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

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

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

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

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

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

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

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Authors are required to submit the following:

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

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

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- 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.

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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.

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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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PREFACE

On behalf of the Turkish Surgical Societies' Council, I would like to present the new changes in our longstanding journal, Turkish Journal of Surgery, which is devoted to surgical sciences. The mission of the journal is to become the voice of surgical communities not only in Turkey but also worldwide.

We have certain goals to reach. The most important one is to increase the quality and visibility of the journal, for which we need very good quality submissions. Very good quality publications are based on well-planned, well-constructed and well-written manuscripts, for which the editorial evaluation processes are also highly important. Therefore, a new, dedicated editorial team under the direction of Prof. Kaya Sarıbeyoğlu has been appointed. We would like to thank them for accepting the job with tremendous workload.

The main difference from the previous establishment is that there will be no one from the Societies' Council acting as editor. Instead, in order to maximize editorial freedom, only one representative will be there as the coordinator. So as to assure reliability of the evaluation process, new strategies have been developed, such as a new referee system based on specialties and sub-specialties. Rather than increasing the number of bulky editorial board members list, the referee pool has been increased.

Since the principle aim is to be included in well-known indexes, changes have also been rung in the journal's design. The cover design of the journal has been re-structured in line with the illustration rules of the indexes. In the design of the new cover, the colors red and white connotate the Turkish flag. Ignorance has been symbolized by the color black on the left-hand side of the cover, which fades away upwards and ceases to exist when it is struck by the emblem of the Turkish Surgical Society. However, we all know that this aim of ours is only reachable with high-quality studies.

As Prof. Sarıbeyoğlu expressed in his first "From the Editor's Desk" report, without your support and passion, we cannot reach any of the above goals.

Sincerely,

On Behalf of The Turkish Surgical Society Council
M. Mahir ÖZMEN MD MS FACS FRCS FASMBS
Professor of Surgery
Coordinator

Turkish
Journal of Surgery

FROM THE EDITOR'S DESK

Dear Authors of the Turkish Journal of Surgery,

I am sure that you have already realized the noticeable changes in this issue of the journal. Starting from this issue, we have a new editorial board, a new publisher and a new look. I am sincerely thankful to the Turkish Surgical Society for expressing us their confidence and support.

It is a great privilege for me to take over the position of Editor of Turkish Journal of Surgery and being a part of the leading surgical society of Turkey.

Needless to say, Turkish Journal of Surgery, which is the official journal of the Turkish Surgical Society and Turkish surgical community, has a strong background and a long tradition in Turkish medical publishing. There have been great efforts to renew and improve the journal throughout the past years. I would like to take this opportunity to thank our former editors and the members of the editorial board for the remarkable endeavours they have made. It is indeed a -relay race- and our goal now is to bring this flag as high as possible.

We wish to ensure that the members of the Turkish Surgical Society have a journal they can be proud of. For this purpose, I feel lucky to be working with two active and self-motivated Associate Editors, Arda Demirkan and Murat Ulaş. Altogether, we have immediately undertaken this uphill task with our new publisher Bilimsel Tıp Yayınevi over the last few months. Frankly, we have received outstanding support and very meticulous work from the office of Bilimsel Tıp Yayınevi so far. Turkish Journal of Surgery has now a whole new look, which will extend beyond the new cover or the journal design. We aim to raise the quality of the content by promoting the publication of relevant original articles, review articles on recent topics and rare case reports in the field of general surgery.

Our current priority is to bring the Turkish Journal of Surgery into international prominent indexes such as Index Medicus and Science Citation Index, the Champions League of medical publishing. We do know that the goal set is not easily attained and we have much to do. A journal, as a large family of authors, editors, reviewers, and publishers, requires the contributions of each member of this family. Success lies behind this teamwork. As the editors, we need high quality manuscripts, and in return, we should provide a proper and fair reviewing process. In brief, the journal needs your interest and contributions.

On behalf of my editorial board, I can promise a fair, quick and high-grade review. We look forward to reviewing your high-quality submissions and are excited to receive your clinical studies, in particular. Finally, please feel free to share with us your opinions, criticisms or suggestions, which are priceless contributions for a scientific journal.

Since we took over the editorial work, we have noticed that there is a long waiting queue for the formerly accepted case reports. As a journal aiming for high rank indexes, we must consider a particular balance between clinical studies and case reports while forming the issues. As the editorial team, we have taken the decision to publish some already accepted case reports uniquely online with special references in the printed form of the journal. In this manner, we would also reduce the waiting time for the authors. It would be a win-win for both the journal and the authors.

Finally, the Turkish Journal of Surgery is our journal, and success can only be achieved with your support and passion. You are invited to submit your best work to the Turkish Journal of Surgery.

Kindest regards,

Kaya SARIBEYOĞLU
Professor of Surgery
Turkish Journal of Surgery
Editor

ORIGINAL ARTICLE
Turk J Surg 2019; 35 (1): 1-5

Repeated stretched or non-stretched small bowel length measurements in healthy individuals

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ABSTRACT

Objective: The aim of the present study was to contribute to the establishment of a standard method of small bowel measurement by comparing repeated small bowel length measurements with and without stretching in healthy individuals.

Material and Methods: Small bowel measurement was randomly performed in 24 healthy liver donors. Three repetitive measurements were performed with complete stretching in 12 cases; whereas, 3 consecutive measurements were made without any stretching in the other 12 patients. Living donor hepatectomy continued uneventfully in all cases.

Results: In the non-stretched group, the second measurement was 199 cm shorter than the first measurement ($p< 0.001$). In the third measurement, this shortening had increased further, and the difference from the first measurement was 234 cm on average ($p< 0.001$). In the stretched group, a shortening of approximately 135 cm between the first and second measurements was noted. In the third measurement, an improvement of 4% was observed in contrast to the non-stretched method, with a mean reduction of 105 cm in the small bowel length compared with the first measurement ($p< 0.001$).

Conclusion: Stretching technique can reduce error rate in repeated small bowel measurements.

Keywords: Bariatric surgery, human anatomy, metabolic surgery

INTRODUCTION

Measurement of all or part of the small bowel is a common and mandatory procedure in surgeries requiring small bowel resection or anastomosis. Depending on the procedure to be performed, the length of the bowel segments to anastomose is known at the beginning of the surgery, particularly in bariatric and metabolic surgeries (1-3). However, different surgeons employ different techniques to measure these lengths, and even if the same surgical technique is applied, the efficiency of the outcome may vary. A standard technique for measuring bowel length has not been established, which presents an obstacle to achieving the desired clinical outcomes and accurately assessing postoperative complications (4-9).

The small bowel is an elastic organ. The use of different techniques involving stretching or non-stretching of the bowel during measurement suggests that the target segment for a standard surgery will, unfortunately, differ in length from surgeon to surgeon. Although bowel lengths measured with and without stretching have been reported in the literature, to our knowledge, no studies have compared the two methods. Another important consideration is that if intraoperative bowel length measurement is repeated for any reason, contraction of the bowel smooth muscle may lead to erroneous results. In this study, small bowel length measurements obtained with and without stretching in healthy individuals undergoing living donor hepatectomy were prospectively recorded and compared. The aim was to compare the results obtained from these healthy individuals in order to facilitate the establishment of a standardized method of small bowel measurement.

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MATERIAL and METHODS

Small bowel length measurements were performed in 24 healthy, prospectively enrolled and randomized liver donors at İnönü University Liver Transplant Institute. The study was approved by İnönü University Ethics Committee. Informed consent was obtained from all the individuals who participated in the study. Completely healthy liver donors > 18 years old who had no previous abdominal surgery were included into the study. Patients who had previous abdominal surgery were excluded from the study. The distance between the Treitz ligament and the ileocecal valve was measured using a 70 cm nylon tape. A sterile ruler was used to measure the final loops that were < 70 cm. All measurements were performed by the same surgeon immediately after laparotomy, before hepatectomy, or any other intra-abdominal manipulations. Twelve consecutive randomized patients were measured while fully stretching the small bowel, whereas the other 12 patients applied no tension when taking measurements. Measurements were performed at the midline between the mesenteric and antimesenteric borders and repeated three times using the same technique, resulting in three small bowel length measurements for each participant. The measurements were repeated in immediate succession. The measurement process lasted a total of approximately 10 min, and living donor hepatectomy proceeded uneventfully after measurements of all cases.

Demographic data, bowel measurement technique used, and bowel lengths were recorded in a Microsoft Excel file.

Statistical Analysis

For homogeneous parameters, the paired Student's t-test was used for comparison of continuous variables of the same patients. For non-homogeneous parameters, the Mann-Whitney U test was applied. Comparison of two continuous parameters was made by Pearson correlation coefficient. Statistical Package for Social Sciences (SPSS) version 17.0. (SPSS Inc.; Chicago, IL, USA) was used for statistical analysis. A $p< 0.05$ was accepted as statistically significant.

RESULTS

There were no significant differences in demographic data, such as age, sex, height, body weight, and body mass index, in the study groups. There were no significant differences between the two groups in the first small bowel measurements. When small bowel lengths obtained in the second and third measurements were compared, the non-stretched group had significantly smaller values than the stretched group (Table 1).

In the non-stretched group, a shortening of 28.8 ± 7.1% between the first and second measurements was observed ($p< 0.001$). The decrease was 33.7 ± 7.7% between the first and third measurements ($p< 0.001$). The small bowel length in the third measurement was approximately 5% shorter than that in the second measurement. When the change in the second measurement (1 vs. 2) was compared with the change in the third measurement (1 vs. 3), the length continued to decrease significantly in the non-stretched group ($p= 0.004$).

In the stretched group, a shortening of 17.9 ± 8.8% in the small bowel length between the first and second measurements was observed ($p< 0.001$). In the third measurement, the small bowel length increased again and was closer to that obtained in the first measurement. As a result, using the stretched method, a shortening of 13.8 ± 5.6% in the third measurement compared with the first measurement was noted ($p< 0.001$). In contrast to the non-stretching technique, there was an improvement of approximately 4% in the third measurement.

When the change in the second measurement (1 vs. 2) was compared with the change in the third measurement (1 vs. 3) in the stretched group, the increase in the small bowel length reduced the statistical significance of the difference from baseline ($p= 0.05$) (Figure 1).

DISCUSSION

Measurement of the length of the human small bowel is not just an anatomic data point but is also important for avoiding short

Table 1. Comparison of the stretched and non-stretched groups

Parameter	Stretched (n= 12)	Non-stretched (n= 12)	p
Age (year)	25.9 ± 7.9	25.9 ± 6.5	1.00
Gender (male/female)	7/5	8/4	0.67
Length (cm)	171 ± 11	172 ± 8	0.87
Weight (kg)	68 ± 7	72 ± 12	0.41
BMI (kg/m^2)	23 ± 3	24 ± 3	0.52
SBL 1 (cm)	748 ± 102	696 ± 112	0.25
SBL 2 (cm)	613 ± 98	497 ± 105	0.01
SBL 3 (cm)	643 ± 90	462 ± 92	< 0.001

BMI: Body mass index; SBL: Small bowel length.

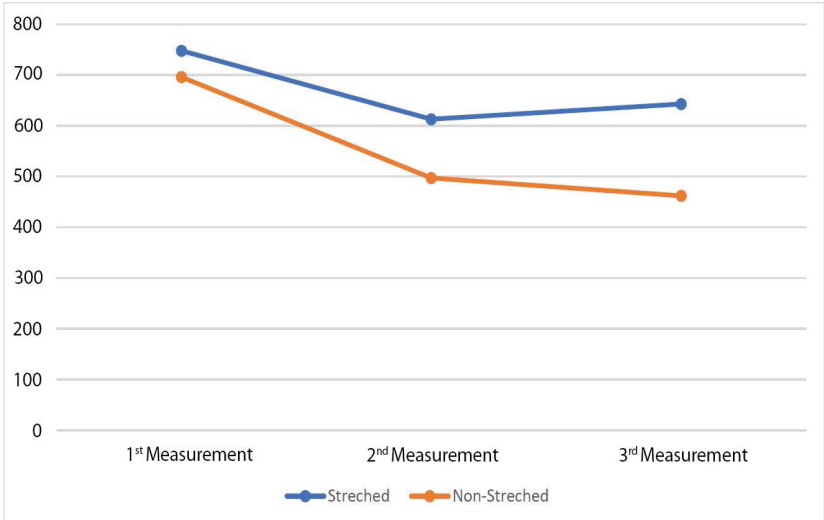

Figure 1. Consecutive small bowel length measurements in the stretched and non-stretched groups.

bowel syndrome or complications of metabolic and bariatric surgeries that may develop postoperatively. Many studies have criticized the fact that measurements cited in the literature are not obtained using a standard method. Nevertheless, there have been relatively few studies aimed at establishing standardization of measurement (8,10,11). The common feature of these studies is that they were all conducted within the last few years. The momentum gained by bariatric and metabolic surgeons has shifted research in this direction.

We believe that the lack of a gold standard procedure is the main reason for this. With current surgical techniques, the length of the bowel limbs must be revised due to complications or unsatisfactory outcomes. Therefore, surgeons are more concerned with how to measure the length of bowel segments than anatomists.

The length of the small bowel has been studied for over a century, initially in cadavers. Various measurement techniques have been used in this process. The primary difference between these techniques is which contour of the small bowel is followed during measurement. The length of the small bowel can be determined based on the mesenteric border, the antimesenteric border, or the midline (4,7,12). Owing to the radial anatomic structure of the small bowel, studies in which the bowel has been measured along different lines are difficult to interpret realistically. For this reason, it is important to be consistent in which aspect of the bowel is used for measurement.

We obtained measurements from the midline between the mesenteric and antimesenteric borders in the present study. It has yet to be determined in the literature which contour is optimal for conducting measurements.

Another critical point that led to the present study is the question of whether or not to stretch the bowel during measurement. Stretching the elastic small bowel segments can result in longer length values measured in the same bowel. Underhill has evaluated small bowel length measurements before and after stretching in cadavers and determined that the small bowel length is increased by 4% in bodies refrigerated for 1 to 3 days (13). Considering that stretching alters small bowel length values even in the tissue that has lost most of its elasticity and tone, this can be expected to pose an even greater challenge in the living tissue. Some studies in the literature have not addressed the issue of tension at all (5,9,12,14).

A previous study has measured and compared small bowel length measured before and after stretching in the same live subjects and reported that stretching results in increases of 72 to 212 cm in the measured values (8). However, the authors of the previous study have overlooked the effect of repeated measurement on bowel length. In our earlier study of bowel length measurements, we demonstrated that repeated measurements yield different results, even when using the same technique (15). When a bowel segment is measured using any technique, contractions induced by manipulation change the length of the bowel prior to the subsequent serial measurement.

Therefore, repeating the measurements using different techniques, as in the study by Tacchino, compromises the validity of the length differences observed (8). The question we would like to answer is which technique will reduce the likelihood of making a surgical error when repeated measures of the bowel are required. Abellan et al. have examined the effect of the ratio of common limb length to total bowel length on clinical

outcomes in patients with Roux-en-Y gastric bypass (16). They have measured the bowel length accurately and repeated the measurement twice each time to ensure greater reliability. In cases of discrepancy between the measurements, a third measurement has been performed. The length of the common limb has been calculated by subtracting the sum of the lengths of the biliopancreatic and alimenteric limbs from the total bowel length. However, repeated measurement performed in the present study in the name of caution was itself a source of inaccuracy. The effect of bowel contractions on measured bowel length was overlooked. Moreover, the length of the common limb was not measured directly but derived based on the total length of the other limbs. It should be recognized that the repeated small bowel length measurement process has been and will continue to be a reflection of the meticulous work of surgeons. Therefore, after each measurement of the stretched or non-stretched bowel in the present study, we repeated the measurement two more times. In order to achieve a repeatable, standardized method, we believed it would be beneficial to first evaluate the repeatability within subjects.

In both the stretched and non-stretched groups, a significant shortening of the small bowel between the first and second measurements was observed. However, the non-stretched group showed a greater reduction in length than the stretched group. Regardless of the technique, repeated measurement resulted in contractile shortening of the bowel. However, in the third measurement, this shortening continued in the non-stretched group, whereas the third value obtained in the stretched group was closer to the initial measurement. These results suggest that stretching the bowel during measurement results in more reliable length values. This information is especially valuable for surgeons today, because bowel length measurement often needs to be repeated in order to form different limbs, especially in bariatric and metabolic surgeries.

When Guzman et al. have stated that no surgeon would operate on a perfectly healthy person, they could not imagine a study where bowel length was measured in healthy subjects (17). One of the main points that make the present study valuable is that all measurements were taken from completely healthy liver donors. Furthermore, all measurements were performed by the same surgeon, thereby reducing subjective factors in the measurement technique.

CONCLUSION

In contrast to all other tissues, standardization of the technique is required for small bowel length measurement. We should keep in mind that just one touch to the small bowel will change all expected outcomes. According to our study, the stretching technique can reduce the error rate in repeated small bowel measurements.

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

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

Peer-review: Externally peer-reviewed.

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

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2019; 35 (1): 1-5

Sağlıklı bireylerde tekrar edilmiş gerilimli ya da gerilimsiz ince bağırsak uzunluğu ölçümleri

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ÖZET

Giriş ve Amaç: Bu çalışmada, sağlıklı bireylerde tekrarlayan gerilimli ve gerilimsiz ince bağırsak uzunluğu ölçümleri yaparak karşılaştırdık. Amacımız, ince bağırsak uzunluğu ölçüm metodunda standardizasyon sağlanmasına katkıda bulunmaktır.

Gereç ve Yöntem: Randomize edilen 24 sağlıklı karaciğer donöründe ince bağırsak ölçümü yapıldı. On iki olguda tam gerginlik oluşturarak, 12 olguda ise gerilimsiz olmak üzere ardışık tekrarlanan uzunluk ölçümleri yapıldı. Tüm olgularda karaciğer donör hepatektomi işlemine sorunsuz devam edildi.

Bulgular: Gerilimsiz grupta ikinci ölçüm birinci ölçümden 199 cm daha kısa bulundu ($p< 0.001$). Üçüncü ölçümde bu kısalma daha da artmış olup birinci ölçüm ile olan fark ortalama 234 cm idi ($p< 0.001$). Gerilimli grupta birinci ve ikinci ölçüm arasında yaklaşık 135 cm fark vardı. Üçüncü ölçümde, gerilimsiz gruba zıt olarak %4 oranında bir düzelme gözlendi ve birinci ölçüm ile karşılaştırıldığında ortalama kısalma 105 cm idi ($p< 0.001$).

Sonuç: İnce bağırsak uzunluğu ölçümünde germe tekniğinin kullanılması hata oranını azaltabilir.

Anahtar Kelimeler: Bariatrik cerrahi, insan anatomisi, metabolik cerrahi

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ORIGINAL ARTICLE
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Risk factors and laboratory markers used to predict leakage in esophagojejunal anastomotic leakage after total gastrectomy

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ABSTRACT

Objective: Esophagojejunal anastomotic leakages, which occur in the reconstruction procedures performed after total or proximal gastrectomy, still account for one of the most significant causes of morbidity and mortality in spite of the developments seen in perioperative management and surgical techniques in gastric cancer surgery. The aim of the present study was to ascertain the risk factors for Esophagojejunal anastomotic leakages.

Material and Methods: A total of 80 patients with gastric cancer, who had total gastrectomy +D2 lymph node dissection and Esophagojejunal anastomotic between January 2013 and December 2016, were retrospectively evaluated. Patients who did not have anastomotic leakages during their clinical follow-ups were allocated to Group 1, whereas those who had anastomotic leakages were allocated to Group 2.

Results: A total of 58 (72.5%) out of 80 patients were males, whereas 22 (27.5%) were females. Mean age of the patients was 61.2 ± 11.2 years. There were no demographic differences between the groups. Postoperative recurrent fever (p= 0.001), C-reactive protein values on postoperative days 3 and 5 (p= 0.01), and neutrophil-to-lymphocyte ratio on postoperative day 5 (p= 0.022) were found to be statistically significant with regard to Esophagojejunal anastomotic leakages and other postoperative complications. The duration of operation (p= 0.032) and combined organ resection (p= 0.008) were ascertained as risk factors for Esophagojejunal anastomotic leakages.

Conclusion: Surgeons should be careful about Esophagojejunal anastomotic leakages which are significant postoperative complications seen especially in cases where the duration of operation is prolonged, and additional organ resections are performed. Recurrent fever, high C-reactive protein levels, and neutrophil-to-lymphocyte ratio may serve as warnings for complications in postoperative follow-ups.

Keywords: Anastomosis leakage, gastrectomy, risk factors

INTRODUCTION

Surgical treatment focuses on the balance between risk and reward. The most important components of postoperative care include predicting the possible secondary problems regarding the procedure, preventing these problems, noticing them early on, and rightly performing the appropriate intervention for treatment on time. In spite of all these, complications may not always be prevented. As long as surgical procedures are performed, surgeons will have to deal with complications as well. Therefore, it is inevitable that novel findings and information on this issue will accumulate, and novel perspectives will develop in modern practices. Anastomotic leakages still prove to be a major problem for surgeons although many studies have been conducted on the issue.

Anastomotic leakage is one of the most significant complications of postoperative gastric surgery and has a high rate of morbidity and mortality (1,2). Securing a safe and sound esophagojejunal anastomosis (EJA) after total gastrectomy is one of the most important problems of gastric surgeons. The incidence of EJA leakages has decreased with experiences achieved during the learning curve and the common use of mechanical stapler tools (3). It is, however, still challenging to completely prevent anastomotic leakage, and the incidence of EJA leakages has been reported to be between 1% and 11% (3-11).

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The aim of the present study was to ascertain the risk factors for EJA leakage in patients who had total gastrectomy +D2 lymph node dissection due to gastric cancer and to unveil the presence of biochemical markers that could be utilized to predict them before they clinically developed.

MATERIAL and METHODS

Patients

A total of 80 patients with gastric cancer, who had total gastrectomy +D2 lymph node dissection and EJA between January 2013 and December 2016 at Kartal Koşuyolu Higher Specialty Training and Research Hospital's Gastroenterology Surgery Clinic, were retrospectively evaluated. The study was approved by the ethics committee of Kartal Koşuyolu Higher Specialty Training and Research Hospital (no. 2017.3/2-36). Informed consent was obtained from each patient for surgical intervention prior to surgery.

Patients who had immunosuppressive treatment; who had inflammatory diseases; who received neoadjuvant treatment; who had D1 lymph node dissection; who had surgical procedures due to gastrointestinal stromal tumor, gastric lymphoma, and other gastric tumors; who had palliative surgeries; and who had missing data in their files were excluded from the study.

All patients had oral intravenous contrasted thoracoabdominal computed tomography (CT) and positron emission tomography in suspected cases prior to surgical procedures. All patients for whom a surgical procedure was planned were started on preoperative enteral feeding. Feeding was reinitiated on postoperative day 1 through intraoperative nasojejunal catheters. Curative resection was performed for those patients without distant organ metastasis or major vascular invasion. Patients who did not have anastomotic leakages during their clinical follow-ups formed Group 1, whereas those who had anastomotic leakages formed Group 2.

Surgical Technique

All patients received total gastrectomy +D2 lymph node dissection and omentectomy. Intestinal reconstruction was performed in the form of Roux-en-Y esophagojejunostomy.

EJA was performed by a circular stapler ILS (Ethicon Endo-Surgery, Inc., Cincinnati, OH, USA) in the form of end-to-side in all cases. The size of the stapler was determined based on the diameter of the esophagus of the patient and the judgment of the surgical team. A 25 mm stapler was generally used for patients with normal sized esophagus. Wider staplers (28-29 mm) were used for patients with a wider esophagus. The circle, which was removed after the anastomosis was completed, was immediately controlled in all cases. Additional organ resection was performed for patients with intraoperative organ invasion and/or iatrogenic additional organ injury (spleen, pancreas, colon, and liver).

Diagnosis of EJA Leakage

Diagnosis of anastomotic leakage was predicted upon clinical and radiological results. Radiological leakage was defined as extravasation outside the lumen seen under endoscopy during the drinking of water-soluble contrast agent (WSCA), observation of the drunk contrast agent outside the lumen in CT, determination of abscess with air collection at anastomotic neighboring, detection of defects at the anastomotic line, and observation of defects in the anastomosis as revealed by endoscopic assessment. Clinical leakage was defined as the leak of intestinal and/or purulent content from the surgical incision or drains, fever, deteriorating abdominal pain, increase in C-reactive protein (CRP) and leukocyte levels, and determination of leakage during relaparotomy for abdominal sepsis. Radiological imaging performed after WSCA was carried out routinely for all patients.

Data

Data on age, sex, body mass index (BMI), left ventricular ejection fraction, respiratory function parameters (forced expiratory volume (FEV) and forced vital capacity (FVC)), preoperative albumin and peripheral blood results, durations of surgical procedures, presence or absence of additional organ resection, need for intraoperative blood transfusion, duration of hospitalization, postoperative clinical characteristics, and CRP and all blood values were recorded. Recurrent fever was defined as fever that lasted for at least 3 days and was over 38°C.

Echocardiography was performed by a 2.5 MHz probe in the left lateral decubitus position. Ejection fraction was calculated according to the modified Simpson method. The height (cm) and body weight (kg) of all patients were used to calculate their BMI for spirometric calculations. Each patient was asked to perform forced expiration after deep inspiration in a sitting position. Calculations were conducted by a dry spirometer tool according to the recommendations of the American Thoracic Society (ATS) (12). The best calculation out of three conducted for each case was recorded. FVC and FEV in one second (FEV_1) were recorded within the scope of spirometric measurements. Expected values were assessed according to the ATS criteria (12).

Peripheral blood samples were extracted to determine hematocrit, leukocyte, neutrophil, lymphocyte, and platelet counts. The neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the number of neutrophils by the number of lymphocytes, whereas the platelet-to-lymphocyte ratio was calculated by dividing the number of platelets by the number of lymphocytes.

The duration of hospitalization was accepted to be the period from the day of surgical procedure to discharge, whereas inhospital mortality was accepted to be the case of mortality seen during hospitalization or during the first 30 days following surgery. Postoperative complications were ranked according to the Clavien–Dindo Classification of surgical complications (13). Patients

without anastomotic leakage but with postoperative complications were set as other complications.

Postoperative other complications included surgical site infection, pneumonia, postoperative atelectasis, cheilosis leakage, evisceration, acute renal failure, and intra-abdominal hemorrhage.

The American Joint Committee on Cancer classification system's seventh TNM staging was used for the histopathological staging of all cases (14).

Statistical Analysis

Statistical Package for the Social Sciences software (SPSS Inc., Chicago, IL, USA) was used in all biostatistical analyses. Data from the study were expressed in mean figures, standard deviation values, and percentages as necessary. Kolmogorov-Smirnov test was used to check the distribution of the collected data. ANOVA test was utilized for the multiple group comparisons of normally distributed data, whereas Student's t-test was used for binary group comparisons.

Multiple group comparisons of non-parametric data were conducted through Kruskal-Wallis analysis, whereas binary group comparisons were performed by Mann-Whitney U test. The comparison of categorical groups was conducted by Chi-square test. Multivariate analysis was conducted for intraoperative results that were found to be statistically significant according to univariate analysis. The results were set at 95% confidence interval (CI). A $p< 0.05$ was considered as statistically significant.

RESULTS

Of the 80 patients, 58 (72.5%) were males, whereas 22 (27.5%) were females. Mean age of the patients was 61.2 ± 11.2 years. There were 67 (83.8%) patients in Group 1 with no EJA leakage findings during their clinical follow-ups, whereas there were 13 (16.2%) patients in Group 2 with EJA leakage. Both groups had similar demographic s and preoperative laboratory results (Table 1).

When intraoperative findings and pathological results were investigated, it was ascertained that additional organ resection (p= 0.002) and prolonged intraoperative time (p= 0.007) significantly increased the rate of EJA leakage. It was seen that all patients with EJA leakage had T3 (69.2%) and T4 (30.8%) tumors, but no statistically significant difference was found. The total number of excised and the number of metastatic lymph nodes, the N stage of tumor, and intraoperative blood transfusion were not found to be statistically significant with regard to EJA leakage. Table 2 shows intraoperative and pathological data of patients. The results of the multivariate analysis revealed that additional organ resection (p= 0.008, odds ratio (OR) 6.329, 95% CI 0.040-0.623) and the duration of operation (p= 0.032, OR 10.416, 95% CI 0.011-0.820) were independent risk factors for EJA leakage (Table 3).

Further, all patients were divided into three subgroups according to those with EJA leakage, those with postoperative complications other than anastomotic leakage, and those without. When data on these patients' postoperative fever and laboratory results up to postoperative day 5 were investigated, it was seen that 7 out of 13 patients with EJA leakage had fever, and 6 had recurrent fever. Of the 21 patients, 12 had postoperative complications, but no anastomotic leakage and fever, and 4 had recurrent fever. The rate of EJA leakage and postoperative complications in patients with postoperative recurrent fever was found to be significantly higher (p= 0.01). When CRP values were assessed, it was observed that CRP values on postoperative days 3 and 5 were higher in patients with postoperative complications including EJA leakage than in those with no complications, and the difference was statistically significant (p= 0.01). There was, however, no statistically significant difference with regard to CRP values between patients with EJA and those with postoperative complications other than anastomotic leakage. Moreover, when the patients were evaluated according to their NLR, it was seen that NLR on postoperative day 5 was significantly higher in EJA leakage and other postoperative complications group (p= 0.022). There was no statistically significant difference regarding NLR on postoperative days 1 and 3. Table 4 shows patients' postoperative laboratory results and fever values.

The average duration from operation to the day on which the leakage was identified among 13 patients with EJA leakage was 6.3 (3-8) days. The average duration of hospitalization for patients with EJA leakage was 35 ± 30 days, whereas it was 13 ± 7 days for patients without EJA leakage. When the cases of patients with EJA leakage were ranked according to the modified Clavien-Dindo Classification of surgical complications, it was seen that 4 patients had grade 2, 4 patients had grade 3a, 2 patients had grade 3b, 2 patients had 4a, and 1 patient had grade 5 complications. Covered self-expandable metal stents were endoscopically placed in 2 out of 13 patients with EJA leakage. One (7.7%) patient with stent died due to multiorgan failure. Two patients needed reoperation. Five patients received radiological percutaneous drainage under local anesthesia due to intra-abdominal abscess. Four patients were treated conservatively.

DISCUSSION

It has been stated that the developments in surgical techniques and perioperative management decreases the rate of EJA leakage after total or proximal gastrectomy. The incidence of EJA leakage has been reported to be between 1.0% and 11.5% (3-11). The rate of leakage reported by high-volume Japanese centers, however, wis 1.0%-2.1% (2,3,5,8). The Japanese National Clinical Database on digestive surgery reported that the incidence of anastomotic leakage after total gastrectomy in 2014 was 4.4% (881/20011) (15). Surgeons should be careful when forming an anastomosis in order to prevent this dangerous complication.

Table 1. Demographic features and preoperative laboratory results of the patients

Variable		Anastomosis leakage (–) n= 67	Anastomosis leakage (+) n= 13	p
Gender#	Male	48 (60)	10 (12.5)	0.696
	Female	19 (23.8)	3 (3.8)	
Age* (year)		61 ± 12	65 ± 9	0.161
ASA#	1	10 (14.9)	1 (7.7)	0.612
	2	27 (40.3)	7 (53.8)	
	3	30 (44.8)	5 (38.5)	
Comorbidities#	HT Yes	17 (25.4)	3 (23.1)	0.861
	No	50 (74.6)	10 (76.9)	
	DM Yes	15 (22.4)	2 (15.4)	0.572
	No	52 (77.6)	11 (84.6)	
	COPD Yes	13 (19.4)	1 (7.7)	
	No	54 (80.6)	12 (92.3)	
	CRF Yes	1 (1.5)	0	
	No	66 (98.5)	13 (100)	
	CAD Yes	7 (10.4)	3 (23.1)	
	No	60 (89.6)	10 (76.9)	
History of smoking#	Yes	21 (31.3)	4 (30.8)	0.967
	No	46 (68.7)	9 (69.2)	
Weight loss#	Yes	30 (44.8)	6 (46.2)	0.927
	No	37 (55.2)	7 (53.8)	
BMI* (kg/m^2)		27 ± 4.5	28 ± 3.2	0.480
LVEF*		61 ± 9	63 ± 9	0.393
Pulmonary function test*	FEV_1	97 ± 17	91 ± 22	0.318
	FVC	97 ± 14	88 ± 21	0.1
Preoperative laboratory results*	Hematocrit	35.7±5.5	37.6 ±4.7	0.249
	Albumin	3.9 ± 0.5	3.9 ± 0.5	0.970
	Creatinine	0.94 ± 0.4	0.76 ± 0.2	0.750

ASA: American Society of Anesthesiologists; HT: hypertension; DM: Diabetes mellitus; COPD: Chronic obstructive pulmonary disease; CRF: Chronic renal failure; CAD: Coronary artery disease; BMI: Body mass index; LVEF: Left ventricular ejection fraction; FVC: Forced vital capacity; FEV_1: Forced expiratory volume in one second; SD: Standard deviation.

