based on clinical findings, imaging modalities, and serological examinations. Direct evaluation of the cyst content aspirated by percutaneous puncture or obtained by surgery with microscopic, histological, and molecular methods can also confirm the diagnosis (2). Up to 60% of the patients are asymptomatic (3). Symptoms and signs that arise with the growth of the cyst over time are nonspecific. The most common symptom is abdominal pain in liver involvement and cough in lung involvement (4,5). Clinical findings depend on the complications that may occur depending on the localization and size of the cyst. Complications such as direct compression of the cyst, inflammatory reaction, distortion of neighboring organs and structures, rupture of the bile duct, pleural space, bronchial tree or peritoneal cavity, infection of the cyst, cholangitis, and pancreatitis may occur. Rupture of the cyst can cause allergic reactions. In the clinical evaluation of patients, it should also be questioned whether they are exposed to the risk of CE (living in an endemic area or having migrated from an endemic area, having a dog, or being in contact with wildlife) (6-8)

1.2. Ulrasound

Radiological imaging is one of the key components in the diagnosis of HCE. US is the primary imaging modality as it can detect pathognomonic findings for diagnosis, has a sensitivity of 88-98% and a specificity of 93-100%, is easily accessible, and is radiation-free (9,10). US has also been used in the classification of HCE, and the standardized classification proposed by the WHO Informal Working Group on *Echinococcosis* (WHO-IWGE) in 2003 is still used (11). US also plays an important role in interventional treatment methods (9,12). It can also be used in community health screenings with its portable feature, high sensitivity, and specificity (13).

1.3. Classification of HCE

In uncomplicated HCE cases, current treatment recommendations follow a stage-specific approach. The cyst type is the most critical determinant of the treatment method to be selected (11,14).

1.4. Role of calcification in HCE classification

Hosch W et al. have followed up 78 CE patients treated with albendazole and a watch-and-wait approach (15). US and, in some cases, additional CT imaging was used in the follow-up. A total of 137 abdominal cysts (116 in the liver) were present in the patients, and calcification was detected in the cyst wall and/or cyst content in 67 *Echinococcal* cysts (48.9% of all cysts). Of the 67 calcified cysts, only 23 were compatible with CE 5 and 18 with CE 4 (46.2% of all CE 4 cysts). In the cyst content-based classification of the remaining 26 patients, one CE 1 (7.1% of all CE 1 cysts), 8 CE 2 (47.1% of all CE 2 cysts), and 17 CE 3 (40.5% of all CE 3 cysts) were detected. During follow-up, progressive involution was observed in two CE 2 cysts, 7 CE 3 cysts, and 5 CE 4 cysts, while a poor course was observed in the form of re-fluid collection in the main cyst and/or new daughter cysts in 5 CE 3 cysts.

1.5. CT and MR imaging

CT and MR imaging are indicated for the subdiaphragmatic location of the cyst, metastatic disease, complicated cyst (abscess, cystobiliary fistula), and preoperative evaluation (2). Obesity, intestinal gases, and postoperative changes are other conditions in which the US is inadequate, and CT and MR imaging are indicated. CT and MR are also used in cases with no pathognomonic findings on US, and differential diagnosis is required (9). While MR imaging (especially T2-weighted sequences) shows very good compatibility with the US in CE 1-CE 4 types, it has shortcomings in identifying the details of the cyst wall in CE 5. On the other hand, CT shows poor performance in CE 1-CE 4 types, while it performs satisfactorily in CE 5 compared to US (16). MRI is also better than CT in visualizing the liquid areas within the matrix structure of the cyst and is preferred to CT whenever possible (17).

1.6. Serological tests

Due to limitations in sensitivity and specificity, serological tests often yield up to 30% false-negative and 25% false-positive results. Therefore, the role of serology in the diagnosis of CE is limited to supporting or confirming the diagnosis rather than being a diagnostic test. Many factors that affect the performance of serological tests have been identified. The most important factors are; the measurement techniques used and the antigens used within, the patient's immune status, the organ involved, the stage, size and number of the cyst, and previous treatment and complications (3,6,9,18). Primary serological tests are:

- ELISA (enzyme-linked immunosorbent assay).
- IHA (indirect hemagglutination)
- LA (latex agglutination)
- IFA (immunofluorescence assay)
- IEP (immunoelectrophoresis) tests.

The generally accepted sensitivity of primary serological tests is 85-98% for liver cysts, 50-60% for lung cysts, and 90-100% for multi-organ involvement (2). It is recommended to use at least two of these primary tests together to improve the performance of serological tests (2,3,19,20). Another recommendation for performance is to use the WB (Western Blot) test as a secondary confirmatory test due to its high specificity of up to 100% (2,6,21-24). It is possible to find different results for each technique in the literature due to the aforementioned factors, especially the type of antigen used in the test (18,25-29).

Detection of antigens in the serum is not preferred in the serological diagnosis of CE due to its low sensitivity of 35% despite its high specificity, and most of the tests are based on the detection of antibodies against antigens in the serum (18). The most commonly used antigen source for this purpose in tests is hydatid cyst fluid (HCS). Overall, HCS provides higher sensitivity (80-99% sensitivity and 60-97% specificity), while tests in which the purified main antigenic structures of Antigen 5 (Ag5) and Antigen B (AgB) or their smaller subunits or their recombinant forms and synthetic peptides are used as antigens provide higher specificity (33-93% sensitivity and 80-100% specificity) (27-30). A double-blind, randomized study on this subject compared the diagnostic performances of HCS, natural AgB, two recombinant AgB subunits, an AgB-derived synthetic peptide, and recombinant cytosolic malate dehydrogenase (EgMDH) in the ELISA method (31). Equivalent diagnostic accuracy was found with HCS, AgB, and AgB8/1 subunit, respectively, of 81.4%, 81.3%, and 81.9%, while synthetic peptide, AgB8/2 subunit, and EgMDH yielded an accuracy of 76.8%, 69.1%, and 66.8%, respectively, and HCS was recommended as the antigen source for the primary serological test (31).

When serological tests were evaluated according to the CE stage, 30-58% false negatives were found in CE 1, 50-87% in CE 4 and CE 5, while this rate was lower in CE 2 and CE 3 with 5-20% (32). False-positive results may be associated with cross-reactions in other parasitic diseases such as alveolar *Echinococcosis*, cysticercosis, fascioliasis, and filariasis, as well as malignancy and chronic immune disorders (6).

1.7. Direct diagnostic methods

In cases where diagnosis cannot be made by clinical, radiological, and serological methods, differential diagnosis can be achieved by direct examination of the aspirated cyst content. Diagnosis can be made by direct microscopic examination by detecting protoscolex and/or free hooks. Histological examination of laminar and germinative membranes is also diagnostic (2,6,9). Another direct diagnostic method is the detection of nucleic acids specific for E. granulosus with molecular biology methods such as Southern blot and PCR (Polymerase Chain Reaction) (2,33). Despite positive experiences with PAIR, diagnostic aspiration and biopsy remain controversial. Anaphylaxis, secondary dissemination, and the risk of tumor seeding during the differential diagnosis in malignant cases are stated as important drawbacks of the procedure (34-36).

1.8. Differential diagnosis of HCE and HAE

The differential diagnosis of HCE and HAE is usually made radiologically. In cases where this is impossible, serological tests should be used. The AgB a 8kDa subunit examined for HCE is also common to HAE, and the WB test performed is positive in 92% of HCE cases and 79% of HAE cases. On the other hand, serological tests Em2-ELISA, Em2^{plus}-ELISA, Em10-ELISA, Em18-ELISA, and Em18-Immunoblot used for HAE have high sensitivity and specificity (90-100% and 95-100%, respectively). In cases where a differential diagnosis cannot be achieved with radiological and serological methods, direct diagnostic methods (direct microscopic examination, histological examination, and PCR) can be used (2,6,9,33,37-39).

Table 2 demonstrates case definition of CE in the article "Expert consensus for the diagnosis and treatment of cystic and alveolar *Echinococcosis* in humans" published by WHO-IWGE in 2010 (2).

In light of the above literature, the following recommendations were formed;

Recommendation 1.1: Most patients are asymptomatic and diagnosed incidentally in radiological examinations performed for other reasons. Since clinical findings are non-specific, HCE should be considered, especially in endemic areas, and radiological imaging should be performed in suspected cases.

Recommendation 1.2: US is the first imaging modality of choice in the diagnosis of HCE. It is diagnostic in cases with pathognomonic signs (CE 1, CE 2, CE 3a, and CE 3b). In uncertain cases, additional diagnostic methods are needed.

Recommendation 1.3: Classification should also be made during the diagnosis of HCE; our treatment approach will be determined accordingly.

Recommendation 1.4: Calcification is also possible in CE 1, CE 2, and CE 3 cysts. Calcification is not reliable for predicting the activity of the cyst. Viability assessment is more reliable with evaluating cyst content rather than wall calcification.

Recommendation 1.5: CT and/or MR imaging are indicated in cases where the patient is obese or has excess intestinal gases, in cases of subdiaphragmatic localization of the cyst or metastatic disease, in cases requiring preoperative and postoperative evaluation, in cases without pathognomonic findings in the US that require differential diagnosis, and in cases of complicated HCE. When CT or MR imaging is required to diagnose HCE, MR has a superior imaging potential and is preferred to CT.

Recommendation 1.6: Negative serological tests do not exclude diagnosis. False negativity may occur due to lack of standardization of the antigens used in serological tests and labo-

Table 2. Case definition of CE in the article "Expert consensus for the diagnosis and treatment of cystic and alveolar echinococcosis in humans" published by WHO-IWGE in 2010

A. Clinical criteria	**B. Diagnostic criteria**	**C. Possible versus probable versus confirmed case**
At least one of the following three: 1.A slowly growing or static cystic mass(es) (signs and symptoms vary with cyst location, size, type and number) diagnosed by imaging techniques. 2. Anaphylactic reactions due to ruptured or leaking cysts. 3. Incidental finding of a cyst by imaging techniques in asymptomatic carriers or detected by screening strategies.	1. Typical organ lesion(s) detected by imaging techniques (e.g. US, CT-scan, plain film radiography, MR imaging) 2. Specific serum antibodies assessed by high-sensitivity serological tests, confirmed by a separate high specificity serological test 3.Histopathology or parasitology compatible with cystic echinococcosis (e.g. direct visualization of the protoscolex or hooklets in cyst fluid) 4.Detection of pathognomonic macroscopic morphology of cyst(s) in surgical specimens.	Possible case. Any patient with a clinical or epidemiological history, and imaging findings or serology positive for CE Probable case. Any patient with the combination of clinical history, epidemiological history, imaging findings and serology positive for CE on two tests. Confirmed case. The above, plus **either** (1) demonstration of protoscoleces or their components, using direct microscopy or molecular biology, in the cyst contents aspirated by percutaneous puncture or at surgery, or (2) changes in US appearance, e. g. Detachment of the endocyst in a CE1 cyst, thus moving to a CE3a stage, or solidification of a CE2 or CE3b, thus changing to a CE4 stage, after administration of ABZ (at least 3 months) or spontaneous.

ratories, the patient's immune status, the organ, type and size of the cyst, etc. A single primary serological test is unreliable to exclude false positives; at least two primary tests should be considered together. If the two primary tests are not positive together, results should be confirmed with WB.

Recommendation 1.7: In cases where US findings are compatible with HCE but not pathognomonic, additional radiological imaging should be performed together with serological tests.

Recommendation 1.8: In cases that cannot be diagnosed by clinical, radiological, and serological methods, a direct diagnostic approach with aspiration may rarely be required for differential diagnosis. In the differential diagnosis, the application should be limited due to the risk of anaphylaxis, secondary dissemination, and tumor seeding in cases of malignancy.

Recommendation 1.9: The "CE case definition" section in the article "Expert consensus for the diagnosis and treatment of cystic and alveolar *Echinococcosis* in humans" published by WHO-IWGE in 2010 is suitable for clinical applications in the light of current information (Table 2).

Recommendation 1.10: The differential diagnosis of HCE and HAE is usually made radiologically. In cases where this is impossible, specific serological tests should be performed for HAE. In cases where a differential diagnosis cannot be achieved with radiological and serological methods, cyst aspiration and/or FNAB can be performed for direct diagnosis (direct microscopic examination, histological examination, and PCR).

All recommendations in this chapter had a Strength of recommendation: B Quality of Evidence: III

Chapter 2. Medical Treatment in HCE

The relevant literature was searched using the Pubmed database, covering 01.01.1900 and 18.03.2018. In Pubmed search, two columns were chosen as keywords. In the first one, the words "albendazole OR mebendazole OR praziquantel OR drug OR drugs OR medical OR benzimidazole* OR flubendazole" were searched in the title, abstract, and keywords of the articles (n= 9633333). In the second column, articles with the words "(*Echinococ** OR hydati*) AND (liver OR hepatic)" in the title were searched (n= 3517). The combination of both columns revealed a total of 963 studies. Narrowing these down to studies that included words in the first column in their title revealed 87 studies. No distinction was made between them in terms of date or language.

A total of 503 articles were found in the Turkish literature search using the keyword "kist hidatik" (hydatid cyst) in the TR Index-Ulakbim database. Of these, 477 were related to medicine. After excluding the articles that did not include liver involve-

ment and were not related to medical treatment in cystic *Echinococcosis*, a total of 17 Turkish articles were evaluated within the scope of the study.

Points to be clarified about drug use in the treatment of cystic *Echinococcosis* (CE) in the liver:

2.1. Drugs used in the treatment of HCE, medicines that have not entered clinical use, drug doses, and drug combinations

The drugs used in the treatment of HCE are mainly benzimidazole group drugs. The drug that first came into use is mebendazole. However, Albendazole has become the primary drug used over time due to its greater effectiveness. Albendazole is determined to be effective in the germinative layer. Its sulfoxide (SO) metabolite is more effective than albendazole itself. Intra-cyst concentrations of Albendazole were also found to be more important than blood levels. It was also revealed that there was no significant difference between the intra-cystic and blood levels of the drug. However, it was noted that intra-cyst concentrations could not be predicted from blood concentrations. Besides, hepatic localization of the cyst and the calcification of its wall were found to cause higher drug concentration in the cyst. The intra-cystic drug concentration is inversely proportional to the diameter of the cyst. While the duration of drug use does not increase the intra-cystic drug concentration, long-term exposure of the germinative layer to the drug increases the effectiveness of the treatment (40). Experimental studies have been conducted with flubendazole as a drug not used in clinical practice to treat HCE. These studies have not yet been put into clinical practice (41). The dose of Albendazole is determined as 10 mg/kg/day. There is no evidence that increasing the drug's dose will increase the drug's effectiveness during medical treatment (2,41,42). The most commonly combined drug with Albendazole is Praziquantel. Praziquantel has been found to increase the blood level of Albendazole significantly. However, this combination has not been shown to increase intra-cystic concentrations. Therefore, the clinical efficacy of combining these two drugs has not been proven (40).

2.2. Role of drug use in the treatment of HCE

In the treatment of HCE, drug therapy is administered either as the sole treatment or as an adjuvant to the interventional procedure.

CE1 cysts with a diameter of less than 5 cm have an indication for drug therapy alone. The rate of transformation of these cysts to inactive cysts after 1-2 years of drug treatment has been reported as 75% in some studies. Studies have also reported that the effectiveness of drug therapy decreases as the cyst diameter increases and the stage progresses. Medical therapy alone has also been used in patients with medical conditions not suitable for surgical treatment, patients with diffuse peritoneal hydatidosis with or without liver cysts, and CE3b patients in some studies. However, no study compared the effectiveness of medical treatment alone with surgical treatment in this patient group. Nevertheless, drug therapy alone has a high recurrence rate. In two-year follow-ups, it was determined that cysts that became inactive with medical treatment became active in 25% in some series and 50-60% in others (11,43-45). The response rate to drug therapy is even lower in CE2 and CE3 cysts (30-50%). There is no definite duration of treatment in patients who will receive drug therapy alone. Different durations have been specified in the literature, such as 1-2 years (46,47). There is no study comparing the duration of medical treatment. Studies predominantly compare drug therapy with watch-and-wait therapy. Nonetheless, WHO/IWGE states that membrane detachment should occur three months after drug initiation in CE1 cysts to evaluate the efficacy of the intra-cystic drug. In some studies, the mean duration of drug intake was reported as 12 months (46). In addition, there are studies suggesting that CE3b cysts should be treated with Albendazole alone instead of surgery or followed by ultrasound without treatment (46). However, these studies are retrospective, and some CE4 cysts have been reported to revert to the CE3b state. The most important criterion for drug therapy success is the cyst stage change. The World Health Organization classifies CE1 and CE2 as active, CE3a and CE3b as transitional, and CE4 and CE5 as inactive cysts. Success in medical treatment can be defined as changes in US appearance (e.g., conversion to CE 3a with membrane detachment in a CE 1 cyst or conversion to CE 4 with solidification of a CE2 or CE3b cyst) after albendazole administration (at least three months). Regarding the complication rate of cysts in HCEs under drug therapy, a study comparing medical treatment with albendazole and wait and watch treatment in CE3b cysts reported the complication rate in cysts treated with albendazole was the same as in other cysts (46). Albendazole has side effects that can sometimes be serious. Except for nausea and rare hair loss, this drug is hepatotoxic and may cause bone marrow depression. Liver functions and hemogram parameters should be followed in long-term treatments.

2.3. Drug therapy and duration before or after intervention (percutaneous or surgical) in HCE

Medical indication for hepatic hydatid cyst is mainly adjuvant therapy used in the preoperative and postoperative period. It is known that Albendazole used before surgery reduces intracystic pressure and scolex vitality. In addition, the intracystic viable scolex ratio decreases as the duration of preoperative use is prolonged. Studies have shown that the concentration of Albendazole in the cyst is close to the values in the blood. Different sources have specified different durations for the use of the drug. Still, various sources recommend using drugs for 15 days-1 month preoperatively and 1-3 months postoperatively (2,41,42).

In light of the above literature, the following recommendations were formed;

Recommendation 2.1: The most effective drug currently in use in the medical treatment of HCE is albendazole. Treatments with other medications have not yet entered clinical use.

Recommendation 2.2: There is no evidence that the concomitant use of praziquantel or any other drug in medical treatment increases the effectiveness of the treatment.

Recommendation 2.3: The dose of albendazole is determined as 10 mg/kg/day. There is no evidence that increasing the drug's dose will increase the drug's effectiveness during medical treatment.

Recommendation 2.4: Indications for medical treatment of HCE; If CE1 cysts have a diameter less than 5 cm medical treatment can be attempted.

Recommendation 2.5: Although some studies consider medical treatment sufficient in patients with CE3b cysts, the primary treatment is interventional or surgical. An appropriate dose of albendazole is first given preoperatively in these patients, and then surgical/interventional treatment is applied.

Recommendation 2.6: There are no definitive studies in patients with peritoneal hydatidosis along with HCE. If surgical treatment is applied in these patients, drug therapy may be preferred as an adjuvant, but it can also be administered alone without surgical treatment.

Recommendation 2.7: The duration of medical treatment without any other treatment approaches should be six months at least and twelve months on average. However, the change in the cyst stage should also be evaluated in the follow-ups.

Recommendation 2.8: Liver function tests and hemogram should be monitored monthly to follow up on drug side effects seen during drug treatment of HCE.

Recommendation 2.9: There is no defined period for the use of Albendazole before and after the intervention (surgery or percutaneous treatment). However, based on limited information in the literature, a minimum of ten days of drug use can be recommended. Similarly, at least two months of postoperative use can be recommended.

Recommendation 2.10: Studies have shown no relationship between Albendazole blood levels and intra-cystic concentration, but these two levels are close to each other, and the intra-cystic concentration is more effective in treatment. Therefore, blood level monitoring has not been included in clinical practice.

Recommendation 2.11: Drug use during pregnancy has been reported as teratogenic and embryotoxic in experimental studies; however, high doses used in experimental studies are not used in humans in clinical practice. Nevertheless, its embryotoxic effects have not been clearly demonstrated. Yet, there is also no evidence that it is safe for use in pregnant women.

Recommendation 2.12: There are two recommendations for drug administration in patients who will use albendazole for a long time (six months or more). Recommended treatments for long-term use are continuous and intermittent therapy. In continuous therapy, the treatment continues with two divided daily doses without interruption, while in intermittent therapy, the drug is given for 20 days, and a break is given for ten days. The more preferred treatment is intermittent therapy.

All recommendations in this chapter had a Strength of recommendation: B Quality of Evidence: III

Chapter 3. Percutaneous Treatment in HCE

The relevant literature was searched using the Pubmed database, covering 01.01.1900 and 18.03.2018. In Pubmed search, two columns were chosen as keywords. In the first one, the words "PAIR OR puncture OR percutaneous" were searched in the articles' title, abstract, and keywords (n= 418508). In the second column, articles with the words "(*Echinococ* OR hydatid) AND (liver OR hepatic)" in the title were searched (n= 3699). The combination of both columns revealed a total of 346 studies. Narrowing these down to studies that included words in the first column in their title revealed 73 studies. Of these, four were comparative clinical studies, five were reviews, 16 were case reports, and one was a meta-analysis, and the remaining majority were retrospective clinical studies. No distinction was made between them in terms of date or language.

A total of 503 articles were found in the Turkish literature search using the keyword "kist hidatik" (hydatid cyst) in the TR Index-Ulakbim database. Of these, 477 were related to medicine. After excluding the articles that did not include liver involvement, were not related to the treatment of cystic *Echinococcosis*, or insufficiently related to the diagnosis, a total of nine Turkish articles were evaluated within the scope of the study.

3.1. Common evaluation

Especially in the last three decades, percutaneous treatments in HCE have increased and improved. It can be performed with low complication rates, especially for CE1 and CE3a cysts (48). Today, the success of percutaneous treatments in HCE is quite high. From this point of view, joint planning of the treatment for HCE by an interventional radiologist, general surgeon, and endoscopist who can perform ERCP will increase the chance of success.

3.2. Cyst localization

Especially cysts located deep in the liver parenchyma are more suitable for percutaneous treatment (PT). There may not be enough parenchyma in exophytic cysts to enter the cyst, and sclerosis of the cyst pouch is often more difficult in these cysts.

Therefore, surgical treatment is more appropriate in these cysts that grow towards the abdomen (49).

3.3. Cyst diameter and type

While PAIR therapy is successful in CE1 and CE3a cysts, it is more likely to fail in CE2 and CE3b cysts. Failure rates of up to 60% have been reported in some series (50,51). Therefore, percutaneous catheter applications are used in this patient group. Generally, PAIR treatment with a needle is appropriate for CE1, CE3a, and CE4 cysts with fluid content up to 10 cm. If possible, catheter treatment should be performed in larger cysts, CE2 medium-large CE3b cysts, cysts with biliary content, and postoperative collections. Different methods have been tried for catheter treatment. However, there are no controlled studies comparing these methods. PT can be performed on all cysts with live or liquid contents. However, since the risk of recurrence is high in CE3b cysts with a high solid component and especially with exophytic extension, primarily surgical treatment should be considered (11,12,48,50-54).

3.4. Treatment in HCE in case of bile leakage into the cyst

If PT is to be performed in these patients, they should be treated with catheter drainage, if possible. Since most cystobiliary fistulas become evident after cyst drainage, the inserted catheter should not be removed immediately but should be removed after waiting for about one week, making sure there is no obvious fistula, and performing cystography and sclerotherapy (12).

3.5. Treatment in HCE in case of bile leakage into collections or cyst pouch after surgery or PT

Cystobiliary fistula is more likely in centrally located cysts close to the porta hepatis. These cysts should be treated with catheter drainage if possible. The catheter should not be removed until the daily bile leakage is below approximately 10 cc. Sclerotherapy should be performed after the presence of cystobiliary fistula is evaluated cystography. If bile leakage is not reduced or is increased, ERCP and ES, Stent, or NBD can be applied. In this process, care should be taken for the cyst not to become infected (12).

3.6. Treatment of recurrent cysts after surgery or PT in HCE

It would be correct to approach the cases with recurrence or residual postoperatively as if they had not been operated on. Since the mortality and morbidity of the second open surgery are higher in these patients, and surgical treatment is more difficult due to surgical adhesions, they should be treated with PT if possible. Similarly, percutaneous treatment should be planned primarily in recurrences or residues after percutaneous procedures (12,55-58).

3.7. Postprocedure follow-up

After the procedure, routine controls with US and blood tests should be performed at the 1st, 3rd, 6th, 9th, and 12th months. Bile leakage into the cyst pouch is usually seen in the first months, while cyst recurrence develops in a longer term. If there is deterioration in blood values, the dose of the drug should be adjusted accordingly, and if there are GI side effects, it should be given with stomach protectors. In the follow-up, recovery criteria such as the absence of fluid in the cyst, collapse of the membranes, reduction in size, and development of calcification should be considered.

In light of the above literature, the following recommendations were formed;

Recommendation 3.1: When planning treatment for HCE, the patients should be discussed in a MDT board including an interventional radiologist or, at least should be consulted with an interventional radiologist prior to surgery.

Recommendation 3.2: In terms of cyst localization, surgical or percutaneous treatment can be planned for superficial cysts or cysts growing towards the abdomen. Surgical treatment is preferred in cases where safe percutaneous access is not available.

Recommendation 3.3: Percutaneous treatment is applied with the PAIR technique in CE1 and CE3a cysts. If the aspirated content has bile, catheterization should be started. PAIR and catheterization can be applied in CE1 and CE3a cysts larger than 10 cm in diameter, but catheterization is preferred for a safer and shorter procedure. If there is no bile content, the catheterization process can be completed in a single session by removing the catheter at the end of the procedure. Surgical treatment is the standard treatment for CE2 and CE3b cysts, but percutaneous treatment is also possible in experienced centers with the modified catheterization technique (MoCaT), in which the cyst content (daughter vesicles and solid degenerative content) is completely evacuated.

Recommendation 3.4: PT should be planned first in recurrent cysts or collections after surgery and PT.

All recommendations in this chapter had a Strength of recommendation: B Quality of Evidence: III

Chapter 4. Surgical Treatment of HCE

The relevant literature was searched using the Pubmed database, covering 01.01.1900 and 30.09.2018. In Pubmed, the keywords (surg* OR lap*) AND [(cystic AND *Echinococ**) OR (hydatid)] AND (liver OR hepatic) were searched in the title, abstract, and keywords of the articles. As a result, 1557 studies were obtained. Of these, 548 were case reports, 25 were comparative clinical studies, 65 were reviews, four were meta-analyses, and the remaining majority were retrospective clinical studies. No distinction was made between them in terms of date or language.

A total of 92 articles were found in the Turkish literature, using the keywords "kist hidatik VE karaciğer VE cerrahi" ("hydatid cyst

AND liver AND surgery") in the TR Index-Ulakbim database. After excluding the articles that did not include liver involvement and were not related to cystic *Echinococcosis* surgery, a total of 47 Turkish articles were evaluated within the scope of the study.

4.1. Surgical treatment

With the increase in percutaneous interventions, surgical treatment indications have narrowed, and their number has decreased. The current indications for surgical treatment are as follows.Surgical treatment indications (2);

1. In large uncomplicated CE2 and CE3b cysts with many daughter vesicles.
2. In uncomplicated large cysts that compress neighbouring vital organs.
3. In cases where percutaneous treatment is not possible.
    a. Against the possibility of spontaneous or traumatic rupture in superficial and large single cysts.
    b. In infected cysts.
4. As an alternative to percutaneous treatment in cysts with cysto-biliary communication.

4.1. Surgical treatment options

The main purpose of surgical treatment in hepatic hydatid cyst is to eliminate the parasite and minimize recurrence, morbidity, and mortality (59). Surgical treatment can be done as radical or conservative. Surgical treatment is chosen according to the patient, the cyst, the surgeon's experience in different surgical treatments, and the institution's facilities.

4.2. Conservative surgery

The principle of conservative surgical treatment is to empty and sterilize the cyst cavity and manage the remaining cavity (60-62). Although conservative surgical procedures are easier to perform than radical procedures, the rate of postoperative morbidity is higher (2).

In conservative surgery, various scolicidal agents are used to evacuate the cyst content and sterilize the inside of the cavity. Mostly, 3-30% NaCl (hypertonic NaCl), chlorhexidine, cetrimide (0.5%), povidone-iodine (10%), hydrogen peroxide (3%), silver nitrate (0.5%) and ethyl alcohol (75-90%) are used as scolicidal agents. The application time of these agents is 5-15 minutes. However, some of these agents are no longer in use. Today, the most commonly used agents are hypertonic NaCl and cetrimide. A concentration below 10% hypertonic NaCl is considered insufficient scolicidal activity. The ideal concentration is 20% (63,64). Contact of all scolicidal agents with the biliary tract should be avoided. Because all of them are likely to cause caustic sclerosing cholangitis.

The part of the emptied cavity outside the liver parenchyma should be removed as much as possible. This procedure is defined as a partial cystectomy. After reducing the cystic cavity, management methods for the remaining space include unroofing, marsupialization, tube drainage, capitonnage, Roux-en-Y cystojejunostomy, and omentoplasty (65). There are studies comparing tube drainage, capitonnage, and omentoplasty in the literature. Comparisons were made in terms of biliary fistula and cavity infection. In general, the risk of biliary fistula and cavity infection was lower in capitonnage than tube drainage and omentoplasty compared to capitonnage (66-70).

Radical surgery

Radical surgical procedures are pericystectomy and hepatectomy. The rate of radical surgery reported in the literature is only 10% of all surgical procedures in the series. Radical surgical treatment is performed without opening the cyst with its contents, either by removing only the pericyst (Pericistectomy-total cystectomy) or removing the pericyst and some parenchyma around it (hepatectomy). The rate of pericystectomy in radical surgical procedures is reported to be 80-90% in the literature (71). Unlike conservative procedures, radical procedures are more complex and challenging and are only applied in units performing advanced HPB surgeries.

Pericystectomy is more preferred among radical procedures. This is because healthy parenchyma is tried to be preserved as much as possible. There is a good dissection plane between the liver tissue and the cyst. Identifying and advancing this plane will provide a comfortable dissection (72). Pericystectomy or cystoprostatectomy method is the removal of the pericyst together with the cyst. This method can be performed closed or open. In the closed method, the cyst content is not opened, while in the open method, the cyst is opened, the pericyst is removed, and its contents are emptied. The open method is especially preferred for deeply located cysts close to the hepatic and portal vein (59).

Considering the series, the rate of hepatectomy in radical surgical treatment remains at 10-20% (59,72-76). Indications for hepatectomy are a large cyst filling a lobe, multiple cysts, complicated cysts, as well as lesions close to hilar vascular structures, according to some authors (77). Erosion of the large bile ducts has been suggested as an indication for hepatectomy. Studies have stated that especially lesions close to the inferior vena cava constitute a partial contraindication. Particular attention should be paid to segment VIII, IV, and I lesions, lesions close to hepatic veins and right atrium (78).

Complications vary depending on the surgical method used in radical surgery. Complications of liver surgery are observed in general, and postoperative morbidity ranges between 3-30% (71). This rate is lower than conservative surgery. The advantage of radical surgery is that there is no cavity infection and less probability of biliary fistula (0-7.7%) (79,80). In patients who undergo radical surgery, the incidence of infection in the operation area after resection is less than 3%. Low postoperative

morbidity naturally reduces hospital stay in patients undergoing radical surgery. Besides, the probability of local recurrence is also lower in radical surgery. The local recurrence rate reported in the literature is 20-25% after conservative methods (59,81,82) and 0-6.4% after radical surgery (71).

Examination of the studies comparing the radical and conservative surgery reveals that the radical surgery group is preferred according to anatomical localization in many studies, indicating a bias. Besides, a significant portion of the comparison studies was conducted in specialized centers (83).

Minimally invasive surgery

The role of laparoscopy in the surgical treatment of liver hydatid cysts has always been discussed. The first studies were reported in the 1990s. The general advantages of laparoscopy, such as less hospital stay, fewer wound problems, and less pain, are also valid here (84). However, the difficulty in reaching the cysts in some localizations and aspiration of the cyst contents have led to concerns about disseminating the contents and question marks about laparoscopy.

Reaching the cysts in the posterior and superior liver segments poses some technical difficulties. However, access to cysts in the II, III, IVB, V, and VI segments can be achieved more easily (85). This also enables patient selection in liver hydatid cysts. In other words, laparoscopic or minimally invasive surgical treatment seems more reasonable in patients with anterior segment cysts (86). It can even be deduced that laparoscopy is a relative contraindication for segment VII and I cysts.

In addition, the complete evacuation of the cyst contents and the possibility of spreading around during evacuation are among the problems experienced. In the current literature, there are various studies on the use of special aspirators, liposuction catheters, or trocar systems (85,87-89). After the cavity is emptied and sterilized, cavity management can be performed with the same methods as in open cases. After the evacuation of the cyst, bile leaks can be detected thanks to the magnification by laparoscopy. Leaks can be sutured (87,90-92).

Conversion to open surgery in laparoscopic surgical treatment is usually due to inaccessibility of the cyst, calcifications, and other complications (bleeding, etc.) (85). The transition to open surgery rate has been reported as 1.7% (86,90). Currently, there is no obstacle to the treatment of liver hydatid cysts with minimally invasive surgical methods (93). In the published series, the recurrence rate in patients who underwent minimally invasive surgery was not higher than in open surgery patients (85). However, it is essential that minimally invasive surgical treatment is well planned and the indications are not forced because it is easy to apply. Minimally invasive radical surgery for hepatic hydatid cysts will increase as minimally invasive hepatectomy becomes more common.

In light of the above literature, the following recommendations were formed;

Recommendation 4.1: Indications for surgical treatment in HCE mainly apply to CE2 and CE3b cysts where percutaneous evacuation of the cavity is difficult, centrally located cysts with cysto-biliary communication, and superficially located or ruptured cysts where percutaneous treatment is not possible.

Recommendation 4.2: Conservative and radical surgery can be safely performed in HCE. Conservative surgical methods are sufficient in all cases with an indication for surgical treatment.

Recommendation 4.3: During conservative surgery for HCE, one of the currently used agents can be preferred for sterilization of the cyst cavity, but attention should be paid to its harmful effects on the biliary tract. Attention should be paid to hypernatremia when using hypertonic NaCL.

Recommendation 4.4: Although there is no difference in postoperative morbidity and mortality between conservative methods in HCE, biliary fistula is seen at a lower rate in omentoplasty than other methods. Therefore, despite the low level of evidence, omentoplasty should be preferred in cases where fistula may develop in conservative surgery. The main drawbacks in the application of omentoplasty are:

- The possibility of not seeing the fistula opening.
- Its ineffectiveness in preventing bile leakage in some studies.
- The fact that sphincter pressure is more important in preventing fistula. In addition, the fact that experienced centers predetermine the cases with fistula and take precautions reduces the interest in this method.

Recommendation 4.5: Radical surgical treatment should be performed in specialized HPB centers. The radical surgical method to be preferred should be parenchyma sparing, if possible. The relevant center should decide on what kind of procedure will be performed in which cases according to the patient's condition.

Recommendation 4.6: Minimally invasive surgical treatment should be preferred according to the patient, the physician's experience, and the institution's facilities. As the experience of minimally invasive surgery and open HPB surgery increases, it should be practiced by HPB surgeons. In other words, laparoscopic interventions should be performed by HPB surgeons.

All recommendations in this chapter had a Strength of recommendation: B Quality of Evidence: III

Chapter 5. Complication Management in HCE

A literature search on the subject, covering the dates 01.01.1990-09.12.2018, was carried out using the Pubmed database for English publications and the TR Index-Ulakbim database for Turkish publications.

Pubmed search with the keywords "Complications of *Echinococcal* cysts, complications of hydatid cysts, complications of cystic *Echinococcosis*" revealed a total of 3124 articles. Of these, 3102 were related to humans. These 3102 articles were subjected to preliminary evaluation. Of these articles, 299 were clinical studies, 351 were reviews, 14 were meta-analyses, and 2438 were case reports. After excluding the articles that did not include liver involvement, were not related to the diagnosis of cystic *Echinococcosis*, or insufficiently related to the diagnosis, 65 clinical study articles, 10 reviews, and 25 case reports were evaluated within the scope of the study.

A total of 24 articles were found in the Turkish literature, using the keywords "kist hidatik VE karaciğer VE komplikasyon" ("hydatid cyst AND liver AND complication") in the TR Index-Ulakbim database. After excluding the articles that did not include liver involvement and were not related to cystic *Echinococcosis* surgery, a total of 11 Turkish articles were evaluated within the scope of the study.

Cysts can remain as they are, enlarge, collapse, or calcify in their natural course. It is also possible for the cysts to become complicated in their clinical course, and the complication rate reaches 30-60%. Complications in HCE can be classified as local complications in the cyst and systemic complications. Systemic complications include allergic reactions. Allergic reactions or anaphylaxis may develop preoperatively or intraoperatively in HCE. Although these allergic findings are not very common, they can be fatal in some cases. Allergic complications can be seen in the preoperative period as well as intraoperatively. Bile duct involvement (cystobiliary fistula), related complications, and free rupture in the peritoneum, pleural, and pericardium are the most common local complications. Infection of the cyst is also one of the most important complications. The suppuration rate of the cyst is over 20%.

5.1. Allergic reactions in the preoperative or intraoperative period due to hydatid cyst

Literature on the management of allergic and anaphylactic reactions due to hydatid cysts are limited to case reports, and recommendations in case-based patient management for the handling of allergic reactions detected in the preoperative period is to administer antihistamines orally for mild skin lesions at first and to start oral prednol (methylprednisolone) treatment if the reaction does not regress. Intravenous steroid administration is recommended as prophylaxis at the beginning of surgery to prevent anaphylaxis and allergic reaction in the perioperative period. In addition, it is recommended to start albendazole treatment to prevent recurrence of allergy and anaphylaxis after an allergic reaction that developed in the preoperative period. In more severe allergic reactions, if hemodynamics are affected, intravenous (IV) use of antihistamines and steroids is recommended. When anaphylaxis develops, it is recommended to provide airway patency, give IV fluid replacement therapy, provide nasal oxygen support, and discontinue other drugs that may cause allergy (anesthesia drugs given when it occurs in the preoperative period) and administer IV antihistamines and steroids (94-97).

5.2. Detection of cysto-biliary fistula in the preoperative period

Retrospective clinical studies are predominant in the literature on predictive parameters in detecting hydatid cysts with biliary fistula in the preoperative period. Many articles have reported elevations in the enzymes (ALP, GGT, Total and Total Direct Bilirubin) that indicate biliary duct obstruction (98-101). Literature indicates an increase in the biliary tract relationship with the increasing cyst size, and studies have reported a cut-off value between 7.5-14 cm (98,99,102-104). There are studies showing that the risk is increased in hydatid cysts located centrally in the liver and located in the liver dome. Literature has revealed that the high white blood cell value and eosinophilia are significant for biliary fistula, although not alone, together with the elevation in the other parameters mentioned above (98,104-112). Several studies have also indicated that male gender and age of the cyst are risk factors for the development of biliary fistula (100,101,108,109).

5.3. Biochemical tests used for the detection of biliary fistula in the preoperative period

For the detection of biliary fistula in the preoperative period, in addition to the biochemical parameters that indicate biliary tract obstruction, which we mentioned in the previous section, studies have also identified elevated AST and ALT enzymes as a risk factor (100,101,113).

5.4. MRCP in the preoperative period

The cysto-biliary communication is divided into two; frank (major, ≥5 mm) and occult (minor, <5 mm) biliary tract communication. Despite a few articles on the use of MRCP in the preoperative period, which either suggest its routine use or argue that it is unnecessary due to its low sensitivity and specificity (approximately 30%) in demonstrating the communication between the occult bile duct in the patient scheduled for surgery, majority of the articles in the literature recommend MRCP in patients with the parameters mentioned in the above sections that may raise suspicion of preoperative cysto-biliary communication, in patients with signs of cholangitis (fever, jaundice, and right upper quadrant pain) or the presence of findings showing biliary involvement in radiological imaging (113-119).

5.5. Preoperative biliary fistula detection

Literature on preoperative biliary fistula detection mentions the symptoms and signs of cholangitis, laboratory markers for biliary fistula mentioned above, demonstration of biliary tract re-

lationship in radiological imaging (germinative membrane dehiscence, daughter vesicle or debris in the biliary tract), and the presence of bile in the cyst content in the aspiration during the PAIR procedure as parameters used in diagnosis (110,113-120).

5.6. Preoperative ERCP

In the preoperative period, MRCP is preferred because it is non-invasive (120-123). Endoscopic sphincterotomy and a nasobiliary drainage catheter placement are recommended to reduce sphincter pressure with ERCP in patients with biliary fistulization in MRCP (123-125).

5.7. Management of hydatid cyst with cysto-biliary communication

Literature in the 90s reported that the treatment of hydatid cyst was surgical, and if the cyst was associated with the biliary tract during surgery, T-tube drainage might be required, and preoperative preparation should be made (126). However, today, with the advancement of radiological imaging, cysto-biliary communication can be better demonstrated preoperatively, and sphincterotomy and preoperative ERCP reduce the risk of postoperative bile leakage (124,126). There are also recommendations in the literature for the use of ERCP to reduce bile duct pressure and clear debris in hydatid cysts with an obvious cysto-biliary communication, since the incidence of detecting bile duct association greater than 5 mm is 65%, while the incidence of detecting biliary fistula below 5 mm is between 10-37% (112,126,127). In patients with signs of sepsis, such as hydatid cyst rupture, which require an emergency operation, it would be appropriate to try surgical methods for the cysto-biliary communication by taking them directly to the operating room without ERCP (107,108,111). Since ERCP is an invasive procedure, it should be performed by an experienced team (123,124).

5.8. Determining whether the intraoperative hydatid cyst is associated with the biliary tract or not.

Various methods have been described to reveal the association of the intraoperative hydatid cyst with the biliary tract, such as putting a clean sponge into the cyst pouch and waiting for 5-10 minutes, then checking whether there is bile contamination, control of the cyst pouch by performing cholecystectomy through the cystic stump or by injecting methylene blue or lipid solution by entering the common bile duct with a thin needle, checking whether there is a yellow color in the white foamy liquid formed after washing the cyst pouch with oxygenated water or filling the cyst pouch with liquid and checking whether the air exhaled from the cystic stump after cholecystectomy creates air bubbles in the cyst pouch, and checking the cyst pouch with videoscopy especially in patients in where the cyst pouch located in the liver dome cannot be fully observed with a direct examination (73,108,111,112,128,129).

5.9. Management of hydatid cyst with intraoperative biliary fistula

In the management of a hydatid cyst with an intraoperative biliary fistula, the literature recommends applying an ERCP procedure by placing an external drainage catheter into the cyst in cases where there is a biliary tract association in the cyst pouch, and no bile leakage area can be detected. If the bile ducts seen in the cyst pouch are not the main bile duct, direct suturing and placing an external drainage catheter into the cyst is recommended. In the case of a major bile duct association, it is recommended to repair the bile duct with a suture and demonstrate that the main bile ducts are not closed by placing a T-tube drainage catheter and taking a cholangiogram after common bile duct exploration. To reduce postoperative bile duct pressure, it is recommended to perform procedures such as sphincterotomy ± stent with ERCP if necessary (108,120,130-133). In addition, few studies suggest using fibrin glue as a useful method for biliary fistula (134,135).

5.10. Management of biliary fistula detected in the postoperative period

The management of biliary fistula detected in the postoperative period should be arranged according to the bile flow. Any signs of sepsis or peritonitis should be investigated immediately. If the amount of drainage is high (over 300 ccs) in the postoperative period, ERCP should be applied immediately. If the bile flow is low and no signs of sepsis or peritonitis develop (less than 300 ccs), it can be followed for three weeks with a drain (112,130). If bile flow continues despite a three-week follow-up, ERCP is performed. If the amount of drainage is high (over 300 ccs) in the postoperative period, ERCP should be applied (108-112,120,130).

5.11. Treatment of hydatid cyst abscess

Interventional or surgical drainage methods are available in the treatment of hydatid cyst abscesses, and both methods are used according to the patient's clinic and the clinician's preference. Both methods have advantages over each other. If there are no systemic and septic findings, percutaneous drainage should be performed first. Surgical perforation drainage is in the foreground if there are systemic and septic findings. Antibiotic and albendazole treatment should be given at least three weeks before percutaneous drainage (113,136-142).

