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Aims and Scope

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

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

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

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

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

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

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

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

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- 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).

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

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

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

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

Review Articles: Reviews prepared by authors who have extensive knowledge on a particular field and whose scientific background has been translated into a high volume of publications with a high citation potential are welcomed. These authors may even be invited by the journal. Reviews should describe, discuss, and evaluate the current level of knowledge of a topic in clinical practice and should guide future stud-



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Tables

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

Figures and Figure Legends

Figures, graphics, and photographs should be submitted as separate files (in TIFF or JPEG format) through the submission system. The files should not be embedded in a Word document or the main document. When there are figure subunits, the subunits

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

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

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

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

References

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

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

Table 1. Limitations	for each	n manuscript type
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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

TURKISH JOURNAL OFSURGERY



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

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

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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.

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REVISIONS

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

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Editorial

Dear colleagues,

We are pleased to present the latest issue of 2017, which includes valuable studies.

There has been important changes in our Journal within last year. First of all, we started to publish our Journal entirely in English. In the meantime, we expanded and strengthened the editorial board by including competent scientists from all over the world.

To improve the quality of our Journal, we requested from our esteemed colleagues to submit their articles. I have to express with pleasure that the interest you have shown to this invitation and the support you provided are worthy of respect.

These improvements had an impact almost immediately, and the number of citations our journal received increased in each issue. In parallel, the ranking of our Journal has increased among the international surgery journals that are indexed in Web of Science.

I would like to express my gratitude to the researchers who have submitted their articles to our Journal, to our referees who have evaluated the manuscripts with great attention, to our staff, and to our editor Prof. Dr. Can ATALAY and assistant Editor Assoc. Prof. Dr. İlhan ECE for their contributions.

I hope that 2018 brings peace and happiness to all humanity.

Sincerely,

Prof. Mustafa ŞAHİN

Editor in chief

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Comparison of the reliability and efficacy of LigaSure hemorrhoidectomy and a conventional Milligan-Morgan hemorrhoidectomy in the surgical treatment of grade 3 and 4 hemorrhoids

Mustafa Celalettin Haksal¹, Ali Ciftci², Cağrı Tiryaki², Murat Burc Yazıcıoğlu², Mehmet Özyıldız², Selim Yiğit Yıldız²

ABSTRACT

Objective: The aim of this study was to compare the clinical results of LigaSure-assisted hemorrhoidectomy and Milligan-Morgan hemorrhoidectomy as a conventional method in our clinic.

Materials and Methods: Patients who underwent LigaSure-assisted hemorrhoidectomy or conventional hemorrhoidectomy for grade 3 and 4 hemorrhoids in our clinic between 2009 and 2014 were included in this study. The patient data were reviewed by screening records. Gender, age, preoperative hemoglobin and hematocrit levels, operation time, presence of thrombosis, number of packages, hospitalization time, early and late postoperative complications, prolonged pain presence, and follow-up period were recorded.

Results: In this period, surgical interventions were performed on 365 patients diagnosed with hemorrhoids. Among these, 159 underwent LigaSure-assisted operations, while 206 were operated on by conventional methods. One hundred forty-four (39.5%) cases were female, while 221 (60.5%) cases were male. The median age of the patients was 40 (19-82) years in the LigaSure group and 41 (16-78) years in the conventional method group. The operation time was 15 (4-60) min in the LigaSure group and 20 (6-40) min in the conventional method group. Postoperative analgesics were given to the 182 (88.3%) cases in the conventional group and 107 (67.3%) cases in the LigaSure group. The time required for returning to normal daily activity was 6 (1-15) days in the LigaSure group and 7 (1-30) days in the conventional method group.

Conclusion: In this study, LigaSure was determined to be superior to a conventional method in terms of operation time, hospitalization period, postoperative analgesic requirements, time required for returning to normal daily activity, and postoperative bleeding.