Datas are presented as *: mean ± standard deviation.

#: n (%)

Therefore, appropriate anastomosis techniques and a detailed observation of anastomosis are required in order to prevent this complication (11).

Esophagojejunal anastomotic leakage prolongs the duration of hospitalization while increasing the risk of reoperation. It, at the same time, may lead to a fatal result. Sierzega et al. have reported that postoperative mortality rates increase, whereas survival rates decrease in patients with EJA leakage after total gastrectomy (5). Migita et al. have also reported that the mortality rate is 1.8% in 327 patients (11). The authors have stated that 3 out of 21 patients with EJA leakage died. Isozaki et al. have concluded that aggressive surgery for advanced stage gastric cancer increases the risk of anastomotic leakage as well (2). The results of our study, however, showed that 16.2% of the patients with EJA had anastomotic leakage, and this figure was higher than those reported in the literature. We believe that the reason why our EJA leakage rates were high is related to the fact that the majority of our patients had advanced stage tumors and received radical aggressive surgery. Although our leakage rate was high, our mortality rate was at an acceptable level at 1.2%.

Deguchi et al. reported that pulmonary failure and the duration of operation are markers of EJA leakage in 1640 patients after

Table 2. Intraoperative and pathological data of the patients

Variable		Anastomosis leakage (–) n= 67	Anastomosis leakage (+) n= 13	p
T stage#	T1	6 (9)	0	0.148
	T2	5 (.5)	0	
	T3	25 (37.3)	9 (69.2)	
	T4	31 (46.3)	4 (30.8)	
N stage#	N0	20 (29.9)	3 (23.1)	0.895
	N1	10 (14.9)	2 (15.4)	
	N2	18 (26.9)	3 (23.1)	
	N3	19 (28.4)	5 (38.5)	
No. of harvested lymph nodes*		26 ± 11	29 ± 14	0.603
No. of harvested metastatic lymph nodes*		5 ± 8	5 ± 6	0.587
Combined organ resection#	Yes	10 (14.9)	7 (53.8)	0.002
	No	57 (85.1)	6 (46.2)	
Duration of operation (min)#	< 300	32 (47.8)	1 (7.7)	0.007
	≥ 300	35 (52.2)	12 (92.3)	
Intraoperative blood transfusion#	Yes	13 (19.4)	1 (7.7)	0.309
	No	54 (80.6)	12 (92.3)	

Datas are presented as *: mean ± standard deviation, #: n (%)

Table 3. Multivariate analysis of intraoperative findings of the patients

Variable	p	OR	95% CI
Combined organ resection	0.008*	6.329	0.040-0.623
Duration of operation (min)	0.032*	10.416	0.011-0.820

OR: Odds ratio; CI: Confidence interval.
* Statistically significant at p< 0.05.

total and proximal gastrectomy in their retrospective study (8). In our study, the duration of operation was markedly longer in the EJA leakage group than in the group with no leakage, and it was found to be statistically significant by both univariate and multivariate analyses. Various studies have also reported that prolonged duration of operation is related to morbidity after gastrectomy (16-18).

Many factors affect prolonged duration of operation. Complicated surgical procedures result in longer duration of operation and increase the risk of morbidity (19). Procedural duration is generally prolonged in advanced tumor cases, but it does not always lead to EJA leakage. Some studies have also reported that patients' risk of postoperative complications related to additional organ resections including splenectomy or pancreatectomy is higher (20,21). Deguchi et al. have found that the effects of additional organ resection on EJA leakage are statistically significant as revealed by univariate analysis (8). They, however, reported that the results of their multivariate analysis reveal that it does not have a determinant role on EJA leakage.

Migita et al. have reported that chronic renal failure, proximal gastrectomy, high levels of hemoglobin A1c, and problems seen in anastomoses during EJA construction are independent risk factors for EJA leakage, whereas combined additional organ resection is not related to EJA leakage in 327 patients (11).

The results of our study, however, showed that additional organ resection was statistically significant. Kiudelis et al. have ascertained that a 4-day average body temperature, leukocyte levels, and CRP levels during the early postoperative period are considerably related to anastomotic leakage as revealed by univariate analysis in 175 patients (22). The results of our study also demonstrated that the rates of EJA leakage and postoperative complications were significantly higher in patients with recurrent fever in the postoperative period (p= 0.01). When CRP values were investigated, it was seen that the CRP values on postoperative days 3 and 5 were higher in patients with postoperative complications including EJA leakage than in those without complications, and the difference between the two groups was statistically significant (p= 0.01). When the patients were assessed with regard to NLR, it was observed that NLR on postoperative day 5 was significantly higher in the EJA leakage and other postoperative complication group (p= 0.022). All these mentioned factors are essentially a result of the inflammatory effect of EJA leakage and are not specific to EJA leakage.

Table 4. Laboratory results and fever values in the postoperative period

Variable	PO	No Complication (n= 46)	Anastomosis leakage n= 13	Another Complication n= 21	p
CRP* (mg/dL)	Day 1	6.8 ± 2.4	9.8 ± 3.9	9.9 ± 8.8	0.201
	Day 3	8.3 ± 3.4	21.1 ± 9.2	22.7 ± 13.3	0.01
	Day 5	8.8 ± 4	17.4 ± 7.2	10.7 ± 5.3	0.01
WBC* (10^3/μL)	Day 1	13.59 ± 4.91	15.88 ± 2.49	13.62 ± 3.72	0.226
	Day 3	8.8 ± 3.11	12.02 ± 3.79	9.87 ± 5.93	0.077
	Day 5	8.44 ± 2.94	9.37 ± 4.84	8.7 ± 3.8	0.800
Neutrophil-to-lymphocyte ratio*	Day 1	16.6 ± 13.8	26.2 ± 19.5	22.1 ± 20.3	0.142
	Day 3	11.2 ± 7.8	16.7 ± 13.5	9.7 ± 7.7	0.146
	Day 5	6.2 ± 2.9	12.0 ± 8.0	9.7 ± 7.4	0.022
Platelet-to-lymphocyte ratio*	Day 1	379.9 ± 315.7	396.6 ± 238.7	492.5 ± 363.5	0.404
	Day 3	290.8 ± 132.1	303.4 ± 221.5	344.9 ± 274.2	0.682
	Day 5	308.6 ± 109.1	327.8 ± 208.6	503.8 ± 726.8	0.340
Fever#		16 (34.8)	7 (53.8)	12 (57.1)	0.168
Recurrent fever#		2 (4.3)	6 (46.2)	4 (19)	0.001

[a] Patients' postoperative complication without anastomosis leakage (surgical site infection, pneumonia, postoperative atelectasis, chylous leakage, evisceration, acute renal failure, and intra-abdominal bleeding).
[b] Postoperative body temperature over 38°C in more than one measurement.
PO: Postoperative; CRP: C-reactive protein; WBC: White blood cell.
Datas are presented as *: mean ± standard deviation, #: n (%)

Study Limitations

The limitations of our study included the fact that it was retrospective, had a small patient population, and was conducted at a single center.

CONCLUSION

Surgeons should be careful about anastomotic leakage, which is a significant postoperative complication, especially in cases where the duration of operation is prolonged, and additional organ resection is required. Recurrent fever, high CRP levels, and NLR may serve as warnings for complications in postoperative follow-ups.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Kartal Koşuyolu Higher Specialty Training and Research Hospital (2017.3/2-36).

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ORİJİNAL ÇALIŞMA-ÖZET
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Total gastrektomi sonrası özefagojejunal anastomoz kaçağında risk faktörleri

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ÖZET

Giriş ve Amaç: Mide kanseri cerrahisinde perioperatif yönetim ve cerrahi teknikteki gelişmelere rağmen, total veya proksimal gastrektomi sonrası yapılan rekonstruksiyonda özefagojejunal anastomoz (ÖJA) kaçağı halen önemli bir morbidite ve mortalite nedenidir. Bu çalışmada, ÖJA kaçağı açısından risk faktörlerinin belirlenmesi amaçlanmıştır.

Gereç ve Yöntem: Ocak 2013 ile Aralık 2016 tarihleri arasında total gastrektomi +D2 lenf nodu diseksiyonu ve ÖJA yapılan 80 mide kanserli hasta retrospektif olarak değerlendirildi. Klinik takipleri sırasında anastomoz kaçağı gelişmeyen hastalar grup 1'i, anastomoz kaçağı gelişenler ise grup 2'yi oluşturdu.

Bulgular: Çalışmaya dahil edilen 80 hastanın 58 (72.5%)'i erkek, 22 (27.5%)'si kadın olup yaş ortalaması 61.2 ± 11.2 idi. Gruplar arasında demografik özellikler açısından farklılık saptanmadı. Postoperatif tekrarlayıcı ateş (p= 0.001), postoperatif 3. ve 5. gün C-reaktif protein (CRP) değerleri (p= 0.01) ve postoperatif 5. gün nötrofil/lenfosit oranı (NLO) (p= 0.022) ÖJA kaçağı ve diğer postoperatif komplikasyonlar açısından istatistiksel olarak anlamlı saptandı. Operasyon süresi (p= 0.032) ve kombine organ rezeksiyonu (p= 0.008) ÖJA kaçak açısından risk faktörleri olarak belirlendi.

Sonuç: Cerrahlar özellikle operasyon süresinin uzadığı ve ek organ rezeksiyonunun yapıldığı durumlarda, ameliyat sonrası önemli bir komplikasyon olan ÖJA kaçağı açısından dikkatli olmalıdırlar. Postoperatif dönemdeki takiplerde tekrarlayan ateş, yüksek CRP değeri ve NLO komplikasyonlar açısından uyarıcı olabilir.

Anahtar Kelimeler: Anastomoz kaçağı, gastrektomi, risk faktörleri

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ORIGINAL ARTICLE
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Malignancy risk for thyroid nodules larger than 4 cm and diagnostic reliability of ultrasound-guided FNAB results

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ABSTRACT

Objective: Our aim in the present study was to investigate the relation between thyroid nodule diameter and malignancy, and the diagnostic accuracy of fine needle aspiration biopsy (FNAB) for thyroid nodules larger than 4 cm.

Material and Methods: Preoperative patient demographics such as age and gender, thyroid nodule diameter, FNAB results and postoperative pathology results were recorded. The relation between age, gender, thyroid nodule size of the patients and malignancy was examined. Also, the sensitivity, specificity, false negativity, false positivity and accuracy rates of FNBA of the patients whose thyroid nodule size was lower than 4 cm and the ones whose thyroid nodule size was higher than 4 cm were analyzed.

Results: There was no significant difference between males and females in terms of malignancy rate (p= 0.15). There was no significant relation between malignancy and patient age (p= 0.92). No significant difference was found between the group with thyroid nodule diameter of > 4 cm and the group thyroid with nodule diameter of < 4 cm in terms of malignancy (p= 0.91). In the group with thyroid nodule diameter of > 4 cm, sensitivity, specificity, false negativity, false positivity, and accuracy rates of FNAB were 15%, 100%, 84%, 0%, and 70%, respectively. In the group with thyroid nodule diameter of < 4 cm, sensitivity, specificity, false negativity, false positivity, and accuracy rates of FNAB were 53%, 100%, 46%, 0% and 80%, respectively.

Conclusion: Our study put forward that thyroid nodule diameter is not the only predictor parameter whilst predicting malignancy. However, it was observed that FNAB sensitivity and false negativity were higher when the thyroid nodules with > 4 cm diameter were compared to the thyroid nodules with < 4 cm diameter.

Keywords: Thyroid nodule diameter, malignancy, fine needle aspiration biopsy, false negativity

INTRODUCTION

Thyroid nodules are very common in the general population. Clinically palpable nodules are observed in 4-7% of the population (1). Prevalence rate is higher when the thyroid gland is evaluated with imaging methods. Thyroid nodules can be found in 17-67% of the adult population when evaluated with cervical ultrasonography (USG) (2). Although most thyroid nodules are benign, the prevalence of thyroid cancer has recently risen dramatically (3). Malignancy rate in thyroid nodules is about 5%-20% (4). In case a nodule is detected on physical examination, the critical question is whether it is benign or malignant. Standard thyroid nodule evaluation protocol consists of patient's history, physical examination, serum thyroid stimulating hormone (TSH) level, cervical USG, and fine needle aspiration biopsy (FNAB). Consideration of clinical factors combined with USG findings gives a clue about the malignancy of the nodule. Particularly hypoechogenic nature of the nodule, presence of calcification, irregular or infiltrative borders, and increased vascularity of the nodule are important predictors of malignancy (5,6). As a reliable, rapid and low-cost method, FNAB is accepted as a gold standard diagnostic tool for the assessment of thyroid nodules. With a false negativity rate under 5%, FNAB is widely used by clinicians. False negativity and non-diagnostic cytology rates are reduced when FNAB is performed under USG guidance (2,7). There are studies reporting that increased nodule diameter is associated with malignancy risk and can be used

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as a predictor of malignancy (8,9). On the other hand, there are also studies reporting that there is no association between nodule diameter and malignancy risk (10,11). Some authors recommend thyroidectomy for nodules larger than 4 cm even when FNAB result is benign due to increased malignancy risk and increased false negativity rate (12,13). Yet, other studies show no difference between small and large nodules with regard to the false negativity of FNAB (14,15).

In many centers, the patient is referred to surgery when the nodule size is greater than 4 cm even if FNAB result is negative. Our aim in the present study was to examine the validity of this approach, to investigate the relationship between nodule diameter and malignancy, and the diagnostic accuracy of FNAB for nodules larger than 4 cm.

MATERIAL and METHODS

The study included 322 patients who underwent thyroid surgery in our clinic between October 2010 and January 2015 due to the diagnosis of nodular goiter. Data were obtained retrospectively from patient files. The study was carried out in accordance with the declaration of Helsinki. Cystic and complex (solid + cystic) nodules were excluded from the study.

Preoperative patient demographics such as age and gender, nodule diameter, FNAB results and postoperative pathology results were recorded. FNAB was performed under USG guidance by radiologists in a radiology clinic. For solitary nodules, FNAB was performed on that nodule, whereas for multinodular cases, FNAB was performed on the nodule showing malignant characteristics in ultrasonographic assessment, or on the largest (dominant) nodule. Nodule diameters were recorded from USG reports in the unit of cm. FNAB results were categorized according to Bethesda classification as non-diagnostic (category 1), benign (category 2), atypia of undetermined significance (AUS)/follicular lesion of undetermined significance (FLUS) (category 3), follicular neoplasm/suspicious for a follicular neoplasm (category 4), suspicious for malignancy (category 5), and malignancy (category 6) groups. Surgical indications for patients with benign and non-diagnostic FNAB results in Bethesda categories 1 and 2 were cosmetic problems and compression findings for nodules larger than 4 cm, whereas for nodules smaller than 4 cm, surgical indications were presence of clinical symptoms (being dysphagia or disphonia, nodule's fast growth) and the existence of nodule malignancy chance radiologically (nodule being hypoechoic, having micro qualifications, nodule having irregular sidelines, increase in vascularity in Doppler). Thyroidectomy was performed by surgeons experienced in the field of endocrine surgery. For evaluation of sensitivity, specificity, false negativity, false positivity and accuracy of FNAB, Bethesda category 2 was accepted as a negative result, while category 6 was accepted as a positive result. Inadequate and suspicious categories were not included in the analysis.

The relation between age, gender, nodule size of the patients and malignancy was examined. Also, the sensitivity, specificity, false negativity, false positivity, and accuracy rates of FNBA of the patients whose nodule size was lower than 4 cm and the ones whose nodule size was higher than 4 cm were analyzed.

Chi-square and independent t-tests were used in statistical analysis. Normality assessment was made with Kolmogorov-Smirnov test. $p< 0.05$ was considered significant.

RESULTS

Of the 322 patients included, 54 (16.8%) were males and 268 (83.2%) were females. Mean age was 48.4 ± 13.9 years with a range of 13-91 years. 222 (68.9%) patients had multiple nodules, whereas 100 (31.1%) patients had solitary nodules. 257 (79.8%) patients had nodules with a diameter of < 4 cm, while 65 (20.2%) patients had nodules with a diameter of > 4 cm. Preoperative FNAB results were nondiagnostic in 39 (12.1%) patients; benign in 131 (40.7%) patients; AUS/FLUS in 14 (4.3%) patients; follicular neoplasm/suspicious for follicular neoplasm in 107 (33.2%) patients; and suspicious for malignancy in 5 (1.6%), Malign cytology was observed in 26 (8.1%) patients. Mean nodule diameter was 2.8 ±-1.3 cm (0.5-9.5 cm). Types of surgery were total thyroidectomy in 266 (82.6%) patients, lobectomy in 53 (16.4%) patients and complementary thyroid surgery in 3 (0.9%) patients. Postoperative final pathology results were benign in 195 (60.6%) patients and malignant in 127 (39.4%) patients. Among patients with malignant results, detected histopathological types were papillary carcinoma in 106 patients, Hurthle cell carcinoma in 9 patients, follicular carcinoma in 6 patients, medullary carcinoma in 2 patients, poorly differentiated carcinoma in 2 patients, and anaplastic carcinoma in 1 patient. Malignancy was seen in 101 (37.6%) of the female patients and 26 (48.1%) of the male patients (Table 1). There was no significant difference between males and females in terms of malignancy rate ($p= 0.15$). Mean age of the patients in the malignant group was 48.7 (22-85) years, and that of the patients in the benign group was 49.3 (13-91) years. There was no significant relationship between malignancy and patient age ($p= 0.92$). Malignancy was seen in 26 (40%) of the 65 patients with a nodule diameter of > 4 cm and in 101 (39.2%) of 257 patients with a nodule diameter of < 4 cm. No significant difference was found between the group with a

Table 1. Malignant and benign distribution according to sex

	Histopathology		
Sex	Benign	Malign	Total
Male	28	26	54
Female	167	101	268
Total	195	127	322

nodule diameter of > 4 cm and the group with a nodule diameter of < 4 cm in terms of malignancy (p= 0.91). In the group with a nodule diameter of > 4 cm, malignancy was observed in 3 of 10 patients in non-diagnostic FNAB category, 11 of 35 patients in benign category, none of the patients in AUS/FLUS category, 10 of 16 patients in follicular neoplasm/suspicious for follicular neoplasm category, and both of the 2 patients with malignant FNAB results while in the group with a nodule diameter of < 4 cm, malignancy was observed in 3 of 29 patients in non-diagnostic category, 21 of 96 patients in benign category, 3 of 12 patients in AUS/FLUS category, 47 of 91 patients in follicular neoplasm/suspicious for follicular neoplasm category, 3 of 5 patients in suspicious for malignancy category, and in all of the 24 patients in the malignancy category (Tables 2,3). In general, the sensitivity, specificity, false negativity, false positivity, and accuracy rates of FNAB were 44%, 100%, 55%, 0%, and 70%, respectively. In the group with a nodule diameter of > 4 cm, sensitivity, specificity, false negativity, false positivity and accuracy rates of FNAB were 15%, 100%, 84%, 0% and 70%, respectively. In the group with a nodule diameter of < 4 cm, sensitivity, specificity, false negativity, false positivity and accuracy rates of FNAB were 53%, 100%, 46%, 0% and 80%, respectively (Table 4).

Table 2. Fine needle aspiration biopsy results in the nodule diameter > 4 cm group

	Postoperative histopathology		
FNAB	**Benign**	**Malign**	**Total**
Non-diagnostic	7	3	10
Benign	24	11	35
AUS/FLUS	2	0	2
Follicular neoplasm/suspicious	6	10	16
Malignancy positive	0	2	2
Total	39	26	65

FNAB: Fine needle aspiration biopsy; AUS/FLUS: Atypia of undetermined significance/follicular lesion of undetermined significance.

Table 3. Fine needle aspiration biopsy results in the nodule diameter < 4 cm group

	Postoperative histopathology		
FNAB	**Benign**	**Malign**	**Total**
Non-diagnostic	26	3	29
Benign	75	21	96
AUS	9	3	12
Follicular neoplasm/suspicious	44	47	91
Malignency suspicious	2	3	5
Malignancy positive	0	24	24
Total	156	101	257

FNAB: Fine needle aspiration biopsy; AUS: Atypia of undetermined significance.

DISCUSSION

In case of detection of a thyroid nodule, determination of its malignancy probability is of key importance for the clinician. Numerous studies have been conducted to investigate many parameters to be used in the prediction of the malignancy-risk of thyroid nodules. Studies examining the relationship between age and malignancy risk of nodules have shown contradicting results. Pinchot et al. have reported a higher prevalence of thyroid cancer among the elderly population in comparison to the young adults (16). Godazaneh; however, has found a higher prevalence of thyroid cancer among young adults compared to the elderly (17). On the other hand, in their studies, Rosario et al. and Rapari et al. have reported that there is no significant association between age and malignancy (8,18). In our study, mean patient age was similar in benign and malignant groups (48.7 and 49.3 years, respectively), and no significant association was found between age and malignancy (p= 0.92> 0.05). Raparia et al. have studied patients with FNAB results as suspicious for follicular carcinoma or Hurthle cell neoplasm or suspicious for malignancy, and they have found a higher prevalence of malignancy among males in comparison to females (8). Kim et al. have studied patients with thyroid nodules larger than > 4 cm, and they have reported that there is no significant difference between males and females with regard to malignancy (p= 0.78) (12). In our study, a significant difference was not found between male and female groups in terms of malignancy (p= 0.15).

Many studies have examined the association between thyroid nodule size and malignancy risk and reported contradicting results. In their study including patients with FNAB results as suspicious for follicular carcinoma or Hurthle cell neoplasm or

Table 4. Sensitivity, specificity, false negativity, false positivity and accuracy rates of fine needle aspiration biopsy

FNAB	Sensitivity	Specifity	False negativity	False positivity	Accuracy
> 4 cm	15%	100%	84%	0%	70%
< 4 cm	53%	100%	46%	0%	80%
Total	44%	100%	55%	0%	70%

FNAB: Fine needle aspiration biopsy, AUS/FLUS: Atypia of undetermined significance/follicular lesion of undetermined significance.

suspicious for malignancy, Rapari et al. have reported a higher frequency of malignancy among patients with nodules larger than 2 cm (p< 0.001) (8). McCoy et al. have reported a higher prevalence of malignancy for nodules ≥ 4 cm (9). In a meta-analysis, Hammad et al. have examined the relationship between nodule size and malignancy and categorized nodules in three groups based on their diameter as < 3 cm, 3-5.9 cm, and ≥ 6 cm. In a comparison of 3-5.9 cm group with < 3 cm group, they have found higher malignancy risk in the group with nodule size between 3-5.9 cm (p= 0.02) (< 3 cm). In a comparison of ≥ 6 cm group with < 3 cm group, they have found that malignancy risk is lower in ≥ 6 cm group (p< 0.001) (19). In another study, McHenry et al. have reported that the mean diameter of malignant nodules is lower than that of benign nodules (p< 0.001), and therefore, the nodule diameter could not be a predictor of malignancy (10). In their study including patients with nodule size > 4 cm, Kim et al. have not found an association between nodule diameter and malignancy (p= 0.13) (12). Godazandeh et al. have not determined a significant difference between patients with nodule size > 4 cm and < 4 cm in terms of malignancy rate (p= 0.29) (17). Megwalu et al. have studied nodules ≥ 4 cm and have not detected an association between nodule size and malignancy (p= 0.7) (20). In our study, there was no significant difference between the > 4 cm group and the < 4 cm group in terms of malignancy (p= 0.91). Conflicting results from various studies suggest that nodule size on its own is not a reliable parameter for predicting malignancy. Deciding on medical follow-up or surgery, based on the nodule diameter alone, would not be a correct approach.

FNAB is currently considered a gold standard diagnostic tool for the evaluation of thyroid nodules. Diagnostic accuracy is particularly higher when it is performed under USG guidance and in experienced hands. Nonetheless, diagnostic accuracy of FNAB is controversial, especially for large nodules. In their study including patients with nodules of > 4 cm, Kim et al. have found general false negativity rate as 11.9%, and because of such a high rate, they have recommended consideration of surgery in case of suspicious USG findings for nodules of > 4 cm, even if FNAB is negative (12). In another study, Wharry et al. have studied patients with nodules of ≥ 4 cm and found false negativity rate of FNAB as 10.4%. They have reported that lack of suspicious USG findings would not rule out malignancy and that therefore, at least lobectomy should be considered for nodules ≥ 4 cm (13). In their study, Godazandeh et al. have found that sensitivity of FNAB is lower and false negativity rate is higher when nodule size is < 4 cm (17). Giles et al. have compared patients with a nodule size of < 3 cm and ≥ 3 cm, and they have reported that false negativity rate is higher when nodule size is ≥ 3 cm. They have stated that thyroidectomy can be considered in patients with a ≥ 3 cm nodule even if FNAB is reported as benign (21). In their study, Koo et al. have categorized thyroid nodules as ≤ 0.5, > 0.5-1, > 1-2, > 2-4, and > 4 cm. They have found high false negativity rate (50%) in the > 4 cm group and recommended frequent FNAB for patients with a > 4 cm nodule even though FNAB is reported as benign (22). Beştepe et al. have reported that false negativity rates of ≥ 4 cm nodules is two times higher than the nodules between the sizes of 1-3.9 cm (23). By contrast to these studies, Shrestha et al. have categorized thyroid nodules in three groups as 0.5-0.9 cm, 1-3.9 cm, and ≥ 4 cm. They have found higher false negativity rate in the 0.5-0.9 cm group and stated that greater nodule diameter should not automatically direct physicians towards thyroidectomy (14). Albuja-Cruz et al. have examined patients with < 4 cm and ≥ 4 cm nodules and reported that diagnostic reliability of FNAB is not influenced by the nodule size. They have recommended not to use nodule size as a single independent factor while making the decision on thyroidectomy for ≥ 4 cm nodules (15). Megwalu et al. have found false negativity rate of FNAB as 0% in their study with ≥ 4 cm nodules, and they have recommended not to perform thyroidectomy automatically in every patient with ≥ 4 cm nodule and a benign FNAB result (20). Kuru et al. have found that false negative rates are 1.3% and 4.3% when they have compared < 4 cm nodules and ≥ 4 cm nodules, respectively. They have stated that FNAB's false negativity rates are lower in < 4 cm nodules and ≥ 4 cm nodules upon comparing ≥ 4 cm nodules with nodules between the sizes of 1-3.9 cm (24). In the present study, when > 4 cm and < 4 cm nodules were compared, it was found that FNAB had lower sensitivity and higher false negativity rate for nodules > 4 cm. In comparison to the literature data, lower sensitivity and higher false negativity rates were found in the present study. Accuracy of FNAB results may vary depending on several factors such as adequacy of sample volume, sampling from correct site, and accurate interpretation of the results. Therefore, the validity of the results of FNAB are significantly dependent on the experience of the pathologist that is in charge of the process of examination of the cytology samples and the radiologist who performs the procedure. Different findings in our series regarding FNAB results may be attributed to such factors.

Major limitation of the present study was its retrospective and single-centered design.

CONCLUSION

Our study put forward that nodule diameter was not the only predictor parameter whilst predicting the malignancy. However, it was observed that FNAB sensitivity and false negatively were higher when the nodules with a > 4 cm diameter were compared to the nodules with a < 4 cm diameter.

Ethics Committee Approval: Ethics committee approval was not obtained because the study was a retrospective file screening study.

Informed Consent: As the study was a retrospective file screening study, informed consent was not obtained.

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ORİJİNAL ÇALIŞMA-ÖZET
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4 cm'den daha büyük tiroid nodüllerinde malignite riski ve ultrason eşliğindeki İİAB sonuçlarının tanısal güvenirliliği

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ÖZET

Giriş ve Amaç: Bu çalışmadaki amacımız tiroid nodül çapı ile malignite arasındaki ilişkiye ve 4 cm' den büyük tiroid nodüllerinde ince iğne aspirasyon biyopsisi (İİAB)'nin tanısal doğruluğunu araştırmak idi.

Gereç ve Yöntem: Hastaların ameliyat öncesi yaş, cinsiyet gibi demografik özellikleri, tiroid nodül çapları, İİAB sonuçları ve ameliyat sonrası patoloji sonuçları kaydedildi. Yaş, cinsiyet ve tiroid nodül çapı ile malignite arasındaki ilişki araştırıldı. Ayrıca tiroid nodül çapı > 4 cm ve < 4 cm olan hastalarda İİAB'nin duyarlılığı, özgüllüğü, yanlış negatifliği, yanlış pozitifliği ve doğruluğu değerlendirildi.

Bulgular: Kadın ve erkek grup malignite açısından karşılaştırıldığında iki grup arasında anlamlı bir fark bulunamadı (p= 0.15). Hastaların yaşları ile malignite arasında anlamlı bir ilişki bulunamadı (p= 0.92). Tiroid nodül çapı > 4 cm olan grup ile tiroid nodül çapı < 4 cm olan grup arasında malignite açısından anlamlı bir fark bulunamadı (p= 0.91). Tiroid nodül çapı > 4 cm olan grupta İİAB'nin sensivite, spesifite, yanlış negatiflik, yanlış pozitiflik ve doğruluk oranları sırasıyla %15, %100, %84, %0 ve %70 idi. Tiroid nodül çapı < 4 cm olan grupta İİAB'nin sensivite, spesifite, yanlış negatiflik, yanlış pozitiflik ve doğruluk oranları sırasıyla %53, %100, %46, %0 ve %80 idi.

Sonuç: Çalışmamız, tiroid nodül çapının tek başına maligniteyi öngörmede güvenilir bir parametre olmadığını ortaya koydu. Fakat > 4 cm tiroid nodüllerinde < 4 cm nodüllerle kıyaslandığında İİAB'nin duyarlılığının daha düşük ve yanlış negatiflik oranının daha yüksek olduğu bulundu.

Anahtar Kelimeler: Tiroid nodül çapı, malignite, ince iğne aspirasyon biyopsisi, yanlış negatiflik

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ORIGINAL ARTICLE
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The diagnostic values of procalcitonin and interleukin 6 in acute appendicitis

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ABSTRACT

Objective: Despite the recent use of computed tomography scan and diagnostic laparoscopy, acute appendicitis is still highly misdiagnosed. Timely diagnosis of acute appendicitis is more crucial in children and elderly patients because of vague symptoms and rapid progression to perforation in these age groups, which may result in high rates of morbidity and mortality. The aim of the present study was to find the diagnostic values of procalcitonin and interleukin 6 (IL-6) for diagnosing acute appendicitis in our center.

Material and Methods: Patients who were suspected of acute appendicitis and referred to the emergency department of a tertiary care urban hospital in 2016 were enrolled in the study. A 5 mL blood sample was obtained from each patient before appendectomy and was examined for procalcitonin and IL-6. Then the resected specimen of the appendix was studied by a pathologist, and a definite diagnosis was made.

Results: Eighty patients including 53 (66.3%) men who underwent appendectomy were enrolled in the study. The diagnosis of acute appendicitis was histopathologically confirmed in 60 (75%) patients including 18, 20, and 22 patients with inflammatory, suppurative, and gangrenous/perforated appendicitis, respectively. The sensitivity and specificity of procalcitonin versus IL-6 for diagnosing acute appendicitis were 65% and 80% vs. 76% and 55%, respectively. The sensitivity and specificity of concurrent procalcitonin and IL-6 for diagnosing acute appendicitis were 95% and 55%, respectively.

Conclusion: Our study suggests that parallel measurement of procalcitonin and IL-6 decreases unnecessary negative appendectomies.

Keywords: Appendicitis, interleukin 6, procalcitonin

INTRODUCTION

Appendicitis is the most common cause of surgery of the abdomen with an incidence rate of 11 in 10.000 annually, and it most commonly occurs in the second to fourth decade of life especially in young adults (1,2). Timely diagnosis of acute appendicitis is crucial especially in children and elderly patients because of vague symptoms and rapid progression to perforation in these age groups, which may result in high rates of complications including wound infection, intra-abdominal abscess formation, and mortality (3,4). Despite the recent use of computed tomography scan and diagnostic laparoscopy, acute appendicitis is still highly misdiagnosed at a rate of 15%, with the highest number of negative appendectomy seen in elderly women (5). Hence, additional preoperative testing may be helpful for the timely diagnosis of acute appendicitis. Although the role of the measurement of inflammatory cytokines, such as procalcitonin, interleukin 6 (IL-6), and C-reactive protein, which are involved in acute and chronic inflammatory responses in addition to the measurement of white cell count and bilirubin for diagnosing acute appendicitis, has been investigated in few studies, the results have varied with no consensus about the best test (6,7).