5.12. Peritoneal rupture of the cyst

There are generally case series in the literature on the peritoneal rupture of the cyst. Based on the case, in which acute rupture of the cyst has the possibility of anaphylaxis and peritoneal spread of the cyst, that was urgently treated with laparotomy or laparoscopy and then albendazole administration for 3-6 months, open or laparoscopic surgery may be considered after albenda-

zole treatment for a certain period before surgery in a patient with a late-detected acute abdomen with self-limited closed perforation in the abdomen or without anaphylaxis or allergy symptoms (94,106,143-146).

5.13. Superinfection of the cyst

Since it usually occurs due to cysto-biliary communication, it is necessary to interrupt the biliary tract association with surgical or ERCP/PTK procedures and add albendazole + antibiotic therapy to the treatment. Invasive or surgical drainage of the cyst should also be provided. After the procedure, antibiotics and at least three months of albendazole treatment should be administered (147-150).

5.14. Opening of liver hydatid cysts into the thoracic cavity or pleura

The daughter vesicles and debris in the thoracic cavity can be cleaned with thoracotomy. It can be treated depending on the surgeon's experience; after laparotomy and treatment of the cyst, the diaphragm is opened, and the cyst pouch in the liver is drained, the daughter vesicle and debris are cleaned, the biliary tract communication is sutured, the diaphragm is repaired after washing with scolicidal agents, the abdominal drainage catheter is placed in the thorax, and the postoperative treatment is with albendazole (151-155).

5.15. Cutaneous fistulization of liver hydatid cysts

It is one of the rare complications. In the literature, there are case-level treatments such as elective surgery after 2-4 weeks of albendazole treatment, emergency surgery performed by removing the skin area and fistula tract if it is suppurative or hemorrhagic, thereby cutting the relationship between the cutaneous region and the cyst, and application of one of the surgical procedures suitable for the lesion in the liver (156).

5.16. Rupture of large vessels (portal vein, inferior vena cava, and aorta)

It is one of the rarest complications. Rupture of *Echinococcal* cysts of the liver into the hepatic veins or inferior vena cava may cause hydatid disease to spread to the lungs or pulmonary arteries. Its symptoms are cough, hemoptysis, and shortness of breath (157). Clinical suspicion should be increased in endemic areas. This complication should be kept in mind in patients presenting with these symptoms, especially those who have undergone liver surgery for a hydatid cyst. Thrombosis has also been reported due to opening into the inferior vena cava. One of the rare vascular complications of liver hydatid cysts is their rupture into the portal vein. A total of four cases have been reported. In this case, symptoms include abdominal pain, fever, and signs of portal hypertension (158-161). Anaphylactic shock may also develop after rupturing into large vessels (157-161). There are case-series-level treatments, but they are not mentioned because of their low success.

In light of the above literature, the following recommendations were formed;

Recommendation 5.1: In HCE, preoperative cyst diameter greater than 8 cm, central localization of the cyst, and/or presence of high ALP, GGT, and bilirubin may be indicators of possible communication between the cyst and the biliary tract.

Recommendation 5.2: In cases with clinical and laboratory suspicion of cystobiliary fistula in the preoperative period, MRCP using hepatocyte-specific agents may increase the diagnosis of cystobiliary fistula, but a standard MRCP does not completely rule out the possibility of fistula.

Recommendation 5.3: Preoperative ERCP should be performed in cases with obstructive jaundice or cholangitis, patients with dilatation of the biliary tract, daughter vesicles or debris in the biliary tract on the US examination, or a biliary tract relationship with MRCP and an obvious cystobiliary fistula (over 5 mm, major biliary tract relationship, common bile duct relationship). It is not absolutely necessary in cases where occult cysto-biliary communication (minor bile duct relationship less than 5 mm) is considered. Routine use is not recommended in uncomplicated cases.

Recommendation 5.4: In cases where intraoperative cystobiliary fistula is detected, if the bile ducts can be seen in the cyst pouch are not the main bile duct, suturing of the bile duct opening and placement of an external drainage catheter should be the choice. If a major bile duct association is observed in the cyst pouch, the repair should be performed so that it does not obstruct/narrow the large biliary tract. Intraoperative cholangiography will be useful for this. In cases where there is a bile in the cyst pouch, and no bile leakage area is detected, an external drainage catheter is placed into the cyst, and postoperative ERCP is performed if necessary.

Recommendation 5.5: If the bile flow rate is low (<300 cc) in biliary fistulas detected in the postoperative period, spontaneous closure of the biliary fistula can be expected for ten days without any action, and if the fistula closes spontaneously within ten days, no additional treatment is required. If the bile flow is high (>300 cc) and continues for more than ten days, ERCP can be planned. If the amount of fistula tends to decrease over time, ERCP can wait. ES, stent, or NBD can also be applied in ERCP. In patients with fistula, it is necessary to ensure that there is no peritonitis and sepsis. Radiological imaging of the cyst cavity is required in patients whose fistula drainage is interrupted.

Recommendation 5.6: When peritoneal rupture is detected in HCE, laparotomy or laparoscopy should be performed urgently if there are signs of acute rupture, as there is a possibility of anaphylaxis and peritoneal spread of the cyst. Afterward, albendazole treatment should be given for at least three months.

Recommendation 5.7: If superinfection of the cyst is detected, it should first be considered that it may be associated with the biliary tract and should be treated appropriately.

Recommendation 5.8: Whether or not there are septic findings or acute abdominal findings in hydatid cyst abscess, surgical or interventional drainage procedures to be preferred should be determined in accordance with the patient's clinical condition clinician's preference, and institutional facilities. Appropriate antibiotic therapy should be initiated after the procedure.

Recommendation 5.9: If liver hydatid cysts are ruptured into the thoracic cavity or pleura, after the treatment of the cyst with laparotomy, the diaphragm is opened, the daughter vesicles and debris are cleaned, the biliary tract is sutured if a relationship is detected, then it is washed with scolicidal agents, the diaphragm is repaired, drainage catheters are placed in the abdomen and thorax, and the operation is terminated.

All recommendations in this chapter had a Strength of recommendation: B Quality of Evidence: III

Chapter 6- Posttreatment Follow-up and Recurrences in HCE

The relevant literature was searched using the Pubmed database, covering 01.01.1900 and 01.0.2018. In Pubmed search, [(cystic AND echinococ*) OR (hydatid)] AND (liver OR hepatic) AND (recurr*) were selected as keywords. A total of 28 studies were found. One of these was a randomized controlled trial. Other studies were case reports and retrospective serial analyses. No distinction was made between them in terms of date or language.

6.1. Medium-long-term follow-up-serology-imaging

Serological tests have become negative over the years. Therefore, its sensitivity is low in recurrence cases. In the follow-up, if the serological tests have become negative and positive results are detected again, then it is significant in terms of recurrence. After the routine baseline US imaging performed in the 1st month after the treatment of hydatid cyst, control should be provided with the US, especially in the 3rd and 6th months of the first year. Then, US control should be done for at least three years in six months intervals. Suspicious cases should be evaluated with CT (162-166).

6.2. Indications for an interventional procedure in recurrences

In recurrences, treatments similar to the primary treatment indications are applied. If it is a univesicular cyst and its localization is unsuitable for surgery, percutaneous treatment and albendazole should be given together. If the cyst is risky for univesicular and radical surgery, percutaneous treatment can be tried in the recurrences of patients who have previously received conservative treatment (167,168).

6.3. Indications for surgical treatment in recurrences

In recurrences after percutaneous treatment, first of all, percutaneous treatment should be tried again. If percutaneous treatment fails, conservative surgery may be tried. Radical surgery is recommended for those who underwent conservative surgery if the patient is suitable for surgery (162,163,169,170).

In light of the above literature, the following recommendations were formed;

Recommendation 6.1: Short and medium-term follow-ups after treatment in HCE should primarily be done with US exams. CT and serological tests can be used in suspected lesions.

Recommendation 6.2: Recurrent cases of HCE are repaired like the primary disease. In cases where percutaneous treatment was applied, first of all, percutaneous treatment can be tried again. Recurrences after conservative surgery should be treated percutaneously, if appropriate. If surgical treatment is to be performed, radical surgery should be applied if possible; otherwise, a conservative approach should be applied.

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Türk Hepato-Pankreato-Biliyer Cerrahi Derneği'nin karaciğerin ekinokok kistleri hakkındakı konsensüs bildirisi

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ÖZET

Giriş ve Amaç: Kistik ekinokokkoz (CE), Avrasya bölgesinin önemli sorunlarından biridir. Bu hastalığın tedavi yaklaşımlarını güncellemek için bir uzlaşı raporu hazırlamayı amaçladık. Bu çalışma Türk HPB Cerrahi Derneği tarafından yapılmıştır.

Gereç ve Yöntem: Bu çalışma, modifiye Delphi modeli ile yapılmıştır. Bu amaçla, üç aşamalı bir fikir birliği oluşturma yaklaşımı yürüttük.

Bulgular: KKE'de tanı, medikal tedavi, perkütan tedavi, cerrahi tedavi, komplikasyonların yönetimi ve tedavi sonrası takip ve nüksler olmak üzere altı konu tartışıldı.

Sonuç: Uzman paneli her konu için önerilerde bulundu.

Anahtar Kelimeler: Karaciğer, kistik ekinokokkoz, uzlaşı raporu

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ORIGINAL ARTICLE
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Intraoperative and postoperative impact of pretransplantation transjugular intrahepatic portosystemic shunts in orthotopic liver transplantations: A systematic review and meta-analysis

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ABSTRACT

Objective: Orthotopic liver transplantation (OLT) remains the definitive treatment for patients afflicted with end-stage liver disease (ESLD). Transjugular intrahepatic portosystemic shunts (TIPS) have been adapted as a bridge to transplantation, allowing partial normalization of portal pressure and associated symptom improvement. Conflicting evidence exists on TIPS' impact on operative procedures. This study aimed to analyze available evidence on patients who underwent OLT with prior TIPS compared to OLT alone with the intent to determine TIPS' impact on surgical outcomes.

Material and Methods: Following PRISMA guidelines, a systematic review was conducted, identifying studies comparing TIPS + OLT versus OLT alone in patients with ESLD. Data were analyzed using Review Manager 5.3.

Results: Thirteen studies were included. Operative time, packed red blood cells transfusions, intensive care unit admission, length of stay, dialysis, serum creatinine levels, ascites, vascular complications, bleeding revisions, reintervention, and other complications rates were similar between both groups. Fresh frozen plasma transfusion -2.88 units (-5.42, -0.35; p= 0.03), was lower in the TIPS + OLT group.

Conclusion: Our study found TIPS can be safely employed without having detrimental impacts on OLT outcomes, furthermore, these findings also suggest TIPS does not increase bleeding or complications.

Keywords: Liver transplant, transjugular intrahepatic portosystemic shunts, shunt, liver, model for end-stage liver disease

INTRODUCTION

Liver transplantation (LT) is the definitive treatment for patients with end-stage liver disease (ESLD) and its related complications (1,2). Orthotopic liver transplantation (OLT) is limited by the disparity between limited available donors and recipients, as well as logistical and infrastructural challenges associated with organ donation (3,4). These difficulties result in long waiting times and risk further progression, and complications related to failing liver function (5,6). Efforts to offset this progression, as well as advances in medical and surgical therapy, have led to the optimization of medical management and refinement of procedures such as portosystemic shunt surgery. Minimally invasive transjugular intrahepatic portosystemic shunts have allowed the treatment of complications derived from portal hypertension such as variceal bleeding and ascites (7-9).

Transjugular intrahepatic portosystemic shunts (TIPS) have been adopted as a bridge to transplantation in patients with portal hypertension, allowing partial normalization of portal pressure and associated symptom improvement (10,11). TIPS; however, is a palliative and not a definitive treatment strategy (2).

Conflicting evidence exists on TIPS' impact on operative procedures. Some authors have described decreased operative bleeding secondary to reduced vascular engorgement and collateral circulation (12,13). In contrast, others postulate additional technical difficulties during the procedure such as reversal of the procedure adding complexity, especially while performing anastomosis (13).

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This review and meta-analysis aimed to analyze available evidence on operative and postoperative data on patients who underwent OLT with prior TIPS compared to OLT alone, with no previous clear-cut evidence on a large scale of TIPS' effect on OLT.

MATERIAL and METHODS

Search Strategy and Screening

Prior to starting the review, protocol registration was done in the National Institute for Health Research's PROSPERO tool. Our protocol is available with ID CRD42020204409 in the said website. Following the Preferred Instrument for Systematic Reviews and Meta-Analysis (PRISMA), a systematic database search was performed in December 2020 with no limit on date search (Figure 1) (14). Studies comparing OLT with and without previous TIPS were identified through the search engines/databases of PubMed, Web of Science, and Google Scholar. The search was performed for studies that included in their title or abstract the following search string: "Transjugular Intrahepatic Portosystemic Shunt", "TIPS", "Orthotopic Liver Transplantation", "Transjugular Intrahepatic Portosystemic Shunt", "TIPS", "Orthotopic Liver Transplantation", and "Surgical Outcomes". Additionally, "similar articles" feature was employed to further screen possible manuscripts. No restrictions were applied to manuscript age and only manuscripts in either English or Spanish language were included. The identified manuscripts were further inde-

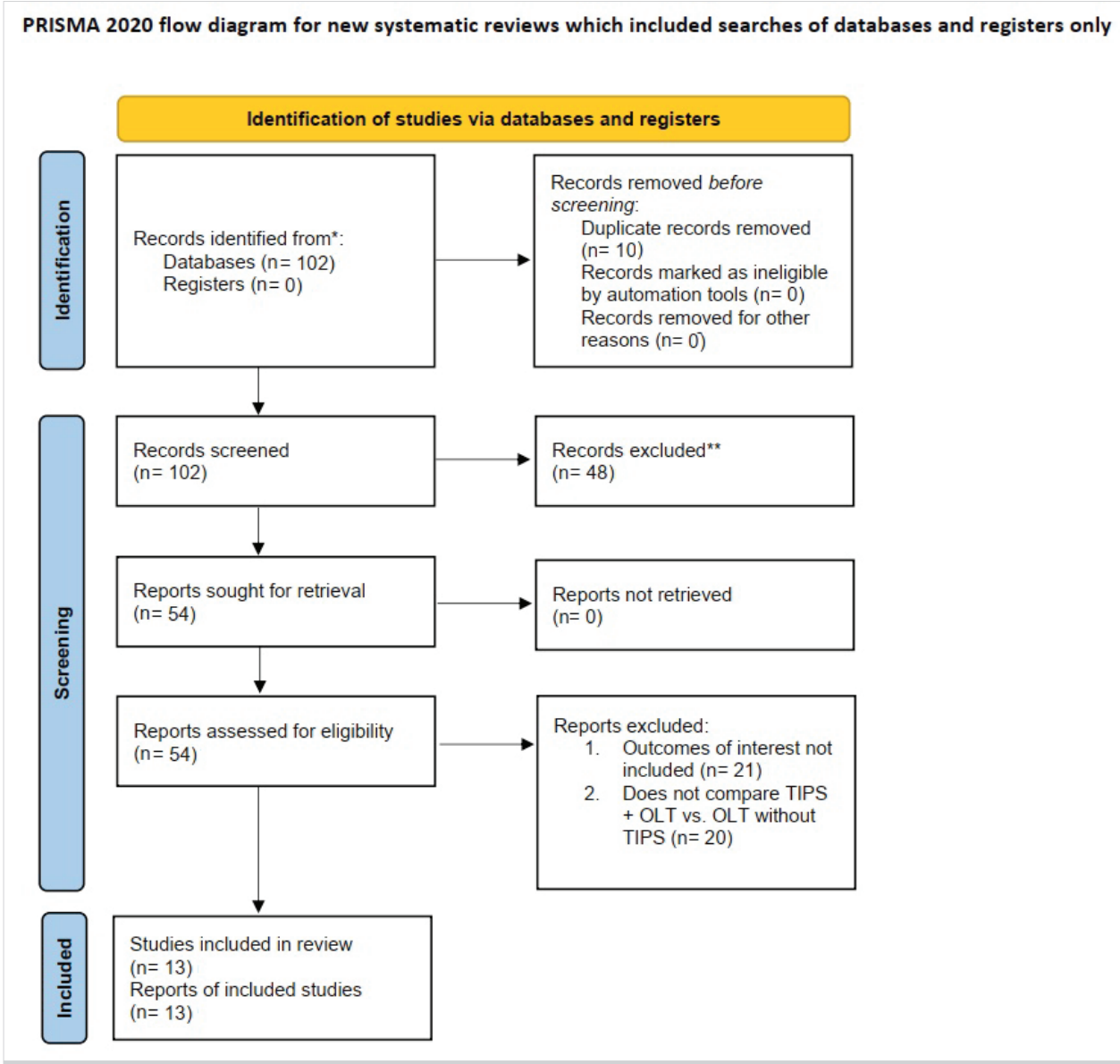


Figure 1. Displays the preferred reporting items for systematic reviews and meta-analyses (PRISMA) Flow Chart for the systematic review.

pendently screened by two authors/reviewers (MAEC, SUVDL) for possible inclusion, evidence grading, and data extraction. Any discrepancy between identified data was mediated by a third reviewer (GSG). Additional articles identified through related articles were also screened.

Study Inclusion

Included studies statistically compared relevant outcomes of patients grouped into either TIPS + OLT or OLT alone in humans. Reporting data on operative time, intraoperative bleeding, time to a normal diet, length of hospital stay, and complications (including cholangitis, anastomosis leak, obstruction, reflux, and intervention) were included. General demographic data including patient age was also taken into consideration. No restrictions were applied for study type or patient age. Only case reports and case series of fewer than eight patients were excluded.

Data Extraction

As previously mentioned, manuscripts were assessed independently by two reviewers for inclusion and data extraction. Data relevant to this meta-analysis besides authorship and year of publication were as follows, for preoperative parameters, age, Model for End-Stage Liver Disease (MELD), and Child-Pugh scores were considered. Within operative variables, operative time, number of transfused packed red blood cells, and units of fresh frozen plaza were included. For postoperative values, variables such as ICU admission and length of hospital stay, the need for dialysis, serum creatinine levels, presence of ascites, vascular complications, bleeding revisions, and reinterventions were included. Studies providing data in median and ranges were used to estimate mean and standard deviation using Wan's method (15). Studies that included means but not standard deviation, but with enough data (p-value and group sizes) were used to estimate standard deviation using the t-value per Cochranes Handbook recommendations (16). In order to avoid by-gone era bias, subgroups of the patient cohort dating prior to and after 2010 were introduced.

Statistical Analysis

The collected data were analyzed using Review Manager v5.4.1 (Cochrane). Heterogeneity was measured using I^2%, with studies obtaining values over 50% being considered heterogeneous and analyzed through random effects models, while studies with values under 50% were considered homogeneous and were analyzed through fixed-effects models. Continuous data including patient age, operative time, estimated blood loss, time to normal feeding, and length of stay was estimated using mean difference with 95% confidence intervals (CI). Dichotomous data such as complications were reported using Odds Ratios (OR) with 95% CI. The resulting values with associated p-values <0.05 were considered significant.

RESULTS

A total of 103 studies were reviewed, of which 13 studies fulfilled the inclusion criteria for the meta-analysis. These 13 studies included 35492 patients, out of which 1885 underwent TIPS + OLT and 33607 underwent OLT alone. The summary of the analysis is displayed in Tables 1-2. Sub-group analysis featuring segregation by publication year cutoff was performed for each variable.

Preoperative

Age

A total of 10 studies described patient age, totaling 1779 patients in the TIPS + OLT group and 33243 in the OLT alone group. Meta-analysis of this data revealed a mean difference of 1.87 (95% CI 0.03, 3.71) p= 0.05. These findings suggest that under our population, patients who underwent OLT without TIPS were older than the OLT + TIPS group. This is further portrayed in Figure 2.A.

Model for End-Stage Liver Disease (MELD)

Five of the included studies described MELD score, totaling 1639 patients in the TIPS + OLT group and 32340 in the OLT alone group. Our analysis showed a mean difference of 0.48 (95%-1.35, 2.31) p= 0.61, suggesting no statistically significant difference between preoperative MELD scores between the two groups. These findings are displayed in Figure 2.B.

Child-Pugh Score

Three studies reported preoperative Child-Pugh scores, with a total of 117 patients in the TIPS + OLT group and 201 in the OLT alone group. Mean Child-Pugh score was higher in the OLT alone population versus the OLT + TIPS group. Mean 0.41 (95% CI 0.01, 0.81) p= 0.04. These findings are displayed in Figure 2.C.

Operative

Operative Time

Ten studies described operative time, totaling 435 patients in the TIPS + OLT group and 1563 in the OLT only group. Meta-analysis of this data showed similar operating times in both groups, with a mean difference of 1.09 (95% CI-8.77, 10.94) p= 0.83 These findings can be seen in Figure 3.A.

Packed Red Blood Cells

We identified 12 studies that reported the number of packed red blood cells (PRBC) transfused intraoperatively, totaling 519 patients in the TIPS + OLT group and 2190 in the OLT alone group. Meta-analysis of this data revealed a mean difference of 0.36 (95% CI-1.61, 2.32) p= 0.93. These findings suggest no greater number of PRBC used during surgery in patients with TIPS undergoing OLT. These findings are displayed in Figure 3.B.

Table 1. Summary of key findings from included studies

Author	Year	Study Type	Evidence Level	Patients (n)			Mean Age		MELD		Child-Pugh		Operative Time		PRBC		FFP		ICU		LoS		Dialysis		Creatinine		Ascites		Vascular Complications		Bleeding Revisions		Reintervention		Other Complications	
				Total	TIPS + OLT	TIPS Alone	TIPS + OLT	TIPS Alone	TIPS + OLT	TIPS Alone	TIPS + OLT	TIPS Alone	TIPS + OLT	TIPS Alone	TIPS + OLT	TIPS Alone	TIPS + OLT	TIPS Alone	TIPS + OLT	TIPS Alone	TIPS + OLT	TIPS Alone	TIPS + OLT	TIPS Alone	TIPS + OLT	TIPS Alone	TIPS + OLT	TIPS Alone	TIPS + OLT	TIPS Alone	TIPS + OLT	TIPS Alone	TIPS + OLT	TIPS Alone	TIPS + OLT	TIPS Alone
Antonini[30]	1996	Retrospective	3	53	27	26	48	42	N.D.	N.D.	N.D.	N.D.	188	212	2.6	2.5	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
John[21]	1996	Retrospective	3	24	12	12	53.2	50.5	N.D.	N.D.	N.D.	N.D.	497	480	13.2	14	8.7	11.7	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	1	0	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Lerut[19]	1996	Retrospective	3	59	23	36	51.5	46.5	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	21.9	8.84	N.D.	N.D.	N.D.	N.D.	17.5	26	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	10	0	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Chui[31]	2000	Retrospective	3	186	8	178	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	486	490	20.6	41.5	15.6	57.1	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Tripathi[24]	2002	Retrospective	3	82	29	53	56	52	N.D.	N.D.	9.9	9.2	414	379	15	10	N.D.	N.D.	6.2	4.6	40.6	26.3	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	0	2	N.D.	N.D.
Moreno[32]	2003	Retrospective	3	76	26	50	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	538	518	7.3	4.7	15.6	17.3	3.5	4.2	19	19.2	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	1	3	N.D.	N.D.	0	2	3	7
Saad[20]	2006	Retrospective	3	28	16	12	54	45.5	18	12.5	8.5	7.5	588	645	21.6	14.5	N.D.	N.D.	15.2	7	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Guerrini[33]	2009	Prospective	3	652	61	591	46	50	17.7	16.5	N.D.	N.D.	N.D.	N.D.	6.7	7.6	5.9	6.2	7.3	5.9	N.D.	N.D.	N.D.	N.D.	1.2	1.1	N.D.	N.D.	4	40	N.D.	N.D.	5	53	N.D.	N.D.
Valdiviveso[34]	2012	Retrospective	3	825	49	776	53.7	49	N.D.	N.D.	N.D.	N.D.	344	322	23.7	17	27	28.2	13	30.7	43	41.2	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	2	6	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Barbier[12]	2014	Retrospective	3	208	72	136	N.D.	N.D.	N.D.	N.D.	9.5	9.2	346	360	4.5	5.2	10.2	12	N.D.	N.D.	25	30.5	1	6	1.7	1.6	5	4	2	5	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Mumtaz[27]	2017	Retrospective	3	32,783	1366	31417	53.5	53.6	23.2	22.6	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	17.5	16.6	N.D.	N.D.	1.2	1.4	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	15	560	N.D.	N.D.
Unger[26]	2017	Retrospective	3	126	66	60	51.2	51.2	15.7	17.9	N.D.	N.D.	348	337	3.3	5	6.6	6.6	N.D.	N.D.	N.D.	N.D.	6	3	1.1	1.1	25	0	4	3	4	6	N.D.	N.D.	N.D.	N.D.
Matsushima[35]	2020	Retrospective	3	390	130	260	57.5	57.1	21.8	21.1	N.D.	N.D.	425	420	8.8	8.2	7.4	7.6	N.D.	N.D.	13.9	12.9	N.D.	N.D.	1.5	1.5	N.D.	N.D.	7	20	N.D.	N.D.	2	5	N.D.	N.D.

TIPS: Transjugular intrahepatic portosystemic shunt, OLT: Orthotopic liver transplantation, N.D.: No Data, MELD: Model for end-stage liver disease, PRBC: Packed red blood cells, FFP: Fresh frozen plasma, ICU: Intensive care unit, LoS: Length of stay.

Table 2. Summary of the findings from our meta-analysis in key variables

						Heterogeneity			
Outcomes	**Studies**	**TIPS + OLT**	**OLT Alone**	**WMD/OR (95%CI)**	**p**	**x^2**	**df**	**I^2%**	**p**
Preoperative									
Age	10	1.779	33.243	1.87 [0.03, 3.71]	p= 0.05	50.39	9	82	p< 0.00001
MELD	5	1.639	32.340	0.48 [-1.35, 2.31]	p= 0.61	48.94	4	92	p< 0.00001
Child-Pugh Score	3	117	201	0.41 [0.01, 0.81]	p= 0.04	1.36	2	0	p= 0.04
Operative									
Time	10	435	1.563	1.09 [-8.77, 10.94]	p= 0.83	15.88	9	43	p= 0.07
PRBC	12	519	2.190	0.36 [-1.61, 2.32]	p= 0.72	143.75	11	92	p< 0.00001
FFP	8	424	2.063	-2.88 [-5.42, -0.35]	p= 0.03	64.96	7	89	p< 0.00001
Postoperative									
ICU	5	181	1.482	-1.86 [-7.85, 4.13]	p= 0.54	186.81	4	98	p< 0.00001
LoS	7	1.695	32.728	0.78 [-3.93, 5.50]	p= 0.74	103.21	6	94	p< 0.00001
Dialysis	2	138	196	0.00 [-0.08, 0.07]	p= 0.93	2.51	1	60	p= 0.11
Creatinine	5	1.695	32.464	-0.02 [-0.16, 0.12]	p= 0.79	75.41	4	95	p< 0.00001
Ascites	2	138	196	11.41 [0.23, 567.75]	p= 0.22	6.29	1	84	p= 0.01
Vascular complications	8	439	1.921	1.38 [0.87, 2.19]	p= 0.17	13.14	7	47	p= 0.07
Bleeding revisions	1	66	60	0.58 [0.16, 2.17]	p= 0.42	N.A.	N.A.	N.A.	N.A.
Reintervention	5	1.612	32.371	0.65 [0.42, 1.00]	p= 0.05	0.87	4	0	p= 0.93
Other complications	1	3	7	0.80 [0.19, 3.40]	p= 0.76	N.A.	N.A.	N.A.	N.A.

DTIPS: Transjugular intrahepatic portosystemic shunt, OLT: Orthotopic liver transplantation, N.A.: Not applicable, ICU: Intensive care unit, LoS: Length of stay.

Fresh Frozen Plasma

We identified eight studies that provided a number of transfused Fresh Frozen Plasma (FFP) units, totaling 424 patients in the TIPS + OLT group and 2063 in the OLT alone group. We found a mean difference of -2.88 (95% CI-5.42,-0.35) p= 0.06, suggesting that the OLT alone group received more FPP units than the TIPS + OLT group. These findings are displayed in Figure 3.C.

Postoperative

Intensive Care Unit

A total of five studies described rates of admission to intensive care unit (ICU) following surgery, totaling 181 patients in the TIPS + OLT group and 1482 in the OLT alone group. There was no difference between the need of ICU in both groups, with a mean of -1.86 (95% CI-7.85, 4.13) p= 0.54. These findings are displayed in Figure 3.D.

Length of Stay

Seven studies described the length of hospital stay after surgery. This resulted in a total of 1695 patients in the TIPS + OLT group and 32728 patients in the OLT alone group. Further analysis of hospital stay showed a mean difference of 0.78 (95% CI-3.93, 5.50) p= 0.74, suggesting no greater length of stay in either group. These findings are displayed in Figure 4.A.

Dialysis

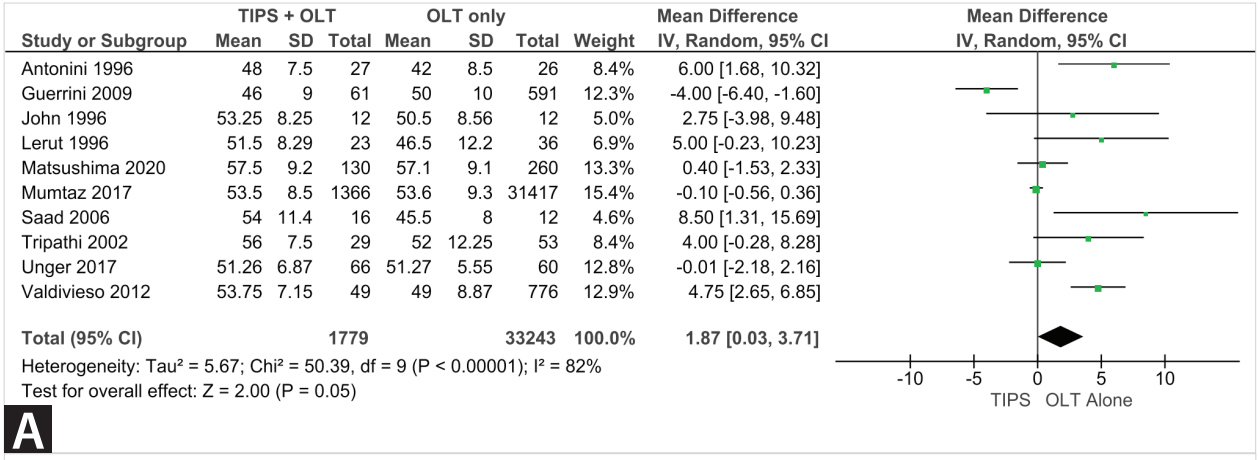
Only two studies described the use of dialysis, with 138 patients in the TIPS + OLT group and 196 in the OLT alone group. Meta-analysis of this data revealed a risk difference of 0.00 (95% CI-0.08, 0.07) p= 0.93. These findings suggest that both groups have a similar risk of undergoing dialysis after OLT. Our findings can be seen in Figure 4.B.

Creatinine

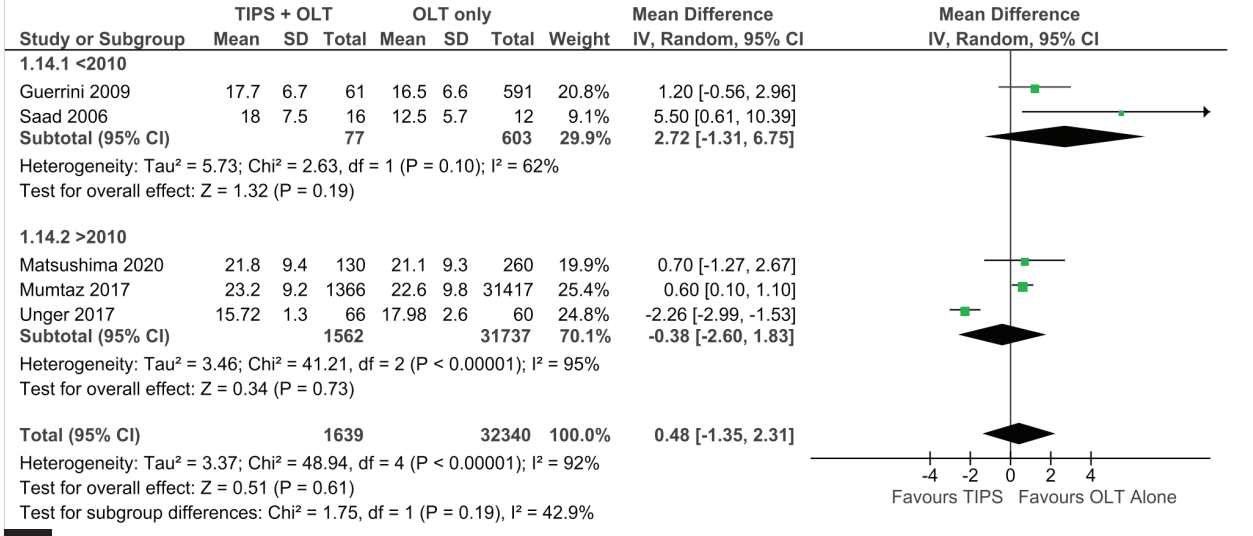
Five studies reported serum creatinine levels after surgery, resulting in 1695 patients in the TIPS + OLT group and 32464 in the OLT only group. Analysis of this data revealed a mean difference of –0.02 (95% CI-0.16, 0.12) p= 0.79, suggesting no difference between serum creatinine between the two groups. Full data is displayed in Figure 4.C.

Ascites

Data associated with patients developing ascites postoperatively was limited to two studies. This resulted in 138 patients in the TIPS + OLT group and 196 in the OLT only group. Comparison shows an odds ratio of 11.41 (95% CI 0.23, 567.75) p= 0.22. This finding suggests that both groups have a similar risk of developing ascites, as demonstrated in Figure 4.D.



A



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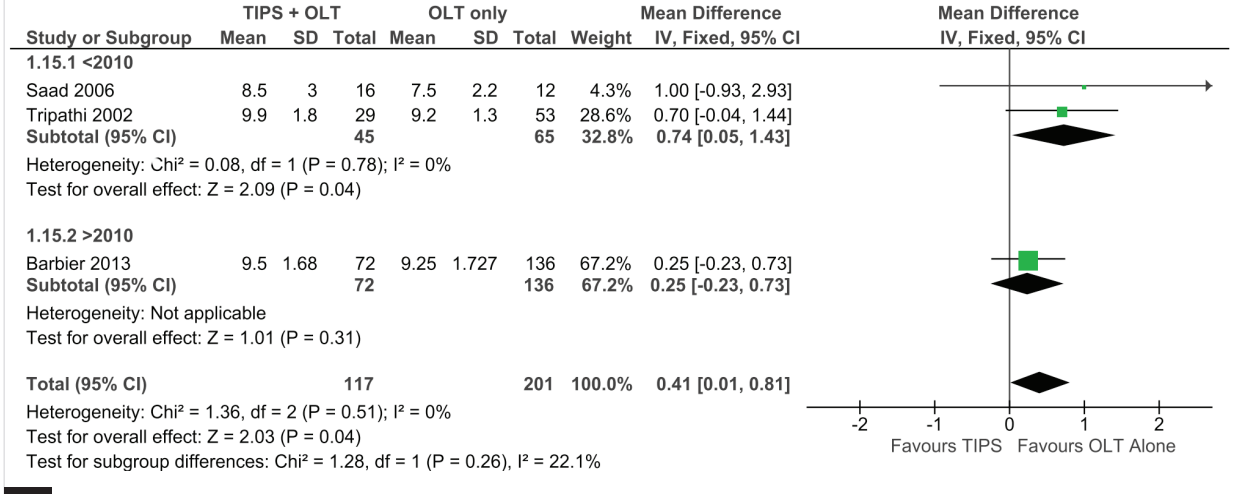


C

Figure 2. Displays forest plots of meta-analysis of the following variables: **A.** Age, **B.** Model for end-stage liver disease (MELD), and **C.** Child-pugh score.

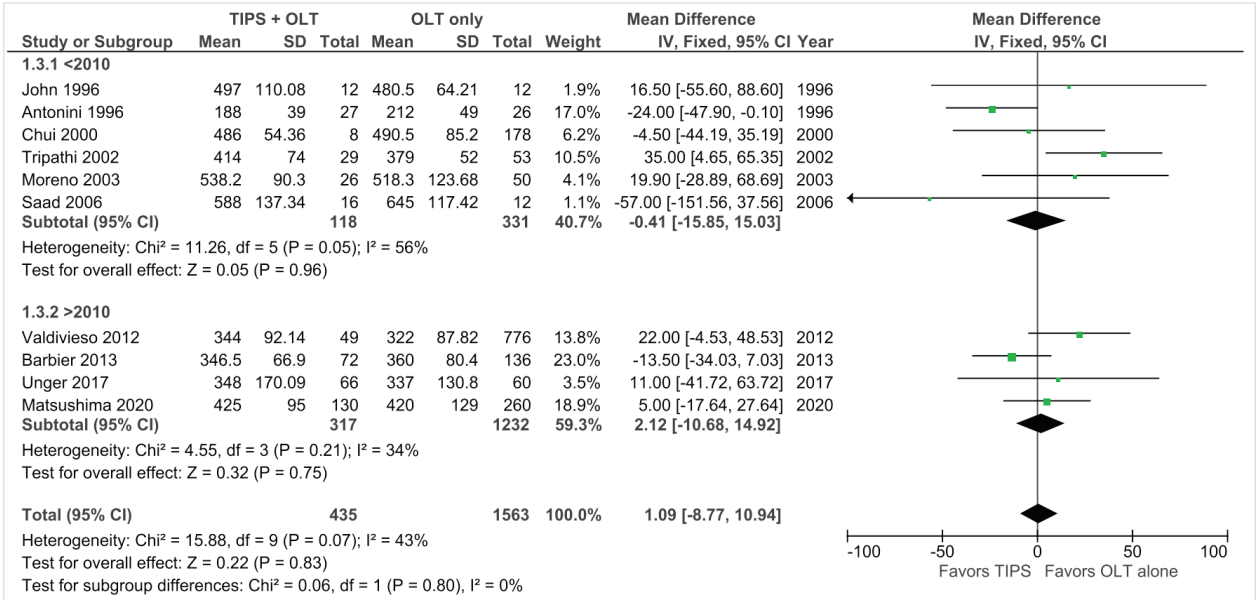


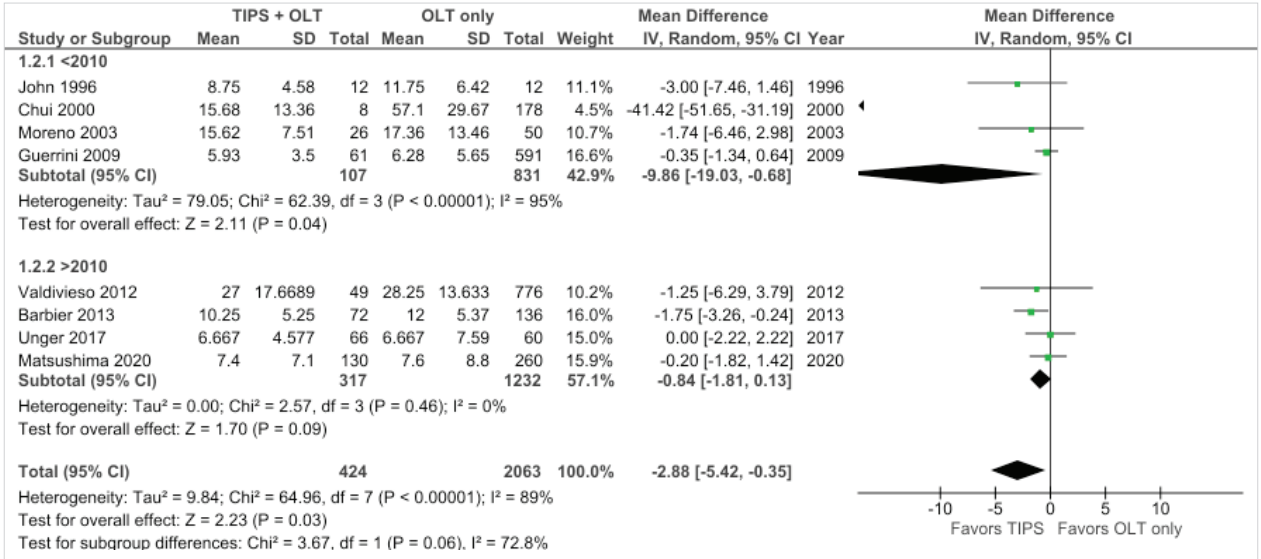
Figure 3. Displays forest plots of meta-analysis of the following variables: **A.** Operative time, **B.** Packed red blood cells, **C.** Fresh frozen plasma and **D.** Intensive care unit admission.

Vascular Complications

Within our included studies, eight described vascular complications within their population. This yields a total of 439 patients in the TIPS + OLT group and 1921 in the OLT alone group. Most notable vascular complications included portal or hepatic vein thrombosis. Analysis of this data revealed an odds ratio of 1.38 (95% CI 0.87, 2.19) p= 0.17. These findings suggest that having undergone prior TIPS does not increase the risk for vascular complications following OLT. Our findings are shown in Figure 5.A.

Reintervention

No significant difference was found between reintervention in TIPS + OLT versus OLT alone. Five studies were included in the analysis, with 1612 patients in the TIPS + OLT group and 32371 in the OLT alone group. Analysis revealed an odds ratio of 0.66 (95% CI 0.43, 1.01) p= 0.06. The forest plot of the association of events is represented in Figure 5.B



C

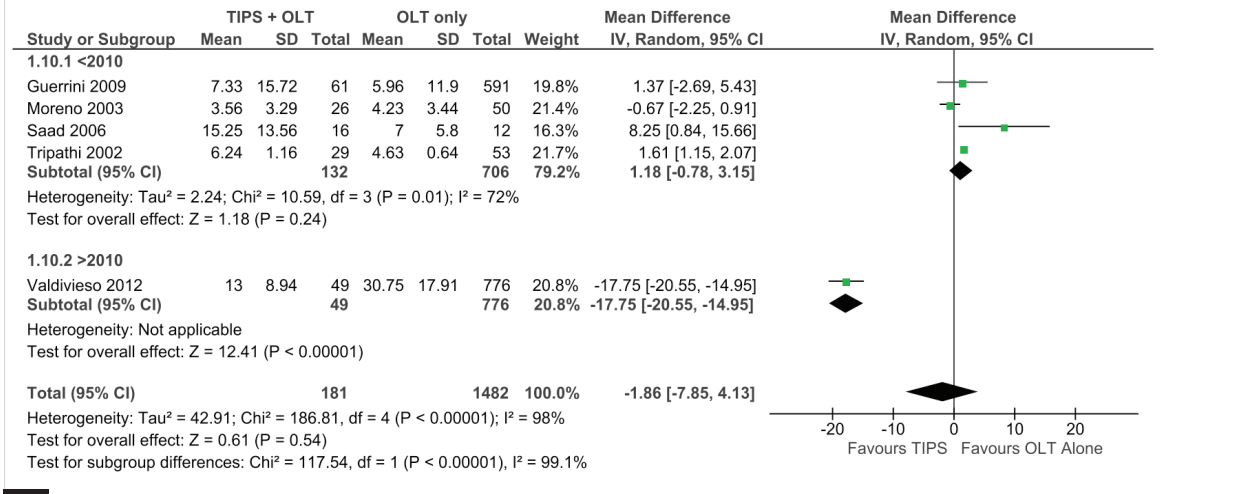


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Figure 3. Displays forest plots of meta-analysis of the following variables: **A.** Operative time, **B.** Packed red blood cells, **C.** Fresh frozen plasma and **D.** Intensive care unit admission (continue).