Keywords: Hemorrhoids, hemorrhoidectomy, LigaSure, milligan-morgan hemorrhoidectomy

INTRODUCTION

Hemorrhoids are submucosal beds containing venules, arterial and smooth muscle fibers that are located on the anal canal. Hemorrhoidal disease is reported in approximately 5% of the general population, especially after 40 years of age (1, 2). Because hemorrhoids are normal anatomical components of the anal canal, treatment is indicated in only symptomatic cases. These symptoms include bleeding, thrombosis, and hemorrhoidal prolapses (3). Various methods are used in the treatment of hemorrhoids, including medical treatment, rubber band ligation, infrared photocoagulation, sclerotherapy, open hemorrhoidectomy, closed hemorrhoidectomy, whitehead hemorrhoidectomy, and stapler hemorrhoidectomy.

Conservative medical treatment is generally effective for grade 1 and 2 hemorrhoids; however, grade 3 and 4 hemorrhoids require surgical intervention. There are two especially well known surgical modalities for hemorrhoidectomy: open (Milligan-Morgan) (4) and closed (Ferguson) (5). These two methods have similar complications, such as blood loss and postoperative pain. Hospitalization time and time to return to work or normal daily activities are similar (6). LigaSure-assisted hemorrhoidectomy is an alternative to open hemorrhoidectomy in the treatment of grade 3 and 4 hemorrhoids (7). The Liga-Sure vessel sealing system (Covidien AS, Baltimore, US), is a hemostatic device that seals vessels by an optimized combination of radiofrequency ablation and pressure (8). LigaSure provides complete closure of arteries and veins with diameters of up to 7 mm. This method has some advantages, it is a fast procedure, easy to learn and providing excellent bleeding control, minimal tissue damage, low postoperative pain, and short time to return to normal daily activity (9-11).

In this study, we aimed to compare the clinical results of LigaSure-assisted hemorrhoidectomy and Milligan-Morgan hemorrhoidectomy in our clinic.

MATERIAL AND METHODS

All patients read and singed a procedural consent form before the operation. Patients who underwent

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LigaSure-assisted hemorrhoidectomy or conventional hemorrhoidectomy for grade 3 and 4 hemorrhoids in our clinic in between January 2009 and January 2014 were included in this study. The patient data were reviewed retrospectively by screening patient records and by telephone calls. Patients of both genders with grade 3 and 4 bleeding hemorrhoids were included in the study. The age range was 16-82 years. Patients with liver cirrhosis, uncontrolled diabetes mellitus, accompanying perianal disease, inflammatory bowel disease, pregnancy, or bleeding diathesis were excluded from the study. Colonoscopy was performed on all patients older than 50 years of age to exclude colon cancer. Anticoagulant or aspirin treatments were terminated five days before the treatment.

Patients underwent surgery under general or spinal anesthesia in the jackknife or lithotomy position. In the LigaSure group, the vessel of the package was sealed with LigaSure and the flaw was left open. In the other group who underwent surgery with the Milligan-Morgan method, the package was excised with cauter; the pedicle of the package was sutured, and the flaw was left open.

Gender, age, preoperative and postoperative 7th day hemoglobin and hematocrit levels, operation time, presence of thrombosis, number of packages, residual disease (untreated residual packages due to anal stenosis risk in patients with more than three packages), hospitalization time, early and late postoperative complications, presence of prolonged pain, follow-up period and time to return to normal daily activity or work were recorded. Postoperative analgesia (a nonsteroidal anti-inflammatory drug) was provided only for patients with pain. Patients were contacted by telephone and asked about the presence of pain 30 days after hemorrhoidectomy in their follow-ups.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences 20.0 for Windows (IBM Corp.; Armonk, NY, USA). Results were given as percentages, mean and standard deviation, or median and range. Quantitative variables were compared with Student's t-test or the Mann-Whitney U test, and qualitative variables were compared with chi-square (Pearson's or Fischer's exact) tests. A p value less than 0.05 was considered to be significant.