The aim of the present study was to find the diagnostic values of procalcitonin and IL-6 in the diagnosis of acute appendicitis and their associations with the severity of the disease in our center.

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MATERIAL and METHODS

Patient Selection

In this prospective study, patients who were suspected of acute appendicitis and referred to the emergency department of a tertiary care urban hospital in 2016 were enrolled in the study. Patients with an Alvarado score of > 5 or in whom diagnosis of acute appendicitis was documented using computed tomography scan were included into the study. Exclusion criteria comprised patients with a history of autoimmune disease; who underwent transplantation; receiving immunosuppressive, antibiotic, and/or immunomodulator drugs; who were in sepsis; or who were markedly overweight with a body mass index > 25. All patients were visited and examined by the same surgeon.

The research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects" (amended in October 2013). Written informed consent was obtained from all participants. Medical University Ethics Committee approved the study.

Study Protocol

A 5 mL blood sample was obtained from each patient before appendectomy. No antibiotic or antipyretic drugs were administered before sampling. Serum samples were stored at -20 °C, and all measurements were performed under similar conditions on the same day. The measurement of procalcitonin and IL-6 was performed using enzyme-linked immunosorbent assay Human Procalcitonin (Eastbiopharm, China) and AviBion Human IL-6 (Orgenium, Finland) kits, respectively. Serum levels of > 0.5 ng/mL for procalcitonin and 5 pg/mL for IL-6 were considered as positive in our study. A pathologist examined the resected specimen of the appendix, and a definite diagnosis was made as normal appendix, inflammatory defined as infiltration of inflammatory cells, suppurative defined as infiltration of inflammatory cells with destruction of the appendiceal wall, with no evidence of abscess or perforation, and gangrenous and/or perforated appendicitis defined as infiltration of inflammatory cells, necrotic appendiceal wall, and macroscopic periappendiceal abscess and/or perforation.

Statistical Analyses

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 20.0 (IBM Corp., Armonk, NY, USA). Qualitative and quantitative data were compared using the Fischer's exact and independent t tests, respectively. A p value < 0.05 was considered as statistically significant.

RESULTS

Eighty patients including 53 (66.3%) men who underwent appendectomy were enrolled in the study. The frequency of patients in the 0-20, 21-40, 41-60, and older than 60 years old age groups were 30 (37.5%), 39 (48.8%), 6 (7.5%), and 5 (6.2%) patients, respectively. The diagnosis of acute appendicitis was histopathologically confirmed in 60 (75%) patients including 18, 20, and 22 patients with inflammatory, suppurative, and gangrenous/perforated appendicitis, respectively.

Figure 1 shows the frequency of positive procalcitonin or IL-6 in patients with the aforementioned different histopathology diagnoses. The sensitivity and specificity of procalcitonin for diagnosing acute appendicitis were 65% and 80%, respectively, with positive and negative likelihood ratios of 3.25 and 0.43, respectively, and positive and negative predictive values of 90% and 43%, respectively. In addition, the sensitivity and specificity of IL-6 for diagnosing acute appendicitis were 76% and 55%, respectively, with positive and negative likelihood ratios of 1.7 and 0.42, respectively, and positive and negative predictive values of 83% and 44%, respectively. On the other hand, the sensitivity and

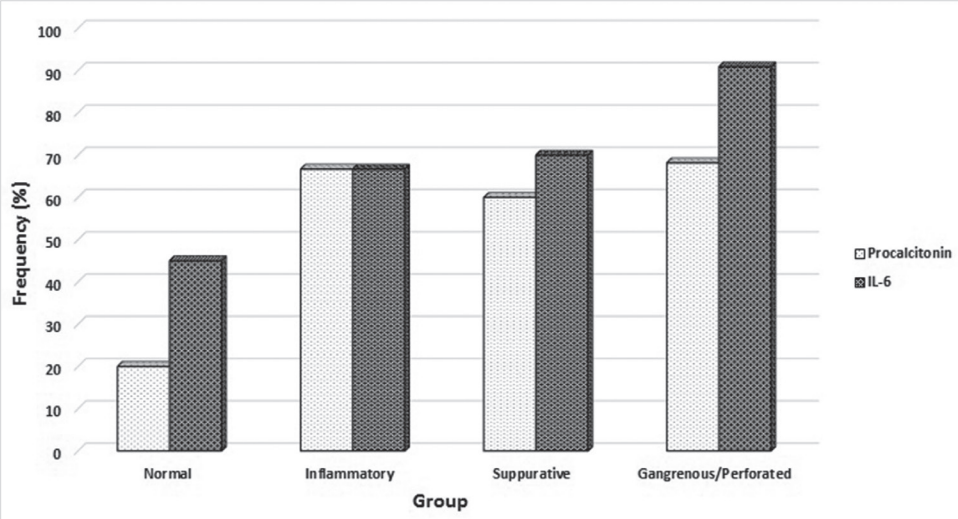

Figure 1. Frequency of positive procalcitonin or IL-6 in patients with different histopathology diagnoses.

specificity of using concurrent procalcitonin and IL-6 together for diagnosing acute appendicitis were 95% and 55%, respectively.

DISCUSSION

Fecaliths or inflammatory hypertrophy of the lymph nodes is a major cause of proximal appendiceal lumen obstruction that may lead to impaired blood supply of the appendix followed by rapid multiplication of resident bacteria of the appendix and bacterial endotoxin release (8). Bacterial endotoxins, in addition to the proinflammatory cytokines, promote the release of procalcitonin as an early marker of systemic bacterial infection associated with the severity of the infection. Moreover, it has been proposed that the expression of calcitonin I gene, which is responsible for the production of procalcitonin, is highly increased during bacterial infection (9). On the other hand, the measurement of serum procalcitonin with a half-life of 24 h has been shown to be reproducible and affordable with a low time spent for obtaining the result, making it a reasonable choice for diagnosing acute appendicitis (10-12). In our study, the sensitivity and specificity of serum procalcitonin for diagnosing acute appendicitis were 65% and 80%, respectively, and for diagnosing perforated appendicitis were 68% and 52%, respectively.

Similarly, in a recent systematic review by Acharya et al., the pooled sensitivity and specificity of procalcitonin for diagnosing acute appendicitis have been found as 36% and 88%, respectively, and for diagnosing perforated appendicitis as 69% and 67%, respectively (13). Similar to our results, some other studies have suggested that the measurement of procalcitonin is more sensitive for diagnosing perforated appendicitis, whereas it has less accuracy for diagnosing uncomplicated appendicitis (14,15).

During acute appendicitis, other proinflammatory cytokines, especially IL-6 as mediators of fever and acute phase reactions, are secreted due to the inflammatory process and neutrophil recruitment following the invasion of bacteria to the appendix (16, 17). In the present study, the sensitivity and specificity of serum IL-6 for diagnosing acute appendicitis were 76% and 55%, respectively, and for diagnosing perforated appendicitis were 91% and 37%, respectively. Similarly, previous studies have shown that the measurement of IL-6 is associated with high sensitivity and low specificity for diagnosing acute appendicitis. Ozguner et al. have shown that the serum level of IL-6 is significantly lower in children with negative appendectomy than in children with complicated or uncomplicated appendicitis, suggesting that the measurement of IL-6 is helpful in reducing the number of negative appendectomies (18).

In the study by Gürleyik et al., the sensitivity and specificity of IL-6 are 84% and 46%, respectively, and a marked elevation of IL-6 level has been reported in patients with perforated appendicitis (19). In the aforementioned systematic review, similar to our study, the pooled sensitivity and specificity of IL-6 for diagnosing acute appendicitis have been found as 73% and 72%, respectively, and for diagnosing perforated appendicitis as 79% and 63%, respectively. Moreover, the overall performance of IL-6 has been reported to be superior to procalcitonin, especially in terms of cost, sensitivity, and prediction of perforation.

However, IL-6 is not specific especially for diagnosing complicated appendicitis and associated with higher time spent for obtaining the result than procalcitonin (13). As previously mentioned, the measurement of procalcitonin was associated with low sensitivity and high specificity, whereas IL-6 was associated with high sensitivity and low specificity for the diagnosis of acute appendicitis. The total sensitivity and specificity of measurement of these two biomarkers combined were 95% and 55%, respectively, for diagnosing of acute appendicitis.

CONCLUSION

Our study suggests that the measurement of combining procalcitonin and IL-6 can provide beneficial evidence for superior decision-making, and owing to high sensitivity, negative results of each of these biomarkers may assist in ruling out acute appendicitis and reducing the number of negative appendectomies.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Hamadan University of Medical Sciences.

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2019; 35 (1): 19-22

Akut apandisit tanısında prokalsitonin ve interlökin 6 değeri

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ÖZET

Giriş ve Amaç: Son yıllarda artan bilgisayarlı tomografi ve tanısal laparoskopi kullanımına rağmen akut apandisit hala yüksek oranda yanlış tanı almaktadır. Bu yaş gruplarında belirsiz semptomlar ve perforasyona çabuk ilerlemesi sebebiyle yüksek oranda morbidite ve mortalite ile sonuçlanması, akut apandisit tanısının çocuklarda ve ileri yaşlı hastalarda zamanında konmasının öneminin altını çizmektedir. Bu çalışmanın amacı, merkezimizde akut apandisiti tanılamak için prokalsitonin ve interlökin 6 (IL-6) tanısal değerlerini ortaya koymaktır.

Gereç ve Yöntem: Çalışmaya, 2016 yılında akut apandisit şüphesi ile üçüncü basamak şehir hastanesi acil servisine sevk edilen hastalar dahil edilmiştir. Appendektomi öncesi bütün hastalardan 5 mL kan örneği alınarak prokalsitonin ve IL-6 incelemesi yapıldı. Daha sonra, apandisin kesip çıkarılan örneği bir patolojist tarafından incelendi ve kesin tanı konuldu.

Bulgular: Elli üç (%66.3)'ü erkek olmak üzere appendektomi alan toplamda 80 hasta çalışmaya dahil edildi. Akut apandisitis tanısı 18'i inflamatuvar, 20'si süpüratif ve 22'si gangrenli/perfore apandis olmak üzere 60 (%75) hastada histopatolojik olarak teyit edildi. Akut apandisit tanısında IL-6'ya karşın prokalsitonin duyarlılığı ve özgüllüğü ardışık olarak %80'e %65 ve %55'e %76 olarak bulundu. Akut apandisit tanısı için eşzamanlı prokalsitonin ve IL-6 duyarlılık ve özgüllüğü ise ardışık olarak %95 ve %55 olarak tespit edildi.

Sonuç: Çalışmamız, gereksiz negatif appendektomilerinin prokalsitonin ve IL-6 paralel ölçümleri ile azaltılabileceğini göstermiştir.

Anahtar Kelimeler: Apandisit, interlökin 6, prokalsitonin

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ORIGINAL ARTICLE
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Ultrasound-guided lateral versus posterior Quadratus Lumborum Block for postoperative pain after laparoscopic cholecystectomy: a randomized controlled trial

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ABSTRACT

Objective: The aim of the present study was to investigate the effect of ultrasound-guided bilateral posterior quadratus lumborum block (QLB) and lateral QLB on postoperative pain scores after laparoscopic cholecystectomy.

Material and Methods: In this prospective, randomized, single-blind study; 60 patients with elective laparoscopic cholecystectomy operations were randomized into two groups as group P (n= 30): Posterior Quadratus Lumborum Block + IV patient-controlled analgesia (PCA) tramadol and group L (n= 30): Lateral Quadratus Lumborum Block + IV PCA tramadol. Primary outcome measures included the amount of total consumption (24 hours) of tramadol. Secondary outcome measures; Visual Analog Scala (VAS) scores at rest and on movement (postoperative 30th minute, 2nd, 6th, 12th, and 24th hours) were recorded. Adverse effects (nausea and vomiting), additional analgesic requirement, and intraoperative opioid requirement were recorded.

Results: Postoperative total consumption amounts of tramadol and VAS scores (rest and on movement) were compared, and there was no statistically significant difference between the two groups (p> 0.05). There was no statistically significant difference in adverse effects (nausea and vomiting), additional analgesic requirement, and intraoperative opioid requirement between the two groups (p> 0.05).

Conclusion: Similar postoperative tramadol consumption values and VAS scores were determined in both lateral QLB and posterior QLB block applications in the results of our study.

Keywords: Cholecystectomy, quadratus lumborum block, postoperative pain, laparoscopy, ultrasound

INTRODUCTION

Laparoscopic cholecystectomy causes less pain and shortens the healing period when compared to open surgery. Today, since it provides a shorter length of hospital stay, it can be admitted in the status of the same-day patient (1,2). Pain type after laparoscopy is different from laparotomy, although detected mostly as parietal pain (with abdominal wall origin), patients also complain of visceral pain resulting from pneumoperitoneum (3). Many analgesic procedures such as nonsteroidal anti-inflammatory drugs (NSAIDs), opioid and regional anesthesia procedures are used as part of multimodal analgesia for postoperative pain (3,4). Among the regional anesthesia techniques of abdominal surgery, thoracic epidural analgesia, paravertebral block and transversus abdominis plane (TAP) block are used (4). TAP block, which is one of the truncal blocks, has been used in many studies in the literature for pain palliation after abdominal surgery (4-6). Another trunk block that has been used in recent years is the Quadratus Lumborum Block (QLB). It is described as the administration of local anesthetic between the quadratus muscle and the medial layer of the thoracolumbar fascia in an ultrasound-guided manner. It has been reported that a wider sensorial block area can be obtained from the single injection of QLB when compared to those obtained from the TAP block (7,8). Different studies have suggested that analgesia could be achieved up to the level of T5-L1 after QLB, and that it has an effect on both somatic pain and visceral pain (8-10). The block, which can be applied in four different ways to the quadratus lumborum muscle, namely, laterally, posteriorly, anteriorly and intramuscularly, has been administered laterally

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for the first time by Blanco et al. using local anesthetic injection (7). The efficacy of QLB administered with different indications in numerous case reports in the literature has been attempted to be determined with a limited number of randomized controlled studies (11,12).

The aim of the present study was to investigate the effect of ultrasound-guided bilateral posteriorly (posterior QLB) and laterally administered (lateral QLB) QLB on the postoperative pain scores after laparoscopic cholecystectomy.

MATERIAL and METHODS

Patients

Sixty-five patients who were planned to undergo laparoscopic cholecystectomy were evaluated within the scope of this prospective, randomized, single-blind study after obtaining the approval of the local ethics committee (Ethical number 2017-13/56). Patients who were aged between 20 and 60 years, who were included in the American Society of Anesthesiologists (ASA) I-III classes and who would undergo elective laparoscopic cholecystectomy were included. Patients with local anesthetic allergy, systemic infection, uncontrolled diabetes and hypertension were excluded from the study.

Randomization

Sixty suitable patients who accepted to participate in the study and who gave written consent were randomized into two groups with random numbers table including group P (n= 30): Ultrasound-guided bilateral Posterior QLB with 0.3 mL/kg 0.25% bupivacaine (Marcaine %0.5 AstraZeneca, İstanbul, Turkey) + IV patient-controlled analgesia (PCA) tramadol (Tramosel®, Haver, İstanbul, Turkey) and group L (n= 30): Ultrasound-guided bilateral Lateral QLB with 0.3 mL/kg 0.25% bupivacaine + IV patient-controlled analgesia (PCA) tramadol (Figure 1).

Interventions

Quadratus Lumborum Blocks were administered before operation and general anesthesia. After abdominal wall muscles were identified as three layers with the linear probe (10-18 MHz, MyLab30; Esaote, Florence, Italy), the probe was directed posteriorly and the fascia transversalis (TF), thoracolumbar fascia and Quadratus lumborum (QL) muscles were visualized (10). After

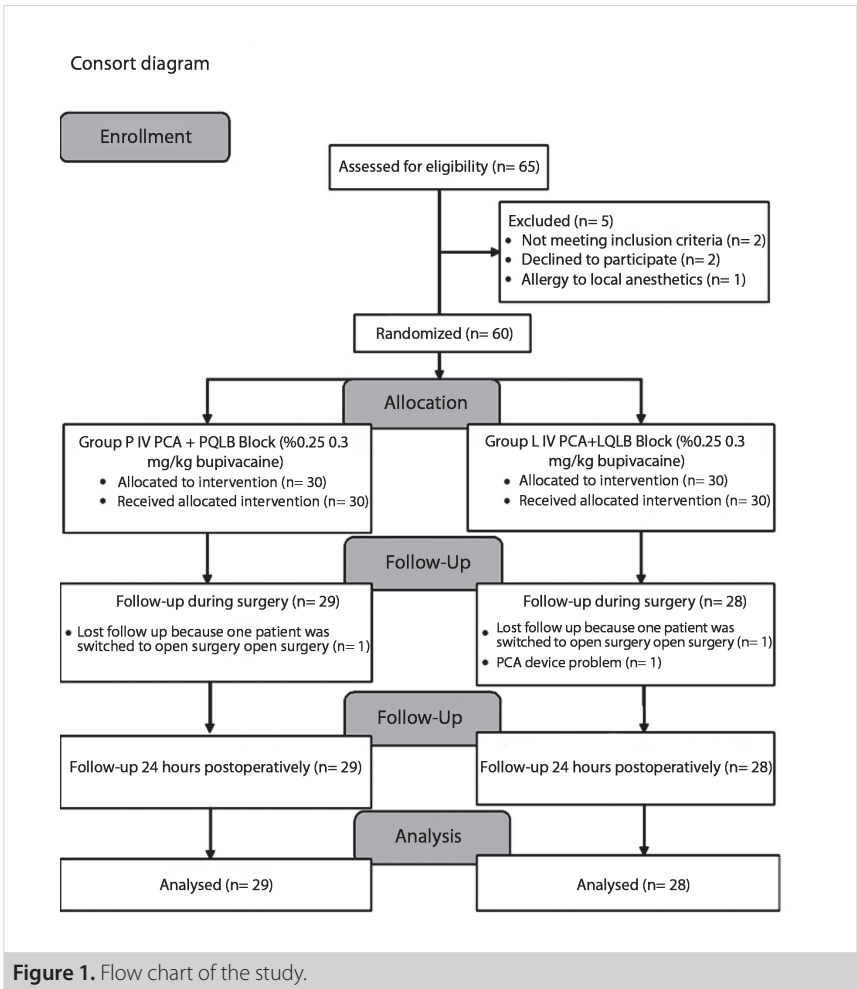

Figure 1. Flow chart of the study.

the area to be intervened was disinfected, the local anesthetic was administered using a 21-gauge, 100-mm needle (Quincke SonoPlex Pajunk, Geisingen, Germany) with the in-plane technique between the middle layer of the thoracolumbar fascia and QL muscle at the posterior edge of the quadratus lumborum muscle for posterior QLB, and between the aponeurosis at the lateral edge of the QL muscle and TF after the place was confirmed with the hydrodissection for lateral QLB (the target point was the junction between fascia and QL muscle) (8,10) (Figures 2,3). Bupivacaine was used at a concentration of 0.25% and at a dose of 0.3 mg/kg in both groups. It was administered to both groups bilaterally by the same regional anesthetist using a 10-18 MHz linear probe (MyLab30; Esaote, Florence, Italy). Propofol (Propofol 2% Fresenius®, Fresenius Kabi, Bad Homborg, Germany) 1-2 mg/kg and rocuronium (Curon®, Mustafa Nevzat, İstanbul, Turkey) 0.8-1.0 mg/kg were used for anesthesia induction. The maintenance of anesthesia was achieved with sevoflurane (Sevorane®Likit %100, AbbVie, Queenborough, England) 3-5% and a flow of 2.5-3L/min including the mixture of air and O2. Analgesia was provided with 1 µg/kg fentanyl (Talinat®, Vem, İstanbul, Turkey) when needed. Twenty minutes to the end of the operation, tenoxicam (Tilcotil, Deva İlaç, İstanbul, Turkey) 20 mg IV was administered for postoperative analgesia. IV PCA (CADD-Legacy® PCA, Smiths Medical, St. Paul, USA) device was connected to the postoperative patient and a bolus dose of tramadol was administered. The saline solution prepared as 5 mg tramadol per mL was mounted on the PCA instrument for the IV PCA protocol. The PCA device was set to the lock duration of 30 min, demand dose of 25 mg and the daily maximum dose of 400 mg. The bolus dose was administrated in the recovery room to those with a postoperative VAS score over 4 points.

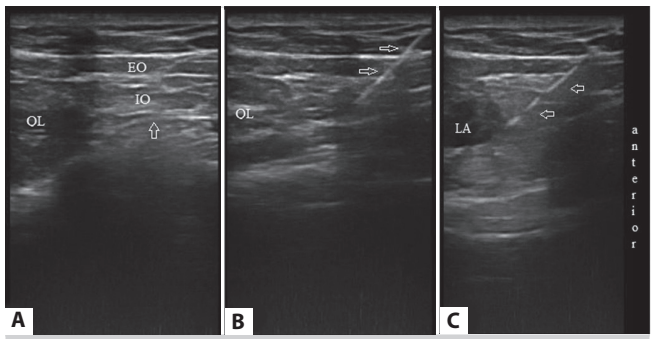

Figure 2. Ultrasound imaging lateral Quadratus Lumborum Block.
(A): QL: Quadratus Lumborum muscle, EO: External oblique muscle, IO: Internal oblique muscle, arrow shows fascia transversalis.
(B): QL: Quadratus Lumborum muscle, arrows show ultrasonic visible needle.
(C): LA: Local anesthesic, arrows show ultrasonic visible needle.

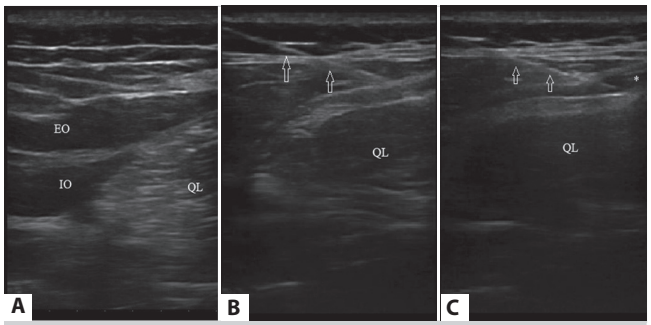

Figure 3. Ultrasound imaging posterior Quadratus Lumborum Block.
(A): QL: Quadratus lumborum muscle, EO: External oblique muscle, IO: Internal oblique muscle.
(B): QL: Quadratus lumborum muscle, arrows show ultrasonic visible needle.
(C): QL: Quadratus lumborum muscle.
* Local anesthesic, arrows show ultrasonic visible needle.

Surgical procedure: The surgical technique applied to all patients was performed in an identical manner by the same team of surgeons. Laparoscopy was performed by a 4 trocar technique (the first trocar was introduced inferiorly to the umbilicus, the second one was introduced inferiorly to the xiphoid process just on the left side of the upper 1/3 portion of the umbilical-xiphoid distance, the third one was introduced at the point of intersection of the umbilicus with the right anterior axillary line below the right costal arch, and the fourth one was introduced on the right midclavicular line). During the procedure, the intraabdominal pressure was maintained at a limit of maximum 14 mmHg.

Outcome Measures

Primary outcome measures; The amount of the total consumption of tramadol was examined. Secondary outcome measures; VAS scores at rest and on movement (Postoperative 30th minute, 2nd, 6th, 12th, and 24th hours) were recorded. Adverse effects (nausea and vomiting), additional analgesic requirement, intraoperative opioid requirement and duration of surgery were recorded.

Statistical Analysis

The analysis of the data was performed using IBM SPSS 22.0 (Chicago, IL, USA) statistical package program. Chi-square (c2) test was used for the comparisons of descriptive statistical methods (frequency, percentage, mean, standard deviation, median, min-max) as well as those of the qualitative data while assessing the study data. Conformity of the data with normal distribution was evaluated by Kolmogorov-Smirnow test (the data were found to be non-normally distributed.). For comparisons among groups, Mann-Whitney U test was used. It was considered that probability (P) values lesser than a= 0.05 were significant and there was a difference among groups while the values higher than that value were insignificant and there was no difference among groups.

Power analysis: In the result of the pilot study conducted in our clinic, a total of 58 patients with the necessary sample size of 29 was calculated for the study power of 90% (α= 0.05) when a 40% reduction was expected in 24-hour tramadol consumption values (82.5 ± 41.17 mg). G * Power3 analysis program (Heinrich-Heine-

Universität Düsseldorf, Düsseldorf, Germany) was used for calculation. In order to increase the power of the study and considering the potential losses, 30 patients were planned to be included in each group.

RESULTS

The study was terminated with a total of 57 patients since it was switched to open surgery in one patient in the posterior QLB group (n= 29), and it was switched to open surgery in one patient and due to a PCA device problem in one patient in the lateral QLB group (n= 28). Patient demographics and fentanyl levels administered during the operation were shown in Table 1. There was no statistically significant difference in terms of these values among the groups (p> 0.05). When postoperative total consumption amounts of tramadol were compared, consumption was determined to be 51.78 (0-175) mg in Group P and 54.46 (0-175) mg in group L. There was no statistically significant difference between the two groups (p> 0.05) (Figure 4). Examining the VAS scores at rest and on movement, no statistically significant difference was detected among all time parameters in inter-group analyses (p> 0.05) (Tables 2,3). There was no statistically significant difference in the frequency of side effects, consumption of paracetamol as rescue analgesia and duration of the operation between the two groups (p> 0.05) (Table 4).

Table 1. Comparison of the demographic characteristics of the patients

	Group P (n= 29)	Group L (n= 28)	p
Age (year)	38 ± 8.51	39.5 ± 7.4	0.834
Height (cm)	164.26 ± 7.63	162.5 ± 7.4	0.367
Weight (kg)	68.7 ± 8.1	69 ± 9.13	0.830
Gender	13 (44.8%)/16 (55.2%)	10 (35.7%)/18 (64.3%)	0.487
Amount of opioid given during operation (µg)	86.78 (60-150)	87 (80-160)	0.980

Mean ± SD for normal distribution and Median (min; max) values for abnormal distribution. cm: Centimeter; kg: Kilogram; M: Male, F: Female; µg: Microgram.
Group P: Ultrasound-guided bilateral Posterior quadratus lumborum block + IV patient-controlled analgesia tramadol and Group L: Ultrasound-guided bilateral Lateral quadratus lumborum block + IV patient-controlled analgesia tramadol.

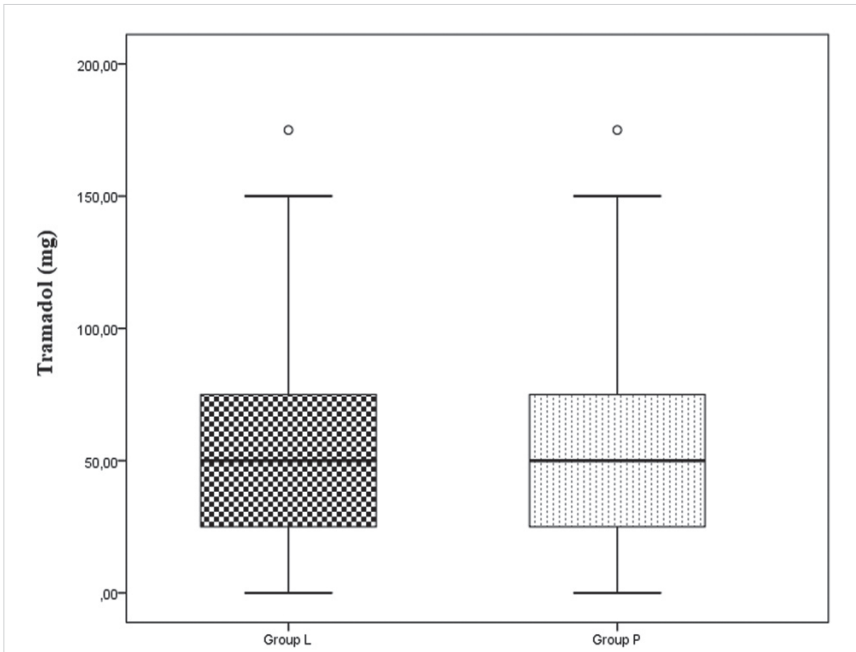

Figure 4. Tramadol consumption in the first 24 hour following surgery. Median (min; max) values for abnormal distribution. The Mann-Whitney U test for the inter-group comparisons. Group P: Ultrasound-guided bilateral Posterior quadratus lumborum block + IV patient-controlled analgesia tramadol and Group L: Ultrasound-guided bilateral Lateral quadratus lumborum block + IV patient-controlled analgesia tramadol.

Table 2. Comparison of VAS scores at rest between groups

VAS (at rest)	Group P (n= 29)	Group L (n= 28)	p
30th minute	0.75 (0-3)	1.07 (0-3)	0.245
2nd hour	0.89 (0-3)	1.1 (0-3)	0.340
6th hour	1.03 (0-3)	1.25 (0-3)	0.343
12th hour	1.1 (0-3)	1.14 (0-3)	0.873
24th hour	0.86 (0-4)	1.10 (0-3)	0.246

VAS: Visual Analogue Scale. Median (min; max) values for abnormal distribution. Group P: Ultrasound-guided bilateral Posterior quadratus lumborum block + IV patient-controlled analgesia tramadol and Group L: Ultrasound-guided bilateral Lateral quadratus lumborum block + IV patient-controlled analgesia tramadol.

Table 3. Comparison of VAS scores at movement between groups

VAS (at movement)	Group P (n= 29)	Group L (n= 28)	p
2nd hour	1.10 (0-3)	1.28 (0-3)	0.627
6th hour	1.17 (0-4)	1.39 (0-4)	0.578
12th hour	1.2 (0-4)	1.64 (0-4)	0.140
24th hour	1.68 (0-4)	1.78 (0-4)	0.766

VAS: Visual Analogue Scale. Median (min; max) values for abnormal distribution. Group P: Ultrasound-guided bilateral Posterior quadratus lumborum block + IV patient-controlled analgesia tramadol and Group L: Ultrasound-guided bilateral Lateral quadratus lumborum block + IV patient-controlled analgesia tramadol.

Table 4. Side effects, additional analgesic requirement, duration of surgery

	Group P (n= 29)	Group L (n= 28)	p
Side effects nausea and vomiting	-	1 (3.4%)	0.309
Additional analgesic requirement	-	1 (3.6%)	0.309
Duration of surgery (minute)	63.5 ± 14	65.7 ± 15.6	0.519

Mean ± SD for normal distribution. Group P: Ultrasound-guided bilateral Posterior quadratus lumborum block + IV patient-controlled analgesia tramadol and Group L: Ultrasound-guided bilateral Lateral quadratus lumborum block + IV patient-controlled analgesia tramadol.

DISCUSSION

Efficacy was investigated in this study by comparing the posterior QLB group with the lateral QLB group after laparoscopic cholecystectomy. In the study results, no statistically significant difference was found between the VAS scores at rest and on movement and PCA tramadol consumption values at all postoperative measurement times.

Trunk blocks are frequently used for laparoscopic cholecystectomy and abdominal surgeries. TAP block is a popular truncal block with shown efficacy in many different studies whereas QLB is a new block which has begun to be used recently. Blanco et al. have used the block application defined as "no pops" for pain after abdominoplasty surgery. Local anesthesia administered by them to the quadratus muscle laterally has been stated to provide effective analgesia (7). Afterwards, the injection performed in the quadratus muscle posteriorly has been reported to be more effective than the injection performed laterally in two different studies, and they have suggested that it causes lesser morphine consumption and need compared to the patients to whom TAP block has been administered (8,10).

Apart from the case reports in the literature, they have attempted to investigate the efficacy of QL block in three different studies (9,13,14). Murocchi et al. have administered QLB and TAP blocks to 22 patients in two studies aiming to determine the efficacy of QLB after laparoscopic surgery in patients with gynecologic disease. In the results examined retrospectively, a sensory block has been found throughout the dermatomes of T7-L1 in the QLB-treated group, and it has been reported to provide analgesia for 24 hours. The spread of local anesthesia administered to the paravertebral area due to the anatomical connection of the fascia transversalis with endothoracic fascia has been suggested as the potential activity mechanism in the study in which posterior QLB has been applied (9). In another study by Ishio et al. in which they have administered posterior QLB and compared it with the placebo group in the RCT, they

have detected that QLB block has lower VAS (on movement and at rest) values than the placebo (13). In this study in which 20 mL of ropivacaine has been used, nausea, vomiting and the time to the first analgesic requirement have been found to be lower in the block administered group. The results of these two studies in which laparoscopic surgery was performed reached to similar results with our study. Although QLB has been found to be effective after inguinal hernia operation in the RCT results performed in pediatric patients, the discussions on the activity mechanism of the block have been addressed. One of the main activity mechanisms is blocking the sympathetic formations in the facial plane with local anesthetic, which has been suggested by Blanco et al (14). Another opinion is the paravertebral spread through the endothoracic fascia which is the continuation of the transversal fascia due to its anatomic structures (8).