DISCUSSION

Transjugular intrahepatic portosystemic shunt (TIPS) has established its role as a bridge therapy to live transplantation ameliorating the remarkable mismatch between the donors and recipients (4,10,11). TIPS' original therapeutic indication for refractory variceal bleeding has expanded other complications related to portal hypertension (17,18). Despite its benefits on palliation of portal hypertension, controversy remains over TIPS' impact on liver transplantation.

Previous authors have described the use of TIPS as a method of reduction of operative bleeding secondary to portal pressure normalization (19-21). A reduction in transfusion requirements and operative time is not described in the current literature. This is in contrast to the notions of other authors who note that TIPS adds technical difficulties during liver transplant (22-24). Other studies demonstrate that TIPS implementation before transplantation does not carry added risk nor advantages during LT (12,13,25,26). TIPS are intrahepatic and under optimal situations are removed with the native liver when performing OLT, not requiring any additional steps during surgery. We found that both groups had a similar length of stay, which contrasts with other meta-analyses that report longer length of stay in TIPS group (27). Notwithstanding, it seems like TIPS performs better than surgical shunts, which are associated with more bleeding (25).

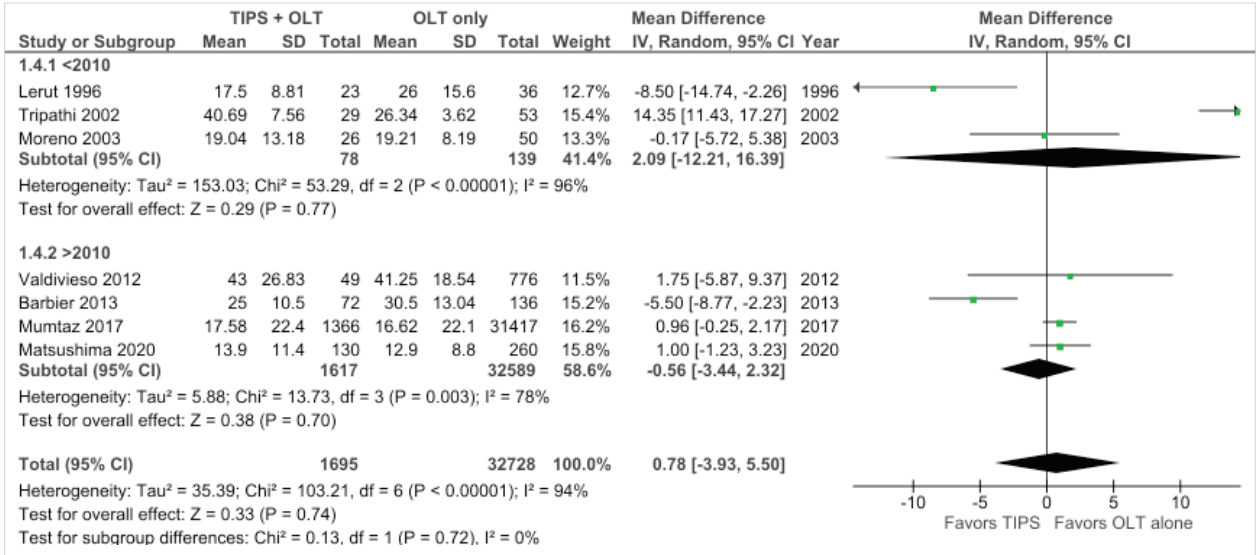

Figure 4. Displays forest plots of meta-analysis of the following variables: **A.** Length of stay, **B.** Dialysis, **C.** Serum creatinine levels, and **D.** Ascites.

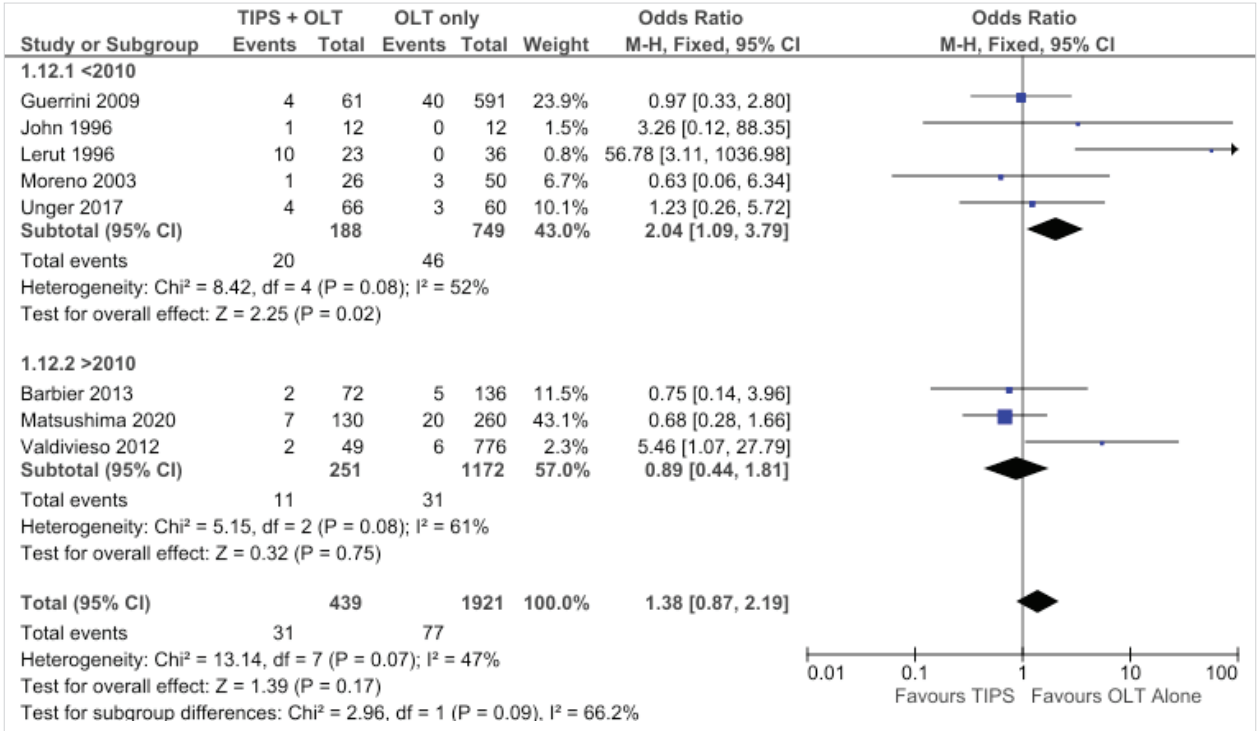

Figure 5. Displays forest plots of meta-analysis of the following variables: **A.** Vascular complications and **B.** Reintervention.

Findings from our own analysis suggest TIPS has no impact on operative and postoperative outcomes during OLT. Baseline characteristics from included studies showed suggested similar patient cohorts. Operative time and bleeding were non-different between the groups, which suggests TIPS presence does not significantly prolong procedures, and its amelioration of portal hypertension does not reduce bleeding. Of note, only fresh frozen plasma use was significantly higher in non-TIPS OLT.

This is driven by a single study by Chui et al. published in 2000 which additionally introduces significant heterogeneity. Sensitivity analysis with exclusion of this study reveals 0% heterogeneity and no significant differences. Similarly, similar length of stays, ICU stays and reinterventions were found.

Concerns on TIPS's impact on waiting list time have been previously raised. TIPS implementation may prolong waiting list time for LT while having comparable post-procedural mortality as non-TIPS counterparts. This increase in waiting list time is a consequence of an improvement in parameters such as MELD score. Non-TIPS patients are thus pushed upwards in the transplant list, causing this group to undergo LT first (27).

TIPS bridging potential must be weighed against possible procedural and postoperative complications (28). These may include migration, occlusion, and worsening of hepatic encephalopathy. Because of this, frequent surveillance is warranted and reinterventions become a possibility (28, 29). The summary of these key findings may be seen in the Table 1 (12,19,20,21,24,26,27,30-35).

From a hospital administration, finances, and resources perspective, there is evidence that there is no significant difference in usage of hospital resources between OLT + TIPS and OLT alone groups; an increased use of resources is described in surgical portosystemic shunts (20).

This study aimed to determine if TIPS has a negative or positive impact on LT and the immediate postoperative period. The study is limited by the lack of robust, high-quality studies on the topic, data estimation and inter study heterogeneity. Additionally, there may be inherent differences in patients who underwent TIPS from those who did not, as the TIPS group may have preserved synthetic function and may be the reason for differences in FFP usage. The wide time frame of included studies may result in by-gone era bias. Lastly, the largest included study is from a UNOS database and as such may bias results; however, sensitivity analysis with the exclusion of this study did not significantly alter results.

CONCLUSION

Analysis of available evidence shows TIPS has no negative or positive impacts on operating time, operative bleeding, ICU admission or complications when compared to patients undergoing OLT without prior TIPS. This suggests TIPS can be safely employed without having detrimental impacts on surgical outcomes if patients undergo OLT, furthermore, these findings also suggest TIPS bleeding or complications are not different from OLT only.

Ethics Committee Approval: Not relevant.

Peer-review: Externally peer-reviewed.

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2022; 38 (2): 121-133

Ortotopik karaciğer transplantasyonunda transplantasyon öncesi transjuguler intrahepatik portosistemik şantın intraoperatif ve postoperatif etkileri: Sistematik bir derleme ve meta analiz

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ÖZET

Giriş ve Amaç: Ortotopik karaciğer transplantasyonu (OKT) son evre karaciğer hastalığında (SEKH) kesin tedavi yöntemidir. Transjuguler intrahepatik portosistemik şantlar (TIPS), transplantasyona bir köprü olarak uyarlanmıştır ve portal basıncın parsiyel normalleşmesine ve ilişkili semptomların iyileşmesine sebep olur. Operatif prosedürlerde TIPS'in etkisi ile ilgili çelişkili kanıtlar vardır. Bu çalışmanın amacı, TIPS'ın cerrahi sonuçlara etkisini belirlemek adına önce TIPS sonra OKT geçiren ve sadece OKT geçiren hastaların verileri analiz etmekti.

Gereç ve Yöntem: SEKH sahip hastalarda TIPS + OKT ve sadece OKT uygulanan hastaların bulunduğu çalışmalar belirlenip PRISMA kılavuz ilkelerini takip ederek bir sistematik değerlendirme uygulandı. Veriler Data Review Manager 5,3 kullanılarak analiz edildi.

Bulgular: On üç çalışma dahil edildi. Her iki grupta da operatif süre, alyuvar transfüzyonu, yoğun bakımda kalış süresi, hastanede kalış süresi, diyaliz, serum kreatinin seviyeleri, assit, vasküler komplikasyonlar, kanama revizyonları, tekrar müdahale ve diğer komplikasyonlar benzerdi. Taze donmuş plazma transfüzyonu -2,88 ünite (-5,42, -0,35; p= 0,03) TIPS + OKT grubunda daha düşüktü.

Sonuç: Çalışmamızda, TIPS'nin OKT sonuçlarına zararlı herhangi bir etkisi olmadan güvenle uygulanabileceğini ve bundan ötürü de TIPS'nin kanamayı veya komplikasyonları artırmadığını bulduk.

Anahtar Kelimeler: Karaciğer transplantasyonu, transjuguler intrahepatik portosistemik şantlar, şant, karaciğer, son evre karaciğer hastalığı

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ORIGINAL ARTICLE
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Comparison of the outcomes of overlapping and direct apposition sphincteroplasty techniques in anal sphincter repair

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ABSTRACT

Objective: Sphincteroplasty is of great importance in the repair of anal sphincter damage. In the present study, we compared the results of overlapping sphincteroplasty and direct apposition techniques used in anal sphincter repair.

Material and Methods: Between 2011 and 2021, 36 patients underwent sphincteroplasty for anal sphincter injury and were analysed retrospectively. Sex, age, etiologic factors, repair technique, degree of laceration, postoperative complications, length of hospital stay, time between injury and repair, follow-up time and postoperative Cleveland Clinic Incontinence Score (CCIS) were recorded for analysis, and the two techniques were compared statistically using SPSS statistics, Version 17.0.

Results: Of the sample, 31 were females and five were males, with a mean age of 31.50 ± 6.7 years. The etiologic factors were obstetric trauma in 25 patients, perianal interventions in seven patients and other traumas in four patients. The overlapping technique was applied to 14 patients and the direct apposition technique was applied to 22 patients. Mean postoperative CCIS of all cases was 5.53 ± 2.59, and was significantly lower in those who underwent overlapping sphincteroplasty technique than those who underwent apposition repair ($p= 0.006$). It was observed that postoperative CCIS decreased as the time between sphincter injury and repair decreased ($p< 0.001$; $r= 0.625$).

Conclusion: It is vital to repair anal sphincter damage as early as possible. The overlapping sphincteroplasty and direct apposition methods can both be considered safe for anal sphincter repair although in terms of faecal incontinence, the outcomes of overlapping sphincteroplasty are better than those of the direct apposition technique.

Keywords: Anal sphincter injury, direct apposition, fecal incontinence, overlapping sphincteroplasty

INTRODUCTION

Most anal sphincter injuries are obstetric and iatrogenic. Sphincter damage identified in postpartum ultrasonographic examinations occurs in 30% of women after first vaginal delivery (1). A study of sphincter damage via transanal ultrasonography following anorectal surgery has revealed 76% and 24% cases of internal and external anal sphincter damage, respectively (2). Perianal fistula surgeries are the most common cause of postoperative faecal incontinence, with the risk of incontinence following fistula surgery reported to be in the 10-20% range, increasing proportionally with the amount of the muscle cut (3). Anorectal traumas are other aetiological factors that usually result from sexual abuse, anal rape, falling on a sharp foreign body and vehicle accidents (4).

Faecal incontinence (FI) is the uncontrolled outflow of liquid or solid faecal matter from the anus, the extent of which depends on the degree of anal sphincter or nerve damage (5). It is a condition that can cause perineal pain and dyspareunia and a reduction in quality of life, which can lead to social withdrawal and postpartum depression and has very high treatment costs (6).

The available surgical approaches to anal sphincter repair include overlapping, direct apposition, post-anal repair, graciloplasty and total pelvic floor repair. Aside from the surgical methods available for the treatment of anal sphincter damage, medical treatments, stem cell treatments, artificial intestinal sphincters, elastomer implants, biofeedback method, rectal balloon, pelvic muscle exercises, digital rectal feedback method, transcutaneous posterior tibial nerve stimulation, sacral nerve

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stimulation, radiofrequency stimulation, etc. have also been described as treatment approaches. Despite the wealth of available information, a standard treatment algorithm for all patients is still lacking (5).

The present study compares the results of the overlapping and direct apposition techniques for the repair of anal sphincter damage resulting from anorectal trauma.

MATERIAL and METHODS

A retrospective analysis was made for 36 patients who underwent direct apposition or overlapping sphincteroplasty for the treatment of anal sphincter injury between January 2011 and June 2021. Ethics committee approval was obtained for the study (approval number: 2021/514/205/5), and the study was conducted following the ethical standards defined in the Declaration of Helsinki, as revised in 2013. In order to determine the sample power, power analysis was performed through the G*Power 3.1.9.4 program. When the margin of error α= 0.05 was accepted and it was assumed that the evaluations made would have a large effect size (d= 0.93), the power of the test was calculated as 0.83 (7). Included in the study were those over 18 years of age with obstetric traumas, perianal interventions and anal sphincter injuries secondary to trauma. Except for direct apposition and overlapping techniques, other sphincteroplasty cases (n= 3, graciloplasty) and patients under 18 years of age were excluded from the study. Patients who underwent sphincteroplasty for such reasons as congenital anomaly, advanced age, rectal prolapse and diabetes mellitus, as other aetiological causes of faecal incontinence, were also excluded from the study.

Age, sex, aetiological factor, degree of perineal laceration, surgical repair technique, presence of ostomy, time between sphincter injury and repair, postoperative complications, hospitalization period (days) and follow-up period (months) were obtained from the patients' epicrisis records and surgery reports. The Postoperative Cleveland Clinic Incontinence Score (CCIS) of the patients was ascertained via telephone or face-to-face interviews. The CCIS scoring system used to evaluate anal incontinence produces a score in the range of 0-20, and is based on such parameters as solid-liquid-gas incontinence, daily pad use and lifestyle change (8) (Table 1). Perineal lacerations are divided into four basic categories in the literature (Grade 1,2,3A-B-C and 4), (9,10).

In the overlapping sphincteroplasty technique, after the existing scar tissue is divided, the two free ends are superimposed and fixed with separate sutures to form a new sphincter complex (11). In the direct apposition technique, the end-to-end suturing of the muscle is carried out, one by one, with the sphincter ends facing each other (12). In the present study, following surgery, the postoperative CCIS, length of hospital stay and rate of postoperative complications of the groups that underwent overlapping and apposition repair surgeries were compared, and the relationship between the time between sphincter injury and sphincteroplasty and postoperative CCIS were analysed.

Statistical Analysis

The statistical analyses were performed using SPSS Statistics (Version 17.0. Chicago: SPSS Inc.). The conformity of the variables to normal distribution was evaluated with histogram graphs and Kolmogorov-Smirnov test. Mean, standard deviation and median values were used for descriptive analyses. Categorical variables were compared with Pearson Chi-square test, and a Mann-Whitney U test was used for the evaluation of non-normally distributed (nonparametric) variables in two groups. Spearman correlation test was used for the comparative analysis of the measurement data. A p-value of <0.05 was considered statistically significant.

RESULTS

Of the 36 patients included in the study, 31 were females and five were males, with a mean age of 31.5 ± 6.7 years. The aetiological factors were obstetric trauma in 25 patients, perianal surgical interventions in seven patients and trauma in four patients. There were four patients with perineal laceration Grade 3a, 10 patients with 3b, 11 patients with 3c, and 11 patients with 4. Repairs were made using the direct apposition technique in 22 patients and the overlapping technique in 14 patients. Mean time between sphincter injury and repair was 11.2 ± 18.1 days. A diversion colostomy was performed in a case with grade 4 perineal laceration resulting from trauma. A perianal fistula developed in two patients and wound infection in one patient as postoperative complications. Mean hospital stay was 2.00 ± 1.1 days; mean postoperative CCIS score of all cases was 5.5 ± 2.6; and mean follow-up period was 9.3 ± 5.2 months (Table 2).

Table 1. Cleveland clinic incontinence score (8)

Type of incontinence	Never	Rarely	Sometimes	Usually	Always
Solid	0	1	2	3	4
Liquid	0	1	2	3	4
Gas	0	1	2	3	4
Wears pad	0	1	2	3	4
Lifestyle alteration	0	1	2	3	4

Table 2. Demographic and clinical characteristics of the patients

	n/mean ± sd
Age	31.5 ± 6.7
Sex	
Male	5
Female	31
Etiology	
Obstetric trauma	25
Perianal surgery	7
Trauma	4
Perineal laceration grade	
3a	4
3b	10
3c	11
4	11
Surgical repair technique	
Overlapping	14
Direct apposition	22
Colostomy	1
Time between sphincter damage and repair (days)	11.2 ± 18.1
Postoperative complication	
Perianal fistula	2
Wound infection	1
Length of hospital stay (days)	2.00 ± 1.1
Postoperative CCIS score	5.5 ± 2.6
Follow-up time (months)	9.3 ± 5.2

CCIS: Cleveland clinic incontinence score.

There was no significant difference between the overlapping and apposition repair groups in terms of age, sex, aetiological factors, perineal laceration degree, postoperative complications, length of hospital stay, and follow-up (p> 0.05), (Table 3). In contrast, the postoperative CCIS mean of the overlapping group was significantly lower than that of the apposition repair group (p= 0.006).

The relationship between sphincter injury-sphincteroplasty interval and postoperative CCIS was evaluated with Spearman correlation test, revealing that postoperative CCIS increased as the time between sphincter injury and repair increased (p< 0.001; r= 0.625), (Figure 1).

DISCUSSION

There can be many causes of anal and perineum trauma, including sexual trauma, pelvic trauma and iatrogenic injuries, with the potential to lead to sphincter damage. In women, vaginal delivery is the most common cause of perineal trauma (13). Labour and vaginal deliveries can lead to the rupture of the perineal striated muscles and damage the pelvic nerves.

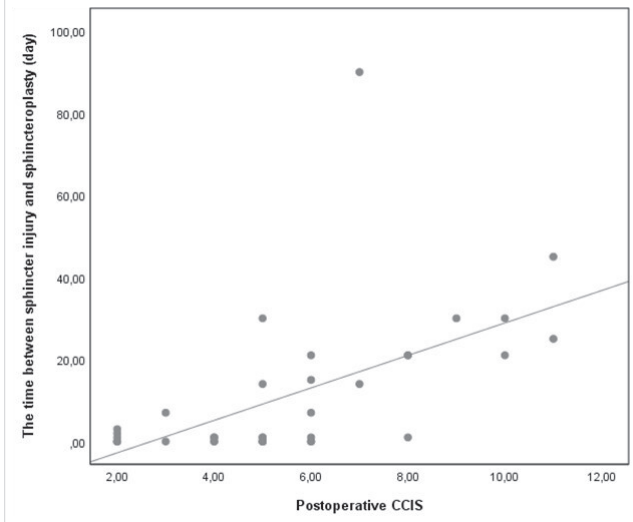

Figure 1. Correlation of time between sphincter injury and sphincteroplasty with postoperative CCIS.

Obstetric anal sphincter injuries (OASIS) are referred to also as third-and fourth-degree spontaneous perineal tears (14). The incidence of OASIS has been reported to be between 0.5% and 17% in the literature (15-20). Primiparous women (5.7%) are at greater risk than multiparous women (1.5%) with no previous OASIS (21). Prolonged second labour stage (>1 hour), advanced maternal age, high birth weight (>4 kg), instrumental vaginal delivery, nulliparity, shoulder dystocia, permanent occiput posterior position, Asian ethnicity, labour induction, epidural analgesia, and midline episiotomy have all been identified as independent risk factors for OASIS (22,23). The incidence of mediolateral episiotomy during vaginal deliveries has been reported to be 45-68%,and has been associated with third-or fourth-degree lacerations in approximately 25% of women (24). In the present study, obstetric trauma was the most common aetiological factor (69%) in anal sphincter injury.

Imaging methods such as anal manometry, magnetic resonance imaging, endoanal ultrasound, electromyography and defecography can be used for the evaluation of sphincter damage secondary to trauma, among which endoanal ultrasound is currently considered the optimum approach to the management of anal incontinence (25).

Sphincter repair aims to restore the anal canal to dimensions of at least 3 cm long and 2 cm thick (6). Lacerations involving the internal anal sphincter (Grade 3c, 4) must be identified and properly repaired to prevent the development of faecal incontinence. The two most common approaches to the repair of damaged external anal sphincter (EAS) are the direct apposition and overlapping techniques. Since the overlap of grade 3a and 3b partial thickness EAS tears will impose excessive stress on the repair, the direct apposition approach should be applied

Table 3. Comparison of the overlapping and direct apposition repair groups

	Overlapping	Direct Apposition	p
	n/mean ± sd	n/mean ± sd	
Age	29.8 ± 5.5	32.6 ± 7.2	0.490[2]
Sex		4	
Male	1	18	0.350
Female	13		
Etiology		13	
Obstetric trauma	12	6	0.225
Perianal surgery	1	3	
Trauma	1		
Perineal laceration grade			
3a	2	2	
3b	2	8	0.550
3c	5	6	
4	5	6	
Postoperative complication			
Perianal fistula	1	1	0.689
Wound infection	0	1	
Length of hospital stay (days)	2.00 ± 1.1	2.00 ± 1.1	0.962[2]
Postoperative CCIS score	4.1 ± 1.9	6.4 ± 2.6	**0.006[2]***
Follow-up time (months)	7.9 ± 3.3	10.3 ± 5.9	0.296[2]

[1]Chi-square test [2]Mann-Whitney U test.

CCIS: Cleveland Clinic Incontinence Score.

in such cases. In this technique, the free ends of the damaged EAS are approximated and sutured. The overlapping technique can be used only for full-thickness lacerations, as two free ends of anal sphincter muscle are required for a tension-free overlapping repair. The torn ends of the EAS are brought together, and 1-1.5 cm of the muscle ends are overlapped and sutured (15). In a meta-analysis, no significant difference has been found between the direct apposition and overlapping repair techniques in terms of flatus incontinence, dyspareunia and perineal pain, although those undergoing overlapping surgery have been shown to have lower faecal urgency and anal incontinence scores than those treated with the direct apposition technique (26). A randomized study comparing the two techniques has revealed the overlapping technique to be associated with worse functional outcomes (7).

For the best results in the treatment of sphincter injury, the repair procedure should be performed as early as possible-immediately after the damage occurs, if possible, but within 24 hours at the latest-and in a centre experienced in anal reconstruction surgeries (4). If sphincter damage is diagnosed after vaginal delivery, surgical repair is recommended within the first 12 hours (27).

Secondary surgical repair refers to surgery performed several months or years after anal sphincter injury. Sphincter repairs should be considered only after failed primary reconstructive surgery when other treatment modalities have been ineffective or there is an identifiable factor responsible for the failure. Sacral nerve modulation (SNM) is a minimally invasive, effective and sustainable treatment option for the treatment of faecal incontinence that improves impaired sphincter function through the continuous, electrical stimulation of the sacral nerves (28). Regardless of the aetiology of faecal incontinence, studies have shown SNM to be effective in the improvement of the continence mechanism (5). In patients with faecal incontinence with low quality of life, faecal referral involving the creation of a colostomy is a treatment alternative in cases where other treatments fail or cannot be applied (29).

Consistent with the literature, obstetric trauma (69.4%) was found to be the main aetiological factor in the patients in our study group. The postoperative quality of life and incontinence scores were higher in the group that underwent overlapping sphincteroplasty than in the group that underwent direct apposition surgery. There have been few studies to date investigating the effect of timing on CCIS. In the present study, a correlation analysis of the time between sphincter injury and surgery with CCIS revealed that early sphincteroplasty resulted in a better quality of life. The limitations of our study are its retrospective design, the fact that the postoperative results were not

supported by such diagnostic methods as endoanal ultrasound and anal manometry.

CONCLUSION

The early repair of anal sphincter injuries is vital. Both the overlapping and direct apposition sphincteroplasty techniques can be considered reliable for anal sphincter repair, although in terms of faecal incontinence, the outcomes of overlapping sphincteroplasty are better than those of the direct apposition technique. Further studies are needed to develop algorithms to steer the repair of sphincter damage secondary to trauma.

Ethics Committee Approval: This study was approved by Kartal Dr. Lutfi Kırdar City Hospital Clinical Research Ethics Committee (Decision number: 2021/514/205/5 Date: 27/10/2021).

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2022; 38 (2): 134-139

Anal sfinkter onarımında overlapping ve direk apozisyon sfinkteroplasti tekniklerinin sonuçlarının karşılaştırılması

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ÖZET

Giriş ve Amaç: Anal sfinkter hasarının onarımında sfinkteroplasti büyük önem taşımaktadır. Bu çalışmada anal sfinkter onarımında kullanılan örtüşen sfinkteroplasti ve direkt apozisyon tekniklerinin sonuçlarını değerlendirmeyi amaçladık.

Gereç ve Yöntem: 2011-2021 yılları arasında anal sfinkter yaralanması nedeniyle sfinkteroplasti uygulanan 36 hasta retrospektif olarak analiz edildi. Yaş, cinsiyet, etyolojik faktör, laserasyon derecesi, onarım tekniği, postoperatif komplikasyonlar, yaralanma ile onarım arasında geçen süre, hastanede yatış süresi, takip süresi, postoperatif Cleveland Kliniği İnkontinans Skoru (CKİS) değerlendirildi. İki teknik SPSS versiyon 17,0 ile istatistiksel olarak karşılaştırıldı.

Bulgular: Hastaların 31'i kadın, beşi erkekti ve yaş ortalaması 31,50 ± 6,7 yıl idi. Yirmi beş hastada obstetrik travma, yedi hastada perianal girişim, diğer dört hastada ise travma etyolojik faktördü. Overlapping tekniği 14 hastaya, direk apozisyon tekniği ise 22 hastaya uygulanmıştı. Tüm olguların ortalama postoperatif CKİS 5,53 ± 2,59 idi. Overlapping sfinkteroplastide CKİS, apozisyon onarımına göre anlamlı ölçüde daha düşüktü (p= 0,006). Sfinkter hasarı ile onarım arasında geçen süre azaldıkça postoperatif CKİS'nin de düştüğü gözlendi (p< 0,001; r= 0,625).

Sonuç: Anal sfinkter yaralanmalarını erken dönemde onarmak oldukça önemlidir. Overlapping ve direk apozisyon teknikleri sfinkter onarımında güvenilir yöntemlerdir. Ayrıca fekal inkontinans açısından overlapping sfinkteroplastinin sonuçları direk apozisyon tekniğinden daha iyidir.

Anahtar Kelimeler: Anal sfinkter hasarı, direk apozisyon, fekal inkontinans, overlapping sfinkteroplasti

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ORIGINAL ARTICLE
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Shabir's "SMART-LAB" score for predicting complicated appendicitis-a prospective study

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ABSTRACT

Objective: Complicated appendicitis needs an aggressive and urgent management, hence there is need of an efficient scoring system for predicting complicated appendicitis. With this in mind, the author developed the present scoring system for predicting complicated acute appendicitis. The study aimed to assess the suitability of this novel (Shabir's SMART-LAB) score for predicting diagnosis of complicated appendicitis.

Material and Methods: In this prospective study, a novel score designated as "SMART-LAB" SCORE, proposed by the author (Shabir) based on his previous observations was calculated in all patients. This score includes sonography (S), migratory right iliac fossa pain (M), anorexia (A), rebound tenderness (R), tenderness (T), leukocytosis (L), Acute phase protein-CRP (A), and serum bilirubin (B).

Results: Of a total of 150 patients included in this study, 52 cases turned out to be perforated and/or gangrenous appendicitis on intraoperative/histopathologic examination. The most commonly affected age group was 10-19 years. SMART-LAB score of >9 was present in significantly higher number of patients in complicated (perforated and gangrenous) appendicitis than uncomplicated appendicitis (p value< 0.001 i.e., highly significant). Hence, high likelihood of complicated appendicitis is reflected by a score >9 (with a sensitivity= 80.7%, specificity= 92.9%, PPV= 85.7%, NPV= 90.1%, and accuracy= 88.7%), while a score 7-9 needs further confirmation to reach a conclusion, and for a score of <7, there is low likelihood of complicated appendicitis.

Conclusion: It seems that this novel score (Shabir's SMART-LAB score) is a reasonably good tool to predict the diagnosis of complicated appendicitis. Early diagnosis of appendiceal perforation is important to limit the associated abdominal sepsis.

Keywords: Gangrenous/perforated appendicitis, SMART-LAB score, bilirubin, leukocyte count, ultrasonography

INTRODUCTION

Appendicitis is the most common general surgery emergency. Appendicitis complicated by gangrene or perforation is a well-known entity. Complicated appendicitis needs an aggressive and urgent management; hence there is need of an efficient scoring system for predicting complicated appendicitis. The author devised the present scoring system for predicting complicated acute appendicitis. Acute uncomplicated appendicitis can be difficult to be distinguished clinically from perforated appendicitis, especially in the elderly and children (1,2) Mortality associated with simple acute appendicitis has been reported to be 0.3%, but increases to 6% in cases with perforation (3). Early diagnosis of appendiceal perforation is important to limit associated abdominal sepsis. Moreover, radiological modalities such as computed tomography (CT) scan and ultrasonography (US) are effective in supplementing the diagnosis of acute appendicitis (4,5), but both modalities have lower sensitivity in detecting perforated appendicitis (6,7). The development of supplementary tools, besides clinical examination and radiology, could be beneficial in the early diagnosis (3). Several studies have found bilirubin to be a useful serological marker for predicting acute appendicitis (8,9) and appendiceal perforation (3,9). Many scoring systems have been proposed, starting from the first score which was presented by Alvarado in 1986 and further more modified Alvarado score was presented by Kalan and colleagues (10). Their score ranges from 0-9 points and includes symptoms, signs and laboratory markers. In Sweden, the Appendicitis Inflammatory Response (AIR)-score was presented in 2008 (11). Adult appendicitis score has been presented by Sammalkorpi and colleagues recently (12). Concerning the pediatric population, a couple of scoring systems are in use, including the Pediatric Appendicitis Score (PAS) (13) and the Lintula score (14).

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There are many scoring systems available for appendicitis, but a comprehensive and acceptable scoring system for predicting complicated appendicitis is lacking. The aim of the present study was to introduce and assess the suitability of a novel (Shabir's SMART-LAB) score for predicting diagnosis of complicated appendicitis. Early diagnosis of appendiceal perforation is important to limit the associated abdominal sepsis. Current scoring systems do not meet such a demand.

MATERIAL and METHODS

Design of the Study

This prospective study was carried out in the Postgraduate Department of Surgery at Government Medical College Srinagar over a period of two years from January 2014 to January 2016. This study consisted of patients admitted with a clinical suspicion of acute appendicitis.

Inclusion Criteria

The study finally included a group of 150 patients who had histologically proven appendicitis and others were excluded as per the pre-framed exclusion criteria.

Exclusion Criteria

Patients initially admitted with a clinical suspicion of acute appendicitis but subsequently unproven by histological examination (negative appendectomies) were excluded from the study. This group included a total of fifteen patients. Other exclusion criteria were patients undergoing interval appendectomies and patients with risk factors for hepatic disease such as alcoholism, a history of viral hepatitis, Gilbert's disease, Dubin-Johnson syndrome, benign recurrent intra-hepatic cholestasis, and other documented biliary, hemolytic or liver diseases associated with hyperbilirubinemia (a total of two patients).

Study Parameters

Subsequent to hospital admission, all patients underwent thorough physical examination and routine laboratory examination. Pre-ultrasound clinical diagnosis was made based on clinical history, physical examination, and laboratory findings. Duration of the symptoms was also recorded. The most common symptom was pain in the right iliac fossa. Real-time, high-resolution (5 MHz, 7.5 MHz) graded compression ultrasound examination was performed by senior radiologists after a clinical diagnosis had been made. The diagnosis of perforation on USG was made by visualization of loculated pericecal fluid, phlegmon or abscess, prominent pericecal or periappendiceal fat and circumferential loss of the submucosal layer of the appendix (15). Sonographic films were taken, and findings were recorded.

"SMART-LAB" Score

A novel score designated as "SMART-LAB" SCORE, proposed by the author (Shabir) based on his previous observations was calculated in all patients. The aim of the present study was to introduce a novel comprehensive and acceptable scoring system for predicting diagnosis of complicated appendicitis. This score includes sonography (S), migratory right iliac fossa pain (M), anorexia (A), rebound tenderness (R), tenderness (T), leukocytosis (L), Acute phase protein-CRP (A), and serum bilirubin (B). Contributing points for these parameters are listed in Table 1.

In our novel score, positive findings of sonography (S) and tenderness (T) are awarded a score of two while migratory right iliac fossa pain (M), anorexia (A), rebound tenderness (R) are given scores of one each. Leukocytosis (L) of the order of 10.0-14.9 x 10^9 Cells/L and ≥15.0 x 10^9 Cells/L is given a score of two and three, respectively. When either CRP (Acute phase protein) of ≥10 mg/L or polymorphonuclear leukocytes of ≥80% or even both where present, a score of only one is given. Serum bilirubin (B)

Table 1. SMART-LAB Score (Shabir's Score)

Findings		Points
Sonography (S)		2
Migratory right iliac fossa pain (M)		1
Anorexia (A)		1
Rebound tenderness (R) or muscular defense		1
Tenderness (T)		2
Leukocytosis (L)	10.0-14.9 x 10^9 Cells/L	2
	≥15.0 x 10^9 Cells/L	3
*CRP (Acute phase protein) ≥10 mg/L or polymorphonuclear leukocytes≥ 80%		1
Serum bilirubin (B)	≥1.5 mg/dL	3
Total possible score		14

CRP: C-reactive protein.

* Use CRP or polymorphonuclear leukocytes, whichever is available or above cut-off, if both are available.

of ≥1.5mg/dL is given a score of three. Maximum total possible score is 14. Parameters more specific for complicated appendicitis are given a maximum individual score of three. ROC curve analysis was performed during the analysis of our novel score.

Management

Preoperatively, the patients were kept nil per oral and received intravenous fluids along with intravenous antibiotics including ceftriaxone or piperacillin tazobactam, with or without metronidazole or tinidazole. No analgesic was given preoperatively. We used the open approach for operative intervention in all study patients. Surgical findings of all patients were recorded separately. All patients were followed for two weeks after surgery, and their histopathological findings were recorded. The initial diagnosis made by the experienced surgical team was based on the usual practice (history/clinical examination/ultrasonography/WBC/differential neutrophil count) before final gold standard diagnosis (operative/histopathology) was reached in our study population of 150 patients as positive or negative for complicated appendicitis. Then the overall sensitivity and specificity of this usually practiced method in predicting complicated appendicitis compared to final gold standard diagnosis (operative/histopathology) was assessed. In addition, sensitivity and specificity of SMART-LAB score for predicting complicated appendicitis compared to final gold standard diagnosis (operative/histopathology) was calculated.

Definitive diagnosis was based on histopathological examination. Patients undergoing interval appendectomies and patients with negative appendectomies confirmed on histological report were excluded from the study. Other exclusion criteria included patients with risk factors for hepatic disease such as alcoholism, a history of viral hepatitis, Gilbert's disease, Dubin-Johnson syndrome, benign recurrent intra-hepatic cholestasis, and other documented biliary, and hemolytic or liver diseases associated with hyperbilirubinemia.

This research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethics Principles for Medical Research Involving Human Subjects"

Statistical Methods

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean ± SD, and categorical variables were summarized as frequencies and percentages. Chi-square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. In order to determine the optimal cutoffs of SMART-LAB Score for prediction of various forms of appendicitis, receiver operating characteristic (ROC) analysis was performed. Further diagnostic accuracy (sensitivity, specificity, PPV and NPV) of SMART-LAB score was obtained by taking operative/histopathological findings as gold standard. A P-value of less than 0.05 was considered statistically significant. All P-values were two tailed.

RESULTS

Design of the Study

This prospective study was carried out in the Postgraduate Department of Surgery at Government Medical College Srinagar over a period of two years from January 2014 to January 2016. The study consisted of patients admitted with the clinical suspicion of acute appendicitis. The study finally included a group of 150 patients who had histologically proven appendicitis, and fifteen patients unproven by histological examination to have appendicitis (negative appendectomies) were excluded from the study. Two more patients were excluded in accordance with other exclusion criteria. Mean age of our patients in years was 15.3 with a standard deviation of 4.39. Majority of the patients belonged to the age groups of 10-19 years and 20-29 years, respectively containing 59 (39.3%) and 51 (34%) patients. There were 97 males and 53 females included in our study.

Mean duration of symptoms (hours) at presentation in our study was 34.8 with a standard deviation of 12.34. Most (36.7%) of the patients presented within 24 hrs of the development of the symptoms. The most common symptom was pain in the right iliac fossa.

All patients with an initial diagnosis of appendicitis were operated up on. The study finally included a group of 150 (Table 2) patients who had histologically proven appendicitis and oth-

Table 2. Demographic distribution & duration of symptoms

Demographic Distribution	
Age group (years)	Number of patients (%)
Up to 9	21 (14%)
10-19	59 (39.3%)
20-29	51 (34%)
>30	19 (12.6%)
Total	150 (100%)
Sex distribution	
Males	97 (64.7%)
Females	53 (35.3%)
Duration of symptoms (hours)	
Hours	Number of patients (%)
<24	55 (36.7%)
24-48	52 (34.7%)
48-72	24 (16%)
>72	19 (12.6%)
Total	150 (100%)

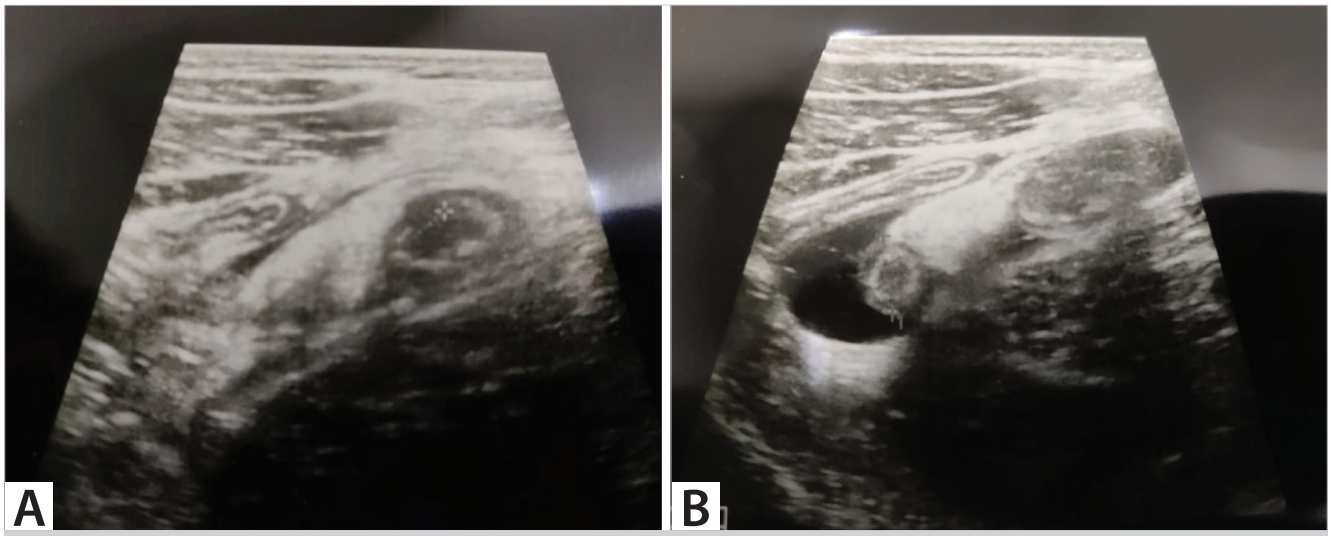

Figure 1. A. USG image. USG image of a patient showing tubular blind ending inflamed gut loop in RIF with marked peri-appendiceal fat stranding with focal breach likely perforated appendix. **B.**, USG image of the same patient showing inflamed appendix with small peri-appendiceal collection suggestive of acute appendicitis with perforation.

ers were excluded. Of the 150 patients included in this study, 52 cases turned out to be of complicated (perforated and/or gangrenous) appendicitis (Figures 1,2) on intraoperative/histopathologic examination. Duration of symptoms is recorded in Table 2. Among the perforated and /or gangrenous and non-perforated cases, the preoperatively calculated SMART-LAB score and the analysis of SMART-LAB score and its diagnostic accuracy are shown in Tables 3 and 4.

We came up with a score of more than nine to be positive in cases of complicated appendicitis and similarly a score of five or more, i.e. more than four, in cases of appendicitis by performing ROC curve analysis (Figures 3,4; Table 5).

Since the majority (82.6) of patients in uncomplicated appendicitis group had SMART-LAB score of ≥5 (i.e.> 4), only 17.4% had a score of 3-4, hence it represents high likelihood of appendicitis for a score ≥5 (i.e.> 4), while a score of 3-4 needs further confirmation to reach a conclusion, and for a score of <3, there is low likelihood of appendicitis.

SMART-LAB score of >9 was present in a significantly higher number of patients in complicated (perforated and gangrenous) appendicitis than uncomplicated appendicitis (p value< 0.001). Cut off was chosen as "nine" because the greatest sum of sensitivity and specificity was achieved at this value. Hence, it sounds high likelihood of complicated appendicitis for a sore >9 (with a sensitivity= 80.7%, specificity= 92.9%, PPV= 85.7%, NPV= 90.1%, and accuracy= 88.7%) while a score of 7-9 needs further confirmation to reach a conclusion, and for a score of <7 there is low likelihood of complicated appendicitis.