RESULTS

In this period, surgical interventions were performed in 365 patients diagnosed with hemorrhoids. Thirty-one (8.5%) cases could not be reached by telephone. Among those 365 cases, 159 underwent LigaSure-assisted operations, while 206 underwent operations by a conventional method. One hundred forty-four (39.5%) cases were female, while 221 (60.5%) cases were male. The median age of all the cases was 41 (16-82) years. Preoperative hemoglobin and hematocrit levels were 13.5 (7.2-17.2) and 39.4±5.9, respectively, in the conventional method group and 13.9 (5.2-18.0) and 40.1±6.0 in the LigaSure group. All patients were asked to return for follow-up on the 7th day after operation in our clinic. The hemoglobin and hemato-

Table 1. Demographic features of patients									
Feature	Milligan-Morgan hemorrhoidectomy	LigaSure-assisted hemorrhoidectomy	р						
Patient number	206	159							
Median age (years)	41	40	0.615						
Gender (%)									
Male	122	99	0.556						
Female	84	60							
Preoperative hemoglobin (g/dL)	13.5 (7.2-17.2)	13.9 (5.2-18.0)	0.242						
Preoperative hematocrit (%)	39.4±5.9	40.1±6.0	0.279						
Postoperative 7 th day hemoglobin (g/dL)	13.1±1.9 (n=119)	13.4±1.9 (n=87)	0.334						
Postoperative 7 th day hematocrit (%)	39.2±5.2 (n=119)	39.7±5.1 (n=87)	0.57						

Table 2. Features of LigaSure and conventional method									
Feature	Milligan-Morgan hemorrhoidectomy	LigaSure hemorrhoidectomy	р						
Operation time [mean (range) min]	20 (6-40)	15 (4-30)	<0.05						
Number of packages	2 (1-4)	2 (1-4)	0.5						
Analgesic requirement n (%)	182 (88.3)	107 (67.3)	<0.05						
Thrombosed hemorrhoids	10 (4.9)	13 (8.2)	0.195						
Hospitalization time (days)	1 (1-16)	1 (1-2)	<0.05						
Re-operation n (%)	3 (1.6)	4 (2.7)	0.704						
Return to normal daily activity [mean (range) days	5] 7 (1-30)	6 (1-15)	<0.05						
Prolonged pain n (%)	27 (14.7)	10 (6.8)	<0.05						
Follow-up (months)	28.3±15.7	25.9±15.6	0.176						

Table 3. Complications									
Complication	Milligan-Morgan hemorrhoidectomy	LigaSure hemorrhoidectomy	р						
Bleeding	24 (12.9)	7 (4.7)	<0.05						
Necrosis	1 (0.5)	0	0.999						
Edema	1 (0.5)	1 (0.7)	0.999						
Residual disease	10 (5.4)	5 (3.4)	0.370						
Anal stenosis	1 (0.5)	4 (2.7)	0.175						
Datas were presented as n (%)									

crit levels in the first follow-up on the 7th day were 13.1±1.9 and 39.2±5.2, respectively, in the conventional method group and 13.4±1.9 and 39.7±5.1, respectively, in the LigaSure group (Table 1). There was no statistically significant difference between the groups regarding age, gender, preoperative hemogram level, or postoperative 7th day hemogram level. The number of packages treated with surgery was similar in the two groups in our study. The operation time was 15 (4-60) min in the LigaSure group and 20 (6-40) min in the conventional method group. Operation time was statistically significantly shorter in the LigaSure group.

Analgesia is not routinely provided to all hemorrhoidectomy cases after surgery in our clinic; it is reserved for patients who complain of pain. Postoperative analgesics were required in 182 (88.3%) cases in the conventional group and in 107 (67.3%) cases in the LigaSure group; the difference was statistically significant (p<0.05). Thrombosis was present in 10 (4.9%) patients in the conventional method group and in 13 (8.2%) cases in the LigaSure group (p=0.195). Re-operation was required because of bleeding in two (1%) patients in the conventional method group and in four (2.7%) patients in the LigaSure group (p<0.05). In one case in the conventional method group, re-operation was required due to necrosis. All patients were discharged in good health after the re-operations.