However, in addition to the studies detecting paravertebral spread in cadaver studies, there are also studies presenting different findings (15-18). Dam et al. have commented rather on the anterior QLB in cadaver studies and reported that paravertebral spread is detected at a significant level (15). Another study has reported that the local anesthetic substance administered to the quadratus muscle laterally and posteriorly has similar spreads. They have stated that the involvement of lumbar plexus by posterior QLB is possible (16).

Whereas Kumar et al. have indicated that paravertebral spread is not possible and presented the fact that the local anesthetics administered though paravertebral route did not spread to the lumbar region in previous studies as the pivotal point (17). Their theory was that the effect of OLB block on visceral pain was through the sympathetic chain or celiac ganglion blockade (17). On the other hand, the inability of cadaver studies to show the full extent of local anesthetic spread in the living body seems to be a disadvantage (18). For the activity mechanism of QLB, which is a new regional block, to meet at a common point, more studies seem to be needed.

Whereas, the results of our study were similar to those studies conducted on QLB. Postoperative VAS and opioid consumption amounts of the injections administered to the quadratus muscle laterally and posteriorly were similar in laparoscopic cholecystectomy operations. The discriminating point between these two types of blocks appears to be the anatomical location of the injection site. Previous studies have noted that interventions directed to the posterior part of the quadratus lumborum muscle may be safer due to the fact that the intervention area is closer to the intra-abdominal organs (10).

Study Limitation

The limitations of the study include not having monitored the block level although block was administered preoperatively and the fact that the patients were not followed up for longer than 24 hours. Another limitation is that we could not calculate tramadol consumption at specific time intervals and we didn't measure the amount of gas used for pneumoperitoneum.

CONCLUSION

Similar postoperative tramadol consumption values and VAS scores were determined in both lateral QLB and posterior QLB applications in the results of our study. Therefore, we suggest that both injections are effective in analgesia after laparoscopic cholecystectomy. The ease in ultrasound imaging and anatomical neighborhoods may be the reason for the preference of QLB type to be administered.

Ethics Committee Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent: Informed consent was obtained from all individual participants included in the study.

Peer-review: Externally peer-reviewed.

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

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

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ORİJİNAL ÇALIŞMA-ÖZET
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Laparoskopik kolesistektomi sonrası postoperatif ağrı için ultrason kılavuzluğunda lateral ve posterior Quadratus Lumborum Bloğu: Randomize kontrollü çalışma

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ÖZET

Giriş ve Amaç: Bu çalışmanın amacı, ultrasonografi eşliğinde yapılan bilateral posterior Quadratus Lumborum Blok (QLB) ve lateral QLB'nin laparoskopik kolesistektomi sonrası postoperatif ağrı skorlarına etkisini araştırmaktır.

Gereç ve Yöntem: Bu prospektif, randomize, tek kör çalışmada; elektif laparoskopik kolesistektomi operasyonu geçirecek 60 hasta grup P (n= 30): Posterior Quadratus Lumborum Blok + IV hasta kontrollü analjezi (PCA) tramadol ve grup L (n= 30): Lateral Quadratus Lumborum Blok + IV PCA tramadol olacak şekilde randomize edildi. Primer sonuç ölçütleri toplam tramadol tüketim (24 saat) miktarını içermektedir. İkincil sonuç ölçütleri ise dinlenme ve hareket halinde "Visüal Analog Scala (VAS)" skorları (postoperatif 30. dakika, 2, 6, 12 ve 24. saat) kaydedildi. Yan etkiler (bulantı ve kusma) ek analjezik gereksinimi, intraoperatif opioid gereksinimi kaydedildi.

Bulgular: Postoperatif toplam tramadol ve VAS skorları (dinlenme ve hareket) karşılaştırıldığında, iki grup arasında istatistiksel olarak anlamlı fark yoktu (p> 0.05).Yan etkiler (bulantı ve kusma), ek analjezik gereksinimi ve intraoperatif opioid gereksinimi açısından iki grup arasında istatistiksel olarak anlamlı fark yoktu (p> 0.05).

Sonuç: Çalışmamızın sonuçlarında hem lateral QLB hem de posterior QLB blok uygulamalarında postoperatif tramadol tüketim değerleri ve VAS skorları benzer olarak belirlendi.

Anahtar Kelimeler: Kolesistektomi, quadratus lumborum bloğu, postoperatif ağrı, laparoskopi, ultrason

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Protoscolicidal effect of oleuropein: an in vitro study

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ABSTRACT

Objective: Hydatid disease is a parasitic disease caused by *Echinococcus granulosus* and is still endemic in many parts of the world. Scolicidal solutions are generally used in any type of intervention, either surgical or percutaneous, to neutralize the cyst contents, although completeness of their effect is obscure and solid evidence is scarce. On the other hand, the use of these scolicidal solutions is not devoid of complications and many serious complications such as caustic sclerosing cholangitis may be seen in relation with their usage. Recent investigations proved protoscolicidal properties of olive leaf extract although the active ingredient has not been attributed to any component. The aim of this experimental study was to isolate oleuropein and test for in vitro protoscolicidal activity.

Material and Methods: Oleuropein, a phenolic compound found in olive leaves, is extracted and prepared in different concentrations. Echinococcal cyst containing livers of sheep are obtained from the government slaughterhouse. Cysts were punctured and live protoscolex suspensions were prepared under aseptic conditions. Different concentrations of oleuropein solutions were prepared and protoscolicidal property is analyzed and compared with positive and negative controls for different exposure times.

Results: Oleuropein 2% concentration was found to be protoscolicidal in all exposure times starting from 5 minutes.

Conclusion: 2% oleuropein is a powerful, natural protoscolicidal agent which should be evaluated clinically before its application in routine treatment practice.

Keywords: Echinococcus granulosus, hydatid cysts, therapy, olive tree

INTRODUCTION

Hydatid disease caused by *Echinococcus granulosus* continues to be a problem in many parts of the world including the Mediterranean Basin. In our country, sporadic cases still exist despite previous efforts to eradicate the disease (1). Surgery is the mainstay of treatment although PAIR (percutaneous aspiration injection and re-aspiration) under sonographic guidance is also available for some stages of the cysts (2,3). During the surgical or interventional treatment of the disease, aspiration of the contents and injecting scolicidal solutions into the cyst cavity to neutralize the parasitic elements are commonly used steps. Cetrimide, alcohol, and hypertonic NaCl solutions are the most preferred solutions to neutralize the parasite during these procedures. However, some has hazardous effects to the biliary epithelium and most are heavily concentration-dependent and does not have the chance to neutralize the contents in large or septated cysts. These unfavorable factors and lack of solid evidence about their effectiveness stimulate continuous and new efforts to find a novel scolicidal effective and yet devoid of complications if there is any. There are different substances used for this purpose and many synthetic and natural products have been investigated in terms of their scolicidal effect.

One of the natural substances is the olive leaf extract. Fresh olives and olive leaves have a bitter taste because of oleuropein, a phenolic compound (Figure 1). It is secoiridoid and its level in olives declines rapidly during maturation (4). Oleuropein has pharmacological effects including antioxidant, anti-inflammatory, anti-atherogenic, anti-cancer and antimicrobial activities (4). Reported antimicrobial and antiparasitic activities stimulate this experimental study, in which the scolicidal properties of oleuropein were evaluated.

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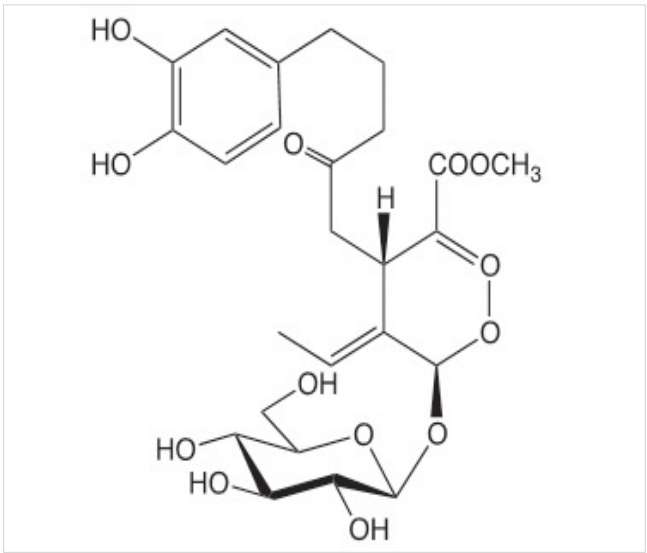

Figure 1. Chemical structure of oleuropein.

MATERIAL and METHODS

This study was conducted in the laboratories of Near East University. Olive leaves were obtained from the olive trees of our country. The voucher specimen was deposited in the Herbarium of Near East University. Ethics committee approval was obtained when this study started (The ethics committee number is Near East University 2018/55-537). The authors do not have any conflict of interest and no financial support from any institution was provided for this study.

Extraction and isolation: The air dried and powdered leaves (200 g) were extracted with 80% EtOH (1000 mL) by shaking three days at room temperature and filtered. The filtrate was concentrated to 80 mL in vacuum at 50°C and washed with chloroform (80 mL 3) to remove lipophilic compounds. The remaining aqueous phase was applied to vacuum liquid chromatography (LiChroprep RP-18; 25-40 mm; column dimensions: 105 x 42 mm) employing H_2O-MeOH mixtures with increasing amount of MeOH in H_2O (0-100% MeOH). For each 100 mL of eluents, the MeOH ratio was increased by 5% MeOH. The fractions eluted with 45, 50 and 55% MeOH were rich in oleuropein (958 mg, 793 mg and 302 mg, respectively). 400 mg of crude oleuropein was further subjected to a Sephadex LH-20 column using a solvent system of MeOH-H_2O (1:1) to yield pure oleuropein (208 mg).

Oleuropein: The ^{1}H- and ^{13}C-NMR (500 and 125 MHz, respectively; CD3OD) data was superimposable with those of the reported (5).

Preparation of protoscolex suspension: Infested sheep livers containing hydatid cysts were collected from the governmental slaughterhouse and locally cleansed with povidone iodine solution in the laboratory. Cysts were punctured under aseptic conditions and hydatid fluid was aspirated and collected in a sterile container. The cysts were opened by a scissor and the hydatid sediment was aspirated by a pipette. Then the germinative membrane was extracted and rinsed with the cyst fluid in the container to free additional protoscoleces and hydatid sand. Cyst fluid was preferred for the short period storage of protoscoleces for mimicking the hydatid cysts conditions. The suspension was allowed to settle, and the protoscolex viability was confirmed under light microscopy. Living protoscoleces show characteristic mobility and do not take the dye (0.1% eosin) (2,3,6).

Study Design

Oleuropein solutions were prepared in 3 different concentrations of 0.1%, 1.0% and 2.0% for the study groups. Two mL of each solution was put in a test tube. 10% formalin, a known powerful protoscolicidal, was used as a positive control and hydatid fluid containing protoscoleces was the negative control group. Definition of the groups was as follows:

Group I: 0.1% oleuropein

Group II: 1.0% oleuropein

Group III: 2.0% oleuropein

Group IV: 10% formalin (positive control)

Group V: Hydatid fluid (negative control)

Time table: A drop of viable protoscolex-rich sediment was added to the oleuropein and positive control solutions with a pipette. Protoscoleces and brood capsules were allowed to settle down and specimens were taken after 5, 10, 15, 20 and 30 minutes from the sediment of the test tube.

Viability evaluation: All specimens were instantly placed on glass slides and a drop of 0.1% eosin was added and the slide was covered by a lamelle. Light microscopy was used instantly for the evaluation of protoscolex viability. The evaluation was performed under blinded conditions. If all protoscoleces are darkly stained and no characteristic movement was seen, it was defined as "Dead = inactive". The result was noted as "Live = active" with the confirmation of at least one live (unstained and/or moving) protoscolex.

RESULTS

Group I (0.1% Oleuropein)

This concentration of oleuropein did show a very weak and slow protoscolicidal effect in our study. Peripheral scoleces in brood capsules were affected after 20 minutes of exposure, but central ones were apparently normal (Figure 2). All specimens contained viable protoscoleces on examination at the end of 30 minutes.

Group II (1% Oleuropein)

This concentration of oleuropein solution did not inactivate protoscoleces for the first 15 minutes. All specimens taken after 5, 10 and 15 minutes contained viable protoscoleces. All protoscoleces were inactivated after 20 and 30 minutes of exposure with 1% oleuropein.

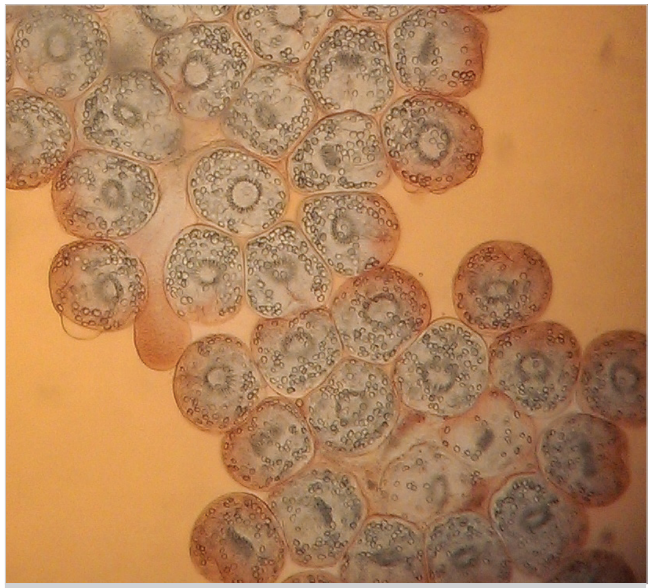

Figure 2. Scoleces in brood capsules after 20 minutes of exposure. Peripheral scoleces were affected but central ones were apparently normal.

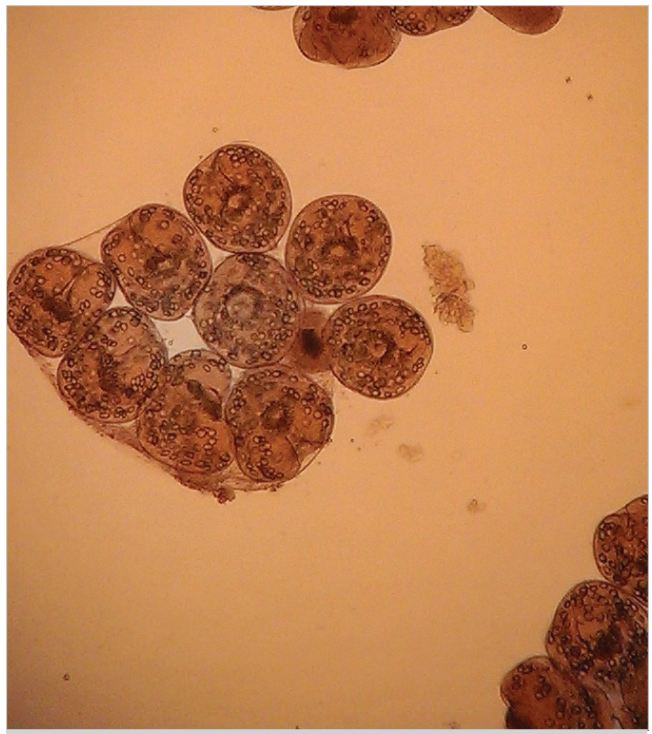

Figure 3. Complete protoscolicidal effect of olueropein. Dead scoleces were darkly coloured and the surroundings were tinted.

Group III (2% Oleuropein)

When the concentration of oleuropein was elevated to 2%, protoscolicidal effect was seen in all exposure times beginning from the 5th minute. The scoleces were darkly colored and the surroundings was tinted (Figure 3).

Group IV (10% Formalin)

All protoscoleces were dead in all exposure times starting from 5 minutes.

Group V (Hydatid fluid)

All protoscoleces were live in all exposure times till 30 minutes.

Results are summarized in Table 1.

DISCUSSION

Although injecting a scolicidal solution is a widely-used practice during surgical or radiological intervention for the treatment of hydatid cyst, the objective evidence regarding the effect of this is controversial as there are studies confirming viable protoscoleces after proper usage of the most effective scolicidal agents, especially in the germinative membrane imprints (6). In addition, the usage of scolicidal agents may be related with serious side effects and complications, such as caustic sclerosing cholangitis, sclerosing peritonitis, metabolic acidosis and some other biochemical abnormalities may be seen (7-9). Despite these unfavorable factors, injecting a scolicidal solution is a must especially in PAIR and in a surgical intervention when the cyst cavity has to be intervened. To enter a cyst cavity that may harbor thousands if not millions of viable protoscoleces without sterilizing is a risk, as each one of these are capable to produce a new cyst in case of a leakage to the peritoneal cavity.

Olive tree (Olea europeana) is an endemic widespread small tree found mainly in Mediterranean countries as well as California, South America and parts of the Indian Ocean. Olive oil and olive fruit is an important component of Mediterranean diet, and products associated with olive tree are known to provide commercial products such as food, cosmetics and medicine. Oleuropein is the most prominent phenolic compound found both in the fruit and leaves of olives (4,10,11) and is the cause of characteristic bitterness of green olive fruits (12). Phenolic compounds are found in all parts of the olive plant and can reach concentrations of up to 140 mg/g on a dry matter basis in young olives and 60-90 mg/g of dry matter in the leaves (4). Oleuropein has pharmacological effects including antioxidant, anti-inflammatory, antiatherogenic, anticancer, antimicrobial and hypolipidemic activities.

Protoscolicidal effect of 0.1% olive leaf extract was confirmed in prior studies. This effect is seen in prolonged exposure and as the extract contains numerous chemicals this effect can be attributed

Table 1. Different oleuropein concentrations and their protoscolicidal activity in exposure times up to 30 minutes

	Exposure time (minutes)-viability				
Group	**5**	**10**	**15**	**20**	**30**
Group I (0.1% oleuropein)	L	L	L	L	L
Group II (1% oleuropein)	L	L	L	D	D
Group III (2% oleuropein)	D	D	D	D	D
Group IV (10% formaline)	D	D	D	D	D
Group V (hydatid fluid)	L	L	L	L	L

L: Live; D: Death.

to various substances (10,13). Primary medical constituents contained in unprocessed olive leaf are oleuropein, hydroxytyrosols and many other flavonoids (10). Oleuropein has been shown to have strong antimicrobial activity against gram-negative and positive bacteria. Antiviral activity against herpes mononucleosis, hepatitis virus, rotavirus, respiratory syncytial virus and parainfluenza type 3 virus is also attributed to oleuropein (4). In terms of antiparasitic effects, oleuropein has been found to show leishmanicidal activity as well as anti-toxoplasmic activity (14,15). To the best of our knowledge, this study is the first in which oleuropein is isolated and used as a single active ingredient in terms of protoscolicidal activity.

In this study, oleuropein showed a considerable protoscolicidal activity in a concentration dependent fashion, as 0.1% oleuropein was unsuccessful in terms of killing the protoscoleces in half an hour but when the concentration was increased to 2%, it acted as a powerful protoscolicidal in relatively shorter exposure times like 5 minutes. An ideal scolicidal agent should be effective in 5-10 minutes as it will be impractical to wait more after injecting a cyst during a surgical intervention. Waiting shorter periods puts the patient theoretically in a risk of secondary hydatidosis in case of a spillage if encountered during the surgery. With the isolated form of oleuropein instead of olive leaf extract, we chose shorter exposure times in contrast to a previous study (13). As stated before, these shorter exposure times are more convenient for surgical intervention, and if oleuropein was the agent responsible from protoscolicidal effect of olive leaf extract, using it as a pure substance may enhance its activity. Longer exposure times may be feasible not for the surgical setting but for PAIR (puncture-Aspiration-Injection-Re-aspiration).

Overall, oleuropein is a rewarding substance found in olive leaves that has protoscolicidal property. It should be thoroughly analyzed for the potential side effects and toxicity in further studies before administering it as the agent of choice.

CONCLUSION

2% oleuropein is a powerful, natural protoscolicidal agent which should be evaluated clinically before its application in routine treatment practice.

Ethics Committee Approval: Ethics committee approval was obtained when this study started. The ethics committee number is Near East University 2018/55-537.

Peer-review: Externally peer-reviewed.

Author Contributions: Consept - K.A., H.B.; Design - A.Ö., K.A.; Supervision - N.Ö., K.A.; Resource - K.A., H.B.; Materials - K.A., H.B., İ.Ç.; Data Collection and/or Processing - K.A, İ.Ç.; Analysis and Interpretation - K.A., H.B., N.Ö.; Literature Search - A.Ö., N.Ö., Writing Manuscript - H.B., K.A., Critical Reviews - N.Ö., K.A., H.B.

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

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ORİJİNAL ÇALIŞMA-ÖZET
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Oleuropeinin protoskolisidal etkisi: Deneysel çalışma

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ÖZET

Giriş ve Amaç: Hidatik kist hastalığı, *Echinococcus granulosus*'un neden olduğu paraziter bir hastalıktır ve hala dünyanın birçok yerinde endemik olarak görülmektedir. Kist hidatik operasyonu sırasında veya perkütan müdahalelerde şimdiye kadar sıklıkla kullanılan skolosidal solüsyonların parazit üzerinde tam etkilerine yönelik sağlam kanıtlarının olmaması ve sklerozan kolanjit gibi ciddi ve diğer komplikasyonlara yol açması başka skolosidal ajanlar üzerinde çalışmalar yapılması gerektiğini zorunlu kılmıştır. Son araştırmalar zeytin ağacı yaprağından elde edilen ekstrelerden hazırlanan oleuropein bileşiğinin protoskolosidal özelliğini kanıtlamıştır. Bu deneysel çalışmanın amacı, oleuropeini izole ederek in vitro protoskolosidal aktivitelerini değerlendirmektir.

Gereç ve Yöntem: Zeytin yapraklarında bulunan bir fenolik bileşik olan oleuropein, farklı konsantrasyonlarda ekstrakte edilerek hazırlandı. Devlet Mezbahasından elde edilen kist hidatikli koyun karaciğerlerinden aseptik koşullar altında protoskoleks solüsyonları ayrıştırıldı. Farklı konsantrasyonlarda hazırlanan oleuropein ekstreleri protoskoloekslerin üzerine tatbik edilerek canlılık süreleri analiz edildi ve pozitif-negatif kontrollerle karşılaştırıldı.

Bulgular: Oleuropeinin %2'lik konsantrasyonunun 5. dakikadan başlayarak tüm zaman birimlerinde protoskolisidal etkisinin olduğu bulundu.

Sonuç: %2'lik oleuropein, rutin tedavi uygulamasından önce klinik olarak değerlendirilmesi gereken güçlü ve doğal bir protoskolosidal ajandır.

Anahtar Kelimeler: Kist hidatik, tedavi, oleuropein

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ORIGINAL ARTICLE
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Comparison of minimally invasive preperitoneal (MIP) single-layer mesh repair and total extraperitoneal (TEP) repair for inguinal hernia in terms of postoperative chronic pain: a prospective randomized trial

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ABSTRACT

Objective: The aim of this study was to compare minimally invasive preperitoneal (MIP) single layer mesh repair with total extraperitoneal (TEP) inguinal hernia repair in terms of complications, recurrence, and chronic pain.

Material and Methods: A total of 240 patients who underwent elective, primary, unilateral inguinal hernia operation between April 2011 and September 2012 were divided into two randomized groups. The f rst group underwent MIP repair and the second group underwent TEP repair. Visual Analogue Scale (VAS) and Shef eld Scale (SS) were used to evaluate chronic pain.

Results: In all, 225 (95%) of the patients completed follow-up and were included in analyses. A signif cant dif erence was not detected between groups in terms of demographics, operative time, or intraoperative, early, or late complications. Length of time before return to work was signif cantly shorter in the TEP group ($p< 0.001$). Recurrence was seen in 1 (0.88%) patient in the MIP group and 1 (0.89%) patient in the TEP group ($p= 0.993$). Evaluation of chronic pain revealed no signif cant dif erence between groups in VAS and SS values at postoperative 6th, 12th, and 24th months.

Conclusion: In conclusion, it was observed that MIP repair for inguinal hernia has all of the advantages of preperitoneal repair and eliminates disadvantages of TEP repair. MIP technique is as safe as TEP repair and has similar qualities in terms of chronic pain, even though it is an open intervention.

Keywords: Chronic pain, inguinal hernia, preperitoneal repair, total extra peritoneal repair

INTRODUCTION

High recurrence rates have been observed in classic hernia repairs due to the tension created when tissue is pulled together to close myopectineal orifice. Newer tension-free techniques have led to greatly diminished recurrence rates. This is an advantage; however, pain and fibrosis that can develop due to the mesh used are important subjects of discussion (1).

Although most related studies have examined Lichtenstein and laparoscopic repairs, it may be a mistake to make direct comparison of the two techniques. In the Lichtenstein repair, mesh is placed on premuscular layer, not preperitoneal surface, as in laparoscopic techniques. Therefore, it may be more useful to compare open and laparoscopic techniques that are similar in terms of dissection site, use of preperitoneal plane for mesh placement, and surfaces covered by the mesh. Review of the literature yielded no prospective randomized trials comparing chronic pain and long-term results of TEP and Kugel methods of repair.

The aim of this study was to prospectively examine minimally invasive preperitoneal (MIP) single-layer mesh repair with total extraperitoneal (TEP) repair in terms of operative time, length of time before return to work, early and late period complications, recurrence, and chronic pain.

MATERIAL and METHODS

This prospective, randomized study was conducted at the General Surgery Clinic of Konya Education and Research Hospital after having received approval of the ethics committee of Uşak University Medical School. Patients who presented to general

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surgery polyclinics of the hospital and who were scheduled to undergo surgery for inguinal hernia between April 2011 and September 2012 were assessed. Patients who met the study criteria were informed about the goals and content of the study preoperatively, and written consent was obtained from participants.

Patients over the age of 18 who were to undergo elective, unilateral inguinal hernia repair were included in the study. Recurrent cases that had already undergone hernia repair to the same side, patients with systemic disease (American Society of Anesthesiology Classification IV patients) that led to general disorders, and those who had undergone laparotomy for prostate, bladder, or in iliac region were excluded.

Patients who met the study criteria were enrolled beginning in April 2011 and inclusion was terminated in September 2012. Study was conducted with a total of 240 patients randomly divided into two groups of 120 using a computer program. One group underwent MIP repair and the other had TEP repair. Follow-up period was determined to be a minimum of 24 months. Study was concluded in September 2014. Information related to the patients who could not be followed up for any reason was not included in the analyses. Calculations were made using the data of the patients who completed follow-up and whose files did not have any missing information or otherwise, the participant was excluded.

Primary endpoints this study assessed were peroperative groin pain and postoperative 6th, 12th, and 24th months with VAS and SS. Secondary endpoints were operation time, length of hospital stay, time of return to work, complications, and recurrence.

The questionnaires were made until the 24th month: however, the patients were followed up until 36 months for recurrence.

Two hundred and twenty patients were included into to this study. This sample size was adequate to determine inter-ratio reliabilities described by Gheorghe D and Robert L. Considering that 10% of the patients would be lost during follow-up, 240 patients were included into the study (2).

Surgical Method

All procedures were performed by two experienced surgeons or under their supervision. General anesthesia was given to all patients in the TEP group. Predominantly, spinal anesthesia was used for the MIP group, and general anesthesia was used when necessary. Local anesthesia was not administered to any patients. All patients were intravenously administered 1 g cefazolin sodium as prophylactic.

Minimally Invasive Preperitoneal (MIP) Single-Layer Mesh Repair

This technique can be defined as a modification of Kugel repair. Surgical technique is similar; however, the mesh used has different qualities. Two-layer mesh with extreme polypropylene load is used in Kugel hernia repair, which leads to greater cost and increased foreign object reaction (Kugel's Patch; Surgical Sense, Inc., Arlington, TX, USA).

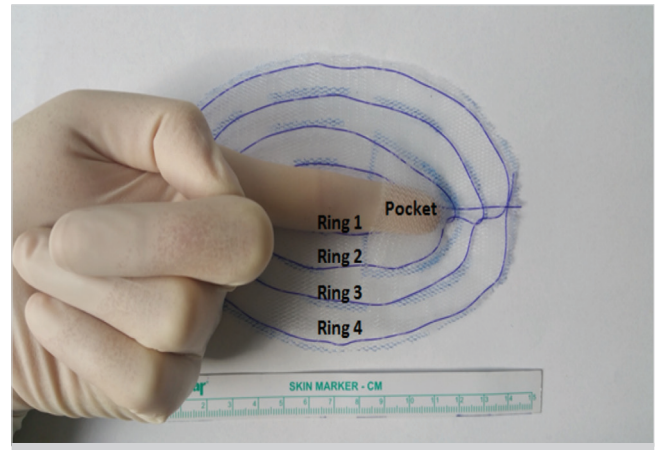

Figure 1. Single-layer mesh used in MIP repair.

Monofilament 38g/m^2 polypropylene mesh, 15 x 15 cm in size, was used in MIP repair (Supromesh; Sayın Tıp Ticaret, İstanbul, Turkey). The mesh was cut to oval shape, 14 x 9 cm in size, and 4 memory recoil rings were added to the prepared mesh with absorbable monofilament synthetic polydioxanone suture (Pedesente, Doğsan Surgical Sutures, Ankara, Turkey). In size 2 x 2 cm pocket added on the prepared mesh with the same material. This pocket was created for the surgeon's index finger during blind placement of the mesh in the preperitoneal space. Polypropylene load is reduced in comparison to the original mesh of Kugel repair. Specially prepared mesh was then sterilized with hydrogen peroxide and packaged for use in MIP repair (Figure 1).

Surgical Technique

A 3-cm skin incision was made two-thirds medial and one-third lateral to the line connecting pubic tubercle with spina iliaca anterior superior. After passing through subcutaneous tissue and Camper's and Scarpa's fasciae, aponeurosis of abdominal external oblique muscle was opened parallel to fibers while protecting nerves.

Transverse fascia was reached by opening in the direction of abdominal internal oblique and transverse muscle fibers. Transverse fascia was opened perpendicularly to the abdominal incision so as not to injure inferior epigastric artery and vein, and preperitoneal space was entered.

In case of indirect hernia, hernia sac can usually be easily separated from the spermatic cord. When that is not possible, the sac is cut at the level of distal deep inguinal ring, left inside the inguinal canal, and closed proximally.

Dissection was continued until there was 3 to 4 cm between the peritoneum and the cord and its elements. After completing the dissection of the hernia sac, a pocket was made in the

preperitoneal space for mesh placement with blunt dissection. Pocket reached to pubic symphysis medially, 3 cm lateral to deep inguinal ring, and 3 cm under inguinal ligament and over conjoint tendon. The mesh was placed blindly in the preperitoneal space. Then with thw help of a retractor, three-fifths of the mesh was over the inguinal ligament and two-fifths was underneath. If spinal anesthesia was used, the patient was asked to cough to check the positioning of the mesh and whether there was any herniation. If necessary, the mesh was re-positioned. In patients under general anesthesia, positioning was confirmed once the patient awoke from anesthesia. The mesh cannot be fixed anywhere after it has been placed; however, the suture is attached by passing from the mesh when transverse fascia is closed. Following layers are closed in their anatomical order.

Laparoscopic Total Extraperitoneal (TEP) Repair

The procedure was performed under general anesthesia. The patient was put in supine and 15-degree Trendelenburg position. The surgeon stood on side opposite to the site where hernia repair would take place, and camera assistant and nurse stood opposite the surgeon. Patients had preoperatively emptied bladder and no urinary catheters were used.

One 10-mm and two 5-mm trocars were used in all patients. Following the incision under umbilicus toward the herniated site, 10-mm trocar was inserted. Two 5-mm trocars were placed over the midline, one 2 cm over the pubic symphysis and the other between the umbilicus and the first trocar. Anterior rectus sheath was reached with 2 cm incision to the sub-umbilical region. Sheath was opened with transverse incision to reach the rectus muscle and posterior rectus sheath. Following blunt dissection, preperitoneal space was enlarged by entering the space formed with 10-mm trocar. At this stage, carbon dioxide was added at pressure of 10 mmHg. Pubic symphysis was reached with angled laparoscope (30°). Dissector with curved tip and flat grasper were generally used for dissection. Dissection continued toward the rectus muscle until reaching the location where sub-umbilical was above, midline medial, Retzius space below, Bogros region inferolateral, and anterior superior iliac spine. Guide points such as pubic symphysis, Cooper's ligament, pubis, inferior epigastric vessels, spermatic cord and its elements, myopectineal openings, and fascia of the psoas muscle were fixed. Hernia sac was revealed and all adhesions were removed as far as the peritoneum. Sac and testicular veins were separated from the posterior margin of vas deferens. Hernia sac was separated from the cord structure. The openings formed in the peritoneum during dissection were sutured. In case of large direct hernia, widened transverse fascia was fixed to Cooper's ligament by rotating it inwardly. Non-absorbable monofilament polypropylene mesh, approximately 16 x 12 cm in size according to patient anatomy, was prepared and inserted to the field in a roll. The mesh was uniformly spread out after placement such that it reached at least 2 cm under Cooper's ligament and passed through midline, covering the pubis bone after stapling to Cooper's ligament. Non-absorbable titanium tack (ProTack 5 mm fixation device, Covidien, Dublin, Ireland) was used for fixation in TEP repair. Five tackers were used (3 on pubis and Cooper's ligament and remainder on medial part of inferior epigastric vessels, transverse fascia, and superior lateral side with bimanual technique) in the fixation procedure to avoid use of stapler on the lateral side of the external iliac artery and vein or the inferior side of the lateral of the ileopubic tract. Gas was released slowly under direct vision. Fascia at location of 10-mm trocar was approximated with absorbable suture material, and skin incision was approximated with non-absorbable suture material.