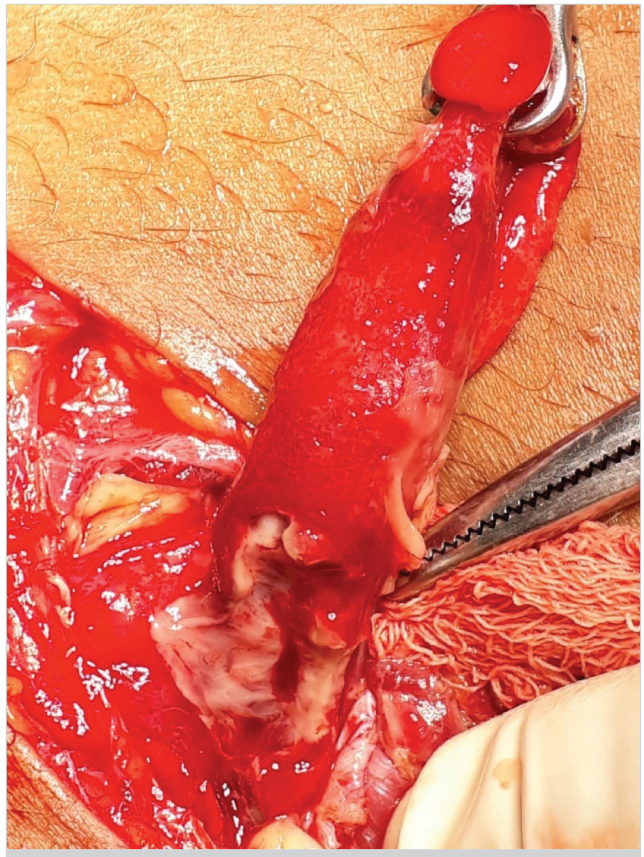

Figure 2. Intraoperative picture of the same patient showing complicated appendicitis.

Table 3. Cut-off values (SMART-LAB Score)				
Cut-off value (SMART-LAB Score) for Complicated appendicitis= 9				
SMART-LAB score in complicated appendicitis	Number of patients (%)			
Score of patients	42 (80.8%)			
>9	8 (15.4%)			
7-9	2 (3.8%)			
<7	52 (100%)			
Total				
Majority of patients with complicated appendicitis had a score of >9.				
SMART-LAB score in non-perforated appendicitis				
Score	Number of patients(%)			
>9	7 (7.1%)			
5-9	74 (75.5%)			
3-4	17 (17.3%)			
Total	98 (100%)			
Analysis of SMART- LAB score with respect to score 9 as cut-off				
Status of appendix	Score positive (>9)	Score negative (≤9)	Total	Positive rate
Perforated &/or gangrenous (complicated)	42	10	52	80.7%
Non perforated (uncomplicated)	7	91	98	7.1%
Total	49	101	150	
$\chi 2$= 83.72; df= 1; P< 0.001				
Cut-off value (SMART-LAB Score) for appendicitis= 4				
Analysis of SMART- LAB score in non-perforated cases of appendicitis				
Status of appendix	Score positive (≥5 i.e.> 4)	Score negative (<5 i.e.≤ 4)	Total	Positive rate
Non perforated/non gangrenous appendicitis	81	17	98	82.6%
No appendicitis	2	13	15	13.3%
Total	83	30	113	
$\chi 2$= 32.06; df= 1; P< 0.001.				
Analysis of SMART- LAB score in appendicitis				
Status of appendix	Score positive (≥5 i.e.> 4)	Score negative (<5 i.e.≤ 4)	Total	Positive rate
Appendicitis	133	17	150	88.66%
No appendicitis	2	13	15	13.3%
Total	135	30	165	
$\chi 2$= 52.02; df= 1; P< 0.001.				

Further information regarding the utility of this score in the diagnosis of uncomplicated appendicitis, and all appendicitis patients, is given in Table 3 and 4.

SMART-LAB score of ≥5 (i.e.> 4) was present in a significantly higher number of patients in uncomplicated (non-perforated and non-gangrenous) appendicitis than in patients who were proven to be negative for appendicitis (p value of< 0.001) on histological examination.

Table 4. Diagnostic accuracy of SMART-LAB score		
Diagnostic accuracy of SMART-LAB score for complicated appendicitis(cut-off value= 9)		
Variable	Value (%)	95% Confidence Interval
Sensitivity	80.7	67.48-90.37
Specificity	92.9	85.82-97.08
PPV	85.7	72.77-94.05
NPV	90.1	82.57-95.14
Accuracy	88.7	
Diagnostic accuracy of SMART-LAB score for simple appendicitis (cut-off value= 4)		
Variable	Value (%)	95% Confidence Interval
Sensitivity	82.6	73.70-89.55
Specificity	86.7	59.57-98.34
PPV	97.6	91.56-99.71
NPV	43.3	25.47-62.54
Accuracy	83.2	
Diagnostic accuracy of SMART-LAB score for appendicitis (both simple & complicated)= cut-off value 4		
Variable	Value (%)	95% Confidence Interval
Sensitivity	88.67	82.48-93.26
Specificity	86.67	59.54-98.34
PPV	98.52	94.81-99.59
NPV	43.3	31.91-55.51
Accuracy	88.48	
PPV: Positive predictive value; NPV: Negative predictive value.		

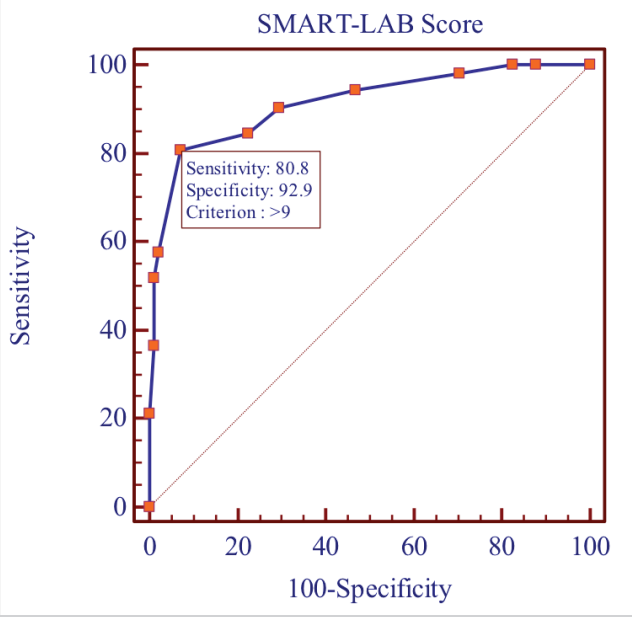

Figure 3. ROC analysis of SMART-LAB score for complicated appendicitis.

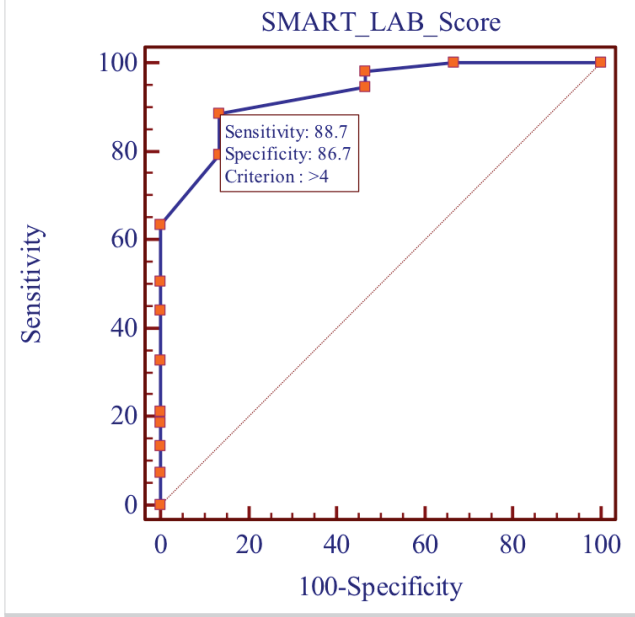

Figure 4. ROC analysis of SMART-LAB score for appendicitis.

Table 5. ROC analysis

ROC analysis of SMART-LAB score for complicated appendicitis			ROC analysis of SMART-LAB score for appendicitis		
Variable	**Value (%)**	**95% Confidence Interval**	**Variable**	**Value (%)**	**95% Confidence Interval**
Optimal cutoff	>9	-	Optimal cutoff	>4	-
Area under ROC curve	0.913	0.856-0.953	Area under ROC Curve	0.932	0.882-0.965

DISCUSSION

Despite being one of the most frequent diagnoses among surgical emergencies, acute appendicitis continues to pose significant diagnostic problems. The difficulty of diagnosing acute appendicitis in old age is reflected by high incidence of perforation, 60-90%, in many reports rather than by a high rate of negative appendicectomy (16,17). Morbidity and mortality rates associated with appendicitis are greatly increased when perforation ensues, wound infection rates may treble, intra-abdominal abscess formation increases 15-fold and mortality may be 50 times greater. Three of our patients in the complicated appendicitis group developed surgical site infection postoperatively and were managed successfully. Appendiceal perforation can also cause tubal infertility (18). In our present study, long term follow up was not available to look for such complications of complicated appendicitis. Early diagnosis of appendiceal perforation is important to limit the associated abdominal sepsis.

In the present study, the author tested a novel score to predict the diagnosis of complicated (perforated/gangrenous) appendicitis. The score included eight components. The components included serum bilirubin, USG (ultrasonography), Acute phase protein-CRP or polymorphonuclear leukocyte percentage, and modified score for leucocyte count, in addition to the few components used in usual Alvarado score. Author recommends use of C-reactive protein (CRP) or percent polymorphonuclear leukocyte count, whichever is available or above cut off if both are available (either one if both are above the cut off).

The author has already found in one of his studies that serum bilirubin, CRP, and ultrasound are effective for differentiating perforated from nonperforated appendicitis. Bilirubin, CRP, and USG are important preoperative biochemical and sonographic markers of perforation, respectively in appendicitis (19). The diagnosis of perforation on USG was made by visualization of loculated pericecal fluid, phlegmon or abscess, prominent pericecal or periappendiceal fat and circumferential loss of the submucosal layer of the appendix (20). Serum bilirubin is an important adjunct in diagnosing the presence of gangrenous/perforated appendicitis (21). Preoperative assessment of Bilirubin, CRP, WBC and Alvarado scoring system together, as a routine procedure for patients admitted in the emergency ward, may help the surgeon determinate the risk of complications in acute appendicitis (22).

We came up with a score of more than nine to be positive in cases of complicated appendicitis and similarly, a score of five or more i.e. more than four, in cases of appendicitis by performing ROC curve analysis (Figures 3,4; Table 5). In the present study, SMART-LAB score of >9 was present in significantly higher number of patients in the group of complicated (perforated and gangrenous) appendicitis than the uncomplicated appendicitis (p value of <0.001). Hence, it sounds high likelihood of complicated appendicitis for a score >9, while a score of 7-9 needs further confirmation to reach a conclusion of complicated appendicitis, and for a score of <7, there is low likelihood of complicated appendicitis. The high predictive power of SMART-LAB score for complicated appendicitis seems to come from the incorporation of specific markers for gangrenous or perforated appendicitis in the novel score like serum bilirubin, USG (ultrasonography), acute phase protein-CRP or polymorphonuclear leukocyte percentage, and modified score for leukocyte count. SMART-LAB score of ≥5 (i.e.> 4) was present in significantly higher number of patients in uncomplicated (non-perforated and non-gangrenous) appendicitis than in patients who were proven to be negative for appendicitis (p value of <0.001) on histological examination. Also, the majority (82.6%) of patients in uncomplicated appendicitis group had SMART-LAB score of ≥5 (i.e.> 4), while only 17.4% had a score of 3-4, hence it sounds high likelihood of appendicitis for a sore ≥5 (i.e.> 4), while a score 3-4 needs further confirmation to reach a conclusion, and for a score of <3, there is low likelihood of appendicitis.

It has been shown that during appendicitis, an ulceration of the mucosa in the appendix occurs due to inflammation which facilitates bacterial translocation from the appendix to the portal blood system (23). The most common bacteria to infect the appendix is *E. coli* when *E. coli* reaches the hepatic tissue through the portal venous system, animal models have shown that the bacteria interferes with the hepatocyte microcirculation, which induces damage to the liver cells and compromises excretion of bile acids into the bile canaliculi (24). Furthermore, *E. coli* has been shown to induce intravascular hemolysis, and both mechanisms may result in an increased amount of bilirubin circulating in the blood (25). Bilirubin can be elevated in cases of sepsis, intra-abdominal abscesses from urological, gynecological or gastroenterological origins, antiviral therapy or in patients with genetic disease such as Dubin-Johnson syndrome, Rotor's syndrome, and Gilbert's syndrome (26). It has been proposed that hyperbilirubinemia is a weak marker of appendiceal perforation among persons with Gilbert's syndrome (27). There exists no single diagnostic test or symptom other than surgery with

pathologic examination that can definitely result in a diagnosis. In a study by Mcgowan et al., the authors have found that biochemical markers (bilirubin, CRP and white cell count) were significantly higher in perforation ($p< 0.001$). The greatest sum of sensitivity and specificity of CRP was at 34.6 mg/L (sensitivity 78.57%, specificity 63.01%), and bilirubin was at 21.5 µmol/L (sensitivity 62.96%, specificity 88.31%). They have concluded that Bilirubin and CRP are markers of perforation in appendicitis, but are not accurate enough to be diagnostic (28).

Cumulative sensitivity and specificity of all components together was significantly more than any individual parameter of "SMART-LAB" score in predicting complicated appendicitis. Sensitivity (80.7%), specificity (92.9%), and diagnostic accuracy (88.7%) of "SMART-LAB" score for complicated appendicitis were better than the initial diagnosis (61.54%, 83.67%, and 76% respectively) made by the experienced surgical team as per routine practice (history/clinical examination/WBC/differential neutrophil count/USG). However, in case of simple appendicitis, "SMART-LAB" SCORE had sensitivity and specificity similar to initial diagnosis made by usual practice method. Hence, our novel score seems to be valuable for predicting complicated appendicitis.

CONCLUSION

It seems that this novel score (Shabir's SMART-LAB score) is a reasonably good tool to predict the diagnosis of complicated appendicitis. Early diagnosis of appendiceal perforation is important to limit associated abdominal sepsis. It also has the potential to predict diagnosis of simple uncomplicated appendicitis. Serum bilirubin seems to be a valuable component of this novel score for predicting complicated appendicitis.

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Ethics Committee Approval: This study was approved Government Medical College Ethical Committee (Decision no: 125/ETH/GMC/ICM, Date: 10.01.2014).

Peer-review: Externally peer-reviewed.

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

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2022; 38 (2): 140-148

Komplike apandisiti öngörmede Shabir'in "SMART-LAB" skoru: Prospektif bir çalışma

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ÖZET

Giriş ve Amaç: Komplike apandisitte agresif ve acil müdahale gerekir, bu sebeple komplike apandisiti öngörmek adına etkili bir skorlama sistemine ihtiyaç vardır. Bu amaçla, yazar tarafından komplike akut apandisiti öngören bir skorlama sistemi geliştirildi. Bu çalışmanın amacı, komplike apandisit tanısının öngörülmesinde bu yeni skorlama sisteminin (Shabir'in SMART-LAB skoru) uygunluğunu değerlendirmekti.

Gereç ve Yöntem: Bu prospektif çalışmada, kendi gözlemleri doğrultusunda yazar (Shabir) tarafından geliştirilen "SMART-LAB SCORE" adındaki bu yeni skor tüm hastalarda hesaplandı. Bu skorlama sistemine sonografi (S), migratör sağ iliyak fosa ağrısı (M), anoreksiya (A), tepkisel duyarlılık (R), duyarlılık (T), Lökositoz (L), akut faz protein-CRP (A) ve serum bilirubin (B) dahildir.

Bulgular: Çalışmaya dahil edilen 150 hastanın 52'sinde perfore/gangrenöz apandisit olduğuna intraoperatif/histopatolojik inceleme sonucunda ulaşıldı. En yaygın olarak etkilenen yaş grubu 10-19 yıl idi. SMART-LAB >9 skoru, komplike (perfore veya gangrenöz) apandisit hastalarında komplike olmayan apandisit hastalarına göre daha fazla bulundu (P değeri< 0,001, yani yüksek oranda anlamlı). Bu doğrultuda, >9 skorda komplike apandisit yüksek olasılıkta (sensitive= %80,7, spesifite= %92,9, PPV= %85,7, NPV= %90,1, ve doğruluk= %88,7), 7-9 arası skorda sonuca ulaşmak için daha detaylı incelemeler gerektiği ve <7 skorda komplike apandisitin düşük olasılıkta olduğu bulundu.

Sonuç: Bu yeni skor sisteminin (Shabir'in SMART-LAB skoru), komplike apandisit tanısını öngörmede makul bir derecede iyi olduğu ortaya çıktı. İlişkili abdominal sepsisi sınırlamak için apandisit perforasyonunun erken tanısı önemlidir.

Anahtar Kelimeler: Gangrenöz/perfore apandisit, SMART-LAB skoru, bilirubin, lökosit sayısı, ultrasonografi

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ORIGINAL ARTICLE
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Experience of endoscopic retrograde cholangiopancreatography with side-viewing duodenoscope in patients with previous gastric surgery

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ABSTRACT

Objective: Endoscopic Retrograde Cholangiopancreatography (ERCP) with conventional side-viewing duodenoscope can be challenging and unsuccessful at altered anatomy in the gastrointestinal tract. This study aimed to evaluate our experience with ERCP in patients with previous gastric surgery.

Material and Methods: Patients on whom ERCP was performed from January 2017 to August 2021 and who had previous gastric surgery were included into the study. Age, sex, comorbidity, Charlson's Comorbidity Index (CCI), ERCP indication, previous gastric surgery (indication, type of resection and reconstruction), history of cholecystectomy, and MRCP results were evaluated retrospectively. The results were compared as successful ERCP (SERCP) or unsuccessful ERCP (USERCP). Also, odds ratio ERCP failure was also evaluated.

Results: Forty-three patients were included into study. Mean age was 68.8 ± 13.6 years. The most common sex was female (51.2%). The most common ERCP indication was choledocholithiasis with 44.2%, gastric surgery indication was peptic ulcer with 72.1%, gastric resection was subtotal with 67.4%, and reconstruction was gastrojejunostomy with 58.1%. The success rate of ERCP was 44.2%. Mean CCI was 4.16 ± 2.28. Only malignancy history was significantly higher in the USERCP group (p= 0.026). Male sex, non-choledocholithiasis indication, history of malignancy, CCI> 4, total gastrectomy, Roux-NY (RNY) reconstruction, history of cholecystectomy, and intercalarily to the bile duct dilatation in MRCP were likelihood for USERCP.

Conclusion: While history of malignancy and cholecystectomy were the only significant factor for unsuccessful ERCP, male sex, total gastrectomy, RNY anastomosis result in a higher likelihood of ERCP failure in patients with previous gastric surgery. Alternative devices to side-viewing duodenoscope will increase success in selected patients.

Keywords: Endoscopic retrograde cholangiopancreatography, gastrectomy, roux ny, gastrojejunostomy

INTRODUCTION

The incidence of biliary tract stones (BTS) increases after gastrectomy as a result of (1) resection of the hepatic branch of the nervus vagus, (2) non-physiologic reconstruction, (3) biliary tract infection, (4) and altered response and secretion of cholecystokinin (1). Biliary tract stones occurs at a rate of 16.6% after gastric surgery, whereas the incidence is 4.4% in the general population. Biliary tract stones is most common after total gastrectomy with 6.6%, proximal gastrectomy with 5.4%, and distal gastrectomy with 4.8%. Biliary tract stones is most common after Billroth II with 18% and Roux-en-Y (RNY) reconstruction with 17.8%. The incidence of BTS reaches 39% after ten years of gastric surgery. Fifty-three percent of BTS occur at the the common biliary duct (CBD). Common biliary duct stones with 70.5% and cholangitis with 14.1% are the most common indication of ERCP in patients with previous gastric surgery (2-4).

Endoscopic Retrograde Cholangiopancreatography (ERCP) is an important and effective diagnostic and therapeutic modality for pancreaticobiliary disorders. The difficulty of ERCP has been graded by Cotton et al. and American Society for Gastrointestinal Endoscopy (ASGE), and previous gastric surgery has been graded as more difficult (5,6). The difficulties of ERCP with previous gastric surgery include (1) identifying the pancreaticobiliary enteral limb; (2) reaching and identifying the major papilla or the pancreaticoenteric and/or bilioenteric anastomoses (3); selectively cannulating the biliary or pancreatic duct from an altered orientation; and (4) performing therapeutic interventions with ERCP (7). The success rate of the ERCP procedure varies from 70.4% to 99% and decreases with higher grades (8,9). The

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success rate of ERCP changes with the type of gastric surgery performed. The overall success rate of ERCP with gastric surgery has been reported as 91.8%; however, the success rate decreases to 86.4% in pancreaticoduodenectomy patients (10-12). Indication of ERCP, type of previous gastric surgery, and type of the previous reconstruction have been reported as significant risk factors for ERCP success in patients with previous gastric surgery (13). The aim of this study was to evaluate our experience with ERCP in patients with previous gastric surgery.

MATERIAL and METHODS

After receiving approval from the ethics committee of İstanbul Prof. Dr. Cemil Taşçıoğlu City Hospital (16/06/2020 date and 250 number), accessible patient records from January 2017 to August 2021 of those with previous gastric surgery on whom ERCP was performed were evaluated retrospectively. No written consent was obtained from the patients because the study was retrospective.

Patient's age, sex, the indication of ERCP, findings of magnetic resonance cholangiopancreatography (MRCP), the success of ERCP (successful ERCP: SERCP, unsuccessful ERCP: USERCP), treatment of unsuccessful ERCP, survival, comorbidities, and Charlson's Comorbidity Index (CCI) were evaluated retrospectively. Additionally, the indication of gastric surgery, previous gastric surgery, type of gastric resection, type of reconstruction, history of cholecystectomy, and the year ERCP was performed were also evaluated. Moreover, all parameters were compared with ERCP being successful or unsuccessful.

All ERCP procedures were performed by an experienced endoscopist surgeon, under sedoanalgesia and in prone position. All patients received nasal oxygen, followed by monitoring oxygen saturation and electrocardiography. Prophylactic antibiotics were explicitly used. ERCP was performed under fluoroscopic control by side-viewing duodenoscope with a total length of 120 cm and a working channel of 3.4 mm in diameter, which allowed the use of a wide range of catheters according to the diagnostic or therapeutic objective (Fujinon XL-4450, Tokyo, Japan). All patients were hospitalized one day to be followed for ERCP complications.

Indication of ERCP was evaluated as choledocholithiasis, cholangitis, suspicion of malignancy, pancreatitis, and biliary fistula. Findings of MRCP were evaluated as normal, dilated biliary tract, dilated biliary tract with calculi, dilated biliary tract with sudden end, dilated biliary tract with external pressure. Treatment of USERCP was evaluated as percutaneous transhepatic cholangiography (PTC), surgery (choledocotomy, choledocoduedonostomy, or hepaticojejunostomy), or conservative treatment.

Indications of gastric surgery were evaluated as peptic ulcer, gastric malignancy, pancreatic malignancy, pyloric stenosis, or obesity. Previous gastric surgery was evaluated as distal subtotal gastrectomy with gastrojejunostomy (Billroth II gastrectomy) (BR-II), total gastrectomy with RNY gastrojejunostomy (TG+RNY-GJ), distal subtotal gastrectomy with RNY gastrojejunostomy (DG+RNY-GJ), gastrojejunostomy (GJ), jaboulay pyloroplasty (JP), or sleeve gastrectomy with bypass (SG+B). Type of gastric resection was evaluated as none, subtotal, or total. Type of reconstruction was evaluated as gastrojejunostomy (GJ), RNY gastrojejunostomy (RNY), jaboulay pyloroplasty (JP), or bypass.

Statistical analysis was performed with SPSS 15.0., age was expressed as mean ± standard deviation. Nonparametric values were analyzed with Mann-Whitney U, parametric values with t test, odds ratio was analyzed for unsuccessful ERCP (95% Confidence Interval, Lower- Upper Bound), and $p< 0.05$ was accepted as significant.

RESULTS

From one thousand three hundred ninety ERCP performed patients, 43 patients with previous gastric surgery were included into the study. Mean age was 68.8 ± 13.6 years, 51.2% of the patients were females. Choledocholithiasis was the most common indication of ERCP with 44.2% (n= 19), cholangitis with 17.9% (n= 12), and suspicion of malignancy with 18.6% (n= 8). Isolated DBT was the most common finding of MRCP as 37.3% (n= 16), DBT with calculi as 27.9% (n= 12), and normal only in two patients (4.6%). The success rate of ERCP was 44.2% (n= 19). Surgery was the most common treatment for unsuccessful ERCP with 45.8% (n= 11), choledochotomy + T tube drainage performed in six patients, choledochoduedonostomy performed in four patients, and hepaticojejunostomy in one patient. Perforation occurred in only two patients; one of them died (2.3%). Hypertension was the most common comorbidity with 39.5% (n= 17), and diabetes mellitus and heart disease with 23.2% (n= 10). Mean of CCI was 4.16 ± 2.28 (Table 1).

Peptic ulcer was the most common indication of gastric surgery with 72.1% (n= 31), gastric malignancy with 14% (n= 6), and pancreatic malignancy with 7% (n= 3). DG+GJ was the most common previous gastric surgery with 51.1% (n= 22), TG+ RNY with 18.6% (n= 8), and DG+RNY with 14% (n= 6). 67.4% (n= 29) of the patients performed distal subtotal, and 18.6% (n= 8) total gastrectomy. 58.1% (n= 25) of the patients performed GJ (Figure 1), and 32.4% (n= 14) RNY (Figure 2) reconstruction. Of the patients, 69.8% (n= 30) underwent cholecystectomy. Higher numbers of ERCP were performed in 2017 with 27.9% (n= 12) and 2019 with 25.6% (n= 11) (Table 2).

Mean age was 66.9 ± 13.5 years in USERCP and 71.1 ± 13.6 years in SERCP, but the difference was not statistically significant (p= 0.322). 62.5% of USERCP and 36.8% of SERCP were males, but the difference was not statistically significant (p= 0.099). Choledocholithiasis was the most common indication of ERCP, both USERCP and SERCP (41.7% vs. 47.4%), 20.8% of the USERCP, and 36.8% of the SERCP had cholangitis. The difference

Table 1. Results of ERCP with previous gastric surgery		
Age (years)*	68.8 ± 13.6	
Sex	n	%
Male	21	48.8
Female	22	51.2
Indication	n	%
Choledocholithiasis	19	44.2
Cholangitis	12	27.9
Suspicion of malignancy	8	18.6
Pancreatitis	3	7
Biliary fistula	1	2.3
MRCP Results	n	%
Normal	2	4.6
DBT	16	37.3
DBT with calculi	12	27.9
DBT with sudden ends	11	25.6
DBT with external pressure	2	4.6
ERCP success	n	%
Yes	19	44.2
No	24	55.8
Treatment of USERCP	n	%
PTC	4	16.7
Surgery	11	45.8
Conservative	9	37.5
Survival	n	%
Mortality	1	2.3
Alive	42	97.7
Complication	n	%
No	41	95.4
Yes	2	4.6
Comorbidities	n	%
Hypertension	17	39.5
Diabetes Mellitus	10	23.2
Heart disease	10	23.2
Malignancy	9	20.9
Neurologic disease	7	16.3
Pulmonary disease	5	11.6
Endocrinologic disease	3	7
Chronic renal failure	2	4.6
CCI*	4.16 ± 2.28	

*Mean ± SD, ERCP: Endoscopic retrograde cholangiopancreatography, MRCP: Magnetic resonance cholangiopancreatography, DBT: Dilated biliary tract, USERCP: Unsuccessful ERCP, PTC: Percutaneous transhepatic cholangiography. CCI: Charlson comorbidity index.

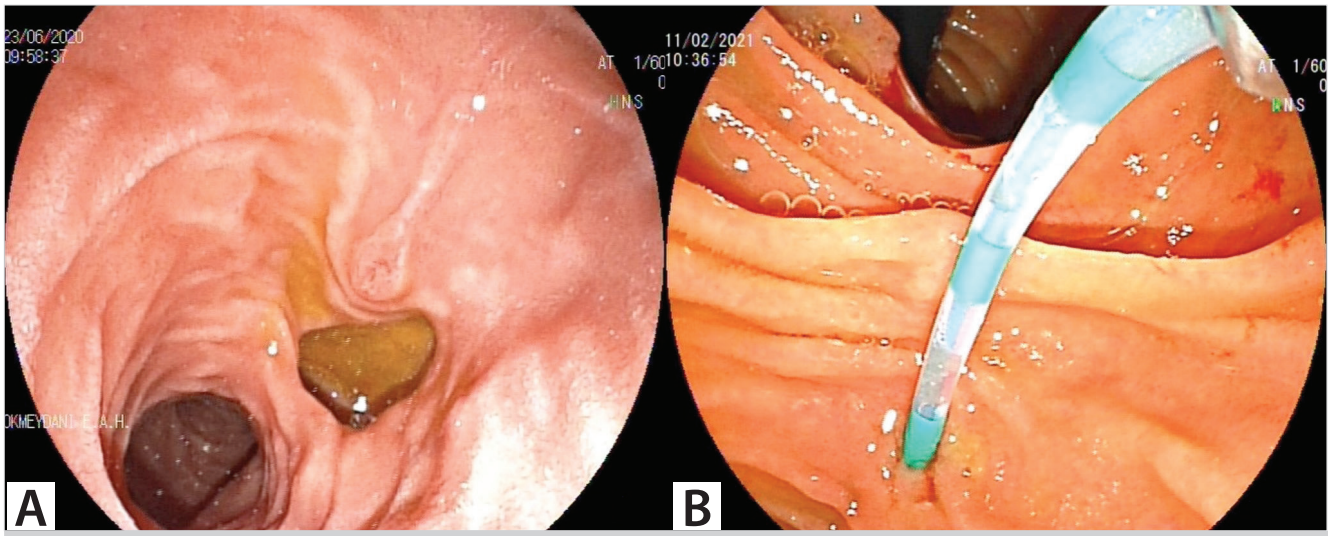

Figure 1. Duodenoscopic images of ERCP in patient with previous gastric surgery **A:** Papilla and duodenum, **B:** Canulation of papilla.

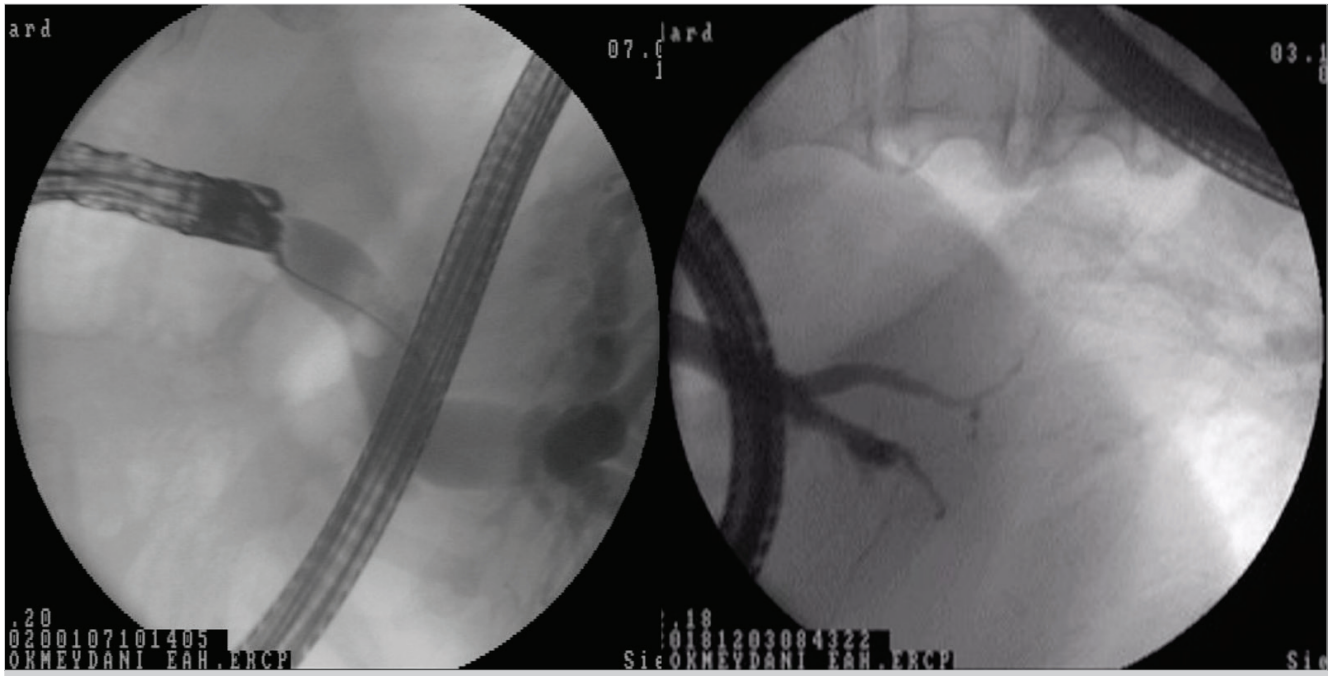

Figure 2. Fluoroscopic images of ERCP in patient with previous gastric surgery.

for ERCP indication was not statistically significant (p= 0.406). From comorbidities, only history of malignancy was statistically higher in USERCP with 33.3% vs. 5.3% (p= 0.026). The mean of CCI for USERCP was 4.04 ± 2.23, for SERCP was 4.32 ± 2.40, but not statistically different (p= 0.701). Peptic ulcer was the most common indication of gastric surgery for both groups (66.7% vs. 73.7%), and the subsequent indication for USERCP was gastric malignancy with 20.8%, for SERCP was pyloric stenosis with 15.8%. The difference in the indication of gastric surgery was not statistically significant (p= 0.588). Subtotal gastrectomy was the most common type of gastric resection for both USERCP and SERCP with 66.7% vs. 68.4%, respectively, and 8.3% (n= 2) of the USERCP and 21.1% (n= 4) of the SERCP had no gastrectomy. The difference in the type of gastric resection was not statistically significant (p= 0.124). Gastrojejunostomy was the most common type of reconstruction for both USERCP and SERCP with 58.3% vs. 57.9%, respectively, and JP and bypass were performed only on SERCP patients. The difference for reconstruction was not statistically significant (p= 0.80). 41.7% of USERCP patients and 15.3% of SERCP patients had history of cholecystectomy. The difference between the history of cholecystectomy was not statistically significant (p= 0.07). The success of

Table 2. Results of previous gastric surgery and time of ERCP		
Indication of gastric surgery	n	%
Peptic ulcer	31	72.1
Gastric malignancy	6	14
Pancreatic malignancy	3	7
Pyloric stenosis	2	4.6
Obesity	1	2.3
Previous gastric surgery	n	%
DG+GJ	22	51.1
TG+RNY	8	18.6
DG+RNY	6	14
GJ	3	7
JP	3	7
SG+B	1	2.3
Type of gastric resection	n	%
None	6	14
Subtotal	29	67.4
Total	8	18.6
Type of reconstruction	n	%
GJ	25	58.1
RNY	14	32.6
Jaboulay	3	7
Bypass	1	2.3
History of Cholecystectomy	n	%
No	30	69.8
Yes	13	30.2
Time of ERCP (year)	n	%
2017	12	27.9
2018	8	18.6
2019	11	25.6
2020	9	20.9
2021	3	7

DG+GJ: Distal gastrectomy with gastrojejunostomy, TG+RNYGJ: Total gastrectomy with RNY gastrojejunostomy, DG+RNYGJ: Distal gastrectomy with RNY gastrojejunostomy, GE: Gastroenterostomy, JP: Jaboulay pyloroplasty, SG+B: Sleeve gastrectomy with bypass. GE/GJ: Gastroenterostomy/gastrojejunostomy, RNYGJ: RNY gastrojejunostomy, ERCP: Endoscopic retrograde cholangiopancreatography.

the ERCP rate increased by years from 25% to 66.7%, but the difference was not statistically significant (p= 0.297). Only DBT was the most common MRCP findings for SERCP with 84.2%; however, DBT with calculi was the most common for USERCP with 37.5%. The difference in MRCP findings was not statistically significant (p= 0.259) (Table 3).

The ODDs ratio for the history of malignancy was 1.889 (1.235-2.889), DBT+findings in MRCP was 1.707 (0.850-3.428), and history of cholecystectomy was 1.648 (1.015-2.677). The ODDs ratio for unsuccessful ERCP is shown in Table 4.

DISCUSSION

Gallstones occur more commonly in patients with gastric surgery, and half of the BTS occur at CBD. Endoscopic retrograde cholangiopancreatography is an important and useful diagnostic and therapeutic modality for CBD stones. However, ERCP in patients with surgically altered gastric anatomy is more difficult and has a lower success rate. Therefore, forward-viewing gastroscope, colonoscope, single or double-balloon enteroscope, endo USG assisted ERCP, or laparoscopic-assisted transgastric ERCP are alternative devices for conventional side-viewing duo-

Table 3. Comparison of USERCP and SERCP

Parameters	**USERCP (n= 24)**		**SERCP (n= 19)**		p
Age (year)*	66.9 ± 13.5		71.1 ± 13.6		0.322
Sex	n	%	n	%	0.099
Female	9	37.5	12	63.2	
Male	15	62.5	7	36.8	
Indication of ERCP	n	%	n	%	0.406
Choledocholithiasis	10	41.7	9	47.4	
Cholangitis	5	20.8	7	36.8	
Suspicion of malignancy	7	29.2	1	5.3	
Pancreatitis	1	4.2	2	10.5	
Biliary fistula	1	4.2	0	0	
Comorbidities	n	%	n	%	p
Hypertension	7	29.2	10	52.6	0.122
Diabetes mellitus	4	16.7	6	31.6	0.256
Heart disease	5	20.8	5	26.3	0.676
Malignancy	8	33.3	1	5.3	0.026
Neurologic disease	3	12.5	4	21.1	0.456
Pulmonary disease	2	8.3	3	15.8	0.454
CCI*	4.04 ± 2.23		4.32 ± 2.40		0.701
Indication of gastric surgery	n	%	n	%	0.588
Peptic ulcer	16	66.7	14	73.7	
Gastric malignancy	5	20.8	1	5.3	
Pancreatic malignancy	3	12.5	0	0	
Pylori stenosis	0	0	3	15.8	
Obesity	0	0	1	5.3	
Type of gastric resection	n	%	n	%	0.124
None	2	8.3	4	21.1	
Subtotal	16	66.7	13	68.4	
Total	6	25	2	10.5	
Type of reconstruction	n	%	n	%	0.80
GJ	14	58.3	11	57.9	
RNY	10	41.7	4	21.1	
Jaboulay	0	0	3	15.8	
Bypass	0	0	1	5.3	

*Mean ± SD, ERCP: Endoscopic retrograde cholangiopancreatography, SERCP: Succeeded ERCPUSERCP: UnsuccessfulERCP, DG+GJ: Distal gastrectomy with gastrojejunostomy, TG+RNYGJ: Total gastrectomy with RNY gastrojejunostomy, DG+RNYGJ: Distal gastrectomy with RNY gastrojejunostomy, GE: Gastroenterostomy, JP: Jaboulay pyloroplasty, SG+B: Sleeve gastrectomy with bypass. GE/GJ: Gastroenterostomy/gastrojejunostomy, RNYGJ: RNY gastrojejunostomy.

Table 3. Comparison of USERCP and SERCP (continue)

Parameters	USERCP (n= 24)		SERCP (n= 19)		p
History of cholecystectomy	n	%	n	%	0.07
No	14	58.3	16	84.2	
Yes	10	41.7	3	15.8	
Time of ERCP (year)	n	%	n	%	0.297
2017	7	58.3	5	41.7	
2018	6	75	2	25	
2019	6	54.5	5	45.5	
2020	4	44.4	5	55.6	
2021	1	33.3	2	66.7	
MRCP results	n	%	n	%	0.259
Normal	2	8.3	0	0	
DBT	6	25	10	52.6	
DBT with sudden ends	6	25	5	26.3	
DBT with calculi	9	37.5	3	15.8	
DBT with external pressure	1	4.2	1	5.3	

ERCP: Endoscopic retrograde cholangiopancreatography, SERCP: Succeeded ERCPUSERCP: Unsuccessful ERCP, MRCP: Magnetic resonance cholangiopancreatography, DBT: Dilated biliary tract.

Table 4. Risk factors of unsuccessful ERCP (Odds Ratio)

Parameters	Odds Ratio	%95 Confidence Interval	
		Lower Bound	Higher Bound
Gender (male/female)	1.591	0.899	2.814
Indication of ERCP (others/choledocholithiasis)	1.108	0.643	1.910
History of malignancy (yes/no)	1.889	1.235	2.889
CCI (CCI> 4/CCI< 4)	1.588	0.843	2.991
Indication of gastric surgery (others/peptic ulcer)	1.292	0.764	2.185
Type of gastrectomy (total/subtotal)	1.359	0.810	2.281
Reconstruction (RNY/GJ)	1.429	0.898	2.272
History of cholecystectomy (yes/no)	1.648	1.015	2.677
Findings of MRCP (+ findings/only DBT)	1.707	0.850	3.428

ERCP: Endoscopic retrograde cholangiopancreatography, CCI: Charlson's comorbidity index, RNY: Roux NY gastrojejunostomy, GE: Gastrojejunostomy MRCP: Magnetic resonance cholangiopancreatography, DBT: Dilated biliary tract.

denoscope in patients with previous gastric surgery (7).

Mean age of ERCP patients with gastric surgery has been reported as >60 years and a higher male rate with 70.3-79.5% (14,15). In our study, mean age of the patients was similar with the literature as 68.8 ± 13.6 years, and ERCP was successful in older patients (71.1 ± 13.6 vs. 66.9 ± 13.7 years). Female was the most common sex for all ERCP (51.2%) and SERCP patients (63.2% vs. 37.5%).

Wu et al. have reported that CBD stone and cholangitis were the most common indication of ERCP in patients with previous gastric surgery (69.1%), and indication of ERCP affected the success of diagnostic and therapeutic ERCP (13). In our study, choledocholithiasis was the most common indication for all ERCP, US-ERCP, and SERCP patients. However, the second most common indication for SERCP was cholangitis, but for USERCP, it was the suspicion of malignancy (36.8% vs. 29.2%). While isolated DBT was the most common MRCP finding of SERCP, additional findings to DBT were more common to MRCP finding of USERCP (52.6% vs. 66.7%).

Indication of previous gastric surgery has affected the success of ERCP due to gastrectomy and reconstruction technique. Peptic ulcer or gastric cancer is the indication of Billroth II gastrec-

tomy; however, RNYGJ is performed for gastric cancer or obesity surgery (16,17). In a recent study, peptic ulcer has been the most common indication of gastric surgery with 69.5%, and in 48% of the operated peptic ulcer patients, ERCP was successful. Also, ERCP was successful in all operated pyloric stenosis and obesity patients.

Type of surgery is the most important factor for ERCP success in patients with previous gastric surgery. Type of gastric resection affects performing ERCP; however, type of reconstruction is a more significant factor affecting ERCP success. The preferred endoscopic device changes with the type of reconstruction from duodenoscope to advanced device endoscope (7). We could only use a side-viewing duodenoscope for ERCP in patients with previous gastric surgery; and therefore, the success rate of ERCP was lower than expected.

Distal gastrectomy or antrectomy with end to side gastrojejunostomy is called Billroth II gastrectomy and performed for peptic ulcer or gastric cancer. The success rate of duodenoscope for reaching the papilla has been reported as 70-90%, and performing biliary cannulation reported as 60-91%. Success rates of other endoscopic interventions reaches to 81-91.5% (18,19). In our study, BR-II was the most commonly performed gastric surgery, but the success rate of ERCP with conventional side-viewing duodenoscope was 41.2%, which is lower than the literature. Independent from the type of gastric resection, gastrojejunostomy was similar for both USERCP and SERCP (58.3% vs. 57.9%)

Total or distal subtotal gastrectomy with RNY gastrojejunostomy performed for gastric cancer or obesity surgery has recently become more popular and useful. There is a controversy for the type of gastric resection that affects ERCP success; however, the length of the RNY limb affects the success of ERCP. Short RNY limb (40-50 cm) is performed in non-bariatric surgery, and long RNY limb (100 cm) is performed at bariatric surgery. Duodenoscope or forward-viewing endoscopes are inadequate for ERCP patients with long RNY limbs. Colonoscope and enterescope (single balloon, double-balloon, or rotational overtube) are more useful endoscopic devices for ERCP patients with long RNY limbs. The success of enteroscopy has been reported as 71-80%, and success of ERCP has been reported as 63-88%. The success of colonoscope has been reported as 50%, and success of ERCP has been reported as 70% (13,18,20). In our study, the success rate of ERCP in patients with previous gastric surgery was affected by the type of gastric resection. Subtotal gastrectomy rate was similar for both groups; however, total gastrectomy rate was higher in USERCP patients (25% vs. 10.5%). RNY-GJ was more common in unsuccessful ERCP patients (41.7% vs. 21.1%).