The median hospitalization time was 1 (1 to 2) day in the LigaSure group and 1 (1-16) day in the conventional method group (p<0.05). The time to return to normal daily activity was 6 (1-15) days in the LigaSure group and 7 (1-30) days in the conventional method group (p<0.05). The follow-up period was 25.9±15.6 months in the LigaSure group and 28.3±15.7 months in the conventional method group (p<0.05). In this study, patients were asked about the presence of pain in the first 30 days after hemorrhoidectomy. Ten (6.8%) of the cases who underwent operations with LigaSure and 27(14.7%) of the cases who underwent operations with a conventional method stated that they had pain (p<0.05) (Table 2). Bleeding was reported in 31 cases in the first seven days. Among these, 24 underwent operations with a conventional method and 7 underwent LigaSure-assisted operations; the difference was statistically significant (p<0.05). Two of the 24 and 4 of the 7 patients underwent re-operations for bleeding. Bleeding stopped spontaneously in the other cases. Regarding early complications, necrosis that was re-operated and then discharged on the 16th day of hospitalization and edema was present in one patient in the conventional method group. In the LigaSure group edema was reported in one case. However dema was spontaneously resorbed in both group. Residual disease was determined in 10 (4.9%) cases in the conventional method group and in 5 (3.1%) cases in the LigaSure group (p=0.370). Gas incontinence was reported in eight cases in the conventional method group and in two cases in the LigaSure group (p=0.195). Anal stenosis was reported in one case in the conventional method group and four cases in the LigaSure group (p=0.175). These five cases were treated with an anal dilatator without any further complications (Table 3).

DISCUSSION

Conventional methods have been used as surgical treatment modalities for grade 3 and 4 hemorrhoids for more than half a century (7). LigaSure is a device used in hemorrhoidectomy that coagulates vessels with diameters of up to 7 mm, with thermal damage to the adjacent tissue of up to 2 mm. This advantage enables rapid dissection of hemorrhoids without blood. Comparative studies of LigaSure with conventional methods can be found in the literature (7, 12).

According to a study by Peker et al., (12) in the LigaSure group, operation and return to work times were shorter than in the conventional group, while hospitalization and complication rates were similar. In a meta-analysis by Mastakov et al. (11) on 11 studies with 1,046 patients, in patients who underwent LigaSure operations, almost all outcome parameters were better than those of the conventional group except complications. In many studies included in the meta-analysis by Mastakov et al. (11), postoperative analgesic requirements were reported to be statistically significantly lower in the LigaSure group. Similarly, in our study, postoperative analgesic requirements were significantly lower in the LigaSure group (107 versus 182 patients). This significant difference is believed to be due to the transfixion suture on the vessel pedicle used in conventional methods. In many studies, the operation time was determined to be significantly shorter in LigaSure-assisted hemorrhoidectomy (12.5 vs. 29) (7), [22.3 vs. 27.4] (13), [9.4 vs.18.2] (14). Similarly, in our study with LigaSure, an easily applicable and trainable method, the operation time was significantly shorter than in the conventional method (15 versus 20 min). In a study by Khanna et al. (7), the hospitalization period after operation (1.4 versus 3.2 days) was significantly shorter in the LigaSure group; however, in a study by Gentile et al. (13), the hospitalization periods of 24±2 h were similar in the two groups. In our study, the median hospitalization period was one day in both groups.

Rapid healing of the injury site accelerates return to normal daily activity. Patients who underwent LigaSure operations returned to their normal daily activities in a significantly

shorter time than patients in the conventional group (6 versus 7; p<0.05). Chung and Wu (15) did not report any difference in these parameters; however, similar to our results. Milito et al. (9) and Sayfan et al. (16) (7.4 versus 18.6 days) defined shorter time periods for returning to normal daily activities in their LigaSure groups. While the postoperative bleeding ratio was 4.7% with LigaSure in our study, this ratio was 3.5% in the study by Khan et al. (7). The postoperative bleeding ratio was 12.9% with the conventional method in our study, whereas this ratio was similar in the study by Khan et al. (10.0%) (7). The incidence of residual hemorrhoid in the study by Khan et al. (7) was lower in the LigaSure group (3.5% versus 5%); similarly, in our study, this ratio was determined to be lower in the LigaSure group (3.4% versus 5.4%). However, in both the literature and in our study, these differences were not statistically significant. Development of anal stenosis due to thermal damage from LigaSure usage has been described in many recent studies. Filingeri et al. (17) reported anal stenosis in 4 of 203 LigaSure-treated patients, Wang (18) determined it in 1 of 42 cases, and Gentile et al. (13) reported it in 1 of 25 patients. In our study, the results for anal stenosis were similar to the literature (2.7%) (9, 11). We treated five cases of anal stenosis with an anal dilator. The key point to prevent development of anal stenosis is to preserve mucosal bridging and the anoderm.