Physical examination determined the type of hernia and was confirmed by findings during operation.

Evaluation of Patient Characteristics and Chronic Pain

Demographic information (age, gender, body mass index [BMI]) of the patients, hernia type according to Gilbert classification as modified by Rutkow and Robbins, operative time from first skin incision to closure, perioperative and postoperative early complications, and length of hospital stay were recorded in files prepared specifically for this study.

Postoperatively, all patients were called for a follow-up visit at the end of 1 week. Patients were then called for routine visits in postoperative 1st, 6th, 12th and 24th months. Annual follow-up was recommended after postoperative first year. Necessary work-up was requested for patients in whom pathological findings or suspected findings were detected during follow-up visits, and those patients were called for follow-up visits at more frequent intervals for appropriate treatment. Postoperative complications and length of time to return to work or return to physical activity for those who were not working were recorded.

A questionnaire was administered to all patients preoperatively and at 6th, 12th, and 24th postoperative months to evaluate pain. Patients who could not come to long term follow-up visits were reached by phone and questioned regarding hernia repair. Visual Analogue Scale (VAS) was used simultaneously with the Sheffield Scale (SS) to determine pain severity and make comparison.

Visual Analogue Scale (VAS)

The scale was composed of a horizontal line, 100 mm in length. The phrase "No pain" appeared at the left end of the line, and the phrase "Excruciating pain" appeared at the right end. Patient was asked to mark the spot on the line best describing their pain. Distance of the mark to the left end is measured in millimeters and reported as "score."

Sheffield Scale (SS)

Pain with regard to physical activity was also assessed with simple three-point scale. Patients were asked to rate their experience as follows: 0: Patient feels no pain; 1: There is no pain during rest but

pain manifests itself during movement; 2: There is occasional pain during rest, but it is mild during movement; 3: Pain is constantly present during rest and intensifies during movement. High values are associated with severity of chronic pain and low quality of life. As scale is simple to understand and does not require the patient to provide excessive detail or time to administer, it is considered a very useful assessment tool.

Statistical Analysis

All statistical analyses were performed by SPSS software, version 16.0 (SPSS, Inc., Chicago, IL, USA). Categorical data were presented as frequencies and percentages, and continuous variables were presented as mean ± standard deviation in tables. Kolmogorov-Smirnov test was applied to determine if numerical values correlated with normal distribution. Mann-Whitney U test was performed to compare two population means. Chi-square test was used to compare categorical variables across groups . p value of less than 0.05 was considered as statistically significant in all analyses.

RESULTS

Of the 269 patients who presented to the general surgery polyclinics and met the criteria of the study, 29 declined to participate and were excluded. A total of 240 patients who accepted the conditions of the study were randomly divided into 2 groups: 120 in MIP group and 120 in TEP group.

In the MIP group, one (0.84%) patient could not be reached for postoperative first month follow-up, 2 (1.7%) patients for 6th month follow-up, 1 (0.84%) patient for 12th month, and 3 (2.5%) patients for 24th month follow-ups. These 7 (5.8%) patients were excluded from the study and data were not included into the analyses. Follow-up rate in the MIP group was 94.2% (Figure 2).

Pneumoperitoneum developed in one patient in the TEP group after perioperative peritoneum damage necessitating Lichtenstein repair. In addition, TEP repair could not be performed on one (0.84%) patient due to surgeon-related and/or technical reasons. One additional patient (0.84%) was excluded upon detecting urolithiasis during follow-up in order not to influence pain scores. Those two (1.7%) patients were excluded from the study. In the TEP group, two (1.7%) patients could not be reached for sixth month follow-up, and 4 (3.4%) could not be reached for 12th month follow-up; therefore, these 6 (5%) patients were also excluded. Follow-up rate in the 120 patients included in the TEP group was 93.4%. Analyses were conducted with the data of a total of 225 patients, 113 (50.2%) in the MIP group, and 112 (49.8 %) in the TEP group.

Majority of the patients had indirect inguinal hernias (Table 1).

General anesthesia was used for all patients in the TEP group (n= 112), and 14 patients (13.3%) of the 113 included in the MIP group; the remainder of the MIP group patients received spinal anesthesia.

No statistically significant difference was detected in terms of age, gender, BMI, operative time, length of hospital stay, or mean follow-up period between the groups (Table 2).

Period before return to work/daily activities was significantly shorter in the TEP group (p< 0.001) (Table 2).

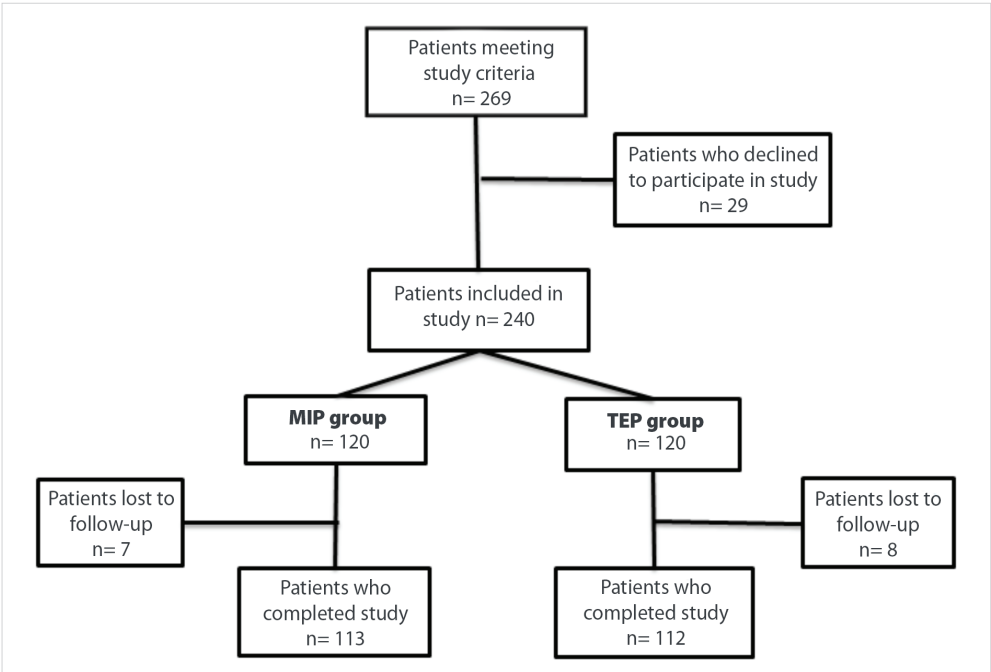

Figure 2. Patient follow-up chart.

Table 1. Hernia type according to Gilbert classification system as modified by Rutkow and Robbins

	MIP n= 113	TEP n= 112
Type 1 Indirect hernia, intact inner ring	18	16
Type 2 Indirect hernia, extended inner ring ≤ 4 cm	52	49
Type 3 Indirect hernia, inner ring > 4 cm	15	16
Type 4 Direct hernia, posterior wall of inguinal canal is defective	18	20
Type 5 Direct hernia, diverticular defect in suprapubic position	1	0
Type 6 Simultaneous direct and indirect component	8	8
Type 7 Femoral hernia	1	3

MIP: Minimally invasive preperitoneal; TEP: Total extraperitoneal.

Table 2. Demographic characteristics and follow-up

	MIP n= 113	TEP n= 112	p
Age	44.8 9 ± 13.692	44.28 ± 14.051	0.738
Body mass index	27.20 ± 8.24	25.92 ± 3.58	0.669
Operative time (minutes)	41.73 ± 16.06	43.26 ± 14.81	0.132
Length of hospital stay (days)	1.05 ± 0.26	1.04 ± 0.28	0.494
Period before return to work (days)	8.66 ± 1.55	7.16 ± 1.43	**< 0.001**
Follow-up (months)	33.12 (24-36)	33.43 (24-36)	0.639

Data expressed as mean value ± SD. Value in bold indicates statistical significance. MIP: Minimally invasive preperitoneal; TEP: Total extraperitoneal.

Complications developed in a total of 16 patients (14.16%) in the MIP group. As perioperative complication, inferior epigastric vessels of one patient (0.88%) were damaged and ligation was performed to stop hemorrhage. No additional complications were observed during postoperative follow-up of the patient. Postoperative early complications included pseudo hernia in 2 (1.76%) patients, seroma in 5 (4.42%) patients, cord edema in 3 (0.88%) patients, scrotal edema in 1 (0.88%) patient, ecchymosis in 1 (0.88%) patient, hematoma in 1 (0.88%) patient, and wound-site infection in 1 (0.88%) patient. At sixth month visit, results for both patients with pseudo hernia were normal. Four instances of seroma had resolved at the end of 1 month, and fifth seroma was aspirated with injector upon observation of swelling. Follow-up was normal after aspiration. Cord edema, scrotal edema, and ecchymosis findings regressed in the first month of follow-up. Though there was no perioperative hemostasis difficulty, hematoma developed postoperatively in one patient. It was medically treated without drainage, as was not large and no growth was detected. First month follow-up of the patient was normal. Oral anti-biotherapy was administered to one patient who developed wound-site infection on postoperative day 5. Skin findings were normal at the second week follow-up visit and no additional treatment was required. Recurrence was detected in one patient (0.88%) in the MIP group. Lichtenstein repair was performed on the 20th month of follow-up, and it was observed that recurrence was the result of migration of the mesh (Table 3).

Complications were observed in a total of 14 (12.50%) patients in the TEP group. Early postoperative complications included pseudo hernia in 6 (5.35%) patients. Swelling in five patients disappeared at third month follow-up; however, upon seeing that it persisted in one patient, ultrasonography was performed and the condition was monitored to make sure there was no recurrence. Pseudo hernia regressed at sixth month follow-up. Seroma developed in 5 (4.46%) patients, but all regressed after 1 month. Hematoma that developed in 1 (0.89%) patient was resorbed on the 45th day without necessitating further intervention. Scrotal edema that developed in 1 (0.89%) patient was seen to have regressed at first month follow-up visit.

Recurrence was detected in the 12th month in 1 (0.9%) patient in the TEP group, and Lichtenstein procedure was performed.

No significant difference between the groups was observed in terms of postoperative early complications or recurrence (Table 3).

Chronic pain was assessed preoperatively and postoperatively at 6, 12 and 24 months using visual analogue scale (VAS) and Sheffield pain scale (SS). Preoperative assessment of the patients revealed that 64 (28.4 %) patients had no pain, 66 (29.3%) patients reported pain in activities but no pain at rest, 71 (31.5%)

Table 3. Complications and recurrence

	MIP n= 113 n (%)	TEP n= 112 n (%)	p
Recurrence	1 (0.88)	1 (0.89)	0.993
Pseudo hernia	2 (1.76)	6 (5.35)	0.147
Seroma	5 (4.42)	5 (4.46)	0.989
Cord edema	3 (2.65)	0	0.083
Scrotal edema	1 (0.88)	1 (0.89)	1.000
Ecchymosis	1 (0.88)	0	0.322
Hematoma	1 (0.88)	1 (0.89)	0.995
Wound-site infection	1 (0.88)	0	0.319
Inferior epigastric vessel damage	1 (0.88)	0	0.319

MIP: Minimally invasive preperitoneal; TEP: Total extraperitoneal.

Table 4. Distribution of preoperative Sheffield Scale scores

	MIP n= 113	TEP n= 112	Total n (%)
0: No pain	31	33	64 (28%)
1: Pain present only during movement	34	32	66 (29%)
2: Occasional pain during rest, mediocre pain present during movement	37	34	71 (32%)
3: Pain present constantly during rest, severe pain during movement	11	13	24 (11%)

MIP: Minimally invasive preperitoneal; TEP: Total extraperitoneal.

Table 5. Mean pain scores of the groups and p value over time

		MIP Group	TEP Group	p
Preoperative Period	Visuale analoque scale (VAS)	23.54 ± 2.13	23.21 ± 2.14	0.893
	Sheffield scale (SS)	1.25 ± 0.09	1.24 ± 0.11	0.925
Postoperative 6th month	Visuale analoque scale (VAS)	3.1 ±0.76	2.86 ± 0.69	0.927
	Sheffield scale (SS)	0.19 ± 0.04	0.16 ± 0.04	0.954
Postoperative 12th month	Visuale analoque scale (VAS)	1.86 ± 0.49	1.52 ± 0.41	0.811
	Sheffield scale (SS)	0.14 ± 0.03	0.13 ± 0.03	0.868
Postoperative 24th month	Visuale analoque scale (VAS)	1.59 ± 0.43	1.07 ± 0.31	0.513
	Sheffield scale (SS)	0.13 ± 0.03	0.11 ± 0.03	0.556

MIP: Minimally invasive preperitoneal; TEP: Total extraperitoneal.

patients reported temporary pain at rest but constant pain during activities, and 24 (10.7%) patients reported pain during activities and at rest (Table 4).

Mean preoperative VAS value was 23.54 ± 21.34 in the MIP group and 23.21 ± 21.40 in the TEP group. A significant difference was not detected between the groups (p= 0.893). Mean preoperative total SS score was 1.247 in the MIP group and 1.241 in the TEP group. Also, a significant difference was not detected between the groups (p= 0.925). Mean VAS and SS scores of both groups were similar in postoperative 6th, 12th, and 24th months in terms of chronic pain (Table 5). Mean VAS and SS scores of both groups were similar in postoperative 6th, 12th, and 24th months in terms of chronic pain (Table 5).

DISCUSSION

Inguinal hernia is a common condition affecting all age groups, and is typically treated by general surgeons. High incidence rate and resulting need for repair surgery equate to high economic cost and loss to work force (3,4). Despite being performed so often, there is no agreed optimal method providing patient comfort and low recurrence rates (5). Problem of recurrence

has been reduced to a minimum in tension-free hernia repairs where mesh is used; however, chronic pain that can develop due to mesh has become the primary issue. The most important factor in determining the success of hernia repair is now patient comfort.

As a result of the studies evaluating anterior and posterior placement of mesh in terms of patient comfort, the European Hernia Society recommended in its 2009 guideline regarding hernia repair in adult patients that posterior repair methods are Level 1 B (6). In posterior repair techniques, complications related to the spermatic cord are reduced since the inguinal canal is not dissected, and possibility of chronic inguinal pain is reduced since neural structures remain outside the surgical area (7). Posterior repairs can be performed laparoscopically or as open surgery. In the literature review we conducted, present study authors did not find a prospective randomized study evaluating the effect of repair types on chronic pain, though there are limited number of studies comparing Kugel and TEP repairs. Therefore, in this study, comparison was made of TEP, which has advantages of minimally invasive surgery, and MIP procedure, which is similar to Kugel hernia repair, since both are preperitoneal and posterior repair methods.

Even though laparoscopic inguinal hernia repair has good results as a posterior intervention in terms of patient comfort and recurrence, it has disadvantages such as long surgical learning curve, requirement of general anesthesia, long operative time, and need for special equipment and related high costs. Another repair method eliminating these disadvantages and simultaneously providing patient comfort would be preferable. In this study, an alternative was compared to the laparoscopic method, and results were presented in order to add clarity to the matter.

The mesh used in original Kugel surgery has two layers and excessive polypropylene load. In addition, it is expensive and increases the cost of the surgery. Tissue compatibility of this 2-layer mesh has not been as expected and serious life-threatening complications have developed due to the fact that the mesh eroded surrounding tissue (8). Therefore, the original Kugel mesh was not used in MIP procedure in this study; single-layer polypropylene mesh modified by Arslan and colleagues was used (9). Thus, the difference between the two groups in terms of the mesh used was eliminated.

Both groups were similar with respect to demographics such as age, gender, and BMI. Patients were operated on by surgeons experienced in both techniques so as to avoid errors stemming from the learning curve. Even though operative time was longer in the laparoscopy group, the difference was not statistically significant. Length of hospital stay was also similar in both groups.

Complication incidence rate was 14.2% in the MIP group and 12.5% in the TEP group. In both groups, complications were minor and at a rate similar to that seen in the literature (10,11).

Although high recurrence rate of 25% has been reported in laparoscopic hernia repair early on, this rate has been later reported as 1.9% in an MRC study (12,13). Rate of recurrence for TEP and transabdominal preperitoneal techniques have been reported as 1% to 2% and 0% to 3%, respectively (14). In some meta-analyses, recurrence rates for open surgery and laparoscopic repair have been reported as 1.2% and 2.7%, respectively (15,16). Kugel, in his own study, has reported a 0.62% recurrence rate (17). Transinguinal preperitoneal repair and laparoscopic repairs have been compared in a recent study and recurrence rates have been found as 1.19% and 0.51%, respectively (11). In the present study, 0.88% recurrence was recorded in the MIP group and 0.89% recurrence was seen in the TEP group, consistent with the literature. There was no significant difference between the groups in terms of recurrence.

Preference to use mesh in hernia repair led to significant improvement in recurrence rates and chronic pain has now become the new focus point. In the literature, frequency of chronic pain has been reported as between 12.9% and 53.6%; it is now a more serious and common complication than recurrence (18-22).

Rate of chronic inguinal pain after inguinal hernia repair has been reported as 12% for all hernia repairs, 18% (range: 0%-75.5%) in cases treated with open surgery, and 6% (range: 1%-16%) in laparoscopically treated cases in a study conducted by Aasvang and Kehlet, and lower rate of chronic pain incidence in laparoscopic repairs has been found to be significant when compared to open repairs (23).

Similar to results in the literature, rate of chronic pain in our study was 14.66% in all patients, 15.9% in the MIP group and 13.39% in the TEP group in postoperative 6^{th} month; 13.27% and 11.60%, respectively, in postoperative 12^{th} month; and 13.27% and 10.71%, respectively, in postoperative 24^{th} month. Although frequency of chronic pain in the MIP group was higher than that of the TEP group, difference was not statistically significant.

Return to daily activities or to work is an important criterion in evaluating the success of surgical intervention and is usually associated with postoperative pain status of the patient. Various studies have indicated that laparoscopic hernia repair causes less pain in both early and late periods when compared to open surgeries (24,25). Patients cannot meet the economic needs of their family and are in need of help until they can carry out daily activities on their own. Hence, the length of this recovery period has effects on economy and social life. In our study, the length of time before returning to work or daily activities was

significantly shorter in the TEP group. Although both methods of treatment are minimally invasive, this advantage of the laparoscopic method, as in other surgical interventions, was significantly different in the early postoperative period.

CONCLUSION

It was observed that MIP repair for inguinal hernia has the advantages of preperitoneal repair and eliminates disadvantages of TEP repair. MIP technique is as safe as TEP repair and has similar qualities in terms of chronic pain even though it is an open intervention. The experience of the surgeon, considering the patient's co-morbidities; MIP procedure with a low rate of recurrence and chronic pain; is an alternative to TEP.

Ethics Committee Approval: This prospective, randomized study was conducted at the General Surgery Clinic of Konya Education and Research Hospital after having received approval of the ethics committee of Uşak University Medical School.

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

Peer-review: Externally peer-reviewed.

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ORİJİNAL ÇALIŞMA-ÖZET
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Kasık fıtıklarında tek yama ile minimal invaziv preperitonial (MİP) onarım ve total ekstra peritonial onarım (TEP) metodlarının postoperatif kronik ağrı yönünden karşılaştırılması; prospektif randomize çalışma

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ÖZET

Giriş ve Amaç: Bu çalışmamızda; inguinal hernilerde minimal invaziv preperitonial (MİP) tek kat yama onarımı ile total ekstraperitonial (TEP) onarımının komplikasyonlar, rekürrens ve kronik ağrı yönünden karşılaştırmayı amaçladık.

Gereç ve Yöntem: Nisan 2011 ile Eylül 2012 tarihleri arasında elektif, primer, tek taraf ı inguinal herni ameliyatı uygulanan toplam 240 hasta iki randomize gruba ayrıldı. İlk gruba MİP onarımı yapıldı ve ikinci gruba TEP onarımı yapıldı. Kronik ağrının değerlendirilmesinde Visual Analog Skala (VAS) ve Shef eld Skalası (SS) kullanıldı.

Bulgular: Hastaların %95 (225 hasta)'i takipte kaldı ve analizlere dahil edildi. Demograf k özellikler, ameliyat süresi veya intraoperatif, erken veya geç komplikasyonlar açısından gruplar arasında anlamlı bir fark saptanmadı. İşe dönüş için geçen süre TEP grubunda anlamlı olarak daha kısaydı ($p< 0.001$). MİP grubunda 1 (%0.88) hastada ve TEP grubunda 1 (%0.89) hastada nüks görüldü ($p= 0.993$). Kronik ağrının değerlendirilmesi post-operatif 6, 12 ve 24. aylarda VAS ve SS değerlerinde gruplar arasında anlamlı bir fark olmadığını ortaya koydu.

Sonuç: Sonuç olarak, inguinal herni için MİP onarımının, preperitoneal onarımın tüm avantajlarına sahip olduğu ve TEP onarımının dezavantajlarını ortadan kaldırdığı görülmüştür. MİP tekniği, TEP onarımı kadar güvenlidir ve açık bir müdahale olmasına rağmen, kronik ağrı açısından benzer niteliklere sahiptir.

Anahtar Kelimeler: Kronik ağrı, inguinal herni, preperitonial onarım, total ekstra peritonial onarım

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Non-surgical acute traumatic perianal injuries

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ABSTRACT

Objective: The diagnosis of fecal incontinence is challenging and complex. One of the most significant causes of fecal incontinence is trauma in the perianal area. The most important cause of such trauma is birth trauma. It is hard to evaluate patients and plan treatment. Surgical method is determined by the severity of sphincter damage and injuries formed in the organs in the perianal area. The aim of this study, therefore, was to analyze the cases of patients who had undergone sphincter repair because of acute injuries in the perianal area.

Material and Methods: The cases of 15 patients with perianal area injuries who had presented to Necmettin Erbakan University Meram Medical School's General Surgery Clinic between 2010 and 2015 were retrospectively analyzed. Data on age, sex, form of injury, severity of injury, time of first response, form of repair, injury problems, and post-operative complications of the patients were investigated. The patients' long-term results were analyzed.

Results: While 5 of the patients were male, 10 were female. 9 of the female patients had birth trauma, while one had injury during sexual intercourse. While all of the patients received sphincteroplasty, 10 had levatoroplasty. All the female patients received vaginoplasty.

Conclusion: We are of the opinion that it is significant to have surgical intervention before tissue edema develops.

Keywords: Fecal incontinence, trauma, perianal

INTRODUCTION

Fecal incontinence is a condition that has social and economic effects and disrupts quality of life (1). It is hard to offer an exact definition of fecal incontinence. It can, however, be defined as the failure to control the anal discharge of intestinal content at an appropriate time and place (2). The prevalence, diagnosis, and treatment methods of fecal incontinence have not been clearly ascertained. Many methods used in diagnosis and treatment have been transformed in time (3). The diagnosis of fecal incontinence is challenging and complex. One of the most significant causes of fecal incontinence is trauma in the perianal area. The most important cause of such trauma is birth trauma. It is hard to evaluate patients and plan treatment. Surgical method is determined by the severity of sphincter damage and injuries formed in the organs in the perianal area. The aim of this study, therefore, was to analyze the cases of patients who had undergone sphincter repair because of acute injuries in the perianal area.

MATERIAL and METHODS

The cases of 15 patients with perianal area injuries who had presented to Necmettin Erbakan University Meram Medical School's General Surgery Clinic between 2010 and 2015 were retrospectively analyzed. Ethics committee approval was received for this study from the ethics committee of Necmettin Erbakan University Meram School of Medicine (10.08.2017-2017/361). Data on age, sex, form of injury, severity of injury, time of first response, form of repair, injury problems, and post-operative complications of the patients were investigated. The patients' long-term results were analyzed. Patients who had not received emergency surgery but undergone repair in the late period and those who had had intraabdominal organ injuries were excluded from the study in line with the exclusion criteria.

RESULTS

While 5 of the patients were male, 10 were female. 9 of the female patients had birth trauma, while one had injury during sexual intercourse. Mean age of the male

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patients was 36 (25-45) and all had injuries because of falling down from height. The injury extended to the right inguinal area in one of the cases. Mean age of the female patients was 24 (19-36) (Table 1). Three of the female patients had type 4, 2 had type 3a, 2 had type 3b, and 3 had type 3c injuries (Figure 1). Six of the female patients had their first labor. 5 of the cases had childbirth with more than 4000 g. While six of the patients had episiotomy, 3 did not receive episiotomy. Moreover, six of the patients had vacuum assisted extraction during labor.

Male patients were taken into surgery at an average of 8 hours (3-15 hours) after the incident. Nine of the female patients received intervention within the first 10 (1-18) hours. One patient was treated at an external center initially and presented to our center on the 3rd day upon the formation of split in the injury. This patient was re-operated.

While all the patients received sphincteroplasty, 10 had levatoroplasty. All of the female patients received vaginoplasty. Post-repair rectovaginal septum was thicker than 2 cm in all female patients. 3/0 Polyglactin sutures were used in all repairs and interrupted repair was completed (Figure 2). All patients had drains placed. Female patients had vaginal tampons which were frequently changed. All patients had colorectal irrigation during the surgical procedure.

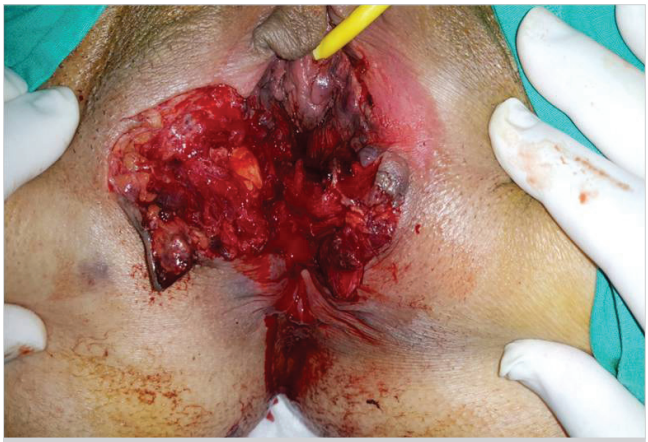

Figure 1. A patients with type 3c injury.

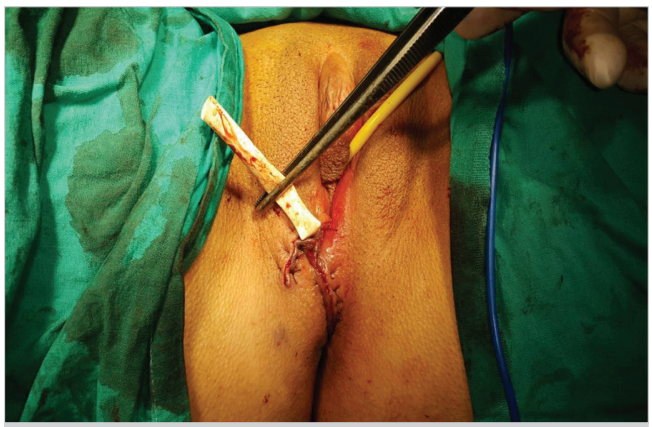

Figure 2. Post-repair image.

Colostomy was not created for any of the patients, while medical ileus was created. Parenteral feeding was continued for six days. The patients were started on third generation cephalosporin and metronidazole. Oral intake was enabled on the fifth day and the patients were discharged between the 7th and 10th days. Female patients were asked to avoid sexual intercourse for 3 months. They were recommended not to have vaginal childbirth in their following labors. All patients were started on laxatives in order to ease stool discharge and to prevent constipation for a month. This period was prolonged for those patients with chronic constipation.

All patients were followed-up in the 1st consecutive month. None of the patients had wound site pathologies. Anal manometric pressure measurements were done in the 3rd month. Mean resting pressure for male patients was 45 (30-70) mmHg, extrusion pressure was 66 (50-120) mmHg, mean duration of extrusion was 30 (20-56) seconds, and coughing reflex was 74 (54-130) mmHg. Mean resting pressure for female patients was 40 (30-60) mmHg, extrusion pressure was 60 (50-100) mmHg, mean duration of extrusion was 26 (20-50) seconds, and coughing reflex was 68 (54-110) mmHg (Table 1).

Four patients contracted gas incontinence in the 6th month. These patients received biofeedback for 2 months upon failure to detect complete sphincter damage by imaging techniques. Patients' complaints got better at the end of two months. The patients have been in the follow-up program for a mean period of 3 years and they do not have complaints of incontinence.

DISCUSSION

Mortality and morbidity following perianal area injuries are high. The most significant cause of morbidity is fecal and urinary incontinence seen in the early and late periods. The early period following injury is a process which necessitates important decision making stages like the prevention of infection, need for colostomy, and repair methods. The root cause of the problem in most of the patients with fecal incontinence is sphincter defects that emerge after obstetric trauma or perianal area surgeries. 53% to 79% of the patients have injuries at varying degrees following vaginal delivery (4,5). Although the rate of such injuries is too high, not all the injuries cause sphincter damage. The rate of primary obstetric anal sphincter injury is about 18% in vaginal deliveries (6). Eight studies have been investigated by a meta-analysis and it has been found that 5.7% of women in their first labor and 6.3% in their following labors have anal sphincter injuries (7). In another study, a total of 700 patients pregnant with twins have been evaluated and the rate of sphincter injury has been found to be 2.8% (8). In a study conducted with patients who had vaginal

Table 1. Patient data

	Female	Male
Cases	10	5
Age	24 (19-36)	36 (25-45)
Severity of injury	Type 4 (n= 3), Type 3a (n= 2), Type 3b (n= 2), Type 3c (n= 3)	Full-thickness injury to internal and external sphincter (n= 5)
Pre-operative time	10 (1-18) hours (n= 1, 3 days)	8 (3-15) hours
Postoperative follow-up time	3 (1-7) years	
Mean resting pressure	40 (30-60) mmHg	45 (30-70) mmHg
Extrusion pressure	60 (50-100) mmHg	66 (50-120) mmHg
Mean duration of extrusion	26 (20-50) seconds	30 (20-56) seconds
Coughing reflex	68 (54-110) mmHg	74 (54-130) mmHg

or c-section deliveries, the authors have found that complaints related to incontinence varied between 13% and 25% (9). The rate of fecal incontinence in patients with sphincter injury following delivery is about 7.7% (10). The rate of incontinence is 6.3% in nulliparous women, while it is 8.8% in uniparous women, 8.4% in secundiparous women, and this rate goes as high as 11.5% in triparous women and women who had more than 3 deliveries (11). Only 27% of endoanal ultrasonography results show occult anal sphincter injuries (12). One third of the patients shown to have damage also had symptoms of incontinence. Asymptomatic patients are at risk in the years to come with regards to incontinence. Almost all female patients presented with trauma at delivery. Male patients, on the other hand, had sphincter injury due to falling down from heights.

The creation of episiotomy during delivery prevents uncontrolled perianal fissures. The results of a meta-analysis; however, has revealed that episiotomy increases the risk of fecal incontinence (13). The most significant parameters for sphincter damage in vaginal delivery are interventional delivery and birth-weight of the baby (14). Tertiary level fissures are frequently seen in interventional deliveries with midline episiotomy. Uncontrolled fissures are seen less after medio-lateral episiotomy procedures. Although 6 of our patients had episiotomy, uncontrolled fissures could not be prevented. We believe that the reason for this was the problematic timing of the episiotomy. Although the starting point of the episio-incision was medio-lateral, it continued towards the medial afterwards. Six of these patients had interventional deliveries. Five of the babies had a birth weight of more than 4000 grams.