Gastrojejunostomy without gastric resection is performed for passage continuity at gastric outlet or pylorus saving pancreaticoduodenectomy. The success rate of endoscope insertion has been reported as 86-93.1%; however, ERCP success rate has been reported as 51-63%. The success rate of ERCP increases with advanced device endoscopes (21,22). In our study, the success rate of ERCP in all GJ patients was 46.2% (12/16), and that of ERCP in GJ patients with and without gastric resection was 45.5% (10/22) and 50% (2/4), respectively. GJ with gastric resection decreased the success rate of ERCP.

JP is a side-to-side gastroduodenal anastomosis, which aims to achieve passage continuity of the pyloric stenosis. The success rate of ERCP in patients with JP has been reported as 75% (23). SG+B is performed for obesity, and gallstone occurred with 21.76%, and common biliary duct stone occurred with 9.63%. The success rate of duodenal insertion has been reported as 80-100%, and the success rate of ERCP has been reported as 60 to 70% with advanced device endoscopes (24-26). In our study, the success rate of ERCP in patients with JP and SG+B was 100% despite using conventional side-viewing duodenoscope.

The success rate of ERCP in patients with previous gastric surgery has been reported higher in experienced endoscopists (66.1% vs. 62.5%); however, complication rate has been reported higher in inexperienced endoscopists (6.25% vs. 3.3%) (27). In a recent study, the success rate of ERCP has increased from 41.7% to 66.7% by the experience of the endoscopist.

CBD stones have been reported as 5-15% after open cholecystectomy and as 0.5-2.3% after laparoscopic cholecystectomy. The success rate of ERCP after cholecystectomy has been reported as 97.7% in the literature (28,29). However, there is no study regarding the effect of cholecystectomy on the success of ERCP in patients with previous gastric surgery. In our study, the history of cholecystectomy in patients with previous gastric surgery was 30.2%, and ERCP success rate of cholecystectomy patients was 15.8%.

The success of ERCP increases by choosing alternative devices due to previous gastric resection and reconstruction. However, a side-viewing duodenoscope can be sufficient for ERCP except for long limb Roux-NY gastrojejunostomy. Wu et al. have evaluated age, sex, the indication of ERCP, type of gastric resection, type of reconstruction, and blood thinner as risk factors for ERCP success with side-viewing duodenoscope. Indication of ERCP, type of gastric resection, and reconstruction have been found significant risk factors of ERCP success (13). In our study, male sex, history of malignancy, history of cholecystectomy, other accompanying findings of DBT in MRCP, total gastrectomy, RNY anastomosis, and CCI> 4 decreased the success rate of ERCP in patients with previous gastric surgery.

The limitation of this study is that it is not a prospective randomized clinical trial. A higher number of patients and using alternative devices for ERCP are needed for further studies.

CONCLUSION

Performing ERCP in patients with previous gastric surgery is difficult due to technical challenges. While history of malignancy and cholecystectomy were the only significant factor for unsuccessful ERCP, male sex, total gastric resection, RN-Y reconstruction, comorbidities (CCI> 4), calculi, sudden end or external pressure of choledochal in MRCP had a higher likelihood of unsuccessful ERCP with conventional side viewing duodenoscope. Forward viewing gastroscope, single or double-balloon enterescope, device enhanced endoscopy, or colonoscopy can be used for total gastrectomy and/or RNY gastrojejunostomy patients. Surgery, especially choledochotomy with T tube drainage, is the primary treatment of unsuccessful ERCP.

Ethics Committee Approval: This study was approved by İstanbul Prof. Dr. Cemil Taşçıoğlu City Hospital Ethics Committee (Decision no: 4870771-514.10, Date: 16.06.2020).

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

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ORİJİNAL ÇALIŞMA-ÖZET
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Mide ameliyatı geçiren hastalarda yandan görüşlü duedoskopi ile endoskopik retrograd kolanjiyopankreatografi deneyimimiz

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ÖZET

Giriş ve Amaç: Gastrointestinal sistem anatomisi değişenlerde konvansiyonel yandan görüşlü duedonoskop ile endoskopik retrograf kolanjiyopankreatografi (ERCP) zor ve başarısız olabilmektedir. Mide ameliyatı geçiren hastalarda ERCP deneyimimizi değerlendirmeyi amaçladık.

Gereç ve Yöntem: Ocak 2017'den Ağustos 2021 tarihleri arasında ERCP yapılmış mide cerrahisi geçirmiş hastalar çalışmaya dahil edildi. Hastaların yaş, cinsiyet, komorbidite, Charlson Komorbidite İndeksi (CCI), ERCP endikasyonu, geçirilmiş mide cerrahisi (endikasyonu, mide rezeksiyon ve rekonstrüksiyon şekli), kolesistektomi öyküsü, MRCP sonuçları geriye dönük değerlendirildi. Sonuçlar başarılı (SERCP) veya başarısız (USERCP) olmasına göre de karşılaştırıldı. Ayrıca ERCP başarısızlığının Odds oranları değerlendirildi.

Bulgular: Kırk üç hasta çalışmaya dahil edildi. Ortalama yaş 68,8 ± 13,6 idi. En sık görülen cinsiyet kadındı (%51,2). En sık ERCP endikasyonu %44,2 ile koledokolitiazis, mide cerrahisi endikasyonu %72,1 ile peptik ülser, %67,4 ile subtotal mide rezeksiyonu ve %58,1 ile gastrojejunostomi rekonstrüksiyonu idi. Endoskopik retrograd kolanjiopankreatografinin başarı oranı %44,2 idi. Ortalama CCI 4,16 ± 2,28 idi. USERCP grubunda sadece malignite öyküsü anlamlı derecede yüksekti (p= 0,026). Erkek cinsiyet, koledokolitiazis dışı endikasyon, malignite öyküsü, CCI> 4, total gastrektomi, roux ny (RNY) rekonstrüksiyonu, kolesistektomi öyküsü, MRCP'de safra kanalı dilatasyonuna ek olarak bulgu olanlarda USERCP olasılığı daha yüksek saptandı.

Sonuç: Malignite ve kolesistektomi öyküsü, başarısız ERCP için tek anlamlı faktörler iken, erkek cinsiyet, total gastrektomi, RNY anastomozu, daha önce mide ameliyatı geçirmiş hastalarda başarısız ERCP olasılığı daha yüksek olmaktadır. Seçilmiş hastalarda yandan görüşlü duodenoskopa alternatif cihazlar başarı oranı artacaktır.

Anahtar Kelimeler: Endoskopik retrograd kolanjiyopankreatografi, gastrektomi, roux ny, gastrojejunostomi

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ORIGINAL ARTICLE
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Short and long term results of anatomical reconstruction of perineal body and sphincter complex in obstetric anal sphincter injuries

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ABSTRACT

Objective: The effective way to reduce the risk of fecal incontinence (FI) in primary repaired obstetric anal sphincter injuries (OASIS) patients is to accurately detect the injury and provide complete anatomical reconstruction. The aim of the study was to evaluate the short-term and long-term results of OASIS cases that were diagnosed by an experienced surgical team and whose perineal body and anal sphincters were reconstructed separately.

Material and Methods: Sixteen patients that required consultations due to anal sphincter damage during vaginal delivery and underwent anatomical reconstruction due to Grade 3c and Grade 4 sphincter damage between 2007 and 2019 were included in the study. These cases were divided into three groups [Group 1 (≤12 months), Group 2 (12-60 months), Group 3 (≥60 months)] according to the time elapsed until anal manometry, and incontinence questionnaires were conducted in the postoperative period. Recto-anal inhibitory reflex (RAIR), mean resting (IB) and squeezing (SB) pressures were measured by anal manometry. Anal incontinence (AI) and FI rates were determined by questionnaires. Anal sphincter damage repair techniques (overlapping, end-to-end) were determined. These parameters were compared between the three groups.

Results: Mean age of the patients was 27.5 (16-35) years. Six (37.5%) patients had Grade 3c, while 10 (62.5%) had Grade 4 injury. The overall mean RP and SP were 35 (26-56) mmHg and 67 (31-100) mmHg, respectively. Mean RP and SP were 46/67 mmHg, 33.5/75.5 mmHg, and 37.5/70.5 mmHg in Groups 1, 2, and 3 respectively. There was no difference between the three groups in terms of mean RP and SP (p= 0.691, p= 0.673). The rate of AI and FI in all patients were 18.75% and 12.5%, respectively while the rate of severe AI incontinence was 6%. Severe AI was observed in 1 (16.7%) case in Group 1, mild AI was observed in 1 (25%) case in group 2, and in 1 (16.7%) case in Group 3. RAIR was positive in all patients. In Group 1, 5 (83.3%) patients underwent overlapping repair, and in Group 3, 6 (100%) patients underwent end-to-end repair. This difference was statistically significant (p= 0.011).

Conclusion: In vaginal births, evaluation of anal sphincter damage, determination of perineal body structures and anal sphincters separately and performing anatomical reconstruction when needed significantly reduce the rate of FI in the short and long term.

Keywords: Obstetric anal sphincter injuries, anal incontinence, fecal incontinence, perineal body, anal manometry, Wexner score

INTRODUCTION

Anal incontinence (AI) is a clinical manifestation of involuntary solid-liquid stool or gas leakage. Fecal incontinence (FI) is defined as the passive leakage of liquid and solid stool (1). Population-based studies have reported that obstetric anal sphincter injuries (OASIS) are responsible for 50% of AI cases (2). Symptoms of liquid-gas incontinence, fecal urgency, and passive FI can also be observed (3). Obstetric anal sphincter injuries is the most common cause of FI in young women. FI is a clinical condition that deeply affects self-confidence, social behavior, and mental state of patients (2). It is not a common manifestation. In a cohort-based study, it has been reported that Grade 3 OASIS was observed 3.3% and Grade 4 OASIS in 1.1% of vaginal deliveries (4). In another study, the rate of sphincter defect has been found to be 11% in the endoanal ultrasonography (EAUS) of patients with AI. The reason for this high rate is because sphincter damage is not noticed during vaginal delivery (3). One study has compared EAUS performed at the 4th week before delivery and at the 4th month postpartum and found that sphincter damage was missed at a rate of 23% (5).

Primary repair of OASIS injuries is the anatomic repair performed within 24 hours (3). Studies have shown that defect rates after primary repair vary between 16-

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90%. The variation in these rates could be due to the inability to detect sphincter damage or improper repair (6). The most common cause of FI developing after OASIS is reported to be failure in primary repair (7). Effective primary repair has been shown to improve anal sphincter functions (8).

The edematous and hemorrhagic tissue in OASIS makes it difficult to assess the damage. In addition, since this clinical manifestation is rare, delivery teams may not have adequate experience. Therefore, sphincter damage is often difficult to identify. Due to lack of effective reconstruction, high rates of FI may occur in the short and long term (3,4). In our study, we aimed to present the short and long-term results of anatomical reconstructions of the perineal body and sphincter complex applied to patients who developed anal sphincter damage during vaginal delivery.

MATERIAL and METHODS

Study Design

This research was conducted with the approval of the local ethics committee (decision no: 2019/18-14). The records of 19 patients that developed Grade 3c and 4 (9) (Figure 1) anal sphincter injuries during vaginal delivery based on the consultation of the experienced surgical team in a tertiary hospital between January 2007 and December 2019 were reviewed. Two patients were excluded from the study because one patient had missing data and one patient had a second birth. One of the 17 cases could not be reached for follow-up. Fourteen of the 16 patients that were called for examination came to the outpatient clinic for face-to-face assessments. Assessments of two cases that did not come to examination were done over the phone. Thus, a total of 16 patients who met the study criteria were included in the study. Demographic characteristics, clinical information, anal manometry results, and operation notes of these cases were analyzed from the hospital data entry system.

In the operation notes, external anal sphincter (EAS) injury accompanied by internal anal sphincter (IAS) injury was noted as Grade 1-4 (Table 1) (9). It was noted whether levator ani muscle examination was performed and there was laceration. The technique of suturing the anal sphincters (primary, overlapping) and whether or not the colostomy was opened were recorded from the operating notes.The degree of sphincter injury, repair technique, follow-up duration, anal manometry findings, Wexner incontinence score (WIS), and rapid assessment fecal incontinence score (RAFIS) questionnaire results of the patients from these groups were evaluated.

Application of Anal Incontinence Scoring Questionnaire and Determination of Groups

In the interviews, AI scoring questionnaires were applied. It was questioned whether the patients developed postoperative wound dehiscence, bleeding and wound infection. They were asked whether they received treatment support due to AI.

WIS and RAFIS questionnaires were used to evaluate AI and FI. In the WIS questionnaire, the results vary between 0, which is the best result and 20, which is the worst result (Table 2) (10,11). Values above the WIS cut-off of nine are considered as poor quality of life (12). In the RAFIS questionnaire, the results vary between 0, which is very good results and 10, which is very bad (Table 3) (13). This questionnaire was used to measure the patients' emotional state due to leakage.

Anal manometry and questionnaires were performed at the same time. Mean resting pressure (RP) and squeeze pressure (SP) of the cases were determined by anal manometry. The presence

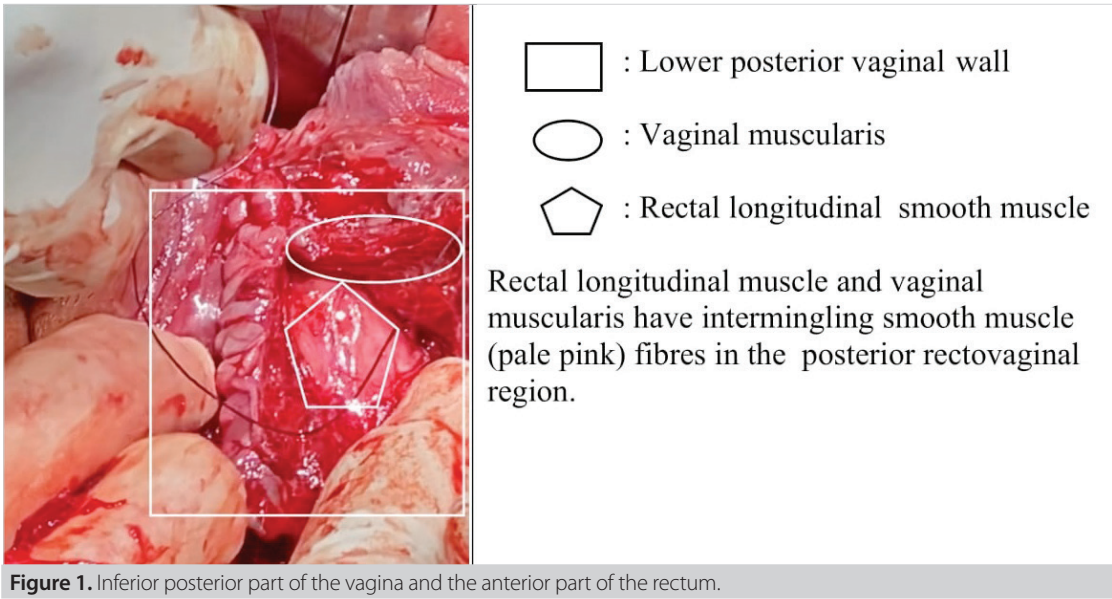

Figure 1. Inferior posterior part of the vagina and the anterior part of the rectum.

Table 1. Grading of the injury in obstetric anal sphincter injuries

First-degree tear: Injury to the perineal skin and/or vaginal mucosa.
Second-degree tear: Injury to the perineum involving perineal muscles but not involving the anal sphincter.
Third-degree tear: Injury to perineum involving the anal sphincter complex:
Grade 3a tear: Less than 50% of external anal sphincter (EAS) thickness torn.
Grade 3b tear: More than 50% of EAS thickness torn.
Grade 3c tear: Both EAS and internal anal sphincter (IAS) torn.
Fourth-degree tear: Injury to the perineum involving the anal sphincter complex (EAS and IAS) and anorectal mucosa.

Table 2. Wexner incontinence scoring system

	Frequency				
Type of incontinence	**Never**	**Rarely**	**Sometimes**	**Usually**	**Always**
Solid	0	1	2	3	4
Liquid	0	1	2	3	4
Gas	0	1	2	3	4
Wears pad	0	1	2	3	4
Lifestyle alteration	0	1	2	3	4

Never: 0; rarely: <1/month; sometimes: <1/week, >1/month; usually: <1/day, >1/week; always: >1/day; 0: Perfect; 20: Complete incontinence.

Table 3. Rapid assessment fecal incontinence score

According to the number of leaks I feel					
Very bad	Bad	Regular	Well	Very well	Excellent
10	8	6	4	2	0

Note down the frequency of leaks	
Several leaks daily	10
Several leaks weekly but not daily	8
Several leaks monthly but there was a week without leaks	6
Leaks from time to time, but there is a full month without leaks	4
Leaks occur rarely	2
No leaks	0

of AI and FI after more than one year following a primary repair was classified as long-term (14). The patients were divided into three groups according to the time elapsed until anal manometry, and incontinence questionnaires were performed after the operation. Cases with a follow-up period of one year or less were classified as Group 1 (n= 6), cases with a follow-up period of 1-5 years were in Group 2 (n= 4), and cases with a follow-up period of 5-12 years were in Group 3 (n= 6).

Rectal Manometer Application Method

Anal manometry was performed with the patient in the left lateral position. The catheter (Latitude Gım 6000A) of a diameter of eight Fr and a length of 60 cm with four pressure sensors arranged in four rows each (360° circumferential). There is a central lumen for inflation of a balloon 5 cm long (capacity of 400 mL). The manometric data are analyzed using the specific MMS-LABORIE analysis software (Laborie Medical Technologies, Canada, USA, and Europe). For each procedure, the parameters including the following were recorded: RP, SP, recto-anal inhibitory reflex (RAIR), and rectal sensitivity.

Determination of Anatomic Localization and Morphological Structures of Damaged Tissues After Oasis and Repair Type

Since OSIS injuries are acute, recognizing the perineal body and internal and external anal sphincter structures was only possible with clinical examination. Striated and smooth anal canal sphincters were determined with different morphological structures in their anatomical localizations. In our study, each of the structures in the damaged area was determined as indicated in the figure and figure descriptions.

The fibromuscular structure that connects the inferior posterior part of the vagina and the anterior part of the rectum is defined as the perineal body (Figure 1). In this structure, there are bulbosupongiosus and superficial transverse perineal muscles, and longitudinal and circular smooth muscles of the rectum. The smooth muscles are morphologically pale pink (Figure 2) (15,16). Each laceration of the lacerated structures in the perineal body was sutured one by one with 2/0 polyglactin. In the anterior anal canal is the EAS, which is composed of striated muscle that surrounds these smooth muscles (pale pink) like a band (Figure 3) (15,16). After the EAS had been determined, if the free muscle bundle was of sufficient length, it was sutured with 2/0

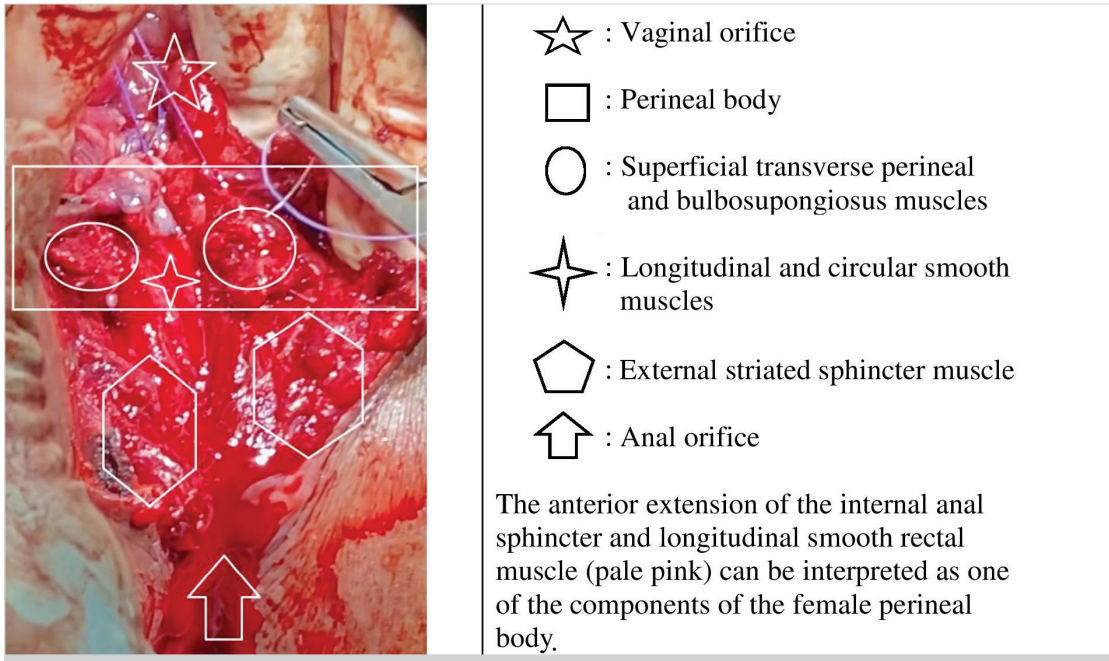

Figure 2. Bulbosupongiosus and superficial transverse perineal muscles, longitudinal and circular smooth muscles of the rectum.

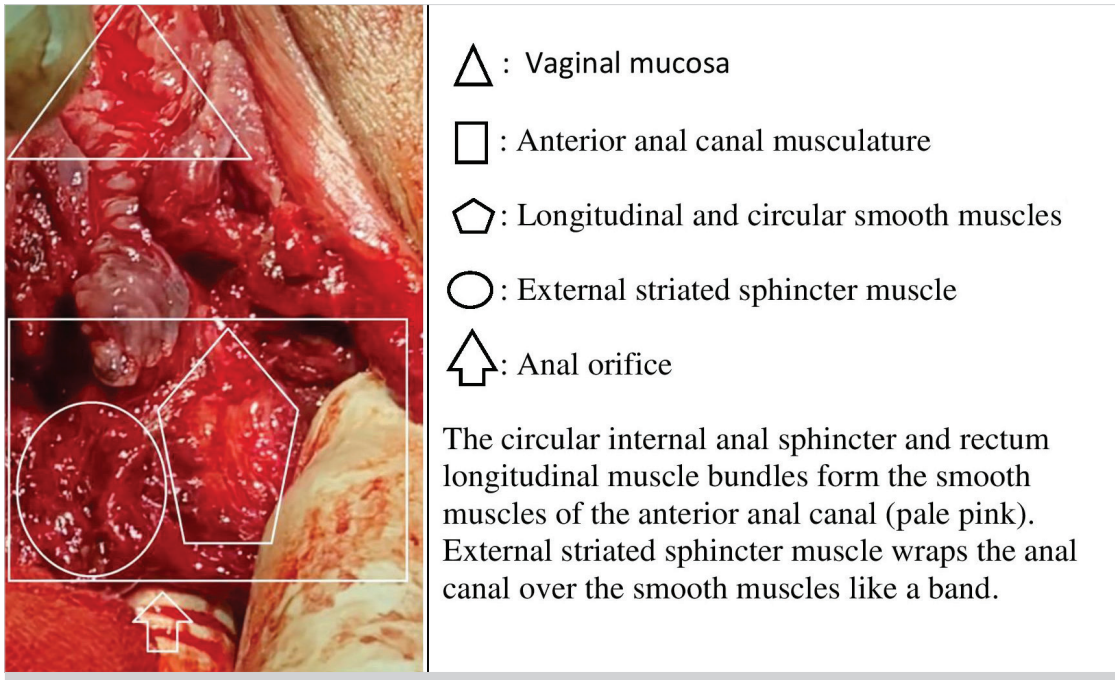

Figure 3. The anterior anal canal is the external anal sphincter, which is composed of striated muscle that surrounds these smooth muscles (pale pink).

polyglactin using the overlapping technique. The external muscle bundle which did not have sufficient length was sutured end-to-end with 2/0 polyglactin without being dissected from the surrounding tissues (in order not to disturb its blood supply and innervation by dissection).

In our study, lacerations were detected in the anterior anal canal and posterior vaginorectal region in the operation notes. Therefore, since the levator ani muscle is located on the right and left lateral of the tear region, no defect information was found.

Statistical analyses; SPSS 26.0 (IBM Corporation, Armonk, New York, United States) program was used in the analysis of the variables. While conformity of the data to normal distribution was evaluated with the Shapiro-Wilk test, the homogeneity of variance was evaluated with the Levene test. One-Way ANOVA (Robust Test: Brown-Forsythe) test with bootstrap results and Jonckheere-Terpstra test and Monte Carlo simulation technique were used in the comparison of quantitative data of more than two groups. Fisher Freeman Halton Test and Monte Carlo simulation results were used to compare categorical variables with each other. Column ratios were compared with each other. P-value with Benjamini-Hochberg correction was expressed according to the results. Spearman's rho test was used to examine the correlations of the variables with each other. Quantitative variables were expressed as mean (standard deviation) and median (minimum/maximum) in the tables. Categorical variables were shown as (%). Variables were analyzed at 95% confidence level, and p value less than 0.05 was considered significant.

RESULTS

Median age of the patients was 27.5 (16-35) years. Six patients (37.5%) had Grade 3c and 10 (62.5%) had Grade 4 sphincter injuries. There were 6 (37.5%) cases in Group 1, 4 (25%) cases in Group 2, and 6 (37.5%) cases in Group 3. Overlapping repair was performed in 6 (37.5%) cases, and end-to-end repair was performed in 10 (62.5%) cases. Median RP of all patients was 35 (26-56) mmHg, and median SP was 67 (31-100) mmHg. RAIR was positive in all patients in the rectal manometry report.

Mean WIS of the cases was 1.88. AI was detected in 3 (18.75%) of 16 patients. FI was detected in 2 (12.5%) of three patients with AI. Mean follow-up time of the patients after primary repair was 23 (2-144) months. The demographic, clinical and manometric findings of the patients are summarized in Table 4.

The groups had a high number of patients with WIS score of 0 (the best). WIS was 0 in 5 (83.3%) patients in Group 1, 3 (75.0%)

Table 4. Demographic, clinical and anal manometry findings of the patients

	n	Mean (SD)	Median (Min/Max)
Age	16	26.81 (5.08)	27.5 (16/35)
Follow-up time (months)	16	46.94 (49.12)	23 (2/144)
Resting pressure (mmHg)	13	38.85 (10.10)	35 (26/56)
Squeezing pressure (mmHg)	13	69.77 (18.23)	67 (31/100)
First sensation(mL)	13	89.23 (28.42)	100 (40/130)
Max-tolerable volume (mL)	13	218.46 (35.32)	230 (160/280)
Frequency of stool incontinence	16	0.88 (2.19)	0 (0/8)
Emotional state related to stool incontinence	16	1.50 (3.14)	0 (0/10)
Wexner incontinence score	16	1.88 (4.69)	0 (0/18)
		n	%
Follow-up time (months)			
≤12 (Group 1)		6	37.5%
(12-60) (Group 2)		4	25%
>60 (Group 3)		6	37.5%
Degree of injury			
3c		6	37.5%
4		10	62.5%
Repair type			
Overlapping repair		6	37.5%
End-to-end repair		10	62.5%

SD: Standard deviation.

patients in Group 2, and 5 (83.3%) patients in Group 3. It was determined that the complaint of severe FI started immediately in the postoperative period in 1 (16.7%) patient and its severity still continued. Anal manometry and face-to-face questionnaire were applied at postpartum 2nd month. A telephone questionnaire was administered 16 months later. In the questionnaires (2nd-16th months) performed in this case, it was determined that WIS (18 points at both time points) and mood score felt due to incontinence (10 points at both time points) did not change throughout time. WIS and RAFIS scores of 13 (81.25%) patients were 0. The RAFIS and WIS scores of the patients are summarized in Table 5. Median RP and SP of the groups were 46 (26-56)/67 (31-90) mmHg in Group 1, 33.5 (31-45)/75.5 (59-87) mmHg in Group 2, and 37.5 (26-52)/70.5 in Group 3 (50-100) mmHg. There was no difference between the three groups in terms of median RP and SP (p= 0.691, p= 0.673). Severe FI (WIS 18, emotional state score (ESS) 10) was observed in 1 (16.7) case in Group 1, mild FI was seen in 1 (25%) case in Group 2 (WIS 7, ESS 8), and mild AI (WIS 3, ESS 2) was observed 1 (16.7%) case in Group 3 (Table 2). There was no significant difference between the three groups in terms of WIDS and RAFIS scores (p= 0.855, p= 772) (Table 6).

When our groups were examined in terms of repair type, it was found that overlapping occurred in 5 (83.3%) patients in Group 1 and 1 (25%) patient in Group 2. End-to-end repair was performed in 1 (16.7%) patient in Group 1, 3 (75%) patients in Group 2, and 6 (100%) patients in Group 3. When repair type was compared between the groups, a statistical difference was observed between Group 1 and Group 3 (p= 0.011) (Table 6).

Except for 1 (6%) patient with severe AI, it was determined that other patients did not go to the doctor. Since the patient with severe AI was short-term (Group 1), it was determined that she was at the stage of patient evaluation and treatment plan.

None of the cases included in the study had a history of previous anal canal and rectal operations. There was no history of serious wound infection or wound dehiscence in any of the patient records and interviews. It was reported that a colostomy was opened in a patient with Grade 4 OASIS in Group 3 and this colostomy was closed six months later.

DISCUSSION

In cases of OASIS undergoing primary sphincter repair, the most common cause of FI is failure of the repair (7). The success rate in the treatment of FI is low (17). Therefore, the primary goal is to prevent the development of FI. Accurate determination of sphincter damage and providing appropriate anatomical reconstruction of the sphincters is crucial in the treatment of OASIS. Therefore, it is recommended that the sphincters be identified and repaired by experienced surgical teams (18). In our study, the perineal body structures and sphincters of patients that developed OASIS were repaired separately by experienced surgeons immediately after delivery. This approach led to low AI and FI rates in the short and long term.

Table 5. RAFIS and Wexner incontinence survey results of the patients according to the groups

	Follow-up time (months)		
	Group 1 n (%)	**Group 2 n (%)**	**Group 3 n (%)**
Stool incontinence score according to RAFIS			
0	5 (83.3)	3 (75.0)	5 (83.3)
2	0 (0.0)	0 (0.0)	1 (16.7)
4	0 (0.0)	1(25.0)	0 (0.0)
8	1 (16.7)	0 (0.0)	0 (0.0)
Incontinence-related emotional state score based on RAFIS			
0	5 (83.3)	3 (75.0)	5 (66.7)
2	0 (0.0)	0 (0.0)	1 (16.7)
8	0 (0.0)	1 (25.0)	0 (0.0)
10	1 (16.7)	0 (0.0)	0 (0.0)
Wexner incontinence score			
0	5 (83.3)	3 (75.0)	5 (83.3)
3	0 (0.0)	0 (0.0)	1 (16.7)
7	0 (0.0)	1 (25.0)	0 (0.0)
18	1 (16.7)	0 (0.0)	0 (0.0)

Group 1: Follow-up time ≤12 months; Group 2: Follow-up time 12-60 months; Group 3: Follow-up time >60 months; RAFIS: Rapid assessment fecal incontinence score.

Table 6. Comparison of the patients' anal manometry findings and incontinence questionnaire results

Follow-up time							
	Group 1		Group 2		Group 3		
	Mean (SD)	Median (Min/Max)	Mean (SD)	Median (Min/Max)	Mean (SD)	Median (Min/Max)	p
Resting pressure (mmHg)	**41.8 (12.40)**	46 (26/56)	**35.75 (6.40)**	33.5 (31/45)	**38.25 (11.56)**	37.5 (26/52)	0.691[a]
Squeezing pressure (mmHg)	**63.8 (21.32)**	67 (31/90)	**74.25 (13.89)**	75.5 (59/87)	**72.75 (20.77)**	70.5 (50/100)	0.673[a]
First sensation (mL)	**90.00 (26.46)**	100 (50/120)	**75.00 (28.87)**	75 (40/110)	**102.50 (30.96)**	110 (60/130)	0.437[a]
Max-tolerable volume (mL)	218.00 (48.17)	**230 (160/280)**	207.50 (34.03)	**215 (160/240)**	230.00 (20.00)	**240 (200/240)**	0.608[j]
Frequency of stool incontinence based on RAFIS	1.33 (3.27)	**0 (0/8)**	0.50 (1.00)	**0 (0/4)**	0.67 (1.63)	**0 (0/2)**	0.994[j]
Emotional state related to stool incontinence based on RAFIS	1.67 (4.08)	**0 (0/10)**	2.00 (4.00)	**0 (0/8)**	1.00 (1.67)	**0 (0/4)**	0.772[j]
Wexner incontinence score	3.00 (7.35)	**0 (0/18)**	2.25 (3.30)	**1 (0/7)**	0.50 (1.22)	**0 (0/3)**	0.855[j]
	n (%)		**n (%)**		**n (%)**		
Repair type							0.011[f]
Overlapping	5 (83.3)[C]		1 (25)		0 (0)		
End-to-end	1 (16.7)		3 (75)		6 (100)[A]		

[j] Jonckheere-Terpstra Test (Monte Carlo), [a] OneWay ANOVA (Robuts Statistic: Brown-Forsythe), [f] Fisher Freeman Halton Test (Monte Carlo), [A] Indicates significance according to the group with a follow-up period of ≤12, [C] Indicates significance according to the group with a follow-up period of >60, SD.: Standard deviation, group 1: follow-up time ≤12 months; group 2: follow-up time 12-60 months; group 3: follow-up time >60 months; RAFIS : Rapid assessment fecal incontinence score.

In our study, manometric measurements showed that median RP of the anal canal was 35 mmHg (normal range= 59-74 mmHg), while median SP was 67 mmHg (normal range= 88.5-111 mmHg). Both values were below normal limits. The rates of AI and FI were 18.75% and 12.5%, respectively, while the rate of severe incontinence was 6%. In their study with 372 cases, Turel et al. (6) have performed anal manometry in 13 of 19 patients with grade 3c/4 sphincter damage and reported RP of 14.7 mmHg and SP of 40.7 mmHg. They have reported FI rate of 12% and AI rate of 51% in those with grade 3c/4 type injuries. In this study, similar to our study, anal canal RP and SP were low, while FI rates were similar. IAS defect and levator avulsion have been found to be independent risk factors for AI. They have stated that the repair of the IAS and levator muscle defect is important. In their study involving 181 patients, Patton et al. (7) have reported Grade 4 injuries in 10 (6%) and Grade 3c injuries in 26 (14%) patients. FI rate has been found as 46% and more common in patients with low anal RP compared to those with normal RP. In addition, patients with low SP and normal SP did not differ significantly in terms of FI rates. This result emphasizes the importance of IAS repair. It has been noted that IAS anal sphincter injuries are often overlooked in OASIS. This was thought to be due to the fact that the IAS is thin and is located behind the larger EAS (3,7). In Gommesen et al.'s (2) study including 575 patients with sphincter injuries, it has been reported that 20 patients had Grade 3c and 15 patients had Grade 4 injuries. The rate of FI has been indicated as 35% in Grade 3c and 33.3% in Grade 4. In this large series study, the high rates of FI after primary repair have been attributed to two reasons: inadequate repair of the sphincters or recurrent injury to the sphincters (6). Anglim et al. (19) have reported major sphincter injury (Grade 4= 28, Grade 3c= 47) in 75 (17%) of 362 patients in their prospective study. The AI score in major sphincter injuries has been found low. The reason behind this low rate was that the degree of injury was determined well and the IAS was detected and repaired separately. Similarly, in our study, the low rate of FI compared to the literature may have been due to detecting and suturing the sphincters separately and careful reconstruction of the lacerated perineal body structures (puborectal muscle, perirectal and paravaginal fascia, bulbocavernosus muscle, superfacial transverse perineal muscle). Soerensen et al. (20) have found that short anterior sphincter length after primary repair correlated with FI. This result increases the importance of reconstruction of the lacerated area as a whole and supports our hypothesis. On the other hand, in our study, it was observed that the AI score of one case (6%) that developed severe AI remained the same in the postpartum short and long term (>1 year long term). The reason for occurrence of severe FI in the early postpartum period and its persistence in the long-term may be the failure of the primary repair.

In recent studies, it has been detected that levator ani muscle injuries are seen at a rate of 21% in OASIS. It has been determined that there is an independent risk factor for the development of AI (6). The levator ani muscle surrounds the rectum posteriorly and is located to the right and left of the rectovaginal region (21). Since the laceration was in the media line in our study, the attention of the repair team might have caused the levator muscle damage to be overlooked. Severe AI seen in 6% may have developed for this reason.

It has been reported in the literature that complications such as severe wound infection, bleeding and wound dehiscence develop after perianal reconstruction. For these reasons, it has been suggested that the primary repair is impaired and AI develops (22). In our study, however, no serious postoperative wound complication developed. This may be a supporting factor in the low rate of AI.

Anal manometry has low sensitivity in determining the degree of sphincter damage. However, it has been reported that the mean sphincter pressures (RP and SP) decreased as the degree of injury increased (23). In the study by Soerensen et al., anal sphincter pressures have been found low in patients who did not develop AI after primary repairs. On the other hand, it has also been determined that the rate of AI increased as the sphincter pressure decreased. However, no correlation has been found between low pressures and severe AI (20). In our study, sphincter pressures were lower than normal in the short and long terms. Pressures were not different between periods. Also, no difference was observed between anal sphincter pressures and AI score between periods. These results show that the pressures did not decrease over time and the anal functions did not deteriorate. Unlike our study, Mous et al. (24) have found that while the rate of incontinence was 38% in 15 years, this rate increased to 60% after five more years. Likewise, Fornell et al. (25) have shown that anal functions deteriorate over time. The reason why our results differed from aforementioned studies might be the prevention of retraction of the lacerated muscle ends with good primary repair.

In IRAIR, there is a sudden increase in pressure in the rectal wall with the accumulation of gas, fluid, and stool in the rectum. This change signals that defecation will begin. This stimulus is the sensorimotor mechanism that activates the mechanisms that help maintain continence or are effective in the realization of defecation (26). This reflex is negative in Hirschsprung's disease without rectal wall sensitivity, in spinal cord injuries, and causes AI to develop (27). Pudendal nerve neuropraxia may develop due to nerve traction during vaginal delivery. This can also cause temporary (28). However, AI due to pudendal nerve injury has not been elucidated in the majority of studies (29). In our study, RAIR positivity in all patients excludes serious nerve damage in our patients. This result indicates that the probability of developing this damage in OASIS may be below.

In their study of 1453 cases, Thomas et al. (17) have performed EAUS evaluations and reported the rate of normal sphincter function after primary repair as 3%, and sphincter defect in 53%. This study is also significant in terms of demonstrating the failure of primary repair. In a study evaluating the adequacy of the delivery team, it has been reported that 87% of midwives, 28% of newly trained doctors, 14% of trained doctors, and 1% of specially trained team overlooked sphincter injuries (30). Another study has compared the outcomes of primary sphincteroplasty repairs performed by surgeons in training and experienced surgeons and reported higher rates of significant sphincter defect in the training group (31). These results support the importance of having an experienced team when diagnosing and treating sphincter injuries. Therefore, having an experienced team was one of the strengths of our study.

In the literature, different results have been reported in overlapping and end-to-end repairs in sphincter repair. However, in the last randomized controlled study, it has been reported that there was no difference between the results of both methods (32). In our study, overlapping was preferred in Group 1 and end-to-end repair type was preferred in Group 3. However, they were cot comparable as follow-up times were different in both groups. In our study, it was the first preferred method if it was suitable for EAS overlapping.

Studies have reported that fecal diversion does not affect the results in Grade 3-4 OASIS injuries (29). In our study, colostomy was opened in 6% of the patients. In our study, it was determined that there were no serious problems in wound infection and stool control in patients who did not undergo fecal diversion. These results show that fecal diversion is not necessary for severe OASIS injuries.

There are serious long-term failures of secondary repair of sphincter insufficiency that develops after primary reconstruction. In secondary repairs, rectal manometric pressures increase at first, and although there are successful results in the short term, the failure rate is high in the long term (3). Barbosa et al. (12) have evaluated long term incontinence in 486 patients that underwent secondary sphincter repair and observed that 75% developed fluid and 54% developed solid incontinence. In another study of 191 cases undergoing secondary repair, complete continence has been achieved in 6% in 10-year follow-up, while 94% developed AI and 58% developed FI (33). According to these results, no matter how well the secondary sphincter repair is performed, the continence score will remain low. Therefore, meticulous primary repair is crucial.

Due to the low success of secondary repair in patients with FI, the preference for sacral nerve stimulation instead of surgery has increased in cases where primary repair was inadequate or sphincter defects was not detected in the initial assessment (12,14). Leo et al. (34) have reported that 381 patients with AI achieved 60% recovery with sacral nerve stimulation.

There are some limitations of our study. These are single center and retrospective design, small number of patients, and lack of EAUS in the follow-up of the patients.

In conclusion, the delivery team should carefully evaluate the injuries that occur in the perineal region. In case of suspected anal sphincter injury, an experienced surgical team (colorectal, gynecology) should be consulted, and primary reconstruction should be performed by an experienced surgical team. We believe that effective anatomical reconstruction of the anal sphincter and perineal body structures significantly reduces the rate of FI in the short and long term.

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ORİJİNAL ÇALIŞMA-ÖZET
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Obstetrik anal sfinkter yaralanmalarında perineal yapıların ve sfinkter kompleksinin anatomik rekonstrüksiyonun kısa ve uzun dönem sonuçları

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ÖZET

Giriş ve Amaç: Primer tamir edilen obstetrik anal sfinkter yaralanması (OASY) hastalarında fekal inkontinans (Fİ) riskini azaltmanın etkili yolu hasarı doğru tespit etmek ve tam anatomik rekonstrüksiyon sağlamaktır. Çalışmanın amacı deneyimli cerrahi ekip tarafından teşhisi yapılan, perineal body ve anal sfinkterlerin ayrı ayrı rekonstrüksiyonu sağlanan OASY olgularının kısa ve uzun dönem sonuçlarını değerlendirmektir.

Gereç ve Yöntem: 2007-2019 yılları arasında vajinal doğum sırasında anal sfinkter hasarı tespit edilmiş, konsültasyon istenmiş, Grade 3c ve Grade 4 sfinkter hasarı nedeniyle anatomik rekonstrüksiyon yapılan 16 hasta çalışmaya dahil edildi. Bu olgular, operasyondan sonra anal manometri ve inkontinas anketleri yapılana kadar geçen süreye göre üç gruba [Grup 1 (≤12 ay), Grup 2 (12-60 ay), Grup 3 (≥60 ay)] ayrıldı. Anal manometri ile rekto-anal inhibitor refleks (RAIR), ortalama istirahat (İB) ve sıkma (SB) basınçları ölçüldü. Anketler ile anal inkontinas (Aİ) ve Fİ oranları belirlendi. Anal sfinkter hasarı onarma teknikleri (overlapping, uç-uca) tespit edildi. Bu parametreler üç grup arasında karşılaştırıldı.

Bulgular: Hastaların yaş ortalaması 27,5 (16-35) yıl idi. Hastaların 6'sı (%37,5) Grade 3c, 10'u (%62,5) Grade 4 idi. Genel ortalama İB ve SB sırasıyla 35 (26-56) mmHg ve 67 (31-100) mmHg idi. Gruplarda ortalama İB ve SB sırasıyla; Grup 1'de 46/67 mmHg, Grup 2'de 33,5/75,5 mmHg, Grup 3'te ise 37,5/70,5 mmHg saptandı. Üç grup arasında ortalama İB ve SB açısından fark izlenmedi (p= 0,691, p= 0,673). Tüm olgularda Aİ oranı %18,75, Fİ oranı %12,5, şiddetli Aİ inkontinans oranı ise % 6 idi. Grup 1'de 1 (%16,7) olguda şiddetli Aİ, Grup 2'de 1 (%25) olguda hafif düzeyde Aİ ve Grup 3'te ise 1 (%16,7) olguda hafif düzeyde Aİ izlendi. Tüm hastalarda RAIR pozitifti. Grup 1'de 5 (%83,3) hastaya overlapping onarım, Grup 3'te ise 6 (%100) hastaya uç-uca onarım yapıldı. Bu fark istatistiksel olarak anlamlıydı (p= 0,011).

Sonuç: Vajinal doğumlarda; anal sfinkter hasarının değerlendirilmesi, perineal body yapıların ve anal sfinkterlerin ayrı ayrı belirlenip anatomik rekonstrüksiyonun yapılması kısa ve uzun dönemde fekal inkontinens oranını önemli oranda düşürmektedir.

Anahtar Kelimeler: Obstetrik anal sfinkter yaralanmaları, anal inkontinans, fekal inkontinans, perineal yapı, anal manometri, Wexner skoru

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Identifying patients with complicated diverticulitis, is it that complicated?

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ABSTRACT

Objective: Discriminating simple from complicated diverticulitis solely on clinical bases is challenging. The aim of this study was to identify clinical predictive factor for the need for invasive treatment for patients presenting with acute diverticulitis in the emergency room.

Material and Methods: The records of all patients, who were discharged from a university hospital between January 2010 and March 2018 with "diverticulitis" diagnosis, were reviewed. Data collected included clinical features, whether this was a first or recurrent episode, WBC, and Hinchey score. Patients were divided into conservative and invasive treatment groups. Groups were compared by age, sex, BMI, fever, WBC and CT findings. Hinchey score groups were also compared by age, sex, BMI, fever, WBC.

Results: A total of 809 patients were included. Mean age was 60.6 years, with 10% below 40 years. Most patients were treated conservatively (95.9%) while only 4.1% were treated invasively. WBC at presentation was significantly higher in those who required invasive treatment in comparison with the conservative group (13.72 vs. 11.46K/uL, p= 0.024). A statistically significant higher WBC was found among patients with a higher Hinchey score (13.16 vs 11.69, p< 0.005). No difference between the groups was found in terms of age, sex, fever or BMI.

Conclusion: This study showed that patients who present with acute diverticulitis and an elevated WBC are prone to a more severe disease and a higher Hinchey score. Prudence should be taken with these patients, and CT scan is warranted as there is a greater chance that invasive treatment will be required.

Keywords: Diverticulitis, invasive treatment, Hinchey score

INTRODUCTION

Diverticulitis, or inflammation of the diverticulum due to micro-perforation (1), is a major health concern in the western world (2). This disease may either follow a benign or a complicated course. One of the major classification systems for acute diverticulitis is the Hinchey classification and its modifications which are solely based on imaging (3,4).

Treatment strategies of diverticulitis are usually based on clinical and laboratory findings in addition to the CT findings, which is considered the gold standard for the diagnosis of diverticulitis (5).

Despite the growing prevalence of diverticulitis, its diagnosis and treatment remain open to debate (6). It is worth noting that recent evidence-based studies are heading towards conservative treatment and many previous strategies, including dietary restriction and bed rest, are now obsolete (7). Although most uncomplicated cases of diverticulitis resolve with conservative treatment (Stages 0-II), larger abscesses or failure of conservative treatment might require percutaneous drainage or surgery (8).

The aim of this study was to identify clinical predictive factors that help discern complicated diverticulitis patients who may require invasive treatment in the emergency room.

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MATERIAL and METHODS

This retrospective study was approved by the ethics committee of the hospital (0058-18-KMC) on 26.06.2018 before the study was started and was conducted in accordance with the principles set forth in the Helsinki Declaration. The records of all patients who had a discharge diagnosis containing "diverticulitis from hospitalization with a" between the years 01.2010 and 03.2018 at a university hospital were reviewed. Patients with diverticulitis of the colon were included in the study. Incomplete records, age <18 and pregnant women were excluded from the study. The following data were collected: socio-demographic characteristics including age, sex, body mass index (BMI) and co-morbidities. Obesity was defined as BMI >25 kg/m^2. Data collection also included length of current illness, pain location, fever (defined as≥ 37.5°C), whether this was a first or recurrent episode, and elective surgery for recurrent disease. Laboratory values were reviewed for white blood count [WBC (normal range 4500-11000)]. Computed tomography findings including disease location and Hinchey score were collected. Patients who presented with diverticulitis and phlegmon only were classified as Hinchey 0. Hinchey score was defined on admission. Treatment was classified as conservative in case of antibiotics only therapy (conservative group), and invasive in case of percutaneous drainage or surgical intervention (invasive group). Groups were compared by age, sex, BMI, fever, WBC and CT findings. Hinchey score groups were also compared by age, sex, BMI, fever, WBC.

Statistical Analysis

Sample size was calculated using bidirectional equivalence study model, based on the minimal age difference between the two study groups. Student's t test, as well as the non-parametric Mann-Whitney U test, was used in order to compare quantitative variables between two independent groups. The non-parametric Kruskal-Wallis test was used to compare more than two independent groups. In order to assess the association between categorical variables, Chi-square and Fisher's exact tests were used. All tests applied were two-tailed, and a p-value of 5% or less was considered statistically significant.

RESULTS

A total of 1350 of the patient records met the inclusion criteria, of which, 358 were duplicate records. One-hundred and eighty-three records were excluded for incorrect diagnosis. A total of 809 patients were included in the study. Characteristics of the cohort are listed in Table 1. Mean age was 60.6 years, with 10.4% (n= 82) below 40 years, and male/female ratio was 58/42%. Most patients (n= 439, 71.3%) were obese, and 28.1% of the cohort had a BMI≥ 30 kg/m^2. Most patients presented with a first diverticulitis episode (n= 619, 76.5%). Most (62.9%) patients had localized abdominal tenderness, and had no fever (80.7%), with a mean WBC of 11.2 K/uL. Computed tomography was performed in 83.2% (n= 673) of the patients. Most patients presented with Hinchey 0, and only 9.1% presented with Hinchey I - IV. A higher rate (95.2% vs. 4.8%) of patients was treated conservatively, but this did not reach statistical significance. No difference was found between invasive and conservative treatment among patient with left or right-side diverticulitis (Table 2).

No statistically significant difference was found between the two groups in terms of age, sex, diabetes, BMI or fever (Table 3). Thirty-five patients had an invasive procedure, of which 13 patients who presented with Hinchey 0 upon admission who had disease progression. Of the patients who underwent invasive treatment, 63% (n= 22) had a laparotomy with resection (either Hartmann`s procedure for left side diverticulitis (n= 20) or ileocecectomy with primary anastomosis for right side diverticulitis due to free perforation (n= 2), 26% (n= 9) had a laparoscopy with either drainage or lavage, and the rest (11%, n= 4) had percutaneous CT guided drainage (Table 1). Of the patients who were operated on, 16% were operated for inaccessible abscess for percutaneous drainage, 11% due to failure of conservative treatment and 19.5% of the patients were operated due to either generalized peritonitis or septic shock.

There was a trend towards invasive treatment among patients with recurrent diverticular disease vs primary episode (6.3% vs. 3.4%, p= 0.078). Patients in the invasive group had a high WBC at presentation compared to the conservative group (13.72 vs. 11.46 K/uL, p= 0.024, Table 3). A statistically significant higher rate of patients with Hinchey scores of I-IV had an invasive procedure compared to patients with Hinchey score of 0 (Table 2). A higher rate of patients with Hinchey score of II-IV had an invasive procedure compared to patients with a score of I (70 vs 28%, p< 0.001, Table 2). A statistically significant higher WBC was found among patients with a higher Hinchey score II-IV vs. score 0 (15.41 vs 11.68, p< 0.005, Table 4). Multivariate analysis showed that Hinchey score was associated with invasive treatment. Elevated WBC on admission showed a trend toward invasive treatment, Table 5.

There was no statistically significant difference between age, sex, BMI subgroups in terms of Hinchey score, treatment, recurrence or elective surgery.

DISCUSSION

Clinical diagnosis of diverticulitis remains challenging, with false diagnosis made in 40-60% of the cases (9,10). In this study, 183 records (18.5%) were excluded for incorrect diagnosis. Due to the retrospective nature of this study, data regarding actual diagnosis was unavailable. This study showed that the most common symptom in patients with diverticulitis was left lower quadrant pain with no significant additional symptoms. However, pain, whether generalized or localized, is not specific for the

Table 1. Cohort`s characteristics

Characteristic	Numbers	Percentage
Sex		
Male	340	42
Female	469	58
Age		
>40	727	89.6
≤40	82	10.4
Diabetes		
Yes	143	17.7
No	666	82.3
BMI*		
≥25 kg/m^2	439	71.3
<24.9 kg/m^2	177	28.7
Episode time		
First episode	619	76.5
Recurrent episode	190	23.5
Abdominal pain		
Localized	509	62.9
Generalized	300	37.1
Fever		
≥37.5°C	156	19.3
<37.5°C	653	80.7
Abdominal CT scan		
Did	673	83.2
Didn't	136	16.8
Treatment		
Conservative	774	95.7
Invasive	35	4.3
Type of invasive treatment		
Hartmann`s procedure	20	57
Ileocecectomy	2	6
Laparoscopic drainage or lavage	9	26
CT guided drainage	4	11
Elective Surgery		
Yes	27	3.3
No	782	96.7

* Data available for only 616 patients; BMI: Body mass index.
CT: Computed tomography.

diagnosis of diverticulitis. Additional clinical factors are required to correctly diagnose acute diverticulitis; Andeweg et al. have found that elevated C-reactive protein (CRP) may be associated with correct clinical diagnosis of acute diverticulitis (9). Other studies have found temperature to be of little clinical importance in this patient population (11), Our findings are in concordance with these results.

As the diagnosis of diverticulitis is challenging when based solely on clinical basis, distinguishing simple from complicated diverticulitis is even more challenging. Van de Wall et al. have shown that body temperature had little value in discriminating complicated from simple diverticulitis, and thus imaging is of paramount importance (12).

This study evaluated the role of several clinical factors in predicting the severity of diverticulitis and found a strong association between elevated WBC count and a more severe disease with a consequent need for invasive treatment.

Table 2. Computed tomography findings

CT findings	Conservative	Invasive	Total	p
Location				
Left & Sigmoid colon	565 (95%)	31 (5%)	596	1
Right colon	74 (96%)	3 (4%)	77	
Total	639 (95%)	34 (5%)	673*	
Hinchey				
0	615	13¥	628	<0.001
I	18	7	25	
II	6	9	15	
III	0	4	4	
IV	0	1	1	
Hinchey I vs II-IV				
I	18 (72%)	7 (28%)	25	<0.001
II-IV	6 (30%)	14 (70%)	20	

CT: Computed tomography.

* A total of 673 underwent abdominal CT scan of the entire cohort.

¥ One patient was operated without undergoing a CT scan.

Table 3. Comparison of conservative and invasive treatment

Risk factor	Conservative	Invasive	p
Age (mean, years)	60.75	60.91	0.953
Sex (m/f)	325/451	15/18	0.684
WBC (K/uL)	**11.76**	13.72	**0.024**
BMI (kg/m^2)	27.62	27.9	0.787
Diabetes (yes/total ratio)	17.5%	21%	0.587
Abdominal Tenderness (localized/generalized)	491/285	18/15	0.309
Fever≥ 37.5°C	19%	30%	0.1
Recurrent episode (yes/total ratio)	**23%**	**36%**	**0.078**

WBC: Wight blood cell count, BMI: Body mass index.

Table 4. Correlation of Hinchey score and WBC

Hinchey score	Number	WBC	p
0	628	11.68	<0.05
I	25	11.72	
II	15	16.15	
III	4	10.82	
IV	1	13.9	
0	628	11.68	0.005
II-IV	20	15.41	

WBC: Wight blood cell count.

This study also found that 70% of the patients who had Hinchey scores between II-IV were treated invasively while only 28% of those with Hinchey I required invasive treatment. These findings are congruous with a study performed by Bates et al, which demonstrated that 80.3% of patients with Hinchey Ia were treated conservatively (13).

Table 5. Correlation of Hinchey score and WBC on admission with invasive treatment

	Odds Ratio	95% Confidence Interval	P
Hinchey score I	14.03	5.58-35.27	<0.001
Hinchey score II-IV	43.5	10.95-172.78	<0.001
WBC on admission	1.07	0.99-1.45	0.077

WBC: Wight blood cell count.

A strong correlation between Hinchey score and WBC levels was found in our study, and similar findings have been reported by van de Wall et al. (12). All of these findings constitute a cornerstone in helping physicians stratify patients who should be further evaluated, preferably by a CT scan, and in turn help them choose the most appropriate treatment.

It is worth mentioning that patients who are younger than 40 years of age constituted 10.1% of the cohort, which means that health professionals should not dismiss this as a potential diagnosis in this age group, taking into consideration that the youngest patient who was treated invasively was 24 years old. On the other hand, the elderly are more prone to misdiagnosis compared to the young, which can be interpreted by the fact that elder patients are more likely to have comorbidities and altered signs and symptoms (11). which in turn necessitates greater clinical attentiveness when evaluating them.

Previous studies showed that younger patients are more prone to complicated or recurrent diverticulitis and thus a more aggressive treatment should be guaranteed. Recently, several studies, as well as our study, have proven that this logic is out-of-date. A study following conservatively-treated diverticulitis cases younger than 50 years of age has demonstrated that during the course of 5-9 years of follow ups, none of them needed colostomies and one third only needed a subsequent surgery (7,14).

Limitations of the Study

The retrospective nature of this study is its major limitation. As a retrospective study, not all parameters were available in patients' records and hence not collected and analyzed. Laboratory test were not uniform across patients' records, especially pivotal parameters as CRP levels.

CONCLUSION

Identifying patients with complicated diverticulitis based on clinical findings solely is challenging. The results of this study suggest that patients with acute diverticulitis and an elevated WBC are more likely to have a severe disease and a higher Hinchey score, but the final decision should be based on a variety of clinical factors, not a single one. Prudence should be taken with these patients, and CT scan is warranted as there is a greater chance that invasive treatment will be required. This diagnosis should not be overlooked even among young patients.

Ethics Committee Approval: This study was approved by the Ethics Committee of the hospital (0058-18-KMC) in 26.06.2018 before the study was started and has been conducted in accordance with the principles set forth in the Helsinki Declaration.

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

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ORİJİNAL ÇALIŞMA-ÖZET
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Komplike divertikülitli hastaların belirlenmesi gerçekten zor mu?

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ÖZET

Giriş ve Amaç: Basit ve komplike divertikül ayrımını sadece klinik bulgulara dayanarak yapmak zorludur. Bu çalışmanın amacı, acil service akut divertikül ile başvuran hastalarda invazif tedavi ihtiyacını öngörücü faktörleri belirlemekti.

Gereç ve Yöntem: Ocak 2010 ile Mart 2018 tarihleri arasında bir üniversite hastanesinden "divertikül" tanısı ile taburcu olan tüm hastaların verileri incelendi. Toplanan verilere klinik özellikler, bunun ilk mi tekrarlayan bir epizot mu olup olmadığı, BKH ve Hinchey skoru dahil edildi. Hastalar konservatif ve invazif tedavi grupları olarak ikiye ayrıldı. Gruplar, yaş, cinsiyet, VKİ, BKH, ateş ve BT bulguları yönünden karşılaştırıldı. Hinchey skor grupları da ayrıca yaş, cinsiyet, VKİ, ateş ve BKH yönünden karşılaştırıldı.

Bulgular: Çalışmaya toplamda 809 hasta alındı. Ortalama yaş 60,6 yıl iken bunun %10'unun 40 yaş altı hastalar oluşturuyordu. Hastaların çoğunluğu konservatif olarak tedavi edilirken (%95,9) sadece %4,1'inde invazif tedaviye ihtiyaç duyuldu. Konservatif tedavi grubuna kıyasla invazif tedavi grubunda hastaneye başvuru esnasındaki BKH anlamlı olarak daha yüksek bulundu (13,72 vs. 11,46 K/uL, p= 0,024). Hinchey skoru daha yüksek olan hastalarda anlamlı derecede yüksek BKH bulundu (13,16 vs. 11,69, p< 0,005). Yaş, cinsiyet, ateş ve VKİ açısından gruplar arası bir fark saptanmadı.

Sonuç: Bu çalışmada, akut divertikül ve yükselmiş BKH ile başvuran hastalarda daha ciddi hastalık ve daha yüksek Hinchey skoru olduğu bulundu. Bu hastalarda ihtiyatli olmakta fayda varken invazif tedavi daha yüksek oranda gerekli olacağı için BT ile görüntülemeye başvurulması da gerekmektedir.

Anahtar Kelimeler: Divertikülit, invaziv tedavi, Hinchey skoru

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ORIGINAL ARTICLE
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COVID-19 outbreak and acute appendicitis: Does the lockdown has a influence on appendectomies?-A single center retrospective cohort study

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ABSTRACT

Objective: Healthcare systems have been negatively affected from COVID-19 pandemic worldwide. Elective surgical procedures were postponed and conservative treatment options were considered even in urgent conditions. This study aimed to explore the influence of the COVID-19 pandemic on urgent appendectomy in a pandemic hospital.

Material and Methods: Patients on whom appendectomy was performed between March 2020- June 2020 were included into the study (pandemic group). For comparison, control group patients were selected in the same period of 2019 (control group). Patients' demographics, laboratory and radiological findings, length of hospital stay, complications and histopathological findings of the groups were compared.

Results: Forty-six patients were included in pandemic group and and one hundred-one in the control group. Patient characteristics were similar in both groups. There were no significant differences in type of surgery, complications, laboratory and histopathological findings. In the control group, length of hospital stay was longer when compared with the pandemic group.

Conclusion: Although the number of appendectomies performed decreased significantly during the COVID-19 pandemic, perioperative parameters were similar in both groups

Keywords: Acute appendicitis, appendectomy, COVID-19, pandemic, lockdown

INTRODUCTION

Appendectomy for acute appendicitis (AA) is the most commonly performed emergency surgical procedure worldwide with very low mortality and morbidity rates (1). Due to the advancements in imaging techniques and accessibility of healthcare services, vast majority of the cases are uncomplicated (2,3).

Since the first COVID-19 case was reported from China, rapid spread of the disease resulted in a pandemic, and the first case was announced on 11 March 2020 in Turkey (4), and the government decided on complete lockdown following the recommendation of the Scientific Committee. Healthcare systems were negatively affected from the COVID-19 pandemic, elective surgeries were postponed for lightening both the burden of the hospitals and healthcare providers to prevent patients from suffering perioperative COVID-19 complications.

This retrospective case control study aimed to explore the influence of the COVID-19 pandemic on urgent appendectomy for AA in a pandemic hospital.

MATERIAL and METHODS

Study Design

This study was conducted retrospectively in Samsun Training and Research Hospital, following the approval of the local ethics committee (protocol number: GOKA/2021/11/11). Patients who underwent appendectomy between March-June 2020 period when the pandemic was at its peak were included as the pandemic group, and patients who underwent appendectomy in the same period in 2019 were included into the study as the control group. Inclusion criteria of the study were as follows:

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1. Patients who were older than 18 years of age,
2. Patients who underwent appendectomy for diagnosis of acute appendicitis.

Exclusion criteria were as follows:

1. Additional surgical procedures with appendectomy,
2. Patients who were younger than 18 years of age or pregnant,
3. Inaccessibility of patients' data.

Study Parameters

Patients' demographics, laboratory and radiological findings, surgery details, length of hospital stay, complications and histopathological findings were recorded.

Diagnosis of AA and Surgery

The diagnosis of AA was made both clinically and radiologically. Choice of laparoscopic or open surgery depended on surgeon's preference. If there was no acute inflammation at histopathological examination, cases were considered as 'negative appendectomy'.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp, Armonk,NY). Chi-square test was used for analyzing categorical variables. Kolmogorov-Smirnov test was used to analyze the distribution of continuous variables, and Mann-Whitney U test or Student's t test was used for analyzing continuous variables. P< 0.005 values were considered statistically significant.

RESULTS

Forty-six patients underwent appendectomy between March-June 2020 period and included into the study as the pandemic group. One-hundred and one patients on whom appendectomy was performed in the same period in 2019 were included into the study as the control group. Patient demographics are summarized in Table 1. Sex, age, and co-morbidity status were similar among the groups. Before the lock-down, more appendectomies were performed, and the difference was significant (p< 0.05) (Table 2). Table 3 shows the differences of the parameters between the groups, and it was found that only the length of hospital stay was significantly longer in the control group statistically. There was an increasing trend for preoperative computed tomography (CT) scan and decreasing trend for preoperative ultrasonography (USG), but these changes were not statistically significant (p= 0.133 and p= 0.238, respectively). There was no 30-day mortality, and no major complications (Clavien-Dindo III-IV) occurred perioperatively (5).

Table 1. Demographic features of the groups

	After COVID-19 outbreak	Before COVID-19 outbreak	p
Age-Median (min-max, SD)	31.5 (18-66,12.34)	31 (19-89,14.43)	0.701*
Sex			
Male (%)	27 (58.7%)	61 (60.4%)	
Female (%)	19 (41.3%)	40 (39.6%)	0.845±
Total (%)	46 (100%)	101 (100%)	
Co-morbidity			
Yes (%)	13 (28.3%)	15 (14.9%)	
No (%)	33 (71.7%)	86 (85.1%)	0.055±
Total (%)	46 (100%)	101 (100%)	

Min: Minimum, Max: Maximum, SD: Standart deviation.
*Mann-Whitney U test.
±Chi-square test.

Table 2. Distribution of the patients per month

	Before COVID-19 lockdown	After COVID-19 lockdown	p*
1st month	27	17	
2nd month	28	7	
3rd month	22	11	
4th month	24	11	
Total number of cases	101	46	***<0.05***
Mean number of operations per month (SD)	25.2 (±2.75)	11.5 (±4.12)	

*Patients were divided four groups in each period and difference of mean number of operations was analyzed using Student's t test.

Table 3. Comparison of the appendectomies; before COVID-19 lockdown vs after COVID-19 lockdown

	Before COVID-19 lockdown	After COVID-19 lockdown	p
Mean length of hospital stay (Min-Max,SD)	2.15 (1-5,0.733)	1.31 (1-6,0.977)	*<0.05*
Surgery type (%)			
Open	96 (95%)	46 (100%)	0.325
Laparoscopic	5 (5%)	0 (0%)	
Total	101 (100%)	46 (100%)	
Early postoperative complications (%)			
Yes	101 (100%)	45 (97.8%)	0.313
No	0 (0%)	1 (2.2%)	
White blood cell count mean (min-max, SD)	12200.9 (5700-25300,3946.7)	13197 (5500-23700, 3764.3)	0.152*
Peri-appendicular abscess (%)			
Yes	11 (10.9%)	6 (13 %)	
No	90 (89.1%)	40 (87 %)	0.705
Total	101 (100%)	46 (100%)	
Histopathological examination (%)			
Acute appendicitis	95 (94%)	43 (94%)	
Normal histology	6 (6 %)	3 (6%)	1.00
Total	101	46 (100%)	
Preoperative radiological tools			
USG			
Yes	41 (40.5%)	14 (30.4%)	
No	60 (59.5 %)	32 (69.6 %)	0.238
CT			
Yes	79 (78.2 %)	41 (89.1 %)	
No	22 (21.8 %)	5 (10.9 %)	0.113

* Student's t test.

DISCUSSION

The COVID-19 pandemic resulted in a dramatic reduction in the number of appendectomies (104 vs 46, p< 0.05). Our results were compatible with previous publications (6-14). There three possible major reasons of those changes. First, our hospital was re-organized for COVID-19 pandemic and transformed as 'Pandemic Hospital' that resulted in limited hospital resources. Second, patients with mild symptoms might not have applied to emergency services due to fear of being infected with coronavirus, and those patients managed by family physician or self-treatment with analgesics and antibiotics. The last possible reason is that the patients might have preferred private hospitals for operation.

Although a downward trend was observed in the appendectomy procedure during COVID-19 lockdown period, we found that preoperative and postoperative parameters were similar when compared with the same period in previous year except length of hospital stay. Mean length of hospital stay was significantly higher before the COVID-19 lockdown period in our study, which was incompatible with the majority of previous reports (6,9,13,15). Although Bajomo et al. have reported higher length of hospital stay time before the lockdown period (three days vs 2.6 days), the difference was not significant (p= 0.35) (16). As a nature of being a 'social state', the healthcare system was supported by the government in our country. Majority of the citizens are free of charge from any medical services in state hospitals. Therefore, some patients wished to stay one or two more days at the hospital because of social reasons including living in a rural area, being far from healthcare centers, and having no relatives to take care of after surgery. However, during the lockdown, patients desired to be discharged as soon as possible, which explains the shorter length of hospital stay in the lockdown period.

During the lockdown period, a slight change was seen in the use of radiological tools. Radiologists wanted to be cautious of COVID-19 infection, and they avoided close contact with the patients. Although there was no significant difference, preoperative use of USG decreased and use of CT increased. Similarly, some authors have reported that use of CT imaging for acute appendicitis diagnosis increased, therefore negative appendectomy rates decreased (15-17). However, in the present study,

our negative appendectomy rates were acceptable and similar in both groups (6% vs 6%).

AA is an urgent situation, and traditionally, it is believed that surgery should not be delayed. However, some authors have suggested that it is safe to delay surgery until obtaining COVID-19 test result without any increase of complication rates (18). It could be logical but due to the limited number of test kits at the beginning of the pandemic, PCR tests were only performed in patients with COVID-19 symptoms in our institution. Now, we have enough PCR test kits, and the patients are hospitalized after obtaining negative PCR results (except critical urgent conditions including trauma, perforation etc.). At the moment, PCR positive cases are operated in isolated operation rooms and followed in isolated COVID-19 beds postoperatively.

Probably the most interesting finding of the studies on COVID-19 and AA association is the efficacy of non-operative treatment of the disease (1,6,17,19). In fact, non-operative treatment is not a novel approach, and various articles have been published about its safety and efficacy but many surgeons are still performing surgery (13). AA is caused by luminal obstruction that leads to stasis, mucosal ischemia and bacterial overgrowth (20). This pathogenesis is similar to acute cholecystitis or intestinal obstruction. In those situations, usually medical treatment is given as first-line treatment (21,22). Lotfallah et al. have reported that with a careful selection, non-operative treatment of appendicitis is safe and effective (1). Both single-center and multicenter studies indicate that non operative treatment is an alternative treatment option to surgery, and also updated guidelines recommend medical treatment of AA during the COVID-19 pandemic (14,23-25). Recent meta-analysis by Emile et al., including fourteen studies and 2140 patients, haas suggested that non-operative AA treatment should be considered in adult patients; however, in the pediatric population, physicians must be aware of treatment failure (19). In our institute, we still prefer surgical treatment for acute appendicitis because of low complication rates, short length of hospital stay, easier to follow-up postoperative patients compared with treated medically.

This study has three major limitations that should be addressed. First, this is a single center retrospective cohort study with small numbers of patients. Second, vast majority of the cases were treated by surgical intervention, and non-operative treatment group was not included to the study. Third, we only included the patients diagnosed with AA in the first wave (March 2020-June 2020) of COVID-19 in Turkey, and the effects of the second and third waves or mutant viruses on AA were unknown.

In conclusion, although the number of performed appendectomy decreased significantly during the COVID-19 pandemic, perioperative parameters were similar in both groups, and appendectomy procedure can be done safely and successfully in patients with AA .

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2022; 38 (2): 175-179

COVID-19 salgını ve akut apandisit: Karantinanın apendektomiler üzerine bir etkisi var mı? Tek merkezli retrospektif kohort calışma

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ÖZET

Giriş ve Amaç: COVID-19 pandemisi tüm dünyada sağlık sistemlerini olumsuz etkilemiştir. Elektif cerrahilerin ertelenmesinin yanısıra acil durumlarda dahi cerrahi tedaviye alternatif olarak konservatif tedavi seçenekleri gündeme gelmiştir. Bu çalışma ile bir pandemi hastanesinde COVID-19 pandemisinin acil apendektomi olguları üzerine etkileri araştırılması hedeflenmiştir.

Gereç ve Yöntem: Mart 2020 - Haziran 2020 tarihleri arasında apendektomi operasyonu yapılan hastalar çalışmaya dahil edilmiştir (pandemi grubu). Bu grup ile karşılaştırmak amacı ile 2019 yılının aynı döneminde apendektomi yapılan hastalar kontrol grubu olarak çalışmaya dahil edilmiştir. Hastaların demografik özellikleri, laboratuvar ve radyolojik bulguları, hastane kalış süreleri ve histopatolojik bulguları kaydedildi.

Bulgular: Pandemi grubunda 46, kontrol grubunda 101 hasta çalışmaya dahil edildi. Hastaların özellikleri her iki grupta benzer idi. Kontrol grubunda hastanede kalış süresi daha uzun olarak bulundu.

Sonuç: COVID-19 pandemisi sırasında apendektomi sayısında azalma görülmesine rağmen perioperatif parametreler her iki grupta benzerdi.

Anahtar Kelimeler: Akut apandisit, apendektomi, COVID-19, karantina, sokağa çıkma kısıtlaması

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ORIGINAL ARTICLE
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Functional outcomes of intersphincteric resection in low rectal tumors

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ABSTRACT

Objective: Currently, sphincter-saving procedures are increasingly performed in the treatment of low rectal cancers. This study aimed to evaluate the outcomes of patients who underwent intersphincteric resection.

Material and Methods: This was a single-center, retrospective, cross-sectional study. We evaluated the electronic data files of 29 patients who had intersphincteric resections at our institute between 2008 and 2018. Bowel function outcomes were assessed prospectively using Wexner incontinence score. Histopathological, surgical and functional outcomes were analyzed.

Results: Mean age of nine female and 20 male patients included in the study was 55.8 ± 12.8 (30-76) years. A tumor-free surgical margin was achieved in all patients. Anastomotic leakage was detected in two patients. Mean Wexner incontinence score of 20 patients who still had functional anastomosis was 8.35, whereas 65% of the patients (n= 13) had a good continence status. There was no relationship between the continence status and sex, tumor distance from anal verge, T stage, distal surgical margin, and lymph node involvement. Twenty-one patients underwent primary coloanal anastomosis and eight patients underwent two-stage coloanal anastomosis.

Conclusion: In the treatment of distal rectal cancer, adequate oncological surgery and relatively acceptable functional outcomes can be obtained with intersphincteric resection technique in suitable patients.

Keywords: Fecal incontinence, rectum cancer, rectum resection, outcome assessment

INTRODUCTION

For more than a century, abdominoperineal resection has been the standard surgical treatment option for rectal cancer located close to the anal canal (1). However, a persistent stoma significantly reduces patients' quality of life (2). Owing to advances in oncology and surgical techniques, several new techniques have been described aimed at preserving gastrointestinal continuity and improving functional outcomes. As a result, the intersphincteric resection (ISR) technique, defined in 1994, has been widely accepted (3,4). Based on the principle of dissection of the anatomical plane between the internal and external anal sphincters, this technique saves the patient from permanent colostomy. Partial functional loss is expected after partial or total excision of the internal sphincter, which is an important part involved in continence mechanism (5). Although there are conflicting results in the literature, studies on functional outcomes show that anal function is preserved satisfactorily in most cases after ISR (6-8).

The aim of this study was to report the functional outcomes after ISR.

MATERIAL and METHODS

This was a single-center retrospective study conducted at a university hospital in Turkey. The study involved patients with low rectal cancer located at <4 cm from the anal verge and who underwent ISR between January 2008 and December 2018.

Surgical electronic data files, histopathological results, and Oncology Department's follow-up files of patients were retrospectively evaluated. Fecal continence conditions of the patients were evaluated prospectively by phone calls or during outpatient clinic visits. Continence was evaluated using the Wexner continence score.

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Wexner continence scores above eight were considered as poor functional outcome (4).

All patients were operated on by two colorectal surgeons with a standard open total mesorectal excision (TME) technique. Annually, an average of 80-100 rectal cancer surgeries is performed in our clinic. The exclusion criteria for ISR were invasion of the levator ani muscle, anal incontinence, and patient preference. Hand sewn coloanal anastomosis technique was used for all anastomoses. Bowel preparation was undertaken, and prophylactic antibiotics were administered routinely.

The patients were divided into two groups, i.e., primary anastomosis group and delayed anastomosis group. In the primary anastomosis group, coloanal anastomosis was performed in the same session, and a protective stoma was routinely used. In the delayed anastomosis group, 5 cm of the colon's segment was exteriorized from the anus in the first session. In the delayed anastomosis group, a protective stoma was not routinely used, and it was performed as surgeon's choice in only two patients. After 7-10 days, the exteriorized segment was excised, and delayed coloanal anastomosis was performed (two-stage Turnbull-Cutait coloanal anastomosis).

The study protocol was approved by the local ethics committee (Medical Research Ethics Committee, Approval Number 19-7T/39) and was conducted in accordance with the principles of the Declaration of Helsinki. Data were analyzed using IBM SPSS v.21.0 software package for Windows. Categorical data were assessed by Fisher's exact test, and numerical data were assessed by Mann-Whitney U test.

Tumor distance from the anal verge was measured with a rigid rectoscope. All patients were staged with preoperative magnetic resonance imaging ,and anal sphincter invasion was excluded. None of the lesions were suitable for local excision. Patients with Stage 2 or Stage 3 disease received preoperative long-term radiotherapy (RT) and concurrent chemotherapy. The total dose of RT was 50.4 Gy with 1.8 Gy/fraction to the gross tumor and 45 Gy to pelvic lymph nodes. For concomitant chemotherapy, capecitabine was administered orally at a dose of 825 mg/m^2 twice daily throughout the radiation therapy or 5 fluorouracil 380 mg/m^2 and leucovorin 20 mg/m^2 were administered every 28 days (days 1-4) for two cycles. All patients underwent standardized TME.

RESULTS

Twenty-nine patients, including 20 males and nine females, were included in the study. The characteristics of the patients included in the study are shown in Table 1. When evaluated in terms of the indications for surgery, two patients had in situ carcinoma that was not suitable for local excision. All of the other patients had well or moderately differentiated adenocarcinoma. Long-term neoadjuvant chemoradiotherapy was administered to 21 patients. When measurement was performed using a rigid rectoscope, mean distance of the tumor from the anal verge was 3.51 ± 0.63 cm. Distal and circumferential surgical margins were tumor-free in all patients. The excision of the posterior vaginal wall was performed in one patient with suspicion of tumor invasion. On pathological examination, mean distal surgical margin distance was 1.79 ± 0.7 cm. Pathological complete response (ypT0N0) was achieved in two patients. The number of removed lymph nodes was 14.6 ± 8.4 (4-32). Postoperative histopathological results are shown in Table 2.

Eight patients underwent delayed coloanal anastomosis, and 21 patients underwent primary coloanal anastomosis. Anastomotic leakage was not detected in the delayed anastomosis group, whereas anastomotic leakage was detected in two (9.5%) patients in the primary anastomosis group. The difference between the rates of anastomotic leakage was not statistically significant (p= 0.517).

Twenty out of the 29 patients still had functional anastomosis, which is shown in Figure 1. Fecal continence status was assessed by reaching all of these twenty patients. In the primary anastomosis group, 14 patients had a functional stoma because five patients had mortality and two patients had a permanent stoma due to anastomotic stricture.

Table 1. Patient characteristics

	Primary Anastomosis (n= 21)	**Delayed Anastomosis (n= 8)**	**Total (n= 29)**	
Age (years)	55.47 ± 12.7	56.75 ± 12.2	55.83 ± 12.8	Range (30-76)
Sex (Female/male)	8/13	1/7	9/20	31.0%/69.0%
Tumor distance from anal verge (cm)	3.57 ± 0.6	3.37 ± 0.7	3.51 ± 0.6	Range (2.0-4.0)
Neo-adjuvant Chemo-radiotherapy (Yes/No)	12/9	7/1	19/10	65.5%/34.5%
Distal surgical resection margin (cm)	1.81 ± 0.7	1.74 ± 0.5	1.79 ± 0.7	Range (0.3-3.0)
Number of dissected lymph nodes	14.52 ± 8.0	14.62 ± 9.4	14.55 ± 8.4	Range (4-32)
Anastomotic leak	2	0	2	6.9 %
Length of stay (days)	10.47 ± 4.8	12.12 ± 1.3	10.93 ± 4.36	Range (5-30)

Table 2. Postoperative histopathological results

		n (29)	(%)
Stage			
	0 (Tis)	2	6.9
	PCR	2	6.9
	I	5	17.2
	II A	10	34.5
	II B	3	10.3
	II C	0	0
	III A	2	6.9
	III B	3	10.3
	III C	0	0
	IV A	2	6.9
PNI (+)		8	27.6
LVI (+)		3	10.3
Satellite tumor (+)		2	6.9
R0 resection		29	100

PCR: Pathologic complete response, PNI: Perineural invasion, LVI: Lymphovascular invasion.

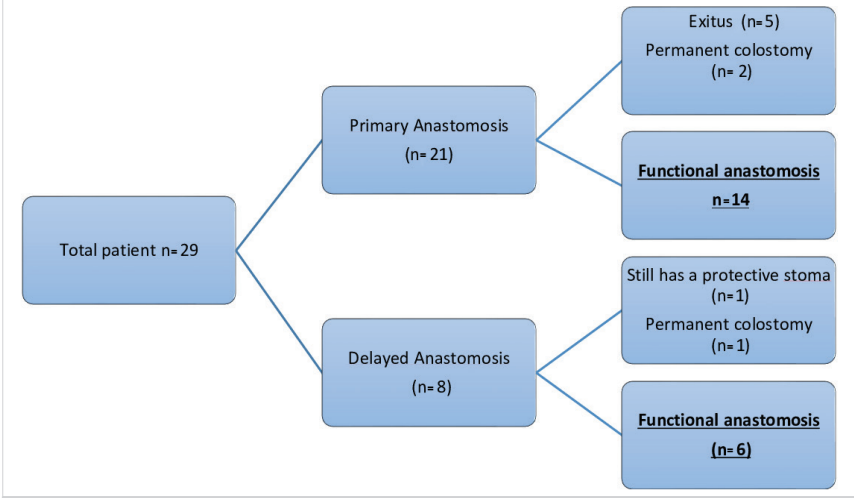

Figure 1. Fourteen of 21 patients in the primary anastomosis group and in eight of patients in the delayed anastomosis group had a functional anastomosis.

In the delayed anastomosis group, six patients had a functional anastomosis as diverting stoma closure had not yet been performed in one individual at the time of the study and one had permanent stoma due to local recurrence. Mean Wexner incontinence score of all patients was 8.35 (0-17) (Figure 2). While 65% of the patients (n= 13) had a good continence status, 35% (n= 7) had poor continence status (Wexner score> 8). According to univariate analysis, no relation was found between continence status and sex (p= 0.651), distance of the tumor from the anal verge (p= 0.608), T stage (p= 0.370), distal surgical margin distance (p= 0.439), and lymph node involvement (p= 0.587).

The rate of severe incontinence in the delayed anastomosis group was 33.3% (n= 2) and 35.7% (n= 5) in the primary anastomosis group (Table 3). No statistically significant difference was found between the two groups in terms of incontinence scores (p= 0.660). The relationship of the variables with severe fecal incontinence was presented in the Table 4."

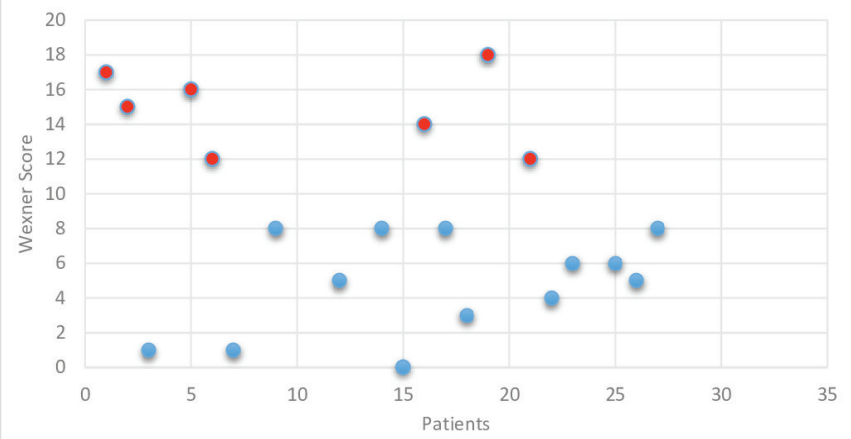

Figure 2. The distribution of Wexner scores (Red dots shows the patients with severe fecal incontinence).

Table 3. Wexner incontinence scores according to type of anastomosis

		Primary Anastomosis (n= 14)	Delayed Anastomosis (n= 6)	p
Wexner score		8.21 ± 5.53	8.67 ± 6.15	0.873
Type of incontinence	Solid	0.71 ± 0.91	0.83 ± 1.16	
	Liquid	1.64 ± 1.00	1.83 ± 1.32	
	Gas	2.93 ± 1.26	2.83 ± 1.16	
	Wears ped	1.07 ± 1.43	1.33 ± 1.75	
	Lifestyle alteration	1.93 ± 138	1.83 ± 1.47	
Severe incontinence[a]		5/14 (35.7%)	2/6 (33.3%)	0.660

[a]Wexner score> 8 defined as severe incontinence.

Table 4. The relationship of the variables with severe fecal incontinence (Logistic regression analysis)

	Odds ratio	95% Confidence interval	p
Age	0.861	0.75-0.99	**0.036**
Sex	0.352	0.024-5.221	0.448
Tumor distance from anal verge	0.515	0.054-4.895	0.563
Distal surgical resection margin	2.049	0.386-10.881	0.4
Type of anastomosis[b]	0.954	0.054-16.861	0.974

[b]Delayed (Turnbull Cutait)/Primary coloanal anastomosis.

DISCUSSION

This study presented functional outcomes of 29 patients undergoing ISR for low rectal cancer. These results revealed that R0 resection could be achieved in all patients using the sphincter preservation technique, and a good functional outcome could be achieved at a rate of 65%. The treatment of rectal cancer is constantly evolving. TME and neoadjuvant therapies have been introduced into routine practice to reduce the high local recurrence rates in the treatment of rectal cancer. Abdominoperineal resection is still used as the gold standard treatment method in many patients with distal rectal cancer (9,10). When adequate oncological outcomes are achieved, the efforts are directed to the development of new methods to avoid performing permanent colostomy in patients and achieve better functional outcomes. As a result of these investigations, Schiessel et al. have described ISR in very low rectal tumors (3).

Accurate patient selection is vital in ISR. The most important goal in rectal cancer surgery is to achieve a tumor-free surgical margin. Nowadays, ISR has been increasingly used with the reduction of acceptable distal surgical margin to 1 cm (11,12). In

terms of oncological outcomes, the most important indicator of rectal cancer surgery's quality is the circumferential and distal surgical margins. In a systemic review of 14 retrospective studies, it has been shown that a negative surgical margin could be achieved in 97% of patients undergoing ISR (13). In our study, mean distal surgical margin distance was 1.79 ± 0.72 cm, and a tumor-free circumferential surgical margin was achieved in all patients. These data are consistent with the literature and indicate that ISR is an oncologically reliable method. In cases in which surgical margin adequacy is suspected, abdominoperineal resection should not be avoided.