The first treatment that should be offered for any incontinence patient with anal sphincter defect is primary sphincter repair. Pre-operative intestinal cleaning should be done very carefully. Perioperative antibiotic prophylaxis is necessary. Randomized controlled studies have demonstrated that prophylaxis with second generation cephalosporin significantly reduces the rate of infection (15). While infection rates following anal sphincter repair done because of vaginal birth injury go as high as 20%, wound healing problems reach up to 25% (16). Surgical site infection was not seen in any of our patients. We administer a combination of third generation cephalosporin and metronidazole prophylaxis to our patients and we continue with the treatment for 3 days. We pay specific attention to keep the vagina dry. We believe that the reason why we do not come across such complications as wound site infection and wound split is the careful attention we pay.

The vaginal wall on the front, anal channel mucosa on the back should be repaired in internal and external sphincter procedures. Sphincter repairs can be done as end-to-end or overlapping forms. The difference between suturing the defect end-to-end and overlapping has not been shown in the literature within one-year of follow-ups (17). We do end-to-end repair in cases with early surgery following injury. We prefer the overlapping method more for chronic cases. We repair all the layers separately with interrupted sutures.

There is no sufficient data on whether a patient who had vaginal injury following vaginal delivery should have her new deliveries by vaginal or c-section delivery. Some studies, however, have reported that the probability of new anal sphincter injury following vaginal delivery is 3% (18). Nevertheless, we do not recommend our patients to have vaginal delivery. These patients have lower anal manometric pressure than normal patients (although the measurements do not have standard values). Micro or macro sphincter injuries happen in all deliveries. We support the idea that patients should not be exposed to the risk of having possible injuries.

Incontinence can be seen in women with sphincter injuries during delivery after repair. The most significant cause of this is residual anterior sphincter defects (3). Adequate continence might not be achieved in the long term by the primary repair of third

and fourth degree sphincter fissures that form during delivery. Although primary repair is done during delivery, 15-61% anal incontinence has been reported. Endoanal ultrasonography results presented in some studies have demonstrated that sphincter injuries up to 91% remain in patients with fissures repaired by interrupted side-to-side sutures (3,19). Follow-ups up to 3 years have not shown any significant continence problems in our cases. The biofeedback therapy offered to patients experiencing gas incontinence and urogenesis problems has proven to be helpful.

CONCLUSION

Sphincter repair should be performed at experienced centers controlled by coloproctologists.

Physicians should note that sphincter injuries may happen after every delivery.

Patients should be informed about the fact that they might experience incontinence problems during the follow-ups. We are of the opinion that it is significant to have surgical intervention before tissue edema develops.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Necmettin Erbakan University Meram School of Medicine (10.08.2017-2017/361).

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

Peer-review: Externally peer-reviewed.

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

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

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ORİJİNAL ÇALIŞMA-ÖZET
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Cerrahi dışı akut travmatik perianal yaralanmalar

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ÖZET

Giriş ve Amaç: Fekal inkotinans tanısı zor ve karmaşıktır. Fekal inkontinansın en önemli nedenlerinden biri perianal bölgede oluşan travmadır. Bu travmanın en önemli nedeni doğum travmasıdır. Hastaları değerlendirmek ve yapılacak tedaviye karar vermek zordur. Sfinkter hasar derecesi ve perianal bölgedeki organlarda oluşan yaralanma cerrahi yöntemi belirler. Perianal bölgede oluşan akut yaralanma nedeniyle sfinkter tamiri yapılan olgularımızı incelemek istedik.

Gereç ve Yöntem: Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi Genel Cerrahi Kliniği 2010-2015 yılları arasında başvuran perianal bölge yaralanması olan 15 hastanın verileri retrospektif olarak incelendi. Hastaların yaş, cinsiyet, yaralanma şekli, yaralanma derecesi, ilk müdahale zamanı, onarım şekli, yara problemleri ve postoperatif komplikasyonları değerlendirildi.

Bulgular: Hastaların beşi erkek ve 10'u kadındı. Kadınların dokuzu doğum travması, biri ise cinsel ilişki esnasında yaralanma gelişmişti. Hastaların tamamına sfinteroplasti yapılırken, 10'una levatoroplasti uygulandı.

Sonuç: Cerrahi müdahalenin doku ödemi gelişmeden yapılmasının önemli olduğu kanaatindeyiz.

Anahtar Kelimeler: Fekal inkontinans, travma, perianal

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Evaluation of local hemostatic effect of microporous polysaccharide hemospheres products in thyroid surgery: a prospective randomized controlled study

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ABSTRACT

Objective: Bleeding is a rare and dangerous complication of thyroid surgery. One of the hemostatic agents used during surgery are microporous polysaccharide hemospheres (MPH) which are local hemostatic agents acquired from purified potato starch. The aim of this study was to evaluate the efficiency of two MPH, produced with different biotechniques, in decreasing hemorrhages and drainage following thyroidectomy.

Material and Methods: A statistical power analysis predicted that totally 20 patients per each group was needed within 95% confidential interval. Patients were randomized into 3 groups as control, Haemocer TM and Arista TM to be 20 patients in each group. Following bilateral total thyroidectomy, no additional procedures were performed in the first group, 5 g Haemocer was administered to the second group, 5 g Arista was administered to the third group into the operational field, and the operation was ended by placing a double-sided hemovac drain. At post-operative day one, drainage amount, calcium (Ca), phosphate (P) and parathyroid hormone (PTH) levels were noted.

Results: No significant difference was noted between the groups for age, gender, removed tissue weight and malignant pathology rates. Also, no significant difference was noted between post-operative drainages and Ca, P, PTH levels of groups either. Hoarseness or hematoma were not observed in any patient.

Conclusion: MPHs are not proven in effectiveness in decreasing post-operative hemorrhages, which might be a key to avoiding unnecessary expenses.

Keywords: Microporous, polysaccharide, hemospheres, thyroid, hemostasis

INTRODUCTION

Thyroidectomy operation is one of the most common endocrine surgical procedures worldwide (1). Thyroidectomy is frequently performed for nodular goiter and thyroid cancer. Major complications include laryngeal nerve injury, hypoparathyroidism and wound complications (hematoma, seroma, infection etc.) (2-5).

Hemostasis is critical during surgery. Inadequate hemostasis can cause postoperative hematoma, wound dehiscence, infection and prolonged hospital stay (6). Most of the time, adequate hemostasis is ensured with proper surgical method, electrocauterization, suturation and bipolar sealing devices (5,7,8). Additionally, adrenaline packs and local hemostatic agents can be used for oozing hemorrhages (9).

Bleeding is a rare complication of thyroid surgery. However, when it occurs, it carries severe morbidity and mortality risks (10-12). Even a hemorrhage of 20-30 ml may result in death by causing tracheal compression and airway obstruction (13). To prevent this complication, generally drainage tubes are placed during the surgical procedure.

One of the hemostatic agents used during surgery is microporous polysaccharide hemospheres (MPH) which are local hemostatic agents derived as a product of advanced BioEngineering from purified potato starch. MPH incorporate

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a sophisticated, plant-based polymer crosslinking that creates ultra-hydrophilic, biocompatible particles. They facilitate the coagulation cascade by absorbing the liquid portion of the blood and increasing the concentration of the platelets and coagulation factors (14-16). Clotting process begins on contact, regardless of patient's coagulation status. MPH provides broad area coverage on rough surfaces and in hard-to-reach areas. MPH are indicated in surgical procedures except neurologic and ophthalmic as an adjunctive hemostatic device to assist when control of capillary, venous, and arteriolar bleeding by pressure, ligature, and other conventional procedures are ineffective or impractical.

This study aimed to evaluate the efficiency of two MPH, produced with different biotechniques including Haemocer TM and Arista TM, in decreasing hemorrhages and drainage following thyroidectomy. Thereby, an effective hemostatic agent would ensure better cosmetic results and extinguish drainage replacement.

MATERIAL and METHODS

Totally, 60 patients (20 patients per each group) were predicted in statistical power analysis within 95% confidence interval. Subsequent to local human ethics committee approval, a group of 60 patients (12 males, 48 females, average age: 45, age range: 12-67 years) were enrolled prospectively. Study group consisted of euthyroid patients admitted to the Endocrine surgery outpatient clinic between January and December 2013, and scheduled to undergo total thyroidectomy. Thyroidectomy indications were malignancy, suspicious malignancy, nodules larger than 4 cm, Basedow-Graves disease and symptomatic multi-nodular goitre like dyspnea and etc. Informed consent was obtained from all participants for both the operation they would undergo and the study they would be enrolled in. Exclusion criteria were administration of anticoagulant agents, central or/and lateral lymph node dissection for malignancy or for any reason, and patient refusal of operation or study participation. Patients were divided into three groups; first being the control group, second being Haemocer^{TM} (Bio Cer Entwicklungs-GmbH, Bayreuth, Germany) group and third being Arista^{TM} (Bard Davol Inc., Werwick, United Kingdom) group respectively. The three treatments are randomized on Microsoft Excel 2016® program for 20 patients in each group. The researcher informed the surgeon in the operation room for each patient. First operation belonging to the control group, all 60 patients underwent the procedure consequently. The same surgeon performed bilateral total thyroidectomy on all patients. Following bilateral total thyroidectomy, no additional procedures were performed in the first group, 5 g Haemocer TM was administered to the second group, 5 g Arista TM was administered to the third group into the operational field. And the operation was ended by placing a double-sided hemovac drain. The thyroidectomy material was weighted perioperatively. Although there is not any effect for hypocalcemia of MPH, they may cause hypoperfusion of the parathyroid glands while covering the surgical site for hemostasis. On post-operative day one, drainage amount, calcium (Ca), phosphate (P) and parathyroid hormone (PTH) levels were noted.

Statistical Analysis

Totally, 60 patients (20 patients per each group) were predicted in statistical power analysis within 95% confidence interval. The statistical analyses were performed using SPSS v20. Kruskal-Wallis Chi-Square test was used for intergroup comparison. Data was evaluated within 95% Confidence Interval and with $p< 0.05$ significance level.

RESULTS

Information regarding age, gender, removed tissue weight and malignant pathology rates of the groups are shown on Table 1. No significant difference was noted between the groups for age, gender, removed tissue weight and malignant pathology rates.

No significant difference was noted between post-operative drainages and Ca, P, PTH levels of the groups, either. Hoarseness, surgical site infection or hematoma was not observed in any patient. Post-operative day one drainage amounts and Ca, P, PTH levels are shown on Table 2.

On post-operative day one, asymptomatic hypocalcemia was noted for four patients in group one, two patients in group two and four patients in group three. Outpatient clinic controls revealed normal calcium levels for all patients on post-operative day 15 after conservative follow-up.

Table 1. Information regarding age, removed tissue weight averages, gender and malignant pathology of the groups

	Group 1 (Control)	Group 2 (Haemocer^{TM})	Group 3 (Arista^{TM})	p
Age	46.0 ± 10.8	44.8 ± 13.1	43.9 ± 13.0	0.946
Gender (female: male)	17:3	15:5	16:4	0.743
Tissue weight (g)	99.7	66.3	50.5	0.129
Malignant pathology	7/20	6/20	9/20	0.617

Table 2. Post-operative drainage; Ca, P, PTH level averages of the groups

	Group 1 (Control)	Group 2 (Haemocer)	Group 3 (Arista)	p
Drainage amount (mL)	53.53 ± 22.41	43.68 ± 27.90	51.94 ± 38.70	0.435
Serum Ca (mg/dL)	8.32 ± 0.70	8.27 ± 0.81	8.19 ± 1.05	0.517
Serum P (mg/dL)	3.30 ± 1.13	3.42 ± 0.77	3.26 ± 0.99	0.741
PTH (pg/mL)	32.30 ± 27.10	40.16 ± 26.58	23 ± 31.37	0.124

Ca: Calcium; P: Phosphate; PTH: Parathyroid hormone.

DISCUSSION

Since the day it was identified, haemorrhage has been one of the most feared complications of thyroidectomy. Despite the advances in surgical method and instruments with its rare occurrence; post-operative hematoma remains to cause severe mortality and morbidity risks (9,11).

Post-operative hematoma may cause airway obstruction due to larynx compression and impairment in venous and lymphatic drainage (11,12).

Slipping of ligatures, re-opening of coagulated veins or leakage from remnant thyroid tissue have been suggested for the etiology of bleeding following thyroidectomy (11,12). Hurtado et al. have stated that postoperative bleeding is present in patients with remnant thyroid tissue, especially the ones with hyperfunctioning thyroid diseases; yet they have failed to prove it statistically (17). Bergamashi et al. have not been able to show the association between the extension of thyroidectomy and post-operative hematoma either (18). However; in a large multicentered study, hematoma consisted 8% of all complications, and with a rate of 2%, it has been found to be most frequent in patients with bilateral subtotal thyroidectomy operation (19). Primary efficiency of local hemostatic agents are seen in oozing hemorrhages (7).

MPH are relatively new additions to the hemostatic agents family. They are acquired from purified potato starch. Absorbing the liquid portion of the blood, they increase the concentration of platelets and coagulation factors and facilitate the coagulation cascade. By this way, a thick, viscose clot formation occurs and then fibrin coat takes place (14-16).

Local hemostatic agents are involved in different fields clinically. They are especially used in liver resections, spleen injuries, kidney operations and orthopedic surgery frequently (14-16,20). For their experimental animal study, Humphrays et al. have evaluated the use of MPH in iatrogenic spleen injuries. Except for one case of splenic artery injury of 12 lesions, MPH have been proven effective in spleen parenchymal injuries (14).

Rajagopal and Hakim have assessed the hemostatic efficiency of MPH on 44 living nephrectomy donors and found hemostasis to be successful for all donors. Therefore, they have stated MPH are efficient and safe hemostatic agents that decrease post-operative complications (21).

There are various studies on local hemostatic agent use in thyroid surgery. Amit M et al., in their randomized prospective study conducted on 190 patients, have compared the efficiency of oxidized cellulose patch hemostatic agent Surgicel® (Ethicon Johnson&Johnson Corp., New Jersey, USA) in thyroid surgery. Group one (n= 92) has received conventional treatment while group two (n= 98) has had Surgicel® (Ethicon Johson&Johnson Corp., New Jersey, USA) in addition to the conventional treatment. No statistically significant difference has been noted between the groups in terms of operation duration, drainage amount and post-operative complications. Duration of hospital stay and drain removal have been found to be significantly shorter for the conventional group (p< 0.001). As a result, routine hemostatic agent use has not been suggested in thyroid surgery (22).

Testini et al. have compared the local hemostatic agent Floseal® (Baxter Healthcare Johnson&Johnson Corp., Illinois,USA) with conventional surgical hemostasis techniques and oxidized regenerated cellulose patch (Tabotamp Fibrillar® 2.5 x 5 cm, Ethicon Johnson&Johnson Corp., New Jersey, USA) in their study of 155 patients. Duration of operation (Floseal vs Surgery, 105 vs 133 min, p= 0.02; Floseal vs. Tabotamp, 105 vs. 122 min, p= 0.0003), drain removal (Floseal vs. Surgery p= 0.006, Floseal vs. Tabotamp p= 0.008) and hospital stay (Floseal vs. Surgery p= 0.02, Floseal vs. Tabotamp p= 0.002) have been determined significantly lower for Floseal (23). Also, Sielaff et al., in their multi-centre study, have assessed the efficiency of gelatine-based sponge as a local hemostatic agent in thyroid surgery. According to the results of 87 thyroidectomy cases, it has been found to be safe and efficient as a local hemostatic agent in thyroid surgery (24).

To the best of our knowledge, this is the first study to evaluate the efficiency of Haemocer™ and Arista™ in thyroid surgery.

This study addressed the efficiency of MPH produced with two different biotechniques, Haemocer™ and Arista™, in terms of post-operative haemorrhage and drainage amounts. Decrease in post-operative haemorrhage was observed for Haemocer™ and Arista™; however, statistical significance could not have

been achieved. Neither product has been found to be superior in terms of bleeding reducing activity. MPH administration had no effect on post-operative Ca, P and PTH levels. It did not affect the hoarseness and infection rates either.

CONCLUSION

MPH are relatively expensive products that got in use empirically in thyroid surgery. However, there is no scientific evidence regarding their role in thyroid surgery. Based on data from our study, MPH are yet to be proven effective in decreasing postoperative hemorrhages and this might be a key to avoiding unnecessary expenses.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Bezmialem Vakıf University (2013/439).

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

Peer-review: Externally peer-reviewed.

Author Contributions: Consept - E.A., E.K.; Design - E.K., E.A.; Supervision - E.A., Y.E.E.; Resource - E.K., O.İ.; Materials - O.İ.; Data Collection and/or Processing - Y.E.E.; H.K.B.; Analysis and Interpretation - E.K., S.Y.; Literature Search - E.K., S.Y., H.K.; Writing Manuscript - E.K., O.İ.; Critical Reviews - E.K, E.A.

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ORİJİNAL ÇALIŞMA-ÖZET
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Mikro gözenekli polisakkarit hemosfer ürünlerinin tiroid cerrahisinde lokal hemostatik etkilerinin değerlendirilmesi: Prospektif randomize kontrollü çalışma

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ÖZET

Giriş ve Amaç: Kanama tiroid cerrahisinin nadir ve tehlikeli bir komplikasyonudur. Ameliyat sırasında kullanılan hemostatik ajanlardan biri, saflaştırılmış patates nişastasından elde edilen lokal hemostatik ajanlar olan mikro gözenekli polisakkarit hemosferlerdir (MPH). Bu çalışmanın amacı, farklı biyotekniklerle üretilen iki MPH'nin, tiroidektomi sonrası hemoraj ve drenajı azaltmada etkinliğini değerlendirmektir.

Gereç ve Yöntem: İstatistiksel güç analizi, her bir grup için %95 gizli aralık içinde toplam 20 hastaya ihtiyaç duyulduğunu tahmin etmiştir. Hastalar her grupta 20 hasta olacak şekilde, Haemocer™ ve Arista™ gruplarına randomize edildi. Araştırmacı, cerrahı ameliyathanede her hasta için bilgilendirdi. Bilateral total tiroidektomi yapıldıktan sonra, ilk grupta ek işlemler uygulanmadı, ikinci gruba 5 g Haemocer™ uygulandı, operasyon alanına üçüncü grupta 5 g Arista™ uygulandı ve operasyon çift taraflı yerleştirilerek sonlandırıldı. Postoperatif birinci günde drenaj miktarı, kalsiyum, fosfor ve parathormon düzeyleri kaydedildi.

Bulgular: Yaş, cinsiyet, çıkarılmış doku ağırlığı ve malign patoloji oranları açısından gruplar arasında anlamlı bir fark saptanmadı. Ayrıca ameliyat sonrası drenajlar ile kalsiyum (Ca), fosfor (P), parathormon (PTH) düzeylerinin gruplar arasında da anlamlı bir fark olmadığı belirlendi. Herhangi bir hastada ses kısıklığı ya da hematom görülmedi.

Sonuç: MPH'lerin postoperatif hemorajinin azaltılmasında etkinliği kanıtlanmamıştır ve bu gereksiz harcamalardan kaçınmanın anahtarı olabilir.

Anahtar Kelimeler: Mikropor, polisakkarit, hemosfer, tiroid, hemostaz

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ORIGINAL ARTICLE
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Analysis of trauma patients with unplanned returns to the operating room

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ABSTRACT

Objective: Trauma patients undergoing damage-control surgery may have a planned return to the operating room. In contrast, little is known about unplanned returns to the operating room (uROR) in trauma. The aim of this study was to identify risk factors for uROR in trauma patients. It is hypothesized that blunt trauma patients with uROR have higher mortality when compared to penetrating trauma patients with uROR. Additionally, it is hypothesized that trauma patients with uROR after thoracotomy have higher mortality than patients with uROR after laparotomy.

Material and Methods: A retrospective analysis of the National Trauma Data Bank from 2011-2015 including any adult patient with an uROR was performed.

Results: From 3.447.320 patients, 9.269 (0.2%) were identified to have uROR. In a multivariable logistic regression analysis, 27 independent predictors were identified for risk of uROR with the strongest independent risk factor being compartment syndrome (OR= 10.50, CI= 9.35-11.78, p< 0.001). Blunt (compared to penetrating) mechanism was associated with higher risk for mortality in patents with uROR (OR= 1.69, CI= 1.14-2.51, p< 0.001) as was re-incision thoracotomy (RT) compared to re-incision laparotomy (RL) (OR= 2.22, CI= 1.29-3.84, p< 0.001).

Conclusion: The strongest risk factor for uROR in trauma is compartment syndrome. Both a blunt (compared to penetrating) mechanism and RT (compared to RL) are independent risk factors for mortality in patients undergoing an uROR.

Keywords: Unplanned return to the operating room, return to the operating room, re-incision thoracotomy, re-incision laparotomy, trauma

INTRODUCTION

A return to the operating room is associated with worse outcomes in surgical patients (1). Up to 50% of elective thoracic cases with a return to the operating room are related to technical failures with 27.3% requiring control of post-operative hemorrhage. These patients have a mortality rate of 5.6% (2). General surgery patients have been shown to have an unplanned return to the operating room (uROR) rate of 5.9% with a mortality rate as high as 33.7%. Up to 70% of uROR in general surgery patients may be related to surgical complications (3). Trauma patients undergoing damage control surgery often have a planned return to the operating room (4). However, the incidence and outcomes of uROR in the trauma population using a large national database has not previously been reported.

The kinematics of blunt trauma and the transfer of energy to the patient are fundamentally different than in penetrating trauma. The larger surface area over which the energy is dispersed can lead to widespread injury and increased severity compared to the localized destruction from penetrating trauma (5). Additionally, trauma patients that have suffered thoracic injuries have a higher rate of mortality particularly with a blunt mechanism of injury (6). Our primary objective was to identify risk factors for uROR in trauma patients. Additionally, it is hypothesized that blunt trauma patients with uROR have higher mortality when compared to penetrating trauma patients with uROR. Finally, it is hypothesized that trauma patients with uROR for re-incision thoracotomy (RT) have higher mortality than patients with uROR for re-incision laparotomy (RL).

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MATERIAL and METHODS

This work was approved by the institutional review board of the University of California, Irvine. Informed consent was not necessary as this study involves a large national database with de-identified information. The National Trauma Data Bank (NTDB) is a multicenter registry of trauma centers in the United States maintained by the American College of Surgeons Committee on Trauma (7). All registered cases with uROR in the NTDB occurring between 2011-2015 were identified. Patients under 18 years of age were excluded. Trauma patients with uROR were compared to those without uROR. The primary outcome was mortality. Secondary outcomes evaluated included total hospital length of stay (LOS), intensive care unit (ICU) LOS, ventilator days, acute kidney injury (AKI), acute respiratory distress syndrome (ARDS), myocardial infarction (MI), pulmonary embolism (PE), deep vein thrombosis (DVT), pneumonia, cerebrovascular accident (CVA), urinary tract infection (UTI), compartment syndrome, severe sepsis, and surgical site infection (SSI). The relation between mortality and baseline patient demographics, comorbidities, injury profile, interventions and hospital outcomes including complications was analyzed.

Patient demographic information including age, gender and prehospital comorbidities were collected. Injury profile included the injury severity score (ISS), mechanism of injury and associated solid organ and extremity injuries. The interventions analyzed included RL and RT based on the appropriate International Classification of Diseases Version-9 procedure codes.

Student's t-test and Mann-Whitney U test were used to compare continuous variables and chi-square was used to compare categorical variables for bivariate analysis. Categorical data were reported as percentages, and continuous data were reported as medians with interquartile range. The magnitude of the association between predictor variables and primary outcomes was measured using a univariable logistic regression model. Covariates with statistical significance ($p \leq 0.20$) were selected into a multivariable logistic regression model. Confounding variables were controlled for using a hierarchical logistic regression model and risk analysis was reported with an odds ratio (OR) and 95% confidence intervals (CI). The reference group used in our logistic regression analysis to identify risk factors for uROR included all trauma patients in the dataset while the reference group for risk of mortality included only patients with uROR. All p values were two-sided, with a statistical significance level of < 0.05. All statistical analyses were performed with IBM SPSS Statistics for Windows, Version 24. (IBM Corporation, Armonk, USA).

RESULTS

Patient Demographics, Injury Profile and Primary Outcomes

From 3.447.320 patients, 9.269 (0.2%) were identified to have uROR with more occurring in penetrating traumas (0.67%) and less in blunt traumas (0.22%). There was an increased incidence of uROR for each consecutive year from 0.11% in 2011 to 0.31% in 2015 ($p< 0.05$). When compared to trauma patients without uROR, those with uROR were younger (median age, 45 vs. 50, $p< 0.001$) and had a higher median ISS (18.0 vs 6.0, $p< 0.001$). Majority of the patients in both groups were involved in blunt trauma. Trauma patients with uROR had higher rates of penetrating mechanism (25.2% vs. 10.2%, $p< 0.001$), hypotension on admission (10.4% vs. 2.9%, $p< 0.001$) and all associated injuries analyzed except for burn injury (1.3% vs. 2.3%, $p< 0.001$) (Table 1). Mortality rate was also higher in patients with uROR (11.8% vs. 3.7%, $p< 0.001$) and higher in patients with RT compared to RL (30.3% vs. 21.0%, $p< 0.05$) (Table 2).

Logistic Regression Analysis for Risk of uROR in Trauma Patients

In a multivariable logistic regression analysis, twenty-seven independent predictors were identified for risk of uROR in trauma patients. The strongest independent risk factors, in order, included compartment syndrome (OR= 10.50, CI= 9.35-11.78, $p< 0.001$), SSI (OR= 5.44, CI= 4.82-6.14, $p< 0.001$), severe sepsis (OR= 3.05, CI= 2.75-3.37, $p<0.001$) and colorectal injury (OR= 3.00, CI= 2.74-3.28, $p< 0.001$). Patients with a blunt mechanism had a lower risk for uROR compared to those with a penetrating mechanism (OR= 0.44, CI= 0.41-0.47, $p< 0.001$). Patients that were ≥ 65 years of age also had a lower risk of uROR (OR= 0.83, CI= 0.78-0.88, $p< 0.001$) (Table 3).

Logistic Regression Analysis for Risk of Mortality in Patients with uROR

In a multivariable logistic regression analysis, nine independent predictors were identified for risk of mortality in trauma patients with uROR. The strongest independent risk factors, in order, included MI (OR= 6.49, CI= 2.19-19.27, $p< 0.05$), CHF (OR= 5.32, CI= 2.07-13.69, $p< 0.05$), AKI (OR= 3.96, CI= 2.84-5.50, $p< 0.001$) and age ≥ 65 years (OR= 3.66, CI=2.47-5.42, $p< 0.001$). Blunt (compared to penetrating) mechanism was associated with higher risk for mortality in patents with uROR (OR= 1.69, CI= 1.14-2.51, $p< 0.001$) as was RT (compared to RL) (OR= 2.22, CI= 1.29-3.84, $p< 0.001$) (Table 4).

Secondary Outcomes in Trauma Patients with uROR

Compared to trauma patients without uROR, those with uROR had a longer LOS (18.0 vs. 3.0 days, $p< 0.001$), ICU LOS (10.0 vs. 3.0 days, $p< 0.001$) and higher rates of all in-hospital complications analyzed (Table 5).

DISCUSSION

This retrospective analysis, encompassing five years of NTDB data, provides an analysis of trauma patients undergoing uROR. The incidence of uROR has increased each year from 2011 to 2015 but remains low at 0.31% in the most recent year analyzed. Majority of the patients were involved in a blunt mechanism of

Table 1. Demographics and injury profile of trauma patients with and without an unplanned return to the operating room

Characteristic	- uROR (n= 3.438.051)	+ uROR (n= 9269)	p
Age, year, median (IQR)	50.0 (37)	45.0 (32)	< 0.001
Sex (male), n (%)	2.158.458 (62.8%)	7042 (76.0%)	< 0.001
Comorbidities, n (%)			
Congestive heart failure	107.411 (3.1%)	31 (2.5%)	< 0.001
Cerebrovascular accident	76.189 (2.2%)	177 (1.9%)	< 0.001
Diabetes	404.651 (11.8%)	1048 (11.3%)	0.17
Hypertension	993.094 (28.9%)	2443 (26.4%)	< 0.001
COPD	249.607 (7.3%)	648 (7.0%)	0.32
ISS, median (IQR)	6.0 (7)	18.0 (16)	< 0.001
Blunt mechanism, n (%)	2.860.547 (89.8)	6544 (74.8%)	< 0.001
Penetrating mechanism, n (%)	326.570 (10.2%)	2208 (25.2%)	<0.001
Hypotensive on admission (SBP < 90 mm Hg), n (%)	99.204 (2.9%)	965 (10.4%)	< 0.001
Injuries, n (%)			
Traumatic brain injury	1.025.301 (29.8%)	3337 (36.0%)	< 0.001
Spine	562.750 (16.4%)	2581 (27.8%)	< 0.001
Rib	522.407 (15.2%)	2505 (27.0%)	< 0.001
Upper extremity	618.191 (18.0%)	2245 (24.2%)	< 0.001
Lower extremity	808.142 (23.5%)	2630 (28.4%)	< 0.001
Lung	411.564 (12.0%)	2779 (30.0%)	< 0.001
Liver	85.203 (2.5%)	1190 (12.8%)	< 0.001
Spleen	87.965 (2.6%)	1196 (12.9%)	< 0.001
Esophagus	1368 (0.1%)	32 (0.3%)	< 0.001
Stomach	8752 (0.3%)	349 (3.8%)	< 0.001
Small intestine	28.778 (0.8%)	1078 (11.6%)	< 0.001
Colorectal	26.260 (0.8%)	1188 (12.8%)	< 0.001
Pancreas	2617 (0.1%)	172 (1.9%)	< 0.001
Kidney	44.193 (1.3%)	646 (7.0%)	<0.001
Burn	79.294 (2.3%)	117 (1.3%)	< 0.001
Crush	13.298 (0.4%)	101 (1.1%)	< 0.001

uROR: Unplanned return to operating room; IQR: Interquartile range; COPD: Chronic obstructive pulmonary disease; SBP: Systolic blood pressure; ISS: Injury severity score.

Table 2. Mortality rates of adult trauma patients

Population	Mortality, %
uROR	11.8%
No uROR	3.7%
Re-incision thoracotomy	30.3%
Re-incision laparotomy	21.0%

uROR: Unplanned return to the operating room.

injury. Multiple predictors were identified for risk of uROR but the strongest risk factor was compartment syndrome. In support of our hypothesis, it was demonstrated that both a blunt (compared to penetrating) mechanism and RT (compared to RL) are independent risk factors for mortality in patients undergoing an uROR.

Trauma patients with uROR have multiple injuries, which may not all be clinically apparent during primary/secondary surveys. We identified higher rates of nearly all associated injuries

Table 3. Multivariable analysis for risk of unplanned return to operating room in adult trauma patients

Predictor	OR	95% CI	p
Blunt vs. penetrating mechanism	0.44	0.41-0.47	< 0.001
Age ≥ 65	0.83	0.78-0.88	< 0.001
Upper extremity injury	1.07	1.01-1.13	< 0.05
Diabetes	1.11	1.03-1.20	< 0.05
Lung injury	1.16	1.09-1.24	< 0.001
Kidney injury	1.17	1.06-1.29	< 0.05
Myocardial infarction-complication	1.17	1.23-1.77	< 0.001
Hypotensive on admission	1.19	1.10-1.29	< 0.001
Hypertension-comorbidity	1.22	1.15-1.29	< 0.001
Spine injury	1.24	1.18-1.31	< 0.001
Liver injury	1.25	1.15-1.35	< 0.001
Traumatic brain injury	1.28	1.22-1.35	< 0.001
Pancreas injury	1.29	1.06-1.29	< 0.05
Lower extremity injury	1.37	1.31-1.45	< 0.001
Male gender	1.39	1.32-1.47	< 0.001
Stomach injury	1.46	1.27-1.67	< 0.001
Pulmonary emboli-complication	2.03	1.78-2.32	< 0.001
Acute kidney injury-complication	2.11	1.91-2.33	< 0.001
Esophagus injury	2.13	1.44-3.14	< 0.001
Urinary tract infection-complication	2.25	2.06-2.45	< 0.001
ISS > 25	2.26	2.12-2.41	< 0.001
Small intestine injury	2.55	2.33-2.79	< 0.001
Deep vein thrombosis-complication	2.62	2.40-2.86	< 0.001
Crush injury	2.63	2.11-3.30	< 0.001
Pneumonia-complication	2.81	2.62-3.01	< 0.001
Colorectal injury	3.00	2.74-3.28	< 0.001
Severe sepsis-complication	3.05	2.75-3.37	< 0.001
Surgical site infection	5.44	4.82-6.14	< 0.001
Compartment syndrome	10.50	9.35-11.78	< 0.001

ISS: Injury severity score; OR: Odds ratio; CI: Confidence interval.

analyzed except for burn injuries in patients with uROR. Injury profile coupled with more severe trauma experienced by patients with uROR likely provided the "perfect-storm" for occult and missed injuries, which may have presented later requiring uROR. This is particularly true in patients with TBI or spine injury since these patients often have unreliable clinical exams (8,9). False-negative rates may continue to be high on subsequent exams. Houshian et. al have performed a retrospective analysis over four years at a Level-1 trauma center and found that 14%, 38% and 48% of injuries are missed in primary, secondary and tertiary surveys, respectively (10). In support of these reports, it was found in the present study that uROR had significantly higher rates of TBI and spine injury. Additionally, trauma patients with TBI were found to have a 28% increased risk for uROR while those with spine injury have a 24% increased risk for uROR. However, the most significant risk factor for uROR was compartment syndrome. This complication is unique because diagnosis is often made clinically without any widespread, highly sensitive or specific imaging or diagnostic modalities to help clinicians. Vigilance and good clinical judgment, especially determining the need for a prophylactic fasciotomy remain the hallmarks of management (11). The difficulty in diagnosing patients correctly may be responsible for the high risk of uROR. For this reason, almost 90% of cases involving compartment syndrome that reach litigation have a delay in diagnosis (12).