There is no standard method for evaluating bowel function after ISR. In this study, we evaluated bowel function with Wexner incontinence score which offers an easily understandable and objective assessment of the patient (14). In this study, mean Wexner incontinence score of the patients was 8.35 (0-17). Different cutoff values have been used in the literature to define the severity of fecal incontinence with the Wexner score. As originally described by Rothbarth et al., a Wexner score of ≥9 is usually associated with complete gas incontinence and more than one fecal incontinence per month, and these patients experience limitations in their social lives (15). Upon considering a Wexner score of nine as a cutoff value for incontinence, 65% (n= 13) of the patients in our study had an good continence status, whereas 35% (n= 7) had poor continence. Although the mean of Wexner scores is 8.35, a score of 8 or less in 65% of patients may seem like a consistency. This can be explained by the fact that some patients have very high scores. The distribution of the patients' Wexner scores can be seen in Figure 2. It is important to manage patient expectations well and inform the patient accurately. Similar to most studies, ISR achieved not perfect but acceptable functional outcomes in our study. A cutoff frequency for acceptable functional outcome has not been defined. Saito et al. have considered a Wexner score less than 10 to be a "good" functional outcome and reported that 70% of the patients in their series had good continence after intersphincteric resection (16). In their series evaluating 101 patients, Denost et al. have found that the median Wexner incontinence score was 11 and 47.5% of the patients were classed as having a good functional result (Wexner score≤ 10) (17). These functional results are not perfect but tolerable for many patients. Consequently, a realistic conversation should be made with the patients before surgery regarding acceptable outcomes. It must be explained that the average expectation will not be complete continence but will involve gas incontinence, partial soiling, and partial liquid incontinence in most patients. During the planning of the surgery, open discussion with the patient is required, mentioning that the procedure is an alternative to permanent colostomy and not to normal defecation (18).

Various researchers have reported considerably different continence outcomes after ISR. In our study, 65% of the patients had an acceptable continence level. Some series have reported a good continence level in 29% of the patients, while others have reported good continence level in 76% of the patients (19-21). One of the main reasons for this difference is that many factors affect the continence status after rectal cancer surgery. As is known, loss of rectal reservoir, damage to autonomic nerves, and neoadjuvant radiotherapy are factors affecting continence status (19). In physiological studies, it has been shown that the basic loss of function in patients undergoing ISR is the decrease in resting pressure due to the loss of internal sphincter (22). It has been shown that the distance of the anastomosis level from the anal verge and the resection of more than half of the internal sphincter affects the continence status after ISR (23). In their study investigating the risk factors for fecal incontinence after ISR, Denost et al. have found that the factors affecting incontinence are the tumor being close to the anal ring and the anastomosis being closer than 2 cm to the anal verge. In our series, we did not find a statistically significant relationship between the level of anastomosis and the distance of the tumor to the anal verge and severe incontinence.

In 1961, Turnbull from Cleveland and Cutait from Brazil independently described a delayed coloanal anastomosis after a pull-through procedure (24,25). With the advent of stapled anastomoses, this method has lost its popularity. The Turnbull-Cutait technique is currently used to prevent the formation of a permanent stoma in selected cases with pelvic sepsis due to anastomotic leakage, rectovaginal or rectourethral fistula, and perianal involvement in Crohn's disease (26). A systematic review of seven retrospective studies has demonstrated that the Turnbull-Cutait technique reduced the likelihood of opening permanent stoma while offering low rate of anastomotic leakage and pelvic morbidity along with reasonable fecal continence (27). The use of Turnbull-Cutait technique has recently gained currency in patients undergoing elective procedures. In a recent randomized controlled trial, Biondo and colleagues have compared the two-stage Turnbull-Cutait anastomosis with the primary anastomosis after ISR in cases with very low rectal cancer (28). They have demonstrated that postoperative complication rates and oncological and functional outcomes of the two groups at one year were similar. Based on the results of this multicenter randomized controlled trial, the authors have argued that a delayed coloanal anastomosis could be a valid alternative strategy to avoid transient stoma. In our study, a two-stage anastomosis was performed in eight patients, and the number of patients was insufficient to make a subgroup analysis.

Retrospective, single-center study design and small size of the study population are important limitations of the present study. Another limitation is that the assessment time of the patients was not homogeneous since the present study evaluated the current functional status of the patients ,and the follow-up

durations were different among the patients. The strengths of the study are the prospective performance of functional assessment, accessibility of all the patients who survived, and being one of the most extensive patient series published in our country.

In conclusion, tumor-free surgical margins and acceptable functional outcomes can be achieved in suitable patients with ISR technique in the treatment of very low rectal cancer. ISR is an alternative that can save patients from permanent colostomy. It is essential to manage patient expectations and thoroughly inform the patient.

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ORİJİNAL ÇALIŞMA-ÖZET
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Alt rektum kanserlerinin intersfinkterik rezeksiyonunun işlevsel sonuçları

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ÖZET

Giriş ve Amaç: Günümüzde alt rektum kanserlerinin tedavisinde sfinkter koruyucu işlemler giderek daha fazla uygulanmaktadır. Bu çalışmanın amacı, intersfinkterik rezeksiyon yapılan hastaların sonuçlarını değerlendirmekti.

Gereç ve Yöntem: Bu çalışma, tek merkezli, retrospektif ve kesitsel bir analizdir. 2008-2018 yılları arasında kliniğimizde intersfinkterik rezeksiyon uygulanan 29 hastanın elektronik veri dosyaları değerlendirildi. Bağırsak fonksiyonları prospektif olarak Wexner inkontinans skoru kullanılarak değerlendirildi. Histopatolojik, cerrahi ve fonksiyonel sonuçlar değerlendirildi.

Bulgular: Çalışmaya alınan dokuz kadın, 20 erkek hastanın yaş ortalaması 55,8 ± 12,8 (30-76) yıl idi. Tüm hastalarda tümörsüz cerrahi sınır elde edilmişti. İki hastada anastomoz kaçağı saptandı. Halen fonksiyonel bir anastomozu olan 20 hastanın ortalama Wexner inkontinans skoru 8,35 idi. Hastaların 13'ünde (%65) iyi bir kontinans durumu mevcuttu. Kontinans durumu ile cinsiyet, tümörün anal verge uzaklığı, T evresi, distal cerrahi sınır ve lenf nodu tutulumu arasında ilişki saptanmadı. Yirmi bir hastaya primer koloanal anastomoz, sekiz hastaya iki aşamalı koloanal anastomoz uygulandı.

Sonuç: Distal rektum kanseri tedavisinde uygun hastalarda intersfinkterik rezeksiyon tekniği ile yeterli onkolojik cerrahi ve nispeten kabul edilebilir fonksiyonel sonuçlar elde edilebilir.

Anahtar Kelimeler: Fekal inkontinens, rektum kanseri, rektum rezeksiyonu, sonuç değerlendirmesi

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ORIGINAL ARTICLE
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Previously operated recurrent pilonidal sinus treated with crystallized phenol: Twenty-year experience in a cohort study

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ABSTRACT

Objective: Postoperative recurrent pilonidal sinus disease is troublesome, and its treatment is a challenge. In this study, it was aimed to present the long-term efficacy of crystallized phenol treatment on postoperative recurrent pilonidal sinus disease through our results collected within the last 20 years.

Material and Methods: Two hundred and twenty-seven patients who had been previously operated on and suffered from recurrent pilonidal sinus disease were enrolled. The operation was applied in our outpatient clinic under local anesthesia. Demographic data of the patients, number of crystallized phenol treatment, duration of follow-up and recurrence numbers were prospectively recorded. Treatment success and factors affecting recurrence were examined.

Results: Our success rate was found as 71.5%. This success rate belongs to the group of patients who never quit treatment and complied with the treatment. The patients were followed up for a mean 45.8 months. Of the post-crystallized phenol treatment recurrences, 72.4% took place within the first five years, while 97.4% did so within the first 10 years. Mean number of crystallized phenol applications was 2.6. The longer the duration of the disease before treatment, the more recurrence was observed after treatment (p= 0.02). There was no correlation between the number of previous operations and recurrence after treatment. As the number of sinus openings increased, so did the number of applications (p= 0.001).

Conclusion: Crystallized phenol treatment yields promising long-term results in recurrent pilonidal sinus disease as well and may be recommended as the first choice in recurrent pilonidal sinus disease treatment since it is an effective non-operative treatment modality.

Keywords: Recurrent pilonidal disease, nonoperative treatment, crystallized phenol

INTRODUCTION

Recurrent pilonidal sinus disease (rPSD) is annoying for both surgeons and patients compared to primary disease. Although many surgical treatment methods in primary pilonidal sinus disease (pPSD) have been reported, long-term recurrence rates after treatment are between 40.2% and 67.9% according to different surgical types (1). Many treatment modalities have been advocated in the treatment of rPSD; however, there is still no consensus in the literature. In addition, a more radical surgical method is generally preferred by surgeons for the failure of the first surgical procedure in rPSD. Due to this approach, various complications such as wound infection, hemorrhage and flap detachment are seen (2).

Some minimally invasive techniques are used alone or as an adjunct to surgery. Injection of various substances into the sinus cavity such as 80% phenol, fibrin glue and cyanoacrylate and destruction of the sinus cavity with laser probe have provided acceptable low recurrence rates compared to simple sinus excision (3-6). Phenol 80% injection has been reported to be applied only in the treatment of pPSD and not of rPSD (3,7). In the nonoperative treatment of pilonidal sinus disease (PSD), crystallized form of phenol has been used for the first time in the world by Dogru O et al. (8), and they have reported the success rate of crystallized phenol treatment (CPT) in pPSD as 95.1%. Aygen et al. (9) have successfully applied CPT in rPSD treatment in a limited number of patients and in a short follow-up period. However, there are no large studies in the literature showing the long-term effects of CPT in rPSD.

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In this study, it was aimed to reveal the long-term efficacy of CPT in rPSD after surgery by publishing our 20-year experience.

MATERIAL and METHODS

Patient Selection

This cohort study was performed in accordance with the declaration of Helsinki protocol and recorded in clinical trials website numbered NCT04423510. The work was reported in line with the STROCSS criteria (10). Patients who were presented to the general surgery clinic of Fırat University Medical Faculty and SBU Konya Training and Research Hospital between March 1995 and January 2015 for previously operated recurrent sinus pilonidal disease were included in the study. Data were collected prospectively and analyzed retrospectively. The aim of this intervention was therapeutic. Informed consent form was obtained from all of the patients. A total of 227 previously operated rPSD patients were included in the study. Of these, 37 patients who discontinued the treatment without any other treatment and at the beginning of the study with a follow-up period of less than 12 months were excluded from the study. The analyzes were performed in a total of 190 patients (Figure 1). In addition to the demographic data of the patients, other parameters such as smoking, whether they sit a lot due to occupation (sitting at work for at least six hours a day), skin tone (whiter, darker), presence of positive family history, BMI (kg/m^2, patients were divided into BMI< 30 and BMI> 30), and pilosity levels were also recorded. Pilosity levels were classified as mild, moderate and severe according to the pilosity levels scale of Dogru et al. (8). The presence of purulent discharge from the sinus opening and the presence of signs of inflammation or abscess formation in this region were evaluated as acute PSD. The presence of serous discharge from the sinus opening and absence of abscess formation were evaluated as chronic PSD. We investigated whether the factors mentioned above affect the number of applications and recurrence after CPT.

The Protocol of CPT

Treatment procedure was applied to all patients as described by Dogru et al. (8). One day before the procedure, the patients were asked to clean the hair from the waist to the middle of the thighs

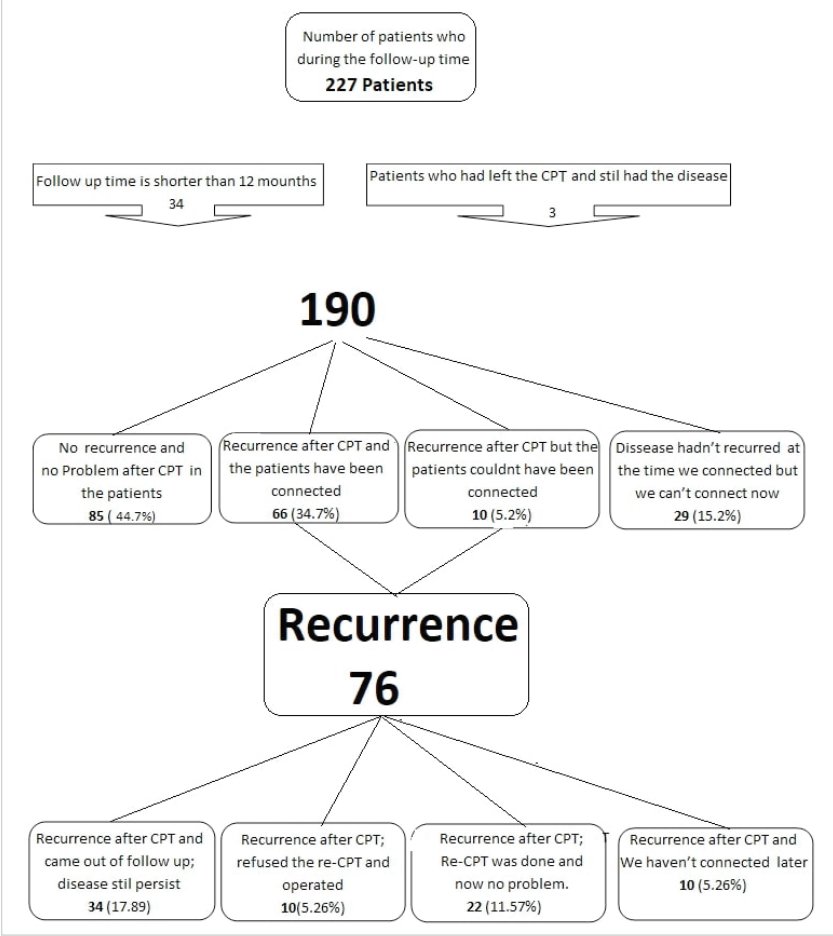

Figure 1. Flow chart for patients' conditions during follow-ups and patient exclusion criteria. CPT: Crystallized phenol treatment.

with depilatory creams or epilation. No antibiotics and analgesic agent were used during intervention. After local anesthesia was performed around the holes, a thin mosquito clamp was inserted into the sinus, the hairs were removed, and the skin around the hole was covered by nitrofurantoin pomade (Furacin, Eczacıbaşı İlaç San. ve Tic. AŞ, İstanbul, Turkey) to prevent chemical irritation. Then crystallized phenol was introduced into the sinus with the same clamp. When an abscess was detected, the abscess was drained first and simultaneous CPT was performed. Patients were allowed to return to their daily activities after the procedure. This procedure was performed every three weeks. If there was discharge from the wound during follow-up examination, the procedure was repeated. The closure of the sinus hole and complete disappearance of the discharge was accepted as healing. After the treatment, follow-up was started. Follow up was done first yearly than with five-year intervals. All of our patients' contact information was recorded by us, and we tried to reach the patients every five years by any means (phone or e-mail). We tried to follow them up by contacting them periodically, whether they contacted us or not. According to this follow-up, patients were analyzed being divided into three groups (1-5 years, 5-10 years, 10-20 years). Patients who could not be reached by any means of communication were included in the unreachable group. Patients were recommended to have hair removal at the wound site once a month for six years.

Post Procedure Follow-up

Number of crystallized phenol application, presence of recurrence and number of recurrences after CPT and follow-up data were evaluated. Recurrence of the sinus hole which was found to occur again at least six months after being determined to be closed was considered as recurrence. If no recurrence was observed during the follow-up or if post-CPT recurrence was healed after treatment, CPT was considered successful.

Statistical Analysis

Distribution of the variables was measured with Kolmogorov Smirnov test. Mann-Whitney U test was used in the analysis of quantitative independent data. Chi-square test was used to analyze the categorical independent data, and Fisher's exact test was used when the conditions for Chi-square test were not met. SPSS (Version 22.0) program was used in the analyses.

RESULTS

During the follow-up period, 85 (44.7%) patients survived without any problems. Among the 66 patients with relapsed disease and who were reachable, CPT was applied again in 22 (11.5%), and 10 (5.26%) patients preferred to have surgery due to recurrent disease after CPT and currently have no problems. Thirty-four (17.89%) of the patients who had relapsed and could be reached received no treatment after the recurrence, and the disease is still present. Twenty-nine (15.2%) patients who could not be reached subsequently had no recurrence within the time they could be contacted. Thus, the number of patients with a successful treatment was 136. Our success rate was 71.5%, which is a result of 20 years.

Demographic information of the patients is shown in Table 1. Mean duration of the disease from surgery to recurrence was 22.2 months. Recurrence was seen most frequently after excision and primary closure. Mean number of previous operations was 1.3 (1-5).

Table 2 shows sinus properties, application data of the procedure, factors accused in etiology and follow up data. Mean duration of follow-up was 45.8 months (range= 12-240 months). Our mean number of applications was 2.6, and mean duration of applications was 8.3 weeks.

Among the rPSD patients treated with CPT, 72.4% recurrences occurred in the first five years and 97.4% in the first 10 years (Table 3). Maximum recurrence was three times after CPT treatment, which was observed in one patient. In Table 3, the distribution of the total number of recurrences in patients with recurrence and data of the patients who could not be reached during follow-up are given with an interval of five years along with the patients who could be followed by us. The most recurrence was observed between 1-5 years and then decreased gradually to 2.6% between 10-20 years. The number of unfollowed patients was similar to this, and there were no patients who were unfollowed between 10-20 years. The number of patients with recurrence after CPT and undergoing re-CPT was 32 (42.1%). Mean number of applications of these patients were 2.38 ± 2.88 (1-16), and mean healing time was 9.41 ± 17.08 weeks (1-92). The number of patients who had recurrence the second time and underwent re-reCPT was 6 (7.89%). Mean number of applications of these patients were 2.33 ± 1.96 (1-6), and mean healing time was 7.17 ± 6.16 (3-20). The remaining one patient who had recurrence three times underwent re-reCPT. When compared to the first CPT performed in the patient with recurrent disease after CPT, fewer applications and shorter application time were required for treatment after each recurrence. In our series, we had 22 patients who accepted our re-CPT again after CPT recurrence and with whom we never lost contact, and now their condition is fine (Figure 1).

Forty percent of the patients recovered after a single procedure; however, we had to perform 14 procedures in two patients. The number of patients on whom we performed 10 or more procedures was only six (Table 4).

Table 5 shows whether demographics, habits and duration of disease affected recurrence after CPT. Patients with habits (cigarette smoking) had a higher rate of recurrence after CPT compared to those without any habits (p= 0.04). The longer the duration of the disease before treatment, the more recurrence was observed after CPT (p= 0.02). There was no correlation between the number of previous operations and recurrence after CPT.

Table 1. Demographic data of patients

Demographic data	Min-Max	Median	Mean ± SD/n (%)		
Age	18 - 50.0	24.0	26.3 ± 8.0		
Sex					
Male			173		91.1%
Female			17		8.9%
Duration of disease (month)	0 - 240.0	12.0	22.2 ± 34.3		
BMI	17.9 - 38.8	26.8	27.2 ± 4.1		
BMI< 30			150		78.9%
>30			40		21.1%
Habits (cigarette smoking)					
None			91		47.9%
Yes			99		52.1%
Previous operation type					
Excision and primary closing			94		49.5%
Limberg flap			68		35.8%
Karidakis flap			18		9.5%
Sinus excision and opening			8		4.2%
V-Y flap			2		1.1%
Sinus excision procedures			102		53.7%
Flap procedures			88		6.3%

Min: Minimum, Max: Maximum SD: Standard deviation, n: Number.

Table 2. Evaluation of the factors accused in etiology, sinus properties and application data of CPT

	Min-Max	Median	Mean ± SD/n (%)	
Number of total openings	1.0 - 12.0	2.0	1.9 ± 1.6	
Follow up duration (month)	12.0 - 251.0	36.0	45.8 ± 32.2	
Number of previous operations	1.0 - 5.0	1.0	1.3 ± 0.6	
Number of applications	1.0 - 14.0	2.0	2.6 ± 2.4	
Time of application (week)	1.0 - 144.0	6.0	8.3 ± 13.0	
Over-sitting story				
None			83	43.7%
Yes			107	56.3%
Skin tone				
Whiter			108	56.8%
Darker			82	43.2%
Pilosity levels				
Mild			11	5.8%
Moderate			99	52.1%
Severe			80	42.1%
Family history				
None			107	56.3%
Yes			83	43.7%
Condition of sinus				
Chronic			173	91.5%
Acute			16	8.5%

Min: Minimum, Max: Maximum SD: Standard deviation, n: Number, CPT: Crystallized phenol treatment.

Table 3. Distribution of the total number of recurrences in patients with recurrence and data of the patients who lost contact during follow up time

Follow-up time (Years)	Number of patients with recurrence n (%)	Number of patients who lost contact n (%)
1- 5	55/72.4	26/66.7
5-10	19/25.0	13/33.3
10-20	2/2.6	0/0

Table 4. Application data of patients

Number of Applications	Frequency	Percent	Cumulative Percent
1	82	43.2	43.2
2	34	17.9	61.1
3	20	10.5	71.6
4	30	15.8	87.4
5	12	6.3	93.7
6	3	1.6	95.3
7	2	1.1	96.3
9	1	0.5	96.8
10	1	0.5	97.4
11	1	0.5	97.9
12	2	1.1	98.9
14	2	1.1	100.0
Total	190	100.0	

Table 6 shows the effect of other features on recurrence after CPT. Recurrence after the procedure was not associated with the number of openings, positive family history and number and duration of applications (p> 0.05).

As the number of sinus openings increased, so did the number of applications (p= 0.001). The number of applications was higher in acute cases, compared to chronic cases (p= 0.001). In darker patients, the number of applications was higher compared to whiter patients (p= 0.01).

DISCUSSION

Although the first method used in the treatment of PSD is often a surgical, the ideal method for treatment is still controversial (11). The most important criteria showing the success of the technique is the recurrence rate. Long-term recurrence rates after surgical procedures are alarmingly high. In a recent meta-analysis by Stauffer et al. (1), recurrence rates of 67.9% after primary midline closure and 40.2% after flap methods have been reported. Lee et al. (12) have suggested primary closure with sinus excision in the treatment of primary disease and flap procedures for the treatment of recurrences. In a study, using sinus excision and flap reconstruction technique in 55 patients with rPSD, 1 (1.8%) patient has had recurrence, who has been reported to be treated using an open technique (13). The authors have suggested that methods such as flap reconstruction or leaving the wound open should be applied after sinus excision in rPSD. Bali et al. (14), in their study comparing Karydakis flap and Limberg flap techniques in rPSD, have reported similar recurrence rates; however, they have favored the Limberg flap technique due to its lower rate of complications. These studies have generally evaluated the surgical results of rPSD treatment. Therefore, it is argued that surgical outcomes are more effective on relapse in the treatment of rPSD. There are few studies with minimal follow-up on minimally invasive or nonoperative treatment methods (9,15,16). Bascom (17) has successfully applied the cleft lift procedure, a minimally invasive technique in rPSD, for the first time. In that study, 91.3% success was achieved in 69 patients who underwent cleft lift procedure. In this present study, it was shown that CPT can be applied in the treatment of rPSD with similar recurrence rates with the surgical methods and minimal complications as in pPSD. This study is also the largest series in the world that have the longest follow-up time with crystallized phenol method used in the treatment of previously operated rPSD.

Crystallized phenol treatment is the most commonly used nonoperative treatment for PSD. Crystallized phenol treatment compared with radical excision of the sinus tract is a procedure that can be performed under local anesthesia, requires no hospitalization, allows patients to return to activities in a short time after the procedure, and causes less pain after the procedure. It is cheaper, wound epithelialization is faster and has a lower risk of complications (18). In addition, CPT has similar success rates compared to other surgical procedures (7).

Table 5. Comparison of demographic data according to the relapse status of the patients

	Recurrence (-)			Recurrence (+)				
Demographic Data	**Mean ± SD/n (%)**		**Median**	**Mean ± SD/n (%)**		**Median**	**p**	
Age	25.7 ± 7.7		24.0	27.3 ± 8.5		27.5	0.234	m
Height (cm)	174.8 ± 6.9		175.0	174.6 ± 7.1		175.0	0.734	m
Weight (kg)	83.6 ± 14.9		82.0	82.6 ± 13.2		82.0	0.594	m
Duration of disease (month)	17.7 ± 25.8		10.5	28.9 ± 43.5		12.0	***0.021***	m
BMI	27.3 ± 4.4		26.9	27.0 ± 3.8		26.3	0.759	m
BMI								
<30	89	59.3%		61	40.7%		0.856	X^2
≥30	25	62.5%		15	37.5%			
Sex								
Male	103	90.4%		70	92.1%		0.678	X^2
Female	11	9.6%		6	7.9%			
Habits (cigarette smoking)								
None	62	54.4%		29	38.2%		***0.040***	X^2
Yes	52	45.6%		47	61.8%			
Previous operation type								
Excision and primary closing	57	50.0%		37	48.7%		0.859	X^2
Limberg flap	42	36.8%		26	34.2%		0.711	X^2
Karidakis flap	11	9.6%		7	9.2%		0.919	X^2
Sinus excision and opening	3	2.6%		5	6.6%		0.184	X^2
V-Y flap	1	0.9%		1	1.3%		1.000	X^2
Sinus excision procedures	60	58.8%		42	41.2%			
Flap procedures	54	61.4%		34	38.6%		0.760	X^2

[m]Mann-Whitney U test/X^2 Chi-square test, Min: Minimum, Max: Maximum SD: Standard deviation, n: number.

Although there are studies reporting some nonoperative methods such as hair removal of the natal cleft, perineal hygiene and laser depilation in addition to CPT in the treatment of pPSD, the number of studies demonstrating its efficacy in rPSD is limited (19,20). Dragoni et al. (16) have reported that no recurrence was observed in the two-year follow-up of 10 patients who were applied nd- YAG laser in rPSD. However, the number of patients and the follow-up period was kept short in that study. Aygen et al. (9) have applied CPT in 36 patients with rPSD and achieved a success rate of 91.7% after a mean follow-up of 4.5 years. Our study is a continuation of this study and gives a longer duration of follow-up results with more patients. The success rate of our study was 71.5%. This success rate includes a patient group that did not give up treatment and was compatible with us. The group of patients who did not come for follow-up visits following recurrence after CPT or who refused treatment and had surgery was accepted as unsuccessful. Complete cure was achieved in all patients who were compatible with the treatment. Perhaps, if the patients in the failing group continued treatment, our success rate would be higher and even higher than the study of Aygen et al. (9). Another reason for the decrease in our success rate compared to the study of Aygen et al is that some patients dropped out of follow-up because of the long follow-up period.

In this study, when we examined the recurrences after CPT, 10 (13.15%) patients stopped to contact us following recurrence after CPT, and 34 (44.73%) patients did not accept our second treatment and the disease was still present in our follow-up, and 10 (13.15%) patients refused our second treatment and underwent surgery (Figure 1). However, 22 (28.94%) patients in this group who relapsed after CPT accepted the additional treatments recommended by our team and never lost contact. All 22 of these patients are now in a healthy state. From these 22 patients, only 3 (13.6%) had second relapses and 1 (4.5%) had a third relapse and treated re-CPT successfully. Thus, it was found that recurrent cases after CPT can be easily treated with crystallized phenol method and will not cause serious complications as in recurrence of surgical treatment.

Table 6. The comparison of sinus characteristics, CPT application data, follow-up time and factors accused in etiology according to recurrence status in the patients

	Recurrence (-)			Recurrence (+)			p	
	Mean ± SD/n (%)		Median	Mean ± SD/n (%)		Median		
Number of total openings	2.1 ± 1.9		2.0	1.7 ± 1.1		1.0	0.316	m
Follow up duration (month)	44.6 ± 30.6		35.0	47.7 ± 34.7		37.5	0.363	m
Number of previous operations	1.3 ± 0.7		1.0	1.3 ± 0.6		1.0	0.272	m
Number of applications	2.7 ± 2.4		2.0	2.5 ± 2.4		2.0	0.241	m
Time of application (week)	8.5 ± 15.2		6.0	7.9 ± 8.6		6.0	0.948	m
Over-sitting story								
None	44	38.6%		39	51.3%		0.083	X^2
Yes	70	61.4%		37	48.7%			
Skin tone								
Whiter	66	57.9%		42	55.3%		0.720	**X^2**
Darker	48	42.1%		34	44.7%			
Pilosity levels								
Mild	7	6.1%		4	5.3%		0.938	
Moderate	60	52.6%		39	51.3%			
Severe	47	41.2%		33	43.4%			
Family history								
None	64	56.1%		43	56.6%		0.952	X^2
Yes	50	43.9%		33	43.4%			
Condition of sinus								
Chronic	107	90.7%		66	88.0%		0.157	X^2
Acute	7	5.9%		9	12.0%			

[m]Mann-Whitney U test / X^2 Chi-square test, Min: Minimum, Max: Maximum SD: Standard deviation, n: number.

The success rate of CPT in a single session in pPSD has been reported to be 62-95% in the literature (21). The success rate of a single session in this present study was 44.4%. In ten sessions of application, the success rate reached 97.4%. Our low rates are due to the fact that we applied this treatment in recurrent cases and did not select the cases. Mean number of applications in this study was 2.6. Aygen et al. (9) have reported an average number of applications in rPSD as 3.7. The number of applications is probably low due to the large size of this present study. In patients with recurrence after CPT, mean number of applications after recurrence was 2.3. In other words, we think that the recurrence of the disease does not lead to an increase in the number of applications, but rather it decreases the number of applications. We also found that flap formation performed in the previous surgical procedure had no effect on the number of applications and recurrence after CPT.

Some etiological factors such as obesity, chronic disease, family history, cigarette smoking and sedentary lifestyle have been proposed as predisposing factors in the development of pPSD (22). Doll et al. (23) have demonstrated a significantly higher recurrence rate in patients who were operated on for PSD and had a positive family history of PSD in first degree relatives. In our study, no relationship was found between positive family history and recurrence after CPT. There are conflicting results about the relationship between recurrence and BMI in PSD (22,24). In this present study, there was no significant difference in recurrence after CPT in patients with BMI> 30 compared to the rest of the patients. However, recurrence was higher after CPT in patients with cigarette smoking (p= 0.04). In addition, recurrence rate after CPT increased with increasing duration from postoperative recurrence to CPT (p= 0.02, Table 5). There was no correlation between skin tone and pilosity levels and recurrence after CPT. However, we recommend hair removal with depilatory cream or laser depilation once a month during treatment and for at least six years following treatment. However, some of the patients complied with this recommendation and some did not. Therefore, we cannot say whether hair growth is effective in relapse after CPT. Kaymakçıoğlu et al. (7) have reported that recurrence rate and recovery time increase as the number of sinus openings increases in pPSD. However, in our study, there was no correlation between the number of holes and the number of applications and recurrence after CPT. According to our study, we think that etiologic factors affecting

recurrence in pPSD are not similar in rPSD. This may be due to previous operations.

There are some limitations of this study. Due to the long follow-up period of our study, we could not contact 20% of our patients within a certain period of follow-up. In addition, since it was not a randomized controlled trial, no patient selection criteria were set. We followed up all patients with previously operated rPSD. Therefore, we obtained data from a very large population. Our study may be supported by a randomized prospective study in a more specific operation group or in a more selected patient group.

CONCLUSION

Long-term results of CPT, which has been proven successful in pPSD, are also effective in previously operated rPSD. In addition, although it has a recurrence rate close to surgical interventions, there is no risk of serious postoperative complications. Cigarette smoking, the duration between time of recurrence after surgical treatment and time of presentation are effective in the development of recurrences after CPT. We believe that CPT can be the first choice of treatment in rPSD treatment as it is an inexpensive nonoperative treatment method that can be applied in outpatient settings with minimal labor loss, excellent cosmetic results, minimal pain and rapid return to daily activities.

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ORİJİNAL ÇALIŞMA-ÖZET
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Pilonidal sinüs nedeniyle opere olan ve nüks gelişen hastalarda kristalize fenol tedavi sonuçları: Yirmi yıllık kohort çalışması deneyimi

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ÖZET

Giriş ve Amaç: Pilonidal sinüste cerrahi sonrası nükslerin tedavisi zor ve can sıkıcıdır. Opere nüks pilonidal sinüs hastalığında kristalize fenol uygulamamızın yirmi yıllık sonuçlarını vererek uzun dönem etkinliğini sunmayı amaçladık.

Gereç ve Yöntem: Pilonidal sinüs cerrahisi geçiren ve nüks nedeniyle başvuran 227 hasta çalışmaya dahil edildi. Müdahale lokal anestezi altında günübirlik müdahale ile yapıldı. Hastaların demografik verileri, sinüs özellikleri, kristalize fenol seans sayısı, takip süresi, nüks ve nüks sayıları prospektif olarak kaydedildi. Tedavinin başarısı ve nüksü etkileyen faktörler incelendi.

Bulgular: Başarı oranımız %71,5 idi. Bu başarı oranı tedaviyi hiç bırakmayan ve tedaviye uyum sağlayan hasta grubuna aittir. Hastalar ortalama 45,8 ay takip edildi. Kristalize fenol tedavisi sonrası nükslerin %72,4'ü ilk beş yıl içinde olurken,%97,4'ü ilk 10 yıl içinde gerçekleşti. Ortalama seans sayısı 2,6 idi. Tedavi öncesi hastalık süresi ne kadar uzunsa, tedavi sonrasında o kadar fazla nüks gözlendi (p= 0,02). Önceki operasyonların sayısı ile tedavi sonrası nüks arasında bir ilişki yoktu. Sinüs deliklerinin sayısı arttıkça uygulama sayısı artmıştı (p= 0,001).

Sonuç: Kristalize fenol tedavisi, tekrarlayan pilonidal sinüs hastalığında da umut verici uzun vadeli sonuçlar verir ve etkin bir ameliyatsız tedavi yöntemi olduğu için tekrarlayan pilonidal sinüs hastalığı tedavisinde ilk seçenek olarak önerilebilir.

Anahtar Kelimeler: Nüks pilonidal sinüs, nonoperatif tedavi, kristalize fenol

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ORIGINAL ARTICLE
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Evaluation of *Echinococcus* DNA by polymerase chain reaction (PCR) in cystic *Echinococcosis* of the liver

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ABSTRACT

Objective: The aim of this study was to determine the DNA and genotypes of *Echinococcus granulosus* in liver cyst hydatids isolated in humans.

Material and Methods: This study was conducted prospectively at the Department of General Surgery of the Cerrahpaşa School of Medicine, University of İstanbul-Cerrahpaşa, between January 2015 and June 2016 in 30 patients who were operated on for cystic *Echinococcosis*. *E. granulosus* DNA was analyzed using the Polymerase Chain Reaction (PCR) method in the cyst samples (protoscolex and/or germinative membrane) obtained during the operation, and genotype was determined in the PCR positive samples by sequence analysis. At the same time, indirect hemagglutination (IHA) was used to test for the presence of antibodies in the patients' blood.

Results: *E. granulosus* DNA was found in 29 out of 30 cystic *Echinococcosis* of the liver samples. All of the 29 cystic *Echinococcosis* samples were found to be G1 (sheep) species. Also, IHA was positive in 22 patients and negative in eight patients.

Conclusion: In the present study, G1 species was the most commonly seen liver cystic *Echinococcosis* species. We suggest that a vaccine, which could be developed against prevalent regional genotypes, would be efficacious in the prevention of the disease with a cause of mortality and morbidity.

Keywords: Liver cystic *Echinococcosis*, *Echinococcus granulosus*, genotype, DNA, PZR, Western-Blot

INTRODUCTION

The disease, caused by the settling of the larva form (metacestode) of *Echinococcus* granulosus in many organs, including primarily the liver and lungs in humans, is called "cystic *Echinococcosis*" (CE: Cystic *Echinococcosis*). CE is a zoonotic disease, caused by *E. granulosus*, *E. multilocularis*, *E. vogeli* and *E. oligarthrus*, which is seen most frequently in the liver, lungs and spleen, as well as in various other localizations in recurrent cases worldwide; however, mainly in countries such as Turkey, where there is widespread animal husbandry (1,2). The main hosts of *E. granulosus* are carnivores such as dogs, wolves, and foxes. Sheep, cattle and humans are intermediate hosts in the life cycle of the parasite. The intermediate host is infected through food contaminated with the eggs of the parasite. (3) Subsequently, the embryos pass to the portal blood circulation through the intestines and settle in the liver (50-70%), lungs (10-30%), spleen, kidney, central nervous system, bone and muscle tissue respectively, and develop the cyst form that is the larval period (3,4). *E. granulosus* is the one among all *Ecinococci*, and 10 different genotypes of *E. granulosus* have been determined as domestic sheep species (G1), The Tasmania sheep species (G2), buffalo species (G3), [G1- G3 species have been grouped as *E. granulosus* sensu stricto (s.s)], horse species (G4), bovine species (G5), camel species (G6), pig species (G7), deer species (G8), wild life species (lion species, lagomorph species) (G9) and Fennoscandian deer species (G10) (5,6). *Echinococcosis* is seen worldwide and most frequently in Eurasia, the Mediterranean, North and East Africa and South America (2,6,7). Genetic diversity has a critical significance in the determination of the phenotypical properties, host specificity, efficacy of spread, pathological processes, antigenicity, antibiotic efficacy and vaccine strategy (1,2). Molecular and immunological tests have been used in the diagnosis of CE. IHA (Immune Hemagglutination), one of the immunological tests, is based on the antigen

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holding properties of tannic acid-sensitized erythrocytes, as a result of change in their surface tension. With a varying sensitivity of 80-94%, IHA has been considered as the most sensitive and easy to apply test in the diagnosis of cystic *Echinococcosis* (7). Polymerase Chain Reaction (PCR) is the enzymatic reproduction of a DNA fragment located in between two oligonucleotide primers. One of the primers is complementary to the one chain of the DNA molecule in one side of the target sequence, and the second primer is complementary to the other chain of the DNA molecule on the other side of the chain sequence. Primers synthesize the sequence by the help of the DNA polymerase that is in between them. PCR based techniques are sensitive techniques used in the diagnosis of *Echinococcosis* (8,9). Many new methods have been developed since the invention of the PCR technique [Multiplex PCR, nested PCR, arbitrary-primed PCR (AP-PCR), real-time PCR (qPCR), polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP)] (10). The most commonly used molecular techniques in the determination of genetic diversity of the *Echinococcus* species are PCR, RFLP, PCR-RFLP, RAPD-PCR (Random Amplified Polymorphic DNA), PCR-SSCP (PCR-Single Stranded Conformation Polymorphism) and DNA sequence analysis. DNA sequence analysis is considered as a gold standard technique among all the molecular techniques, although it requires specialty and interpretation of the results is difficult (2,6). The aim of this study was to evaluate the reproduction of *E. granulosus* DNA using the PCR technique and the genotypical characterization of it by DNA sequence analysis and to scrutinize the results in terms of clinical and pathological aspects.

MATERIAL and METHODS

This study was conducted prospectively at the Department of General Surgery of the Cerrahpaşa School of Medicine, University of İstanbul-Cerrahpaşa, between January 2015 and June 2016 in 30 patients who were operated on using different techniques for CE diagnosed clinically, radiologically and serologically. The various surgical techniques used in this study were defined in previous studies, and surgical techniques that would not result in postoperative recurrence were preferred (11,12). Prior to the start of the study, ethics board approval was obtained from the Ethical Committee of Cerrahpaşa School of Medicine (approval number and date: 83045809- 604.01.02/07.12.2014) and informed consents from the patients were obtained. Patients with an age of less than 18 years were excluded from the study. Prior to the study, age, sex, additional disease or history of previous surgery, history of drug use, family history, occupation, place of birth, history of previous cystic *Echinococcosis* disease or treatment received for it if applicable, history of CE in the relatives, location of the cyst, radiological findings and laboratory results of the patients were evaluated and recorded.

Sample Collection

Cyst samples (protoscolex, germinative membrane and laminar membrane) were stored at -80°C in 70% alcohol (Figure 1).

DNA Extraction

The cyst samples were washed several times in order to clear the alcohol. Cyst samples of 25-50 mg each were divided into multiple pieces, as small as possible. DNA extraction was performed using a commercial tissue extraction kit (High Pure PCR Template Preparation Kit, Roche Diagnostics GmbH, Manheim, Germany).

Polymerase Chain Reaction

PCR method was applied as described previously by Bowles et al. (13) to the extracted tissue samples in order to analyze *E. granulosus* DNA by using primer sequences that belong to the mitochondrial cytochrome c oxidase subunit 1 (CO1) gene region of the *E. granulosus* (Table 1). To this end, 1 mL forward primer (50 pmol/mL), 1mL reverse primer (50 pmol/mL), 5 mL 10 x reaction buffer, 3 mL 25 mM MgCl2, 1 mL dNTP, (200 mM deoxynucle-

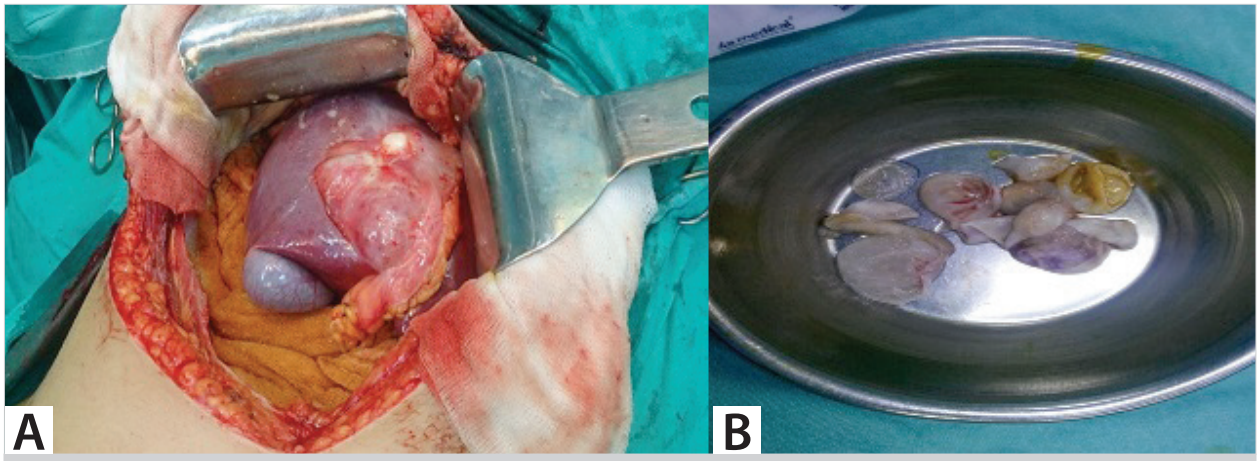

Figure 1. A. Appearance of intraoperative liver cystic *Echinococcosis*; **B.** *Cystic Echinococcosis* obtained from the liver (*E. granulosus*, daughter vesicles).

Table 1. Primer sets used in the study

Name of the Primer	Region	Sequence (5′-3′)	Product Dimension
F-JB 3	Sense CO1	5′ ttt ttt ggg cat cct gag gtt tat 3′	
R-JB 4.5	Anti-sense CO1	5′ taa aga aag aac ata atg aaa atg 3′	446 bp.*
Beta-globin	Sense	5′ aca caa ctg tgt tca cta gc 3′	
	Anti-sense	5′ gga aaa tag acc aat agg ctg 3′	251 bp.*

*bp: Base pair.

otide triphosphate for each) (Fermentase®, Lithuania), 0.25 mL Taq DNA polymerase (Fermentase®, Lithuania) and a 28.75 mL mixture containing water and no DNase-RNasef was prepared. 10 mL of extraction product was added to the 40 mL mixture.

Amplification was performed as follows: Initially, the mixture was denaturated for two minutes at 95°C, and then 30 cycles were applied, with 30 seconds at 94°C, 30 seconds at 55°C and 30 seconds at 72°C. The final lengthening was performed at 72°C for eight minutes. The amplification products were viewed under UV light through application in a 10 mL/mL ethidium bromide added 1.5% agarose gel. All the samples were analyzed for the presence of inhibitors using beta-globulin primers.

Genotype Determination

Genotype determination was performed in cases in which *E. granulosus* DNA positivity was detected. In order to determine the genotype, a commercial purification kit (High Pure PCR Product Purification kit, Roche Diagnostic, GmbH, Germany) was used, positive PCR products were purified and cycle-sequencing was performed using a big-dye terminator kit (ABI®, USA). Subsequently, the cycle sequencing products were cleared with the sephadex G-50 fine column method and analyzed in an automated DNA sequencing device (ABI®, 310). The obtained sequences were prepared using "Bioedit software (Hall, 1999)" and were compared with the sequences in GenBank™.

RESULTS

CE involved the liver in all 30 patients. Among the patients 11 were male (36.6%) and 19 were female (63.3%) with a mean age of 43.7 years. The location of the cyst was the right lobe of the liver in 24 patients (80%) and left lobe in six patients (20%). IHA tests performed in the preoperative period were positive in 22 (73.4%) and negative in eight (26.6%) patients. Among the eight IHA negative patients, the diagnosis of CE was proven radiologically and pathologically in seven (23.3%).

E. granulosus DNA was found to be positive in 29 out of the 30 patients in the study. The DNA sequence analysis method was used in the reproduced and purified isolates. From a comparison of the sequence analysis with the reference sequences (http://www.ncbi.nlm.nih.gov./BLAST/BLASTdatabases.html), all 29 isolates were determined to be the G1 (sheep) species.

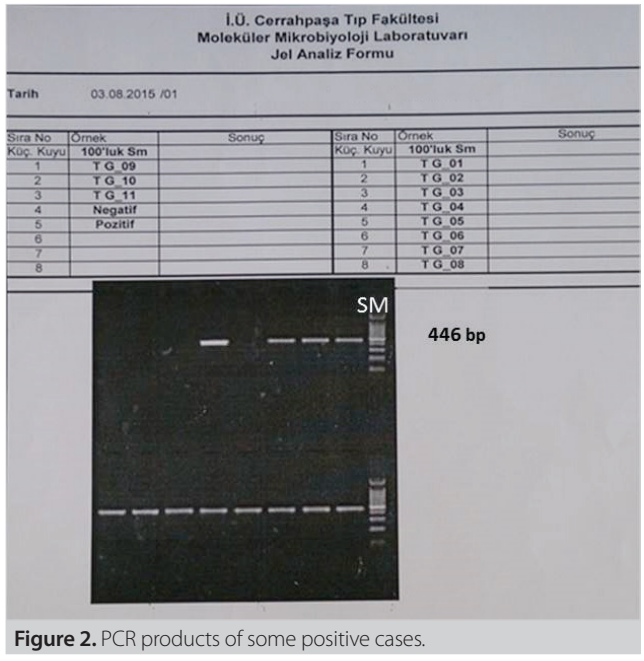

Figure 2. PCR products of some positive cases.

An approximately 446 bp band was formed as a result of reproduction of *E. granulosus* using primer sequences of the mitochondrial cytochrome c oxidase subunit 1 (CO1) gene region using the PCR method. The band profiles of the mitochondrial cytochrome c oxidase subunit 1 (CO1) gene region of the positive controls and the samples following electrophoresis can be seen in Figure 2.

DISCUSSION

E. granulosus is a small parasite, 2-6 mm in length, that can be transmitted by its eggs and through the ingestion of contaminated food, but also through the skin. The hatching embryo (oncosphere) in the intestine attaches to the mucosa and produces cystic *Echinococcosis* by passing to the liver through the gastrointestinal venous circulation and portal system. If the oncosphere is unable to attach here, it may pass to the lungs through the pulmonary artery, and CE may develop either in the lungs or in other organs (spleen, peritoneum, kidney, bone, orbital space, brain, heart and reproductive organs) (1,7).

E. granulosus is quite common worldwide, and is a very important cestode in terms of public health since it causes serious

zoonotic infestations. It produces structural and functional disorders in various tissues and organs of animals, leading subsequently to economic losses (14). Different species are important in the lifecycle of the parasite and also in host selectivity, rate of development, pathogenicity, antigenicity, sensitivity to chemotherapeutics and transmission properties, as well as the epidemiology and controllability of the disease. The determination of the genotype distribution in endemic areas of the disease, and successful application of control and eradication programs in such areas is, therefore, extremely important (2,15).

The most common genotype in humans and animals in this country and around the world is considered to be the G1 (sheep) species, based on genoepidemiological studies that have made use of molecular techniques (16,17). The G1 genotype has been reported to be the most frequently seen genotype in humans and animals in Mediterranean countries on the same continent as Turkey (18,19). Elsewhere, the G6 camel species in Egypt and the G7 pig species in Poland have been reported to be more common (4,20).

Geographical circumstances and social structure affect the prevalence of the *Echinococcus* type in this region. In Turkey, *Echinococcus* infestations are most often seen in sheep and dogs, and these animals and the G1 species are also the most common and most frequent origin of human infections (21).

Studies of hydatid cysts in humans and animal origin studies are quite scarce in Turkey. Vural et al. (22) identified G1 (sheep) and G3 (bovine) genotypes following a sequence analysis of the CO1 gene region of *E. granulosus* isolates obtained from sheep and bovines in different cities in all regions of the country. Simsek and Eroksuz (23) have reproduced the agent using the mitochondrial CO1 gene region in a cyst sample obtained from wild Anatolian sheep (Ovis gmelinii Anatolica) and determined it to be the G1 species based on a sequence analysis. Utuk et al. (24) on the other hand, found that all of the *E. granulosus* isolates were of the G1 genotype in their wide series involving humans, dogs, camels, sheep and bovine. Engin et al. (25) determined G1 species in all of the human isolates in their study of patients from different regions of Turkey using primers belonging to the mitochondrial CO1 gene region in the cyst samples. Snabel et al. (26), on the other hand, identified for the first time the presence of the G7 (pig) species in Turkey in sheep and human isolates collected from various cities in the Aegean region. Eryildiz et al. (27) carried out a sequence analysis of the mitochondrial cytochrome oxidase c subunit one and NADH dehydrogenase subunit one gene regions in their molecular study, and identified the presence of two different genotypes in their study, being G1 and G7.

In the present study, the presence of the G1 (sheep) species was detected in all 29 of the samples in which the sequence analysis of the mitochondrial CO1 gene region of the *E. granulosus* could be performed among the 30 samples of CE located in the liver. This finding concurs with those of studies in which the G1 (sheep) species was identified as the most common genotype in this country and around the world.

CE is still a threat to public health in Turkey, as an endemic region. Screening immigrants through field studies with rapid tests is required in regions where immigration from neighboring countries where the disease is endemic, and where the prevalence of the disease is high. Further molecular tests should be conducted to determine the species when necessary, for which the subject should be evaluated by public health specialists and molecular epidemiologists in collaboration, and risk maps of Turkey's regions should be prepared based on risk analysis methods. The extent and nature of the precautions taken to control the disease may vary based on the characteristics of the species. Large-scale genoepidemiological studies should be carried out and control and eradication programs should be launched, either periodically or during extraordinary mass immigration events, to bring cystic *Echinococcosis* under control.

CONCLUSION

CE is a significant public health problem in several countries around the world. Many *E. granulosus* subtypes have been identified through molecular analyses, and the most common species was found to be the G1 sheep species in the preset study performed in the Cerrahpaşa Medical Faculty. Studies should be conducted in this region into the sheep-dog cycle, as the main path of transmission, as a means of preventing human transmission in rural areas and on animal farms in the region. Studies involving the PCR technique in different regions would aid in the prevention of transmission and distribution of CE by determining the predominant subtypes in a particular region. A vaccine developed for the most commonly seen genotypes identified through larger scale geno-epidemiological studies may serve as a solution for this global public health problem.

Ethics Committee Approval: This study was approved by Cerrahpaşa Faculty of Medicine Research Ethics Committee (Decision no: 442684, Date: 07.12.2016).

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2022; 38 (2): 196-201

Karaciğer hidatik kisti hastalarında polimeraz zincir reaksiyonu (PZR) yöntemi ile ekinokok DNA'sının araştırılması

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ÖZET

Giriş ve Amaç: Bu çalışmada insandan izole edilen karaciğer hidatik kistlerinde *Echinococcus granulosus* DNA ve genotiplerinin belirlenmesi amaçlandı.

Gereç ve Yöntem: Çalışma prospektif randomize olarak, 2015 Ocak-2016 Haziran tarihleri arasında İstanbul Üniversitesi, Cerrahpaşa Tıp Fakültesi Genel Cerrahi Anabilim Dalı'nda karaciğer hidatik kisti tanısı ile ameliyat edilen 30 hasta üzerinde gerçekleştirildi. Ameliyat sırasında elde edilen kist örneklerinde (protoskoleks ve/veya germinatif membran) Polimeraz Zincir Reaksiyonu (PZR) yöntemiyle *E. granulosus* DNA'sı araştırıldı ve pozitif bulunan örneklerde dizi analizi yöntemiyle genotip tayini yapıldı. Aynı zamanda ameliyat öncesinde hastaların kanlarında indirekt hemaglütinasyon testi (IHA) ile antikor varlığı araştırıldı.

Bulgular: İncelenen 30 karaciğer hidatik kisti örneğinin 29'unda *E. granulosus* DNA'sı saptandı. 29 hidatik kist örneğinin tamamının G1 (koyun) suşu olduğu görüldü. Ayrıca 22 hastada IHA pozitif, sekiz hastada ise negatif idi.

Sonuç: Çalışmamızda en sık görülen hidatik kist genotipi G1 suşudur. Bölgesel olarak yaygın görülen genotiplere uygun geliştirilebilecek bir aşının bu morbidite ve mortalite kaynağı hastalığın önlenmesinde etkili olacağını düşünüyoruz.

Anahtar Kelimeler: Karaciğer hidatik kisti, *Echinococcus granulosus*, genotip, DNA, PZR, Western-Blot

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ORIGINAL ARTICLE
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A rare type of burn : Nylon burns

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ABSTRACT

Objective: In this study, it was aimed to examine nylon burns in paediatric patients and compare the results with other causes of hot object contact burns.

Material and Methods: A 10-year retrospective study was conducted on 77 paediatric patients hospitalized for hot body burns at Gazi Yaşargil Training and Research Hospital Burn Center.

Results: Of those patients with hot body burns, 72.7% (n= 56) were males and 27.3% (n= 21) were females. Male-to-female ratio was 2.67:1. Mean age of the patients was 4.79 (min= 1, max= 16) years. There were 42 patients who applied to our hospital on the day of their burn, while four patients applied one day after the burn, one patient applied two days after the burn, 13 patients applied three days after the burn and 17 patients applied five days after the burn. Most burns (79.3%) were third-degree burns, whereas 19.5% were seconddegree and 1.2% were fourth-degree burns. The most common causes of hot body burns were hot nylon and hot stoves, followed by hot ash and hot irons. The number of nylon burns was the highest in the summer and the highest number of hot stove burns occurred in the winter. Nylon burns were most common in the three to eight age group and then gradually decreased. The highest burn rate was observed in nylon burns.

Conclusion: The most common cause of all burns in the Turkish paediatric population is scalding. Although nylon burns are rare, they draw attention due to their higher burn degrees.

Keywords: Nylon burns, hot object contact burns, pediatric burns, epidemiology

INTRODUCTION

Burns are events causing serious material and morale problems that can lead to death and disability. Despite medical and technological advances, burns are still a serious, lifethreatening problem. For this reason, the cheapest and most effective method to prevent burns is by taking precautions before they occur.

Hot object contact burns are caused by direct contact with a hot material, such as hot metal, a stove or an iron, or by being unprotected due to immobilization as a result of various neurological illness for a long time. Burns usually occur in limited areas and may occur at various depths. Nylon is a substance used in all areas of our lives. This material burns rapidly, shrinks and catches fire. After being ignited, the material slowly burns and melts. Nylon extinguishes itself, but can drip dangerously, stick to the site where it drips, and continue to burn until it drains (1).

The aim of this study was to investigate hot body contact burns in patients and compare nylon burns with other contact burns as described in the literature.

MATERIAL and METHODS

Study Design

This 10-year retrospective study was conducted on 77 paediatric patients with hot object contact burns who were admitted to the Gazi Yaşargil Training and Research Hospital Burn Center between January 2010 and January 2020. The study was approved by Research Ethics Committee (Gazi Yaşargil Training and Research Hospital Ethics Committee/29.01.2021/E-615).

Study Parameters

The American Burn Association admission criteria were applied to all patients presenting to our department. Patients' medical histories were taken to reveal the ae-

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tiology of the hot body contact burn. Medical records of each patient were reviewed, and demographic characteristics, burn depth, total burned body surface area (TBSA), the duration of their hospital stay, treatment methods, and rates of morbidity and mortality were determined.

General Management of Pediatric Burn Cases

The overall management of pediatric burn cases includes the same immediate concerns for life support as for any other trauma patient: Establishing an open airway, initiating adequate volume resuscitation to stabilize circulation, and evaluating additional injuries. The patient is then followed up in a specialized burn center with a well-trained multidisciplinary team under the leadership of a burn surgeon.

Statistical Analysis

Descriptive statistics for continuous variables were presented as mean and standard deviation, while count and percentages for categorical variables. SPSS (Chi. Ill. USA) statistical program was used for all statistical computations.

RESULTS

The patient group was comprised of 72.7% (n= 56) males and 27.3% (n= 21) females. Male-to-female ratio was 2.67:1. Mean age of the patients was 4.79 (min= 1, max= 16) years. There were 42 patients who applied to our clinic on the day of the burn, four patients one day after the burn, one patient two days following the burn, 13 patients applied three days after the burn and 17 patients applied five days after the burn. Third-degree burns made up 79.3% of all burns, while 19.5% were second-degree and 1.2% was fourth-degree burns (Table 1).

The most common causes for burns were hot nylon and hot stoves, followed by hot ash and a hot iron (Figure 1). The anatomical areas with the most burns were the left upper extremity, followed by the right lower extremity and then the right upper extremity (Figure 2).

The highest burn injury rate was seen in patients in the 0-2 age group (n= 4; 44.1%), with the highest rate in the 0-1 age group (23.3%). After the age of four years, the number of patients gradually decreased.

Table 1. General information about the patients

	Number	Percent
Boy	56	72.7%
Girl	21	27.3%
Age	1-16 years mean= 4.79 ± 4.2	
Burn degree		
2nd degree	15	19.5%
3rd degree	61	79.2%
4th degree	1	1.3%
Burn percentage	1-15%	Mean= 3.9 Std= 2.6
Hospital length of stay	1-15 days	Mean= 3.86 Std= 2.6

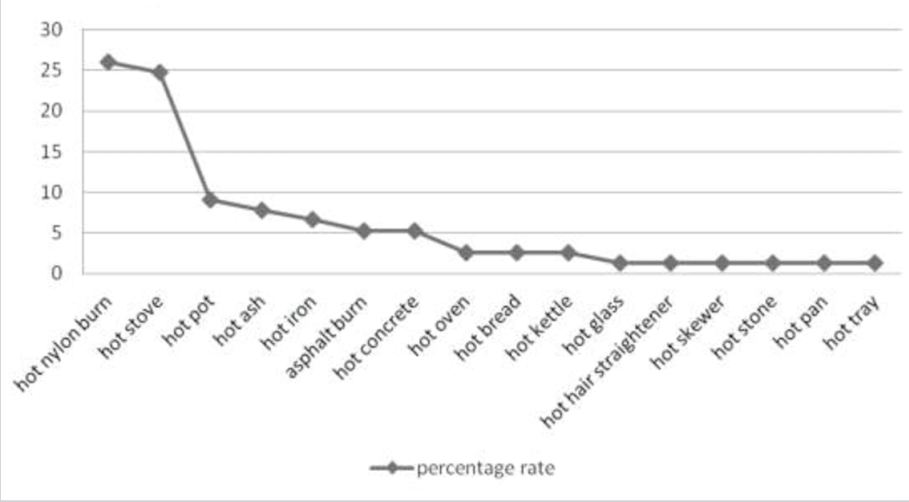

Figure 1. Etiology of hot object contact burns.

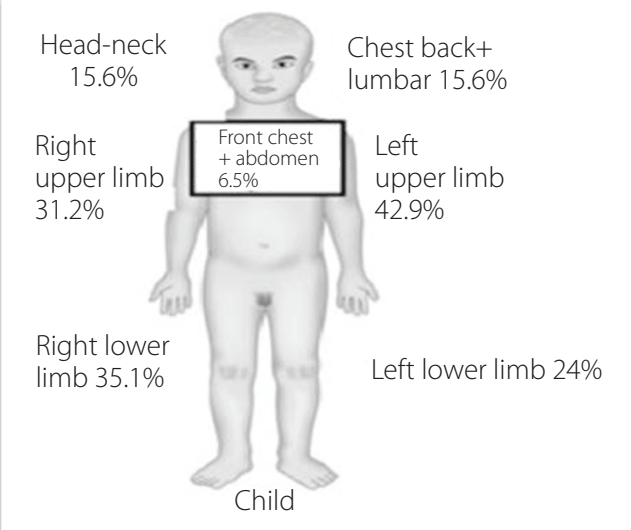

Figure 2. Percentage of area affected by hot object contact burn.

Nylon burns accounted for 25.9% of all burns and were most common between the ages of 3-8 years and then gradually decreased (Figure 3). Nylon burns were the highest during the summer. Of the patients, 25% had second degree burns, and 75% had third degree burns. Wound culture results were 10% (+) in nylon burns (Table 2). There was no additional disease in nylon burns.

Hot stove burns accounted for 24.7% of all patients and were most common between the ages of 0-2 years and then gradually decreased (Figure 3). Hot stove burns were the highest during the winter. Of the patients, 31.5% had second degree burns, and 68.5% had third degree burns (Table 2). Wound culture results were 15.7 % (+) in hot stove burns. Two (10.5%) patients with hot stove burns also had meningomyelocele as additional disease.

Most of the patients were admitted during the summer months (Figure 4). Approximately 6.5% of the patients had a meningomyelocele and 1.3% had paraplegia as additional diseases.

With regard to patients' homes, 62.3% came from urban centres and 37.7% were from rural areas.

Wound culture result was positive in 23.4% of the patients. The most abundant microorganism was *Staphylococcus aureus* with 5.2%. Antibiotics were given according to the culture results.

Silver nitrate dressing was covered after escharectomy in 97.4% of the patients, and grafting was performed in 1.3% of the patients. In 1.3% of the patients, the wound was closed by turning the skin flaps.

The average length of stay of the patients ranged from one to 15 days, with an average of 3.86 ± 2.62 days. We did not have any patients who received an amputation or any that subsequently died following their injuries.

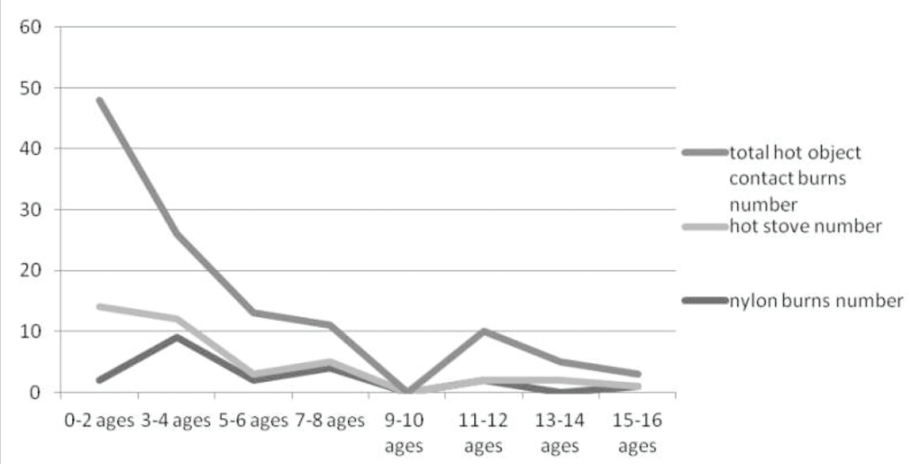

Figure 3. Distribution of the numbers of hot nylon, hot stove and total hot object contact burns by ages.

Table 2. Comparison of children's hot object contact burns

	Patient Percentage	2nd Degree Patient Percentage	3rd Degree Patient Percentage	Infection Rate
Hot Nylon	25.9%	25.0%	75.0%	10.0%
Hot Stove	24.7%	31.5%	68.5%	15.7%
All Patients	100%	19.5%	72.9%	23.4%

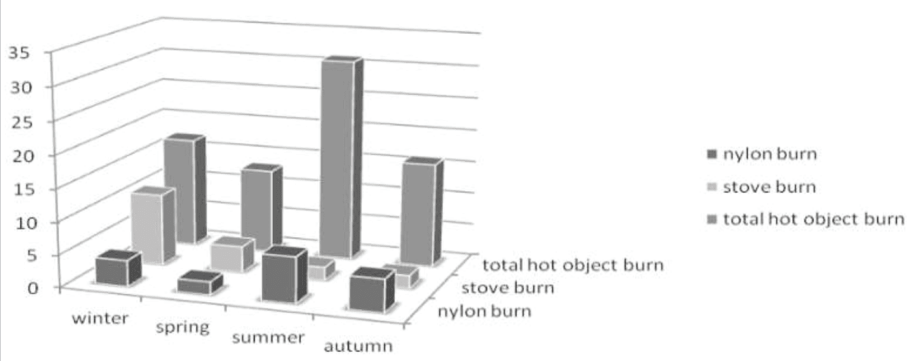

Figure 4. Seasonal distribution of inpatients by hot object contact burns.

Figure 5. Children who stubble.

DISCUSSION

Contact burns with hot objects are burns caused by direct contact of the skin with hot objects. It has been reported that contact combined with the sudden withdrawal reflex is usually short term, and the burn is limited but tends to be deep. These burns have also been found to be the second most common type of burn in various studies (2,3). It has been emphasized that such burns are more common in young children and people with restricted movements, as the contact time may be longer (3). Consistent with our study, some studies have reported a higher incidence of burns in males than in females (4,5).

Paediatric burn injuries affect low-and middle-income countries more than high-income countries (6,7). Hot object contact burns occur more in rural areas than in urban centres (7). Rural houses in Diyarbakır consist of one or two rooms at most, and they usually do not have a separate kitchen. This makes it difficult for children to be effectively protected from the burn hazards associated with cooking. For instance, in Diyarbakır, the urban population is 72.9% and the rural population is 27.1% (8). Of the patients in our study, 62.3% came from the city centre and 37.7% from rural areas. However, in comparing the percentages, there was a higher rate of hot object contact burns in rural areas than in urban areas.

Our results were consistent with those of Kemp et al. (9). In addition, the causes of burns, such as hot nylon, hot tiles, hot concrete and hot soils, which are common in our region, can be added to hot contact burns. Unlike previous studies, contact burns are a common cause of burns in children under five years of age (9-12).

In our region, air temperatures are higher in the summer with longer periods of daylight, during which the temperature is at its highest. Air temperatures reach as high as 40-45°C (13). High temperatures and longer days inevitably increase the temperature of materials, such as soil, tiles and concrete. As a result, hot object contact occurs unavoidably and causes an increase in the proportion of hot objects in the summer. In our region, with a low socioeconomic level, rural children are usually barefoot. This may be one of the reasons for the high rate of hot object burns in the lower extremities in our region (Figure 5). Nylon burns are a rare type of burn in children. In our study, it was the most common cause of hot body burns between the ages of 3-8 years. The reason for this is that children coming from rural areas often burn unwanted dry grass for planting after the summer. They perform this task by traversing the field and by taking advantage of the drip feature of burning nylon to burn the whole field. Inevitably, this sometimes causes accidents and nylon burns occur (Figure 5).

People with low socioeconomic levels use nylon-made textiles a lot. Any kind of burning nylon suit sticks to the body. This increases the depth and complications of the burn. The government and the textile industry both need to investigate the problems associated with burnt and combustible fabrics (14). Two of our patients were burned in this way. Their treatment

was difficult, and their hospitalization periods were long. In our results, we had a higher rate of third-degree burns due to the dripping of hot nylon adhering to the skin.

The author argued that although home safety education with the provision of home safety equipment is effective in increasing some thermal injury prevention practices, there is insufficient evidence to determine whether this also reduces injury rates (15). In our study, we found that hot object contact burns are not only related to household items. Moreover, environmental and socioeconomic factors were found to be related with hot object burns.

CONCLUSION

Our study supports previous findings that contact burns are common thermal injuries in children under 16 years of age. This highlights the need for more prevention strategies for the most common hot object contact burns, which are caused by hot nylon, hot stoves, ash and irons. The causes of hot object contact burns vary in relation to the socio-cultural and consumer lifestyle of the society. Families should be made aware of hot nylon and other causes of burns. The government and the textile industry also need to make adjustments for the amount of nylon used in fabrics.

Ethics Committee Approval: This study was approved by Health Sciences University Gazi Yaşargil Training and Research Hospital Clinical Research Ethics Committee (Decision no: 615, Date: 29.01.2021).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - E.Y.; Design - E.Y.; Supervision - E.Y.; Data Collection and/or Processing - E.Y.; Analysis and/or Interpretation - E.Y.; Literature Search - Y.D.Y.; Writing Manuscript - Y.D.Y.; Critical Reviews - E.Y.

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2022; 38 (2): 202-207

Nadir görülen bir yanık türü: Naylon yanıkları

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ÖZET

Giriş ve Amaç: Bu çalışmada, pediatrik hastalarda gözlenen naylon yanıklarının incelenmesi ve elde edilen sonuçların, diğer sıcak cisim yanık nedenleri ile karşılaştırılması amaçlandı.

Gereç ve Yöntem: Gazi Yaşargil Eğitim ve Öğretim Hastanesi Yanık Merkezinde sıcak cisim yanığı nedeniyle hastaneye yatırılmış 77 pediatrik hasta üzerinde 10 yıllık geriye dönük bir çalışma yapıldı.

Bulgular: Sıcak cisim yanıkların %72,7 (n= 56) erkek ve %27,3 (n= 21) kızdı. Erkek/kız: 2,67:1 oranı vardı. Hastaların ortalama yaşları 4,79 (min= 1, max= 16) yıldı. 42 hasta yanık oluştuğu gün, dört hasta yanık oluştuktan bir gün sonra, bir hasta yanık oluştuktan iki gün sonra,13 hasta yanık oluştuktan üç gün sonra, 17 hasta yanık oluştuktan beş gün sonra bize başvurmuştu. Yanıkların %79,3'si üçüncü derece %19,5'i ikinci derece ve %1,2'si dördüncü derece idi. Sıcak cisim yanık nedeni başında en çok sıcak naylon ve sıcak soba gelmekteydi ve daha sonra sıcak kül ve sıcak ütü gelir. Naylon yanıklarının sayısı yazın en yüksek sayıda, sıcak soba yanıklarının ise kışın en yüksek sayıda idi. Naylon yanıkları en çok 3-8 yaş aralığında görüldü sonra giderek azaldı. En yüksek yanık derecesi oranı naylon yanıklarında gözlemlendi.

Sonuç: Türk pediyatrik popülasyonunda en sık görülen yanık nedeni haşlama yanığıdır. Naylon yanıkları nadir görülmekle beraber daha yüksek yanık dereceleri ile dikkat çekmektedir.

Anahtar Kelimeler: Naylon yanıkları, sıcak cisimle temas yanıkları, pediyatrik yanıklar, epidemiyoloji

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CASE REPORT
Turk J Surg 2022; 38 (2): 208-210

Heterotopic ossification of the anterior abdominal wall

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ABSTRACT

Heterotopic ossification (HO) is a bone formation in a tissue other than the skeletal system. It is more often seen as a complication of orthopedic surgery; however, it is a pathological condition that might be observed during the healing process of abdominal incisions in the midline. The aim of this study is to present a case of a 63-year-old male patient with the complaints of induration and pain on the region of his previous incision through which he had been operated for achalasia. HO is also discussed in the light of the current literature.

Keywords: Heterotopic, ossification, abdominal incision

INTRODUCTION

Heterotopic ossification (HO) is the formation of new bone tissue in soft tissues in which no ossification is present normally. Based on the etiology, HO is classified as neurogenic HO, traumatic HO and myositis ossificans progressiva. It is more common in large joints after orthopedic surgery. The hypothesis of stimulation of mesenchymal cells through tissue hypoxia and metabolic or genetic factors to form a bone tissue by metaplastic transformation is generally accepted, although the pathophysiology of the condition has not been clearly understood yet.

Development of HO in an abdominal midline incision is rare. However, Kim et al. reported the incidence of development of HO in a midline incision as 25% (1). The increased incidence has been observed especially in cases of supraumbilical midline incisions. The aim of this study is to present an extraordinary case of an HO developed in a supraumbilical incision line in a patient who had been operated for achalasia two years ago.

CASE REPORT

A 63-year-old male patient who had undergone esophago-cardiomyotomy at another center two years ago for achalasia applied to our clinic with the complaints of induration and pain in the incision area. His past medical history was otherwise nonspecific. Upon physical examination, a palpable mass was present on the upper half of the midline incision. Abdominal ultrasonography (US) revealed an area of the increased density measuring 1 cm in width and 5 cm in length which was considered a collection. No opacity could be seen on chest X-ray at the region of the lesion. A hard mass on linea alba in the subcutaneous fatty tissue, measuring 8 cm in length was found to be fixated to the surrounding tissue at laparotomy. The mass was seen to be close to xiphoid process with no direct contact with it. The mass was excised, and the wound was primarily closed. The specimen was sent for pathological examination. Macroscopic examination revealed a bone tissue measuring 8.5 x 1 x 0.5 cm (Figure 1). Microscopic examination disclosed organized cortical and medullary lamellar bone and fatty bone marrow in fat and connective tissue (Figure 2). The mass was diagnosed as heterotopic ossification when its localization was also taken into account.

The patient was discharged on postoperative day four because he was from another city. There were not any postoperative complications. The lesion was seen to be completely resolved during the follow-up visits.

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Figure 1. Macroscopic view of the heterotopic ossification.

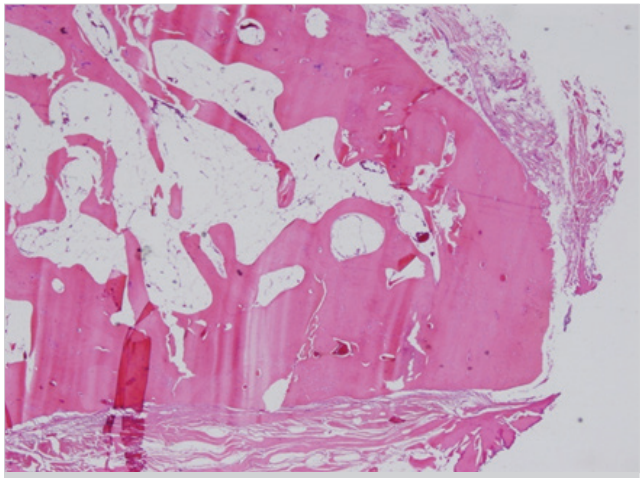

Figure 2. Organized cortical and medullary bone and fatty bone marrow in connective tissue (H & E X 40).

DISCUSSION

Heterotopic ossification is the formation of bone tissue in areas other than the skeletal system such as skin, subcutaneous fat, scars or mesenteric tissue (2,3). The etiology and pathogenesis of HO demonstrated to have a real osteoblastic activity and bone formation at histological examination have not been fully explained yet. The hypothesis of stimulation of mesenchymal cells through tissue hypoxia and metabolic or genetic factors to form a bone tissue by metaplastic transformation is generally accepted for the pathogenesis of the condition. The condition is generally evaluated in three groups: a) Neurogenic HO: The spasticity, long-term comatose condition and exposure to immobilization in patients with head trauma play role in the etiology in this group (4,5); b) Traumatic HO: It develops following fractures of the hip, elbow, and knee and after orthopedic surgery (5); c) On the other hand, myositis ossificans progressiva is a congenital disease with an autosomal dominant inheritance (5).

HO might be seen following abdominal and vascular surgery, although it has been known to be a complication of orthopedic surgery. Kim et al., in their study, reported the incidence of HO to be 25% by postoperative computed tomography evaluation of 152 cases that had abdominal incisions (1). It is more common in men compared to women (89%) (6). It was proposed by some authors that increased abdominal pressure caused an increased suture line tension in men due to heavy work load (7, 8).

Another assumption is inoculation of pieces of periosteum or perichondrium separated from the xiphoid process or the symphysis pubis during a surgical operation (2). In this case reported here, no connection was seen between the xiphoid process and ectopic bone during the exploration.

Patients may suffer from limited mobility, pain and induration in the area of the incision. A palpable mass can be found at the incision line on physical examination. Direct X-rays, US, CT, and magnetic resonance (MR) imaging can be used for diagnosis in case of suspicion of HO. Differential diagnosis includes postoperative complications such as foreign materials and wound infection and neoplasms. This formation was reported as a fluid collection in the US performed in our radiology department. We believe that the presented pathology is infrequent and radiologists are not familiar with this image. Some insufficient evidence is present in the literature on the use of non-steroidal anti-inflammatory drugs such as indomethacin and bisphosphonates in the prevention or treatment of HO in the early period (9,10). Although there is no standard method for the treatment of the condition, the most frequently used surgical treatment option is excision and primary closure. Some authors, considering the differentiation effect of mechanical stress on pleuri-potent stem cells, prefer some reconstruction techniques such as tension-free repair or component separation in surgical treatment (11,12).

The application of radiation therapy following abdominal surgery is debatable due to its side effects, while it is recommended after orthopedic surgery to prevent the development of HO.

Rarely some complications associated with HO might be seen. A tissue of histologically proven HO that was capable of producing triple hematopoiesis with normal function was reported in two case reports during our literature search (13,14). Although HO is a benign lesion, osteosarcoma transformation and fracture of mature lesions following direct trauma are among the reported complications in the literature (15).

CONCLUSION

HO, generally known to develop following orthopedic surgery can also be seen rarely in abdominal incisions. Radiological examination is important in differential diagnosis. Excision and primary closure is an appropriate and safe method in treatment. The authors declare that there is no conflict of interest regarding the publication of this article.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - S.E., O.A.; Design - S.E., S.Y.; Supervision - S.E., S.Y., A.P.; Materials - F.K., S.C., O.A.; Data Collection and/or Processing - F.K., S.C.; Analysis and/or Interpretation - S.E., A.P.; Literature Search - O.A., S.E.; Writing Manuscript - O.A., S.E.; Critical Reviews - S.Y., S.E., A.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.

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OLGU SUNUMU-ÖZET
Turk J Surg 2022; 38 (2): 208-210

Karın ön duvarında heterotropik ossifikasyon

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ÖZET

Heterotopik ossifikasyon (HO), iskelet sistemi dışındaki bir dokuda kemik oluşumudur. Ortopedik cerrahide görülmekle birlikte, orta hattaki karın kesilerinin iyileşme sürecinde gözlemlenebilecek patolojik bir durumdur. Bu çalışmanın amacı, akalazya operasyonu geçirdiği insizyon ve ağrı şikayetleri ile başvuran 63 yaşındaki erkek hastanın bir olgusunu sunmaktır. Mevcut literatür gözden geçirilmiştir.

Anahtar Kelimeler: Heterotropik, ossifikasyon, abdominal insizyon

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CASE REPORT
Turk J Surg 2022; 38 (2): 211-213

Laparoscopic resection of retroperitoneal bronchogenic cyst clinically presenting like adrenal cyst

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ABSTRACT

Bronchogenic cyst that is localized to retroperitoneum is a rare clinical entity. It is a congenital malformation generally occuring in the posterior mediastinum due to abnormal development of the foregut. We report the case of a retroperitoneal cyst presented like left adrenal cyst. A 38 years old female was presented with left upper abdominal pain. Endocrinologic evaluation was done and no adrenal hormonal secretion was detected. The cyst was removed laparoscopically. It was confirmed in pathologic examination as a bronchogenic cyst. Bronchogenic cysts should be considered in the differential diagnosis of retroperitonal cysts. Laparoscopic resection of retroperitoneal cysts results in better outcome.

Keywords: Retroperitoneal cystic mass, bronchogenic cyst, adrenal, laparoscopic

INTRODUCTION

Bronchogenic cysts are rare clinical malformations due to the abnormal development of the primitive foregut between the third and seventh weeks of embryonic life. They are generally localized in the posterior mediastinum because of abnormalities resulting from embryological budding of the bronchial tree. They are rarely localized in the abdomen or in the retroperitoneum (1-3). Bronchogenic cysts are usually asymptomatic unless they are infected or are enlarged enough to compress a nearby organ. Symptoms are variable, related to the location and the diameter of the cyst (3-5). In most cases, retroperitoneal bronchogenic cysts occur on the corpus of the pancreas or left adrenal gland (6).

In this case, we report a laparoscopic total resection of an incidental bronchogenic cyst that looked like a cyst of the left adrenal gland.

CASE REPORT

A 38-year-old female who had no significant past medical history was admitted with left upper abdominal pain. A complete blood count, serum liver function tests, amylase and lipase were within normal limits. There was no history of palpitation, sweating, hypertension, or exhaustion. All the secretory hormone levels of the adrenal gland were normal. Also, plasma and urine catecholamine metanephrine concentrations and the aldosterone/renin ratio were normal. CEA and CA 19-9 were not elevated. Abdominal MRI axial turbo spin-echo T2-weighted (a) and T1-weighted (b) images revealed a 63 x 25 x 55 mm well-defined, ovoid, heterogenous lesion with hyperintense components (arrows) in the left suprarenal region elevating the crus (Figure 1).

To confirm the diagnosis and to document the risk of malignant transformation, the cyst was removed laparoscopically. The operation was performed in the left lateral decubitus position. Intraoperatively, the mass lesion was associated with the left adrenal gland and diaphragm, It was 60 x 80 mm in diameter. The mass included mucous and fluid as in an abscess. The patient was discharged on the fourth postoperative day.

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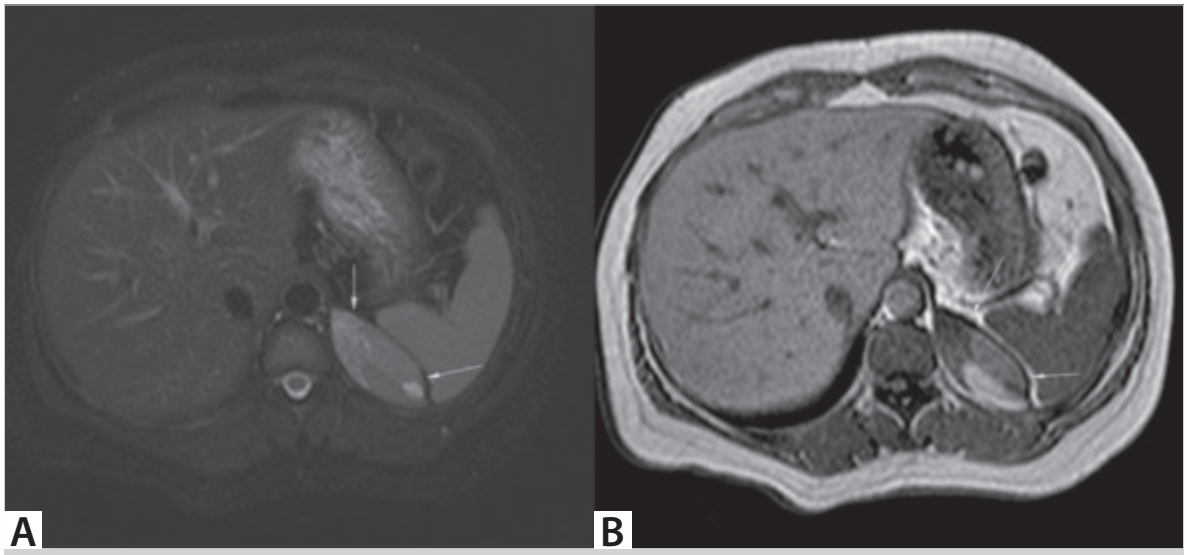

Figure 1. Axial turbo spin-echo T2-weighted **A.** and T1-weighted **B.** images reveal a well-defined, ovoid, heterogenous lesion with hyperintense components (arrows) in the left suprarenal region abutting the diaphragmatic crus.

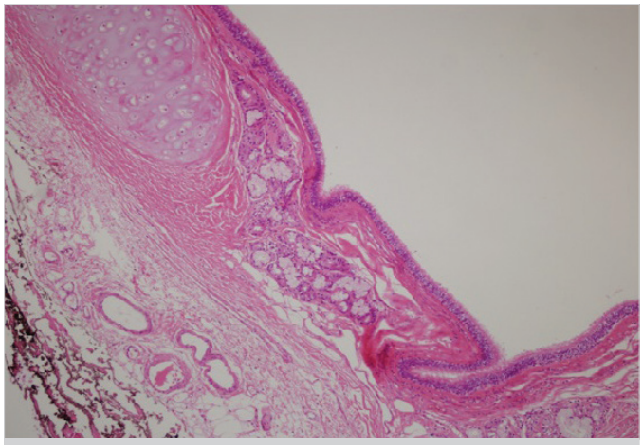

Figure 2. Cartilagenous tissue and mucous glands in the cyst wall which is laid down with the pseudostratified ciliary epithelium of the respiratory system (H&E, x100).

Pathological examination supported the diagnosis of a bronchogenic cyst. There was no malignant transformation. The examination also revealed cartilage tissue and a mucous gland under the cyst wall (Figure 2).

DISCUSSION

Bronchogenic cysts are the malformations that occur due to the abnormal development of the embryologic foregut in the early period. Their pathogenesis is not fully clear (3,7).

Most of the time, these cysts are localized in the posterior of the carina or are embedded in the pulmonary parenchyma. If total separation occurs during abnormal budding, a cyst may migrate to a different location. The cysts migrate particularly to the subcutaneous tissue around the sternum, shoulder, neck, pericardium, and diaphragm. But retroperitoneal location is extremely rare, at 0.03% (1,2,6,8,9).

Generally, a bronchogenic cyst is asymptomatic and is discovered incidentally. But sometimes back pain and epigastric pain can occur. A cyst can lead to secondary complications; its diameter is under 5 cm normally, but sometimes it can lead to infection, acute hemorrhage, perforation, and the compression of other organs (1,2,6,7,10). Our patient was suffering from left abdominal pain.

Histologically, bronchogenic cysts are well defined, because they contain ciliary respiratory epithelium, mucinous glands, and well differentiated cartilage (3,6). A pancreatic pseudocyst, adrenal cyst, cystic lymphangioma, and cystic teratoma should be considered in the differential diagnosis of retroperitoneal bronchogenic cysts (2). In our case, the decision of surgery is taken because of diagnosis of the adrenal cyst. Retroperitoneal bronchogenic cyst can take wrong diagnosis, as in this case.

Endocrinologic evaluation must be done for the cases in which the bronchogenic cyst is adherent to the adrenal gland or is localized in it. But this study may not be helpful for the diagnosis (3).

Surgery is recommended to make the diagnosis certain, reduce the symptoms, prevent infection, and document the risk of malignant transformation (11,12). An operation can be performed by an experienced laparoscopic surgeon. The laparoscopic approach results in less postoperative pain, a shorter hospital stay, and less cost. Postoperative outcomes are reliable and no complications have been reported (1,7). We did the laparoscopic excision successfully in our patient and there have been no postoperative complications.

CONCLUSION

A retroperitoneal bronchogenic cyst is a rare clinical entity. For retroperitoneal cysts, a differential diagnosis must be considered. It is difficult to make a preoperative diagnosis, so surgery is recommended to confirm the diagnosis. Laparoscopic surgery can be performed by an experienced surgeon, and postoperative outcomes are reliable.

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OLGU SUNUMU-ÖZET
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Böbrek üstü bezi kistini taklit eden retroperitoneal bronkojenik kistin laparoskopik rezeksiyonu

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ÖZET

Retroperitoneal yerleşimli bronkojenik kist nadir görülen bir durumdur. Ön bağırsağın anormal gelişimi sonucunda oluşur. Genellikle posterior mediastende yerleşimli konjenital malformasyondur. Biz bu olgu sunumunda sol böbrek üstü bezi kistine benzeyen retroperitoneal bronkojenik kisti sunduk. Otuz sekiz yaşında kadın hasta sol üst kadran ağrısı ile başvurdu. Endokrin değerlendirmesinde böbrek üstü bezi hormon değerleri normal bulundu. Kist laparoskopik olarak çıkarıldı. Histopatolojik inceleme sonucunda bronkojenik kist olarak raporlandı. Bronkojenik kist, retroperitoneal kistlerin ayırıcı tanısında göz önünde bulundurulmalıdır.

Anahtar Kelimeler: Retroperitoneal kistik kütle, bronkojenik kist, böbrek üstü bezi, laparoskopi

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