Table 4. Multivariable analysis for risk of mortality in adult trauma patients with an unplanned return to operating room

Predictor	OR	95% CI	p
Deep vein thrombosis-complication	0.31	0.18-0.53	< 0.001
Urinary tract infection-complication	0.34	0.21-0.57	< 0.001
Pulmonary emboli-complication	0.39	0.18-0.85	< 0.05
Pneumonia-complication	0.49	0.35-0.69	< 0.001
Blunt vs. penetrating mechanism	1.69	1.14-2.51	< 0.001
ARDS-complication	2.10	1.41-3.11	< 0.001
ISS ≥ 25	2.11	1.53-2.92	< 0.001
Re-incision thoracotomy vs. re-incision laparotomy	2.22	1.29-3.84	< 0.001
Hypotensive on admission	2.34	1.74-3.16	< 0.001
Age ≥ 65	3.66	2.47-5.42	< 0.001
Acute kidney injury-complication	3.96	2.84-5.50	< 0.001
Congestive heart failure-comorbidity	5.32	2.07-13.69	< 0.05
Myocardial infarction-complication	6.49	2.19-19.27	< 0.05

ARDS: Acute respiratory distress syndrome; ISS: Injury severity score.

Table 5. Analysis of clinical outcomes in trauma patients with and without an unplanned return to the operating room

Outcome	- uROR (n= 2290)	+ uROR (n= 6698)	p
LOS days, median (IQR)	3.0 (4)	18.0 (21)	< 0.001
ICU days, median (IQR)	3.0 (4)	10.0 (15)	< 0.001
Ventilator days, median (IQR)	3.0 (7)	8.0 (13)	< 0.001
Complications, n (%)			
Acute kidney injury	22.774 (0.7%)	723 (7.8%)	< 0.001
ARDS	28.466 (0.8%)	559 (6.0%)	< 0.001
Deep vein thrombosis	25.911 (0.8%)	869 (9.4%)	< 0.001
Pulmonary emboli	11.055 (0.3%)	310 (3.3%)	< 0.001
Surgical site infection	5382 (0.2%)	435 (4.7%)	< 0.001
Urinary tract infection	49.157 (1.4%)	840 (9.1%)	< 0.001
Myocardial infarction	7957 (0.2%)	79 (0.9%)	< 0.001
Compartment syndrome	7358 (0.2%)	472 (5.1%)	< 0.001
Pneumonia	71.001 (2.1%)	1812 (19.5%)	< 0.001
Severe sepsis	10.866 (0.3%)	705 (7.6%)	< 0.001
Mortality, n (%)	125.041 (3.7%)	1090 (11.8%)	< 0.001

uROR: Unplanned return to operating room; LOS: Length of stay; ICU: Intensive care unit; IQR: Interquartile range; ARDS: Acute respiratory distress syndrome.

Most of the patients with uROR in our study were involved in blunt trauma. In support of previous reports, we demonstrate that blunt trauma carries a higher risk for mortality compared to penetrating trauma (13-17). A blunt mechanism of injury has the potential for multi-system injury and often involves TBI, which is considered one of the leading causes of death in trauma patients (18-20). Almost half the patients in our study with blunt trauma undergoing uROR had an accompanying TBI and nearly 60% of blunt trauma patients undergoing uROR that died had a TBI diagnosis. Furthermore, blunt trauma patients with uROR had a significantly higher rate of extremity fractures (64.9% vs. 24.2%) when compared to patients with uROR after penetrating trauma, which may predispose them to more bleeding. Femur fractures undergoing surgical fixation require, on average, more

than three units of packed red blood cells due to peri-operative blood loss (21). Lastly, the trajectory of a penetrating injury is often easily found upon surgical exploration allowing for the early identification of all significant injuries. Patients with blunt trauma may have an occult injury without other surrounding associated injuries leading to increased mortality associated with delays in diagnosis (22-24).

Thoracic trauma has been shown to be involved in up to 50% of trauma-related deaths (25-27). In our study, we were able to demonstrate that trauma patients enduring uROR for RT had higher risk for mortality compared to patients undergoing uROR for RL. A previous study has demonstrated hemorrhage as the predominant factor requiring uROR for RT (2). Since hemorrhage is also the number one cause of mortality in trauma patients in general, it follows that uROR for RT had a higher mortality rate compared to those who underwent RL (28). Pujol et al. have reported that technical skills and expertise contribute to uROR and therefore, this may be a factor contributing to the increased mortality rate as well (29). From 2007-2015, there were 137.575 patients who underwent exploratory laparotomy in the NTDB while only 21.579 cases of exploratory thoracotomy were reported. A possible explanation for increased mortality in the RT group is that trauma surgeons have less experience working in the chest. Additional studies stratifying outcomes of uROR based on the operating surgeon's volume of thoracotomy cases appears warranted.

The overall mortality rate in our study population of trauma patients undergoing uROR was 11.8%, which is significantly lower than the reported mortality rate in general surgery patients undergoing uROR (33.7%) (3). These populations are quite different and the reason for this disparity is undoubtedly multifactorial. Some possible explanations include that the median age of trauma patients with uROR in the NTDB was lower than the aforementioned general surgery cohort (45 vs. 61 years), and the nature of the reason of the uROR may be very different (i.e. hemorrhaging trauma patients versus infection) (3).

The rate of uROR may be useful for comparison of hospital outcomes and for identifying opportunities for quality improvement (30). Our study identified an alarming trend of increased annual incidence of uROR. This is concerning as uROR poses a financial burden on the patient and a strain on hospital resources. An uROR has been shown to be associated with an eightfold increase in hospital readmission (31). In order for uROR to be a comparable metric across institutions, data collection must include documentation of the surgical findings at re-exploration, as well as the interventions performed. Only with this data can a comparison of results between centers yield meaningful quality improvement by demonstrating how high performing centers can achieve improved outcomes comparatively to low performing centers.

Study Limitations

There are several limitations to our study including those inherent to retrospective large databases such as participation being voluntary and coding error, which may lead to misclassification bias due to the under-reporting of pre-existing medical conditions and complications. Furthermore, our analysis was restricted to data fields available in the NTDB and were subject to input error. We were also missing important data such as timing of the index operation and reason for and time of uROR. Therefore, adjustment for these potential confounders was not possible. Finally, because this was an observational study, the role of unmeasured or unobserved confounding variables cannot be excluded.

CONCLUSION

Trauma patients undergoing uROR appears to be on the rise. Most patients are involved in a blunt mechanism. Multiple predictors were identified for risk of uROR, but the strongest risk factor was compartment syndrome. Both a blunt (compared to penetrating) mechanism and RT (compared to RL) are independent risk factors for mortality in patients undergoing uROR. The overall mortality in trauma patients undergoing uROR is less than emergency general surgery patients undergoing uROR. Future prospective research regarding uROR in all trauma patients appears warranted to better elucidate the exact causes and interventions to prevent and/or successfully treat uROR in trauma patients.

Ethics Committee Approval: This study was approved by the Institutional Review Board at the University of California, Irvine.

Informed Consent: This research involved humans. However, since this retrospective study was performed using a national database with deidentified patients, risk to participants is minimal. There is no consent required.

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ORİJİNAL ÇALIŞMA-ÖZET
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Travma hastalarında plansız ameliyathaneye dönüş analizi

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ÖZET

Giriş ve Amaç: Hasar kontrol cerrahisi geçiren travma hastalarında ameliyathaneye planlı bir dönüş olabilir. Bunun aksine, travmada plansız ameliyathaneye dönüşler (PAD) hakkında çok az şey bilinmektedir. Bu çalışmanın amacı, travma hastalarında PAD risk faktörlerini belirlemekti. Ayrıca, plansız ameliyathaneye dönüşlü künt travma hastalarının plansız ameliyathaneye dönüşlü penetran travma hastalarına kıyasla daha yüksek mortalite oranına sahip olduğu varsayımında bulunduk. Buna ek olarak, torakotomi yapılan PAD travma hastalarının laparotomi yapılan hastalara oranla daha yüksek mortaliteye sahip olduğu da öne sürülmüştür.

Gereç ve Yöntem: 2011-2015 yılları arasını kapsayacak şekilde Ulusal Travma Veri Bankasının plansız ameliyathaneye dönüşlü erişkin hastaların verileri üzerine geriye dönük analiz yapıldı.

Bulgular: 3.447.320 hasta içerisinde 9269 (%0.2)'unun plansız ameliyathaneye dönüşlü hastalar olduğu belirlendi. Çok değişkenli lojistik regresyon analizinde, kompartıman sendromunun (OR= 10.50, CI= 9.35-11.78, p< 0.001) en güçlü bağımsız risk faktörü olduğu 27 bağımsız risk faktörü saptandı. Reinsizyon laparotomiye kıyasla reinsizyon torakotomide de olduğu gibi (OR= 2.22, CI= 1.29-3.84, p< 0.001) (penetran mekanizmaya kıyasla) künt mekanizma, plansız ameliyathaneye dönüşlü hastalarda daha yüksek mortalite riski ile ilişkiliydi.

Sonuç: Travmada PAD için en güçlü risk faktörü kompartıman sendromudur. Plansız ameliyathaneye dönüşlü hastalarda hem penetran mekanizmaya kıyasla künt mekanizma hem de reinsizyon laparotomiye kıyasla reinsizyon torakotomi bağımsız risk faktörlerini oluşturmaktadır.

Anahtar Kelimeler: Plansız ameliyathaneye dönüş, ameliyathaneye dönüş, reinsizyon torakotomi, reinsizyon laparotomi, travma

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Roux-en-Y fistulojejunostomy in the management of persistent external pancreatic fistula: is it olde worlde?

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ABSTRACT

Objective: This article aimed to identify patient selection criteria and approach in treating persistent external pancreatic fistulas surgically with Roux-en-Y fistulojejunostomy, and the study evaluated the outcomes of Roux-en-Y fistulojejunostomy with a review of the relevant literature.

Material and Methods: A retrospective data analysis from January 2010 to May 2017 revealed 6 patients managed with Roux-en-Y fistulojejunostomy for persistent external pancreatic fistulas, and their details were entered in a proforma. Standard surgical steps were performed in all patients, and the patients were followed up postoperatively for 1 year. Data were analyzed for outcomes, and the literature was reviewed.

Results: Four of 6 patients had persistent external pancreatic fistulas following pancreatic necrosectomy, 1 had surgery for pancreatic pseudocyst, and 1 after pancreaticoduodenectomy for pancreatic head mass. An average duration of conservative management was 14 weeks, and Roux-en-Y fistulojejunostomy was performed at a median distance of 6 cm from pancreas via a midline laparotomy. All patients recovered without major complications. Only 1 patient developed diabetes at a 1-year follow-up.

Conclusion: Fistulojejunostomy is a safe and effective treatment for persistent pancreatic fistula having the benefit of avoiding a difficult major pancreatic resectional surgery in an already debilitated patient with frozen tissue planes, along with low postoperative morbidity and mortality. The short- and mid-term outcomes in the literature for this procedure are good, as it has also been seen in our study on diverse indications.

Keywords: Fistula, necrosectomy, pancreas, pancreaticoduodenectomy, surgery

INTRODUCTION

Pancreatic fistulas can result from surgery for various indications, including pancreatic necrosis, pancreatic pseudocysts, pancreatic masses (benign or malignant), chronic pancreatitis, trauma, or pancreatic ascites, and percutaneous interventions for fluid collections/pseudocysts (1-3).

Pancreatic fistulas, whether internal or external, can lead to locoregional complications such as abscess formation, hemorrhage, pseudoaneurysms, peritonitis, and sepsis (1,3). High mortality rates ranging between 13% and 36% have been reported. Initial conservative management is often successful in 90% of the patients without development of fever, tachycardia, leucocytosis, severe wound infection, or peritonitis (1,3,4). Clinical deterioration warrants a step-up approach, with total parenteral nutrition, optimal wound care, drainage of intra-abdominal collections via percutaneous drains, repositioning of previously placed drains, and occasionally, re-exploration with abdominal lavage. Prevention of wound complications, percutaneous dilatation of stenotic segments in anastomosis, and pancreatic duct stenting are all adjuncts for management.

The emergent surgical options include lavage with wide drainage, reinforcing or refashioning of anastomosis in case of a minor leak, disconnection of anastomosis with external pancreatic drainage in feding jejunostomy, and rarely a total pancreatectomy, which leads to debilitating brittle diabetes and carries a prohibitively high mortality (5-7). Persistent external pancreatic fistula (PEPF) is defined as an external pancreatic fistula not resolving with these measures for longer than 6 weeks (1).

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There are few surgical options to treat PEPF: internal drainage by Roux-en-Y fistulojejnuostomy (RYFJ) or fistulogastrostomy, and pancreatic resection procedures are the available surgical options to treat PEPF not resolving with endoscopic, percutaneous, and combined endoscopic–percutaneous procedures (2).

Optimal time for performing fistulojejunostomy is a matter of debate (1,3). We present our algorithmic approach for the management of PEPF and our experience with RYFJ for this indication along with a brief review of the relevant literature.

MATERIAL and METHODS

A retrospective analysis of hospital records of the PEPF patients managed with RYFJ from January 2010 to May 2017 in the department of gastrointestinal surgery was carried out.

An institutional ethics committee approval was obtained, and patients were included into the study after providing a written informed consent. Data recorded in a dedicated proforma included patient demographics, etiology, details of conservative management, duration of conservative management, fistula output, investigations for complications and surgical planning, surgical indication and surgery details. A magnetic resonance cholangiopancreatograpy (Ingenia 3.0 T; Philips, Eindhoven, Netherlands) was done to evaluate the distal duct, the origin of the fistula tract, and confirm findings of disconnected duct syndrome. A contrast-enhanced computed tomography (Somatom definition flash; Siemens, Erlangen, Germany) was done for preoperative planning to evaluate the size of the tract and its wall thickness and rule out any associated intra-abdominal collections. Drain tube diameter, site of anastomosis, intraoperative blood loss, postoperative complications, and length of hospital stay were noted from inpatient hospital records.

At a formal laparotomy, a mature fistula tract was isolated by limited adhesiolysis to prevent devascularization of the tract, and it was dissected as close to the pancreas as possible, avoiding the immediate peri-pancreatic area (Figure 1).

The distance between the pancreas and the anastomotic site was measured. Single layer anastomosis was constructed to a 45-cm-long Roux loop of the jejunum using interrupted 4-0 polydioxanone sutures. A trans-anastomotic tube or stent was not used in any of the cases (Figures 2,3). Drains were placed at the end of the procedure. Intraoperative and postoperative complications were recorded from the inpatient case records.

Patients were followed in the outpatient department with clinical examination and ultrasonography of abdomen and pelvis. An algorithm for our approach to these patients is shown in Figure 4. The observations were tabulated, and the statistical data representation in the form of mean, median and range was done manually without any software.

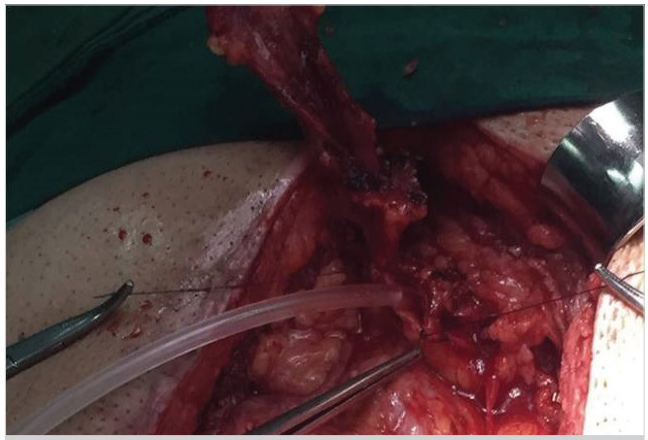

Figure 1. Intraoperative image showing the identification of the fistula tract along the abdominal drain.

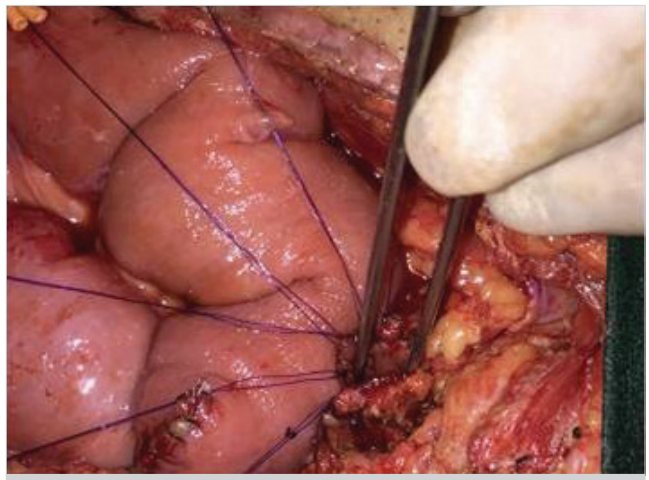

Figure 2. Intraoperative image showing the posterior layer sutures for Roux-en-Y fistulojejunostomy.

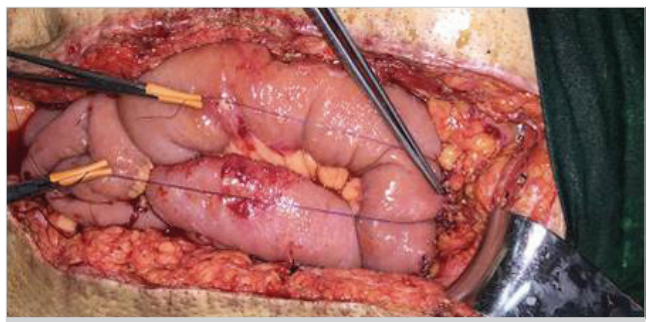

Figure 3. Intraoperative image showing completed Rouxen-Y fistulojejunostomy.

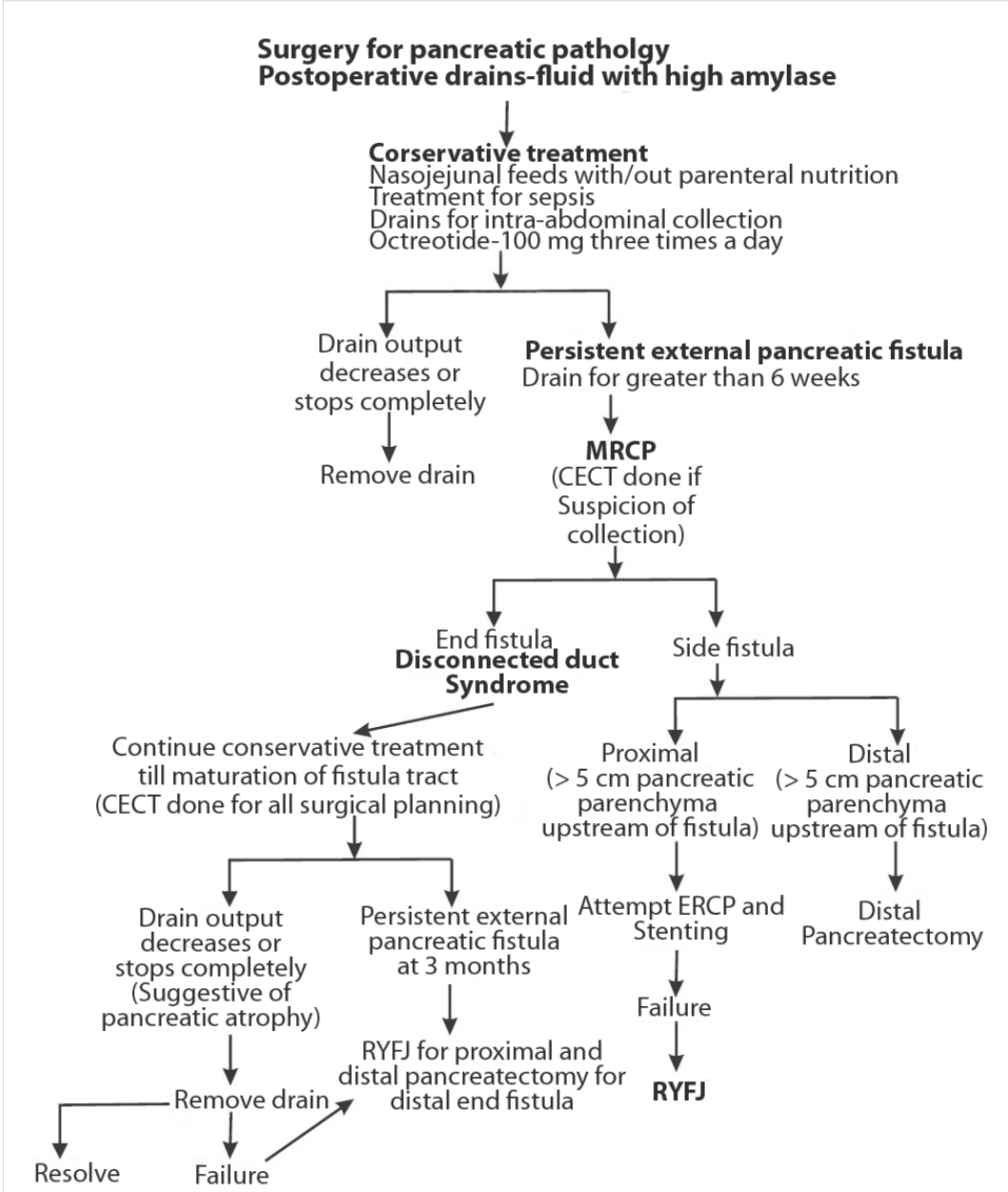

Figure 4. Our algorithmic approach to diagnosis and management of the persistent external pancreatic fistula.

RESULTS

The details of each case are as follows.

Case 1

A 46-year-old man presented with obstructive jaundice due to a pseudocyst and a suspicious mass in the head of the pancreas (HOP), with a background of chronic pancreatitis. The patient underwent a pancreaticoduodenectomy (PD). He postoperatively developed a pancreatic fistula with an output of approximately 200-225 mL/day. He was managed conservatively with enteral feeding by a nasojejunal tube. A percutaneous drain was placed for an intra-abdominal collection detected on CECT at 4 weeks postoperatively, and it was serially upgraded to 32 F. After 14 weeks of conservative management, the patient underwent RYFJ. The fistula tract was divided near the root of the mesocolon, approximately 4 cm from the pancreas, for anastomosis. The surgery lasted 150 minutes, and the blood loss was 100 mL. The patient recovered uneventfully and is doing well at a 60-month follow-up being on the pancreatic enzyme replacement therapy.

Case 2

A 48-year-old man was diagnosed with alcohol-induced acute pancreatitis, with walled-off pancreatic necrosis and splenic vein thrombosis. The patient underwent laparotomy with necrosectomy and splenectomy with a 32 F catheter drainage of the cavity, 6 weeks after the diagnosis. The patient postoperatively developed persistent pancreatic fistula with an output of 150-175 mL/day and was managed conservatively with nasojejunal tube feeding. After 12 weeks of conservative management, the patient underwent RYFJ. Anastomosis was supracolic infrahepatic, approximately 5 cm from the pancreas. The surgery lasted 160 minutes, and blood loss was 120 mL. The patient had a postoperative wound infection managed with dressings in the outpatient setting. The patient recovered without any major morbidity and is doing well on a 13-month follow-up, receiving diabetes therapy.

Case 3

A 52-year-old man was diagnosed with gall stone-induced severe acute pancreatitis with walled-off pancreatic necrosis and underwent laparotomy with necrosectomy, 32 F catheter drainage of the cavity, and cholecystectomy 8 weeks after the diagnosis. The patient postoperatively developed a persistent pancreatic fistula with an output of approximately 50-75 mL/day and was managed conservatively with nasojejunal tube feeding. After 13 weeks of conservative management, the patient underwent RYFJ. The site of anastomosis was at the root of the mesocolon to the left of the middle colic vessels, at a distance of approximately 8 cm from the pancreas. The surgery lasted 200 minutes, and blood loss was 150 mL. The patient recovered uneventfully and is doing well at a 12-month follow-up.

Case 4

A 60-year-old man was diagnosed with alcohol-induced acute pancreatitis with walled-off pancreatic necrosis. The patient underwent percutaneous drainage of a necrotic collection at 3 weeks, followed 3 weeks later by a formal laparotomy with necrosectomy and the 30 F catheter drainage of the cavity. Having ostoperatively developed a persistent pancreatic fistula with an output of approximately 100-150 mL/day, the patient was man-

Table 1. Patient details, diagnosis, conservative measures, and duration of conservative measures in our series

Patient number	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age (years)	46	48	52	60	25	52
Sex	Male	Male	Male	Male	Male	Male
Primary pancreatic disease	Malignancy in chronic pancreatitis with pseudocyst in the pancreas head with obstructive jaundice	Alcohol-induced acute pancreatitis with walled-off pancreatic necrosis	Gall stone-induced severe acute pancreatitis with walled-off pancreatic necrosis	Alcohol-induced acute pancreatitis with walled-off pancreatic necrosis	Alcohol-induced acute pancreatitis with pseudocyst	Gall stone-induced acute sever necrotizing pancreatitis with infected walled-off pancreatic necrosis
Primary surgery	Whipple procedure	Open necrosectomy with splenectomy	Open necrosectomy and cholecystectomy	Open necrosectomy following a percutaneous drainage	Cystogastrostomy cystojejunostomy Hepaticojejunostomy (1 year later)	Laparoscopic transmesocolic necrosectomy
Splenic vein thrombosis	No	Yes	No	No	No	Yes
Conservative measures used before surgery	- Nasojejunal tube feeding - Catheter drainage of collection	- Nasojejunal tube feeding - Catheter drainage of the necrotic cavity	- Nasojejunal tube feeding and maintenance of drain of primary surgery	- Nasojejunal feeding - Catheter drainage of collection	- Percutaneous pseudocyst drainage (After 6 months) - Pancreatic duct stenting - Nasojejunal feeds	Nasojejunal tube feeding - Catheter drainage of collection - Laparoscopic lavage of intra-abdominal collections
Duration of conservative management	14 weeks	12 weeks	13 weeks	14 weeks	6 months	6 months
Fistula output (daily)	200-225mL	150-175mL	50-75mL	100-150mL	50-75mL	100-150 mL

Table 2. The table shows the drain tube diameter used, the approximate distance of the fistula anastomosis from the pancreas, intraoperative blood loss, postoperative complications, and the length of hospital stay in our patients

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Tube/drain diameter	32 F	32 F	32 F	30 F	18 F	32 F
Approximate distance from the pancreas	4 cm	5 cm	8 cm	4 cm	7 cm	4 cm
Site of anastomosis on the fistula	Left side near the root of mesocolon	Right-side infrahepatic area	Left side root of the mesocolon	Right side supracolic	Right side infrahepatic	Left-side root of the mesocolon
Intraoperative blood loss	100 mL	120 mL	150 mL	100 mL	180 mL	200 mL
Operative time	150 min	160 min	200 min	130 min	140 min	260 min
Length of stay	7 days	8 days	10 days	9 days	8 days	8 days
Complication	None	Wound infection	None	None	None	Wound infection
Follow-up duration	60 months	13 months	12 months	24 months	13 months	15 months
Follow-up method	Clinical evaluation and abdominal USG every 3 months					
PERT requirement	Yes	No	No	No	No	No
Postoperative leak/ Collections	No	No	No	No	No	No
Diabetes	No	Yes	No	No	No	No

F: French; cm: Centimeter; Ml: Milliliters; min: Minutes; PERT: Pancreatic enzyme replacement therapy.

aged conservatively with nasojejunal tube feeding and needed a percutaneous catheter drainage of an undrained collection diagnosed on CECT 6 weeks after surgery. After 14 weeks of conservative management, the patient underwent RYFJ. The site of anastomosis was supracolic infrahepatic, at approximately 4 cm from the pancreas. The surgery lasted for 130 minutes, and blood loss was 100 mL. The patient recovered uneventfully and is doing well at a 24-month follow-up.

Case 5

A 25-year-old man was diagnosed with a pancreatic pseudocyst following alcohol-induced acute pancreatitis and underwent a cystogastrostomy. However, cyst drainage was not adequate, and cystogastrostomy was revised to a Roux-en-Y cystojejunostomy. A year later, the patient presented with obstructive jaundice for which he underwent hepaticojejunostomy. He again developed an infected pseudocyst, which was drained percutaneously with a 18 F catheter. The patient developed a pancreatic fistula with an output of approximately 50-75 mL/day and was managed conservatively with nesojejunal enteral feeding. After 12 weeks of conservative management, the patient underwent pancreatic duct stenting for his disconnected duct syndrome. However, the fistula persisted, and the patient was taken up for RYFJ, 6 months after the diagnosis of pancreatic fistula. The site of anastomosis was supracolic infrahepatic, at approximately 7 cm from the pancreas. The surgery lasted 140 minutes, and the blood loss was 180 mL. The patient recovered uneventfully and is doing well at a 13-month follow-up.

Case 6

A 52-year-old man was diagnosed with gall-stone-induced acute severe necrotizing pancreatitis with infected walled-off pancreatic necrosis for which he underwent laparoscopic transmesocolic necrosectomy, 32 F catheter drainage of the cavity, and cholecystectomy 6 weeks after the diagnosis. Having postoperatively developed a pancreatic fistula with an output of approximately 100-150 mL/day, the patient was managed conservatively with nasojejunal enteral feeding. The patient developed intraabdominal collection postoperatively at 4 weeks, which was managed with a percutaneous drainage followed by laparoscopic lavage. After 12 weeks of conservative management, the patient was diagnosed with disconnected duct syndrome, and conservative management was continued for 3 more months due to a decreasing drain output. Pancreatic duct stenting was attempted but was not successful in cannulating the disconnected duct, and he was finally planned for RYFJ. The site of anastomosis was at the root of the mesocolon to the left of the middle colic vessels, approximately 4 cm from the pancreas. The surgery lasted 260 minutes, and blood loss was 200 mL. The patient developed wound infection postoperatively, which was managed by dressings and antibiotics. He is doing well at a 15-month follow-up.

Thus, 6 male patients underwent RYFJ for PEPF during the study period. Patient details, indication of primary surgery and postoperative management, duration of fistula, and other conservative measures taken before surgery are summarized in Table

1. Median delay from the diagnosis of fistula to surgery was 14 weeks (range: 12 weeks to 6 months). The use of a 32 F drain in 5 out of 6 patients helped in the development of a mature fistula tract with an adequate diameter. Mean intra-operative blood loss was 140 mL (range: 100 mL to 200 mL). Intra-operative surgical details are as shown in Table 2. Median follow-up was 15 months (range: 12 months to 60 months). The patients with chronic pancreatitis required the pancreatic enzymes replacement therapy 2 years following the RYFJ surgery. None of the patients had residual or recurrent intra-abdominal collections.

DISCUSSION

External pancreatic fistulas have been classified as side fistulas and end fistulas. End fistulas include disconnected duct syndrome (DDS), which is the most common cause of PEPF. DDS, which can be partial or complete, is necrosis of a pancreatic duct segment along with a large segment full-thickness parenchymal necrosis leading to the disconnection of distal viable pancreas. Side fistulas have been further subdivided into postoperative and postinflammatory sequelae (1). The fistula may originate in the head, neck, body, or tail of the pancreas. Sometimes, the proximal pancreatic duct is strictured, preventing spontaneous fistula healing, which results in PEPF (4).

DDS can be managed by endoscopic sphincterotomy with a bridging stent placement across the discontinuity in the pancreatic duct. The management of complete DDS depends on the presence or absence of a significant fluid collection (> 2 cm), demonstrable duct disconnection, and presence or absence of an external drain. When these factors are present, endoscopic or endoscopic-ultrasound- (EUS) guided transmural drainage with/without stenting or percutaneous transfistulous distal pancreatic duct drainage or embolization with prolamine, ethylene-vinyl alcohol, fibrin sealant, or cyanoacrylate glue can be attempted with variable results. When the duct is not demonstrable, an outside-in (percutaneous) approach followed by an endoscopy- or EUS-guided transmural drainage is required (1,4,7).

These procedures need high technical expertise and are so far recommended for low-output [< 200 cc/day] fistulas with a short tract [< 2 cm]. The availability of expertise, stent blockage or migration, hemorrhage, post-procedure pancreatitis, and need for multiple interventions are some of the limitations (7).

Pancreatic surgeries (resection or drainage) for PEPF require difficult dissection in inflamed and friable tissues, which lead to an increased blood loss, longer operative times, and an extended hospital stay with higher treatment costs. Resection procedures have higher postoperative morbidity and mortality (1-3). DDS itself increases the incidence of diabetes mellitus development and metabolic and nutritional abnormalities due to a chronic protein loss and pancreatic enzymatic insufficiency.

Portal hypertension and its complications can be exacerbated after surgery. The first fistulojejunostomy for PEPF was performed by Lahey and Lium in 1937 (8). Ihse in 1994 treated the persistent pancreatic fistula using fistulogastrostomy (9). Bassi et al. have given the classical description of the standard technique (3). Over the years, RYFJ has also been suggested for the treatment of chronic external refractory biliary fistula and post-sleeve gastrectomy fistula, and it has been attempted laparoscopically.

Fistulojejunostomy is performed at our center based on principles put forward by Bassi et al., and it preserves the pancreatic parenchyma and function (3). Dissection in the lesser sac and difficult pancreatic re-surgery are avoided. Dissection is simpler and guided by the drainage tube, leading to shorter operating times, with less blood loss. As a result, associated costs and hospital stay are also reduced (3,6,9).

Vascularity of the fistula tract improves as we move closer to the pancreas, and chances of a delayed pseudocyst formation due to tract obliteration reduce as the length of the fistula tract reduces. Hence, anastomosis should be performed as close to the pancreas as possible. Bassi et al. question the notion of going very close to the pancreas (3). In their experience, the difference in outcomes with different distances from the pancreas is not significant (1-3,9).

Over subsequent years, variants of fistulojejunostomy have been described with similar outcomes and no demonstrable superiority of one technique over other (5,6,10).

Embedding fistulojejunostomy has been suggested by Luo et al., in which the fistula tract is disconnected from the abdominal wall and drained externally through a transluminal tube drain, with both the drain and the tract fixed to a Roux loop of the jejunum with seromuscular sutures (5). The drain is also fixed to the abdominal wall with absorbable sutures and removed after 30 days. It is an easy and safe technique with very limited entry into the abdominal wall, but drawbacks include a 1-month longer waiting period and the need of pancreatic enzyme supplementation as long as the drainage tube is present (6).

The binding fistulojejunostomy technique involves suturing a 2 cm length of fistula tract (with a tube drain) to an everted cut end of the Roux loop after carbolic acid ablation of the jejunal mucosa in the everted segment. The everted bowel is then wrapped over this anastomosis site with seromuscular sutures.

The drainage tube is brought out transjejunally and through the abdominal wall, and it is removed after a month (10). Subcutaneous fistulojejunostomy involves bringing out a Roux loop of jejunum in the subcutaneous plane followed by anastomosis in that area with the disconnected fistula tract.

The proponents of this technique suggest that there is necrosis or stenosis of the embedded or buried part of the fistula along

with the anastomotic segment. The technique requires minimal dissection of the tract, and the anti-gravity position ensures that there is no enteric contents entering the loop, minimizing the chances of leak (5).

The optimal time of performing fistulojejunostomy is still a matter of debate. Across various studies, timing ranges from 2 months to 1 year (1,5,6,9,10). Bassi et al. have recommended 6 to 12 weeks after identification of PEPF as the appropriate time (3). A delay allows adhesions to soften, inflammation to subside, and the tract wall to thicken and mature enough to allow a secure anastomosis. In the present study, the procedure was performed 12-14 weeks from the first identification of fistula in 4 cases and in 2 cases after 6 months. Fistulojejunostomy was successful in all of the 6 patients without any major complications in our series. The study has the limitations of being a single-center experience, and hence including a small number of patients.

CONCLUSION

Fistulojejunostomy is a safe and effective treatment plan for PEPF with benefits of avoiding a difficult major pancreatic resectional re-surgery in an already debilitated patient with frozen tissue planes. This procedure has a relatively low postoperative morbidity and mortality with good short- to mid-term outcomes.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Lilavati Hospital and research Centre.

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - D.K., H.M., P.V.; Design - G.D., R.N., P.P.; Supervision - H.M., P.V., D.K.; Resource - R.N., P.P., G.D.; Materials - G.D., R.N., P.P.; Data Collection and/or Processing - P.V., D.K., H.M.; Analysis and/or Interpretation - D.K., H.M., P.V.; Literature Search - P.P., G.D., R.N.; Writing Manuscript - G.D., R.N., P.P.; Critical Reviews - D.K., H.M., P.V.

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

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OLGU SERİSİ-ÖZET
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Persistan eksternal pankreatik fistül tedavisinde Roux-en-Y fistülojejunostomi: Modası geçmiş bir yöntem mi?

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ÖZET

Giriş ve Amaç: Bu çalışmanın amacı, persistan eksternal pankreatik fistülün Roux-en-Y fistülojejunostomi ile cerrahi tedavisinde hasta seçimi ve yaklaşımın tespit edilmesi olmakla birlikte çalışma, ilgili literatürün gözden geçirilmesi ile Roux-en-Y fistülojejunostominin sonuçlarını da değerlendirmiştir.

Gereç ve Yöntem: Ocak 2010 tarihinden Mayıs 2017 tarihine kadar yürütülen retrospektif veri analizi persistan eksternal pankreatik fistül için altı hastanın Roux-en-Y fistülojejunostomi ile tedavi edildiğini ortaya koydu ve bu hastaların bilgileri bir proforma üzerine girildi. Bütün hastalarda standart cerrahi adımlar uygulandı ve hastalar postoperatif bir yıl boyunca takip edildi. Sonuçlar açısından veriler analiz edildi ve literatür tarandı.

Bulgular: Altı hastanın dördünde pankreatik nekrosektomiyi takiben persistan eksternal pankreatik fistül vardı, bir hasta pankreatik psödokist için opere edildi ve bir diğeri de pankreatikduodenektomi sonrası pankreas başında kitle sebebiyle opere edildi. Konservatif tedavinin ortalama süresi 14 haftaydı ve Roux-en-Y fistülojejunostomi orta hat laparotomi yoluyla pankreastan medyan 6 cm uzaklıkta yapıldı. Tüm hastalar majör komplikasyonlar geliştirmeden iyileşti. Sadece bir hastada, bir yıllık takip süresinde diabetes mellitus gelişti.

Sonuç: Fistülojejunostomi, persistan pankreatik fistül için zaten zayıflamış ve donmuş doku düzlemlerine sahip hastada zorlu majör pankreatik rezeksiyonel cerrahiden kaçınmaya yarayan güvenilir ve efektif bir tedavidir. Postoperatif morbidite ve mortalite oranı düşük olmakla birlikte bu prosedür için literatürde belirtilen kısa ve orta dönem sonuçlar iyidir ve bizim çeşitli endikasyonlara sahip bu çalışmamızda da bu sonuçlar görülmektedir.

Anahtar Kelimeler: Fistül, nekrosektomi, pankreas, pankreatikoduodenektomi, cerrahi

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CASE REPORT
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Perineal stapled rectal resection without a contour transtar: a modified approach

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ABSTRACT

Perineal stapled prolapse resection is a novel approach for treating rectal prolapse in elderly and frail patients. This study aimed to report a modified technique using only a straight linear stapler. A 94-year-old female with 15-cm full thickness rectal prolapse was treated using a linear cutter in the left and right lateral quadrants, and then resection was completed by using the same instrument in the anterior and posterior flaps. The procedure was performed under local anesthesia and in a prone jackknife position. There was no morbidity or mortality, and the patient was discharged on postoperative day 2. Follow-up at 9 months revealed no recurrent prolapse, and the patient was asymptomatic. This technique is easy, safe, and fast to perform without using contour transtar (Ethicon Endo-Surgery, Cincinnati, OH).

Keywords: Contour transtar, rectal prolapses, stapled resection

INTRODUCTION

The preferred treatment for frail and elderly patients with rectal prolapse is a perineal approach. Various techniques including Altemeier et al. and Delorme have been more commonly performed in such patients with full rectal prolapse (1,2). In 2008, Scherer et al. described a new perineal approach [perineal stapled prolapse (PSP) resection] and a further refinement of this technique was described by Romano et al. in 2009 (3,4). Main drawbacks of PSP are the high cost of two different kinds of staplers employed and a potential risk of damaging adherent peritoneal tissue.

CASE REPORT

A 94-year-old patient presented with a 3-month history of rectal pressure, bright red bleeding per rectum and a prolapsing mass that came out of her rectum after bowel movements. Her past medical history was significant for hypertension and degenerative joint disease. On examination, a 15-cm reducible rectal prolapse was noted. The patient denied symptoms of constipation or incontinence. After alternative procedures were discussed and lack of long-term data about PSP was disclosed, the patient gave consent for PSP. A full bowel prep was conducted and perioperative antibiotics were administered.

Surgical Technique

The patient underwent colonoscopy before the procedure with conscious sedation in the left lateral position. Subsequently, she was put in a prone jackknife position. A 10-inch roll was put under her hips and the buttocks were taped apart. This position is optimal as it gives good visualization and any potential organ in the pouch of Douglas that is pushed cranially away resulting from the prolapse. The patient received 1% lidocaine in 1:200.000 epinephrine as anesthetic, which was infiltrated with a 27-gauge needle to the perianal area and anal canal (total 22 cc of local anesthetic was used). The prolapse was corrected with Babcock clamps and bimanually examined to ensure that there were no intraperitoneal organs between the walls of the rectum. A linear straight stapler was used to divide the prolapse in the right and left lateral quadrants approximately 2 cm above the dentate line (Figures 1,2). After the stapler was fired, a 2-0 Vicryl suture (Ethicon Inc.; Somerville, NJ) was placed at the end of the staple line in each quadrant (Figure 3). Subsequently, the flaps were held and gently pulled with the Babcock clamp; then first the posterior and then

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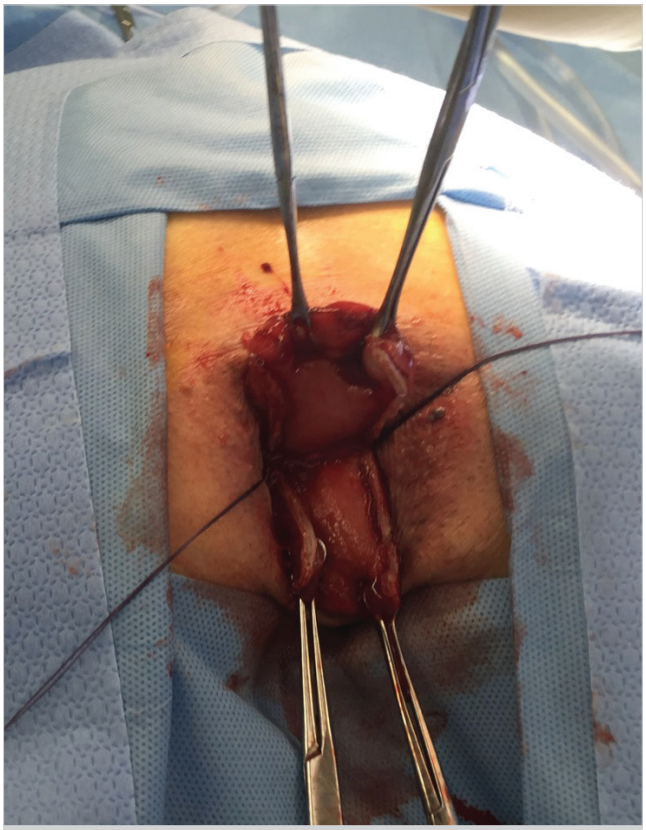

Figure 1. Division of the prolapses through the right and left quadrants.

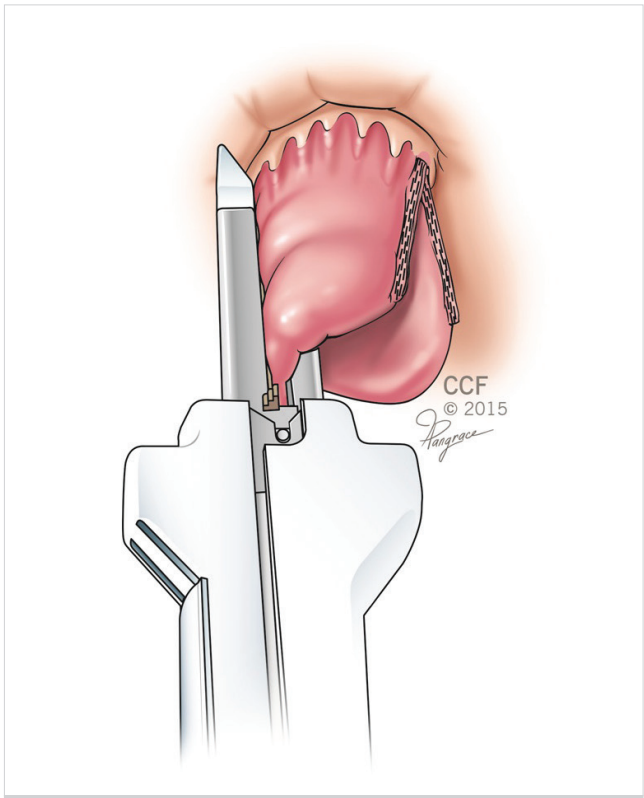

Figure 3. Placement of sutures at the end of staple lines in each quadrant.

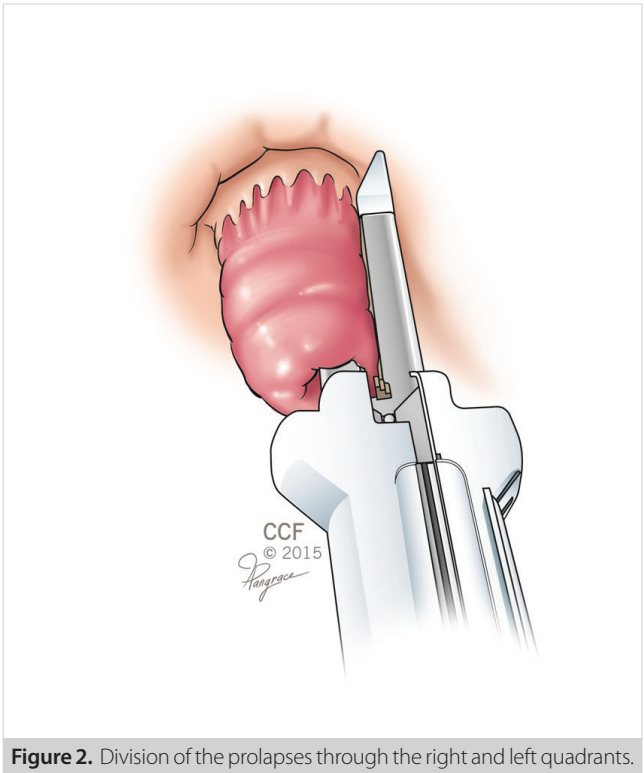

Figure 2. Division of the prolapses through the right and left quadrants.

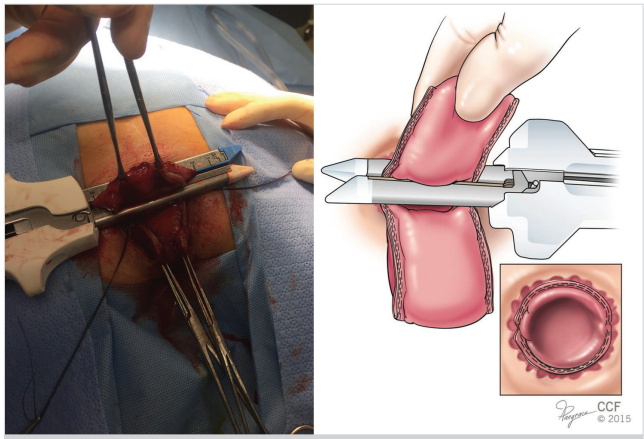

Figure 4. Division of the posterior and anterior flaps with linear stapler.

the anterior flap was again divided with the linear stapler (Figure 4). The stapler was positioned 2 cm proximal to the dentate line. Before stapling and cutting the anterior flap, the back wall of the vagina was checked. During this procedure, traction of the anterior flap with the Babcock clamp was maintained. After the last firing, the neorectum fell back. After each firing, the integrity of the staple line was checked. We routinely use a lighted bivalve anoscope and over-suture the staple line with a 2-0 Vicryl suture.

At the end of the procedure, a rigid proctoscopy was performed along with irrigation and suction. Postoperatively, a regular diet was administered.

RESULTS

The operative time lasted 48 min. No morbidity occurred, and the patient was discharged after 2 days. At follow-up of 9 months after surgery, no recurrent prolapse or incontinence was noted.

DISCUSSION

Rectal prolapse in old, frail patients with multiple comorbid conditions can be challenging. Perineal procedures are generally preferred in this group of patients but the optimum procedure in terms of safety, recurrence, and functional results is still debated. After Scherer described PSP in 2008 and a modification of this technique was reported by Romano in 2009, various authors have reported their experiences in this relatively new technique (3-7). The safety, technical ease, and comparable outcome have been confirmed in these reports (3-8).

A major concern with this technique has been the potential vaginal and even small bowel injury, especially in women with a history of hysterectomy (9). A steep Trendelenburg position in a patient who is in a lithotomy position and checking the vagina has been recommended to prevent such injuries. An alternative of using laparoscopic guidance during anterior stapling has been suggested as well. In our technique and in Romano's modification, the patient was operated in a prone jackknife position, which forces the small bowel to migrate cranially and away from the prolapse and minimizes this potential complication. In addition, the vagina falls away from the prolapse by gravity. Another concern with this technique is the increased cost and whether the cost-to-benefit ratio of PSP is justified.

The cost of linear staplers and a contour stapler varies due to contracts and geographic sites. However, the cost of four firings of a linear stapler compared to two firings of a linear stapler in addition to two firings of a contour transtar (Ethicon Endo-Surgery, Cincinnati, OH) is less. In our technique, contour transtar was not used but only a linear stapler with multifirings was, which decreased the cost by more than 50%. Although such cost saving is significant, it needs to be determined whether this overall cost is offset by the shorter operating and hospitalization time.

In addition, we performed this procedure under local anesthesia, in this way the patient was not subject to potential complications of general or spinal anesthesia.

CONCLUSION

The procedure is easy to perform and is suitable in a select group of frail, elderly patients. Long-term recurrence rate needs to be analyzed perhaps in a multicenter study.

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

Peer-review: Externally peer-reviewed.

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

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OLGU SUNUMU-ÖZET
Turk J Surg 2019; 35 (1): 70-73

Kontur transtar kullanılmadan perineal stapler rektal rezeksiyon: Modifiye yaklaşım

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ÖZET

Perineal staple prolapsus (PSP) rezeksiyonu yaşlı ve zayıf hastalarda rektal prolapsus tedavisi için yeni bir yaklaşımdır. Bu çalışmada, sadece düz çizgisel stapler (straight linear stapler) kullanarak modifiye teknik bildiriyoruz. Doksan dört yaşındaki bir kadın hastanın 15 cm tam kat rektal prolapsusu anterior ve posterior kapakları aynı enstrüman ile sol ve sağ yan kadranda lineer kesici kullanılarak tedavi edildi ve daha sonra rezeksiyonu tamamlandı. İşlem, lokal anestezi altında ve yüzüstü jackknife pozisyonda yapıldı. Postoperatif dönemde morbidite veya mortalite bildirilmedi ve hasta ikinci günde taburcu edildi. Dokuz ay takibi tamamlayan hastada rekürrens bildirilmedi. Bu teknik gerçekleştirmesi kolay, güvenli, hızlı ve kontur TranStar kullanılmadığı bir yöntemdir.

Anahtar Kelimeler: Transtar kontur, rektal prolapsus, stapler rezeksiyon

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CASE REPORT
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Laparoscopic partial cecum resection in appendiceal intussusception

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ABSTRACT

Appendiceal intussusception (AI) is a difficult disease to diagnose. Various features of the disease were analyzed in a 35-year-old female patient admitted with abdominal pain and diagnosed with AI. The diagnosis was made with colonoscopy and abdominal computed tomography. Laparoscopic partial cecum resection was performed. Pathology examination revealed foci of endometriosis externa, which infiltrated the muscular layer of the appendix. AI should be kept in mind in the differential diagnosis of recurrent abdominal pain. Colonoscopy is an indispensable examination for differential diagnosis. Laparoscopic partial cecum resection, preserving the ileocecal valve, is an appropriate treatment approach in irreducible cases that are not suspected to be malignant.

Key words: Appendix, intussusception, laparoscopy

INTRODUCTION

Appendiceal intussusception (AI), which is one of the rare types of intussusception, is seen in 0.01% of the patients who undergo appendectomy (1). Anatomical changes such as partially mobile meso-appendix or large proximal appendicular lumen may be the cause of AI. Appendiceal intussusception-related symptoms include lower abdominal pain, irregular defecation, nausea, vomiting, or rectal hemorrhage. Making a preoperative diagnosis of AI is quite difficult, and usually a computed tomography (CT) of the abdomen and colonoscopy are required (2). The aim of this study was to report a case of AI, secondary to endometriosis, on whom laparoscopic partial cecum resection was performed, preserving the ileocecal valve.

CASE REPORT

A 35-year-old female patient presented to the general surgery outpatient clinic with lower abdominal pain, nausea, and vomiting persisting for the past one week. The patient did not have any defecation problems, did not describe weight loss, altered defecation habit, or urinary tract complaints but had a history of left oophorectomy performed due to endometriosis 6 years ago.

On physical examination, the patient was hemodynamically stable. There was no abdominal distention. Tenderness was found in the right lower quadrant, and a palpable mass could be detected on deep palpation. No defense or rebound was determined. Rectal examination was normal. Intestinal sounds were active. Routine blood tests demonstrated C-reactive protein (CRP) of 16 mg/L, white blood cell count of 8490/mm^3, hemoglobin of 9.5 g/dL, hematocrit of 31%, and platelet count of 340.000/mm^3.

A polypoid mass lesion measuring 3 x 2.5 cm, protruding toward the cecum lumen in the right lower quadrant, was detected on abdominal CT (Figure 1). On colonoscopic examination, a mass lesion, which had exudative and necrotic fields, appearing as the appendix, protruding into the cecum was detected at the appendix root site (Figure 2). Pathology of the colonoscopic biopsy revealed that the findings could be related to gangrenous appendicitis and also an inflammatory condition involving the ileocecal region.

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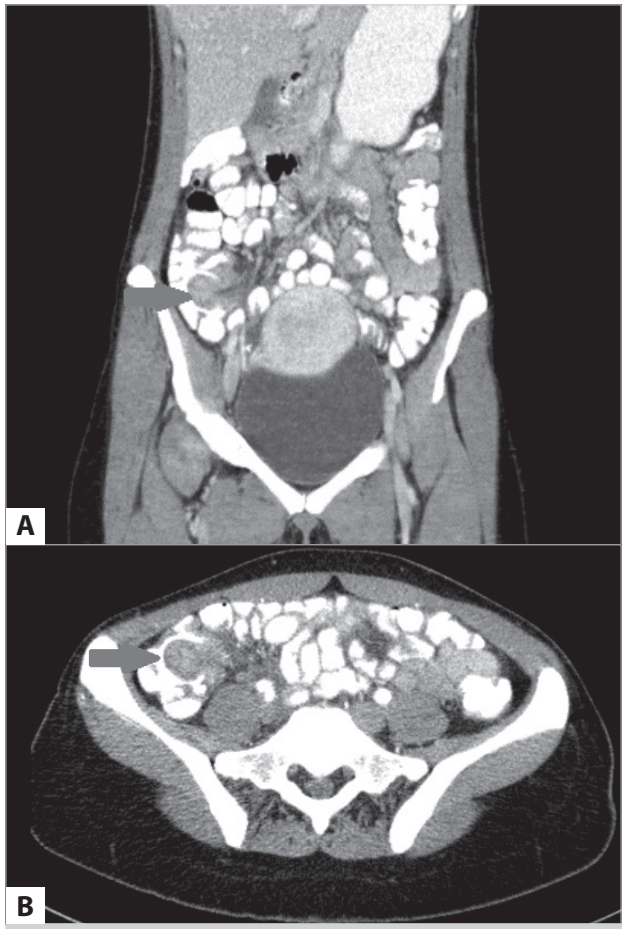

Figure 1 (A,B). Coronal **(A)** and axial **(B)** CT images of AI.

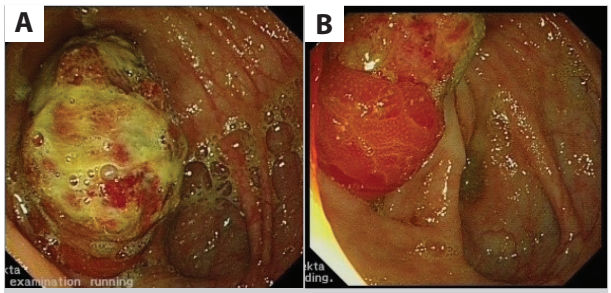

Figure 2 (A,B) Colonoscopy images of AI.

Laparoscopic surgery was planned with a preliminary diagnosis of AI. The patient was informed that different interventions could be applied if needed during the operation. Verbal and written informed consent were obtained from the patient. First, diagnostic laparoscopy was performed. On exploration, the appendix was found to be completely inverted into the cecum (Figure 3). After having decided that the inverted appendix could not be reduced, laparoscopic partial cecum resection was performed, preserving the ileocecal valve (Figure 4).

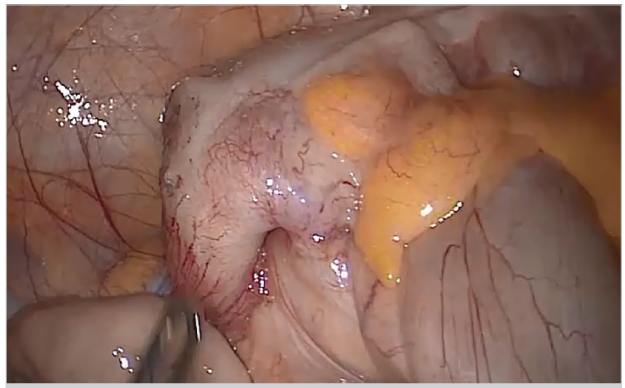

Figure 3. Intraoperative image of inverted appendix.

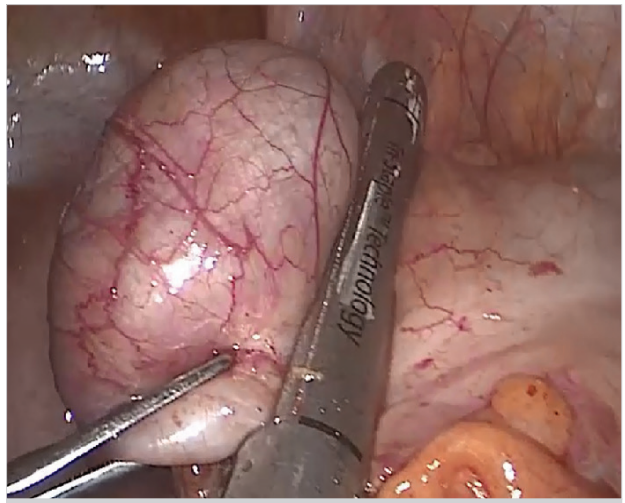

Figure 4. Intraoperative image of laparoscopic partial cecum resection.

The patient was followed in the hospital for 3 days without any complications. No complications developed during the postoperative 30 days. Foci of endometriosis externa infiltrating the muscular layer were detected on histopathological examination.

Laparoscopic surgery was planned with the pre-diagnosis of AI. The patient was informed that different interventions could be applied if needed during the operation. Verbal and written informed consent was obtained from the patient. First, diagnostic laparoscopy was performed. On exploration, the appendix was found to be completely inverted into the cecum (Figure 3). After having decided that the inverted appendix could not be reduced, laparoscopic partial cecum resection was performed, preserving the ileocecal valve (Figure 4).

The patient was followed in the hospital for 3 days without any complications. No complications developed during the postoperative 30 days. Foci of endometriosis externa infiltrating the muscular layer were detected on the histopathological examination.

DISCUSSION

AI is a rare condition. It was first reported by McKidd in 1858 (3). Collins have reported the incidence of AI as 0.01% as a result of the study conducted with 71.000 patients suffering appendicitis over the course of 40 years (4). Chaar et al. have reported in his study investigating 191 AI cases that 76% of the cases were adult and 24% were children (2).

Anatomical changes such as partially mobile meso-appendix or large proximal appendicular lumen may be the cause of AI. While inflammation is the most common cause of AI in children, endometriosis is the most common cause in adults (2, 5, 6). Other common causes include mucocele, adenoma, carcinoid, and adenocarcinoma (7-14). Papilloma, hamartoma, juvenile polyp, Crohn's disease, and melanosis coli are rare causes of AI (15-18).

Endometriosis is a common disease, which affects approximately 15% of the menstruating women in the United States. In the review of Robert et al. including 29 studies, appendix endometriosis has been reported in 336 out of 87.343 patients (0.4%) undergoing appendectomy (19).

Four different clinical types of AI have been reported. The first type mimics the classical type of acute appendicitis. The second type shows typical intussusception signs, which include abdominal pain and sometimes vomiting, accompanied by diarrhea and melena. The third type has signs and symptoms such as melena, vomiting, and recurrent right lower quadrant pain that can persist for weeks or months. The forth type includes patients who are completely asymptomatic (20). The most common signs are abdominal pain (78%), vomiting (26%), and rectal hemorrhage (23%). A mass lesion is detected in the right lower quadrant in 13% of adult patients and 37% of pediatric patients (2).

Preoperative diagnosis of AI is difficult. It is made postoperatively in many cases (57%). Diagnosis is made with postoperative pathological examination in 11% of the cases. Consequently, correct preoperative diagnosis has been made in only 32% of the cases (2). Barium contrast studies and abdominal ultrasonography have a limited value in the diagnosis of this rare condition. Abdominal CT is the most common imaging method. Colonoscopy is a very useful method in the diagnosis of AI in cases with abdominal pain and suspicious imaging findings (21). Our patient was evaluated with abdominal CT and the diagnosis was made with colonoscopy.

Different approaches have been used in the treatment of AI. Despite reports of successful colonoscopic appendectomy using the endo-loop ligation system, this approach may be harmful in patients who have partial intussusception (22-24). Spontaneously reduced AI cases have also been reported in the literature (25).

A total of 191 cases have been analyzed in one of the largest series in the literature, and appendectomy has been reported as the most common intervention (42% in adults, 71% in children). Ileocecectomy (27%) and right hemicolectomy (21%) have been performed in the remaining patients. Treatment with colonoscopy has been reported in four adult patients (3%) (2). While appendectomy is sufficient in cases with only intussusception, right hemicolectomy is more appropriate for patients who are suspected to have neoplasia (26,27). In our case, laparoscopic partial cecum resection was perfomed, preserving the ileocecal valve, as appendix reduction was not possible.

CONCLUSION

Preoperative diagnosis of AI, which is a rare condition, is important. We consider that laparoscopic partial cecum resection through preservation of the ileocecal valve anatomy is an appropriate approach in patients who are not suspected to have malignancy and whose appendix cannot be reduced.

Informed Consent: Verbal informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

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

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

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

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Turk J Surg 2019; 35 (1): 74-77

Apendiks intususepsiyonunda laparoskopik parsiyel çekum rezeksiyonu

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ÖZET

Apendiks intususepsiyonu klinik tanısı zor bir hastalıktır. Bu olgu sunumunda karın ağrısı nedeniyle başvuran ve apendiks intususepsiyonu tanısı ile tedavi edilen 35 yaşındaki kadın hasta vesilesiyle, hastalığın değişik yönleri incelenmiştir. Tanı kolonoskopi ve karın tomografisi ile konuldu. Laparoskopik parsiyel çekum rezeksiyonu uygulandı. Patolojik değerlendirmede apendiksin kas tabakasına infiltre olan endometriozis eksterna odakları tespit edildi. Apendiks intususepsiyonu tekrarlayıcı karın ağrısının ayırıcı tanısında düşünülmelidir. Kolonoskopi ayırıcı tanıya ulaşmada vazgeçilemez bir incelemedir. Redükte edilemeyen ve malignite şüphesi olmayan olgularda, ileoçekal valvi koruyarak laparoskopik parsiyel çekum rezeksiyonu uygun bir tedavi yaklaşımıdır.

Anahtar Kelimeler: Apendiks, intususepsiyon, laparoskopi

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