CONCLUSION

This retrospective study demonstrates the advantages of Liga-Sure compared with a conventional method in the treatment of grade 3 and 4 hemorrhoids. In this study, LigaSure was determined to be superior to a conventional method in terms of operation time, hospitalization period, postoperative analgesic requirements, time to return to normal daily activity, and postoperative bleeding.

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

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

Peer-review: Externally peer-reviewed.

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Contribution of an educational video to surgical education in laparoscopic appendectomy

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ABSTRACT

Objective: With recent widespread advances in laparoscopy, providing education on this subject has become a significant challenge. The aim of this study was to determine the degree of contribution made by surgeons to laparoscopic education through an educational video.

Material and Methods: A total of 40 volunteer general surgery residents and specialists participated in our study. Before watching the approximately six-minute educational video prepared for laparoscopic appendectomy, the participants were asked to fill out participant information forms and information measurement questionnaire forms. After the video, the participants were asked to fill out the information measurement questionnaire forms a second time; additionally, attitude evaluation forms and education evaluation questionnaire forms were presented to the participants for completion, and statistical analysis was performed. Furthermore, the total watching duration and the number of times the video was paused were recorded.

Results: A total of 40 surgeons participated in the study (75% residents and 25% specialists). When the results of the information determination questionnaire forms filled out by the resident and specialist groups before and after the video were compared, it was observed that the scores of both groups significantly increased after watching the video (p=0.001). A statistical significance was identified between the length of time the video was watched and the education evaluation form scores of the participants (p<0.01). It was observed that the longer the video was watched, the greater the increase in the education evaluation scores. The results of the attitude evaluation forms implied that the video could be produced more professionally.

Conclusion: Although education is an inevitable requirement of laparoscopic surgery, many teaching methods are available. Awareness-enhancing videos prepared on this topic can be efficient in providing laparoscopic education.

Keywords: Education, laparoscopic surgery, video

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INTRODUCTION

Laparoscopy is becoming an essential procedure for surgeons. Laparoscopy is frequently being used in very simple to complicated operations and is threatening to replace conventional surgery (1, 2). For surgeons to safely apply laparoscopic procedures in daily practice, they should enhance their cognitive and psychomotor skills; surgeons often first perform these procedures on devices such as training boxes or simulators (3, 4). In general surgery, advanced laparoscopic surgery procedures are being used daily in many clinics, from basic laparoscopic surgeries such as cholecystectomy and appendectomy to colectomy, bariatric surgery, fundoplication, splenectomy, surrenalectomy, hepatectomy, and the Whipple procedure. These surgical procedures are being taught in two ways. Simulators, such as simple educational boxes, can be used as educational models by increasing skill level and simulating operations without intervention on live patients; they can also be used as video models for measuring surgeons' levels of knowledge of laparoscopic surgery, demonstrating the surgery, and describing technical errors. Furthermore, simulators can be educational tools for determining the contribution of the videos to this subject by re-evaluating the surgeons' knowledge after the education program (5-7). Despite current technological advances, laparoscopic education cannot be sufficiently provided through only a master-apprentice relationship; therefore, it can be useful to provide this education on a periodic basis (5, 8).

The aim of this study was to measure the level of knowledge of surgeons on laparoscopic appendectomy, which is one of the most performed operations in surgery clinics; after asking the surgeons to watch an educational video, we evaluated its contribution to their education.

MATERIAL AND METHODS

This study was performed between October 2015 and November 2015 with approval from the local ethics committee. The study was sponsored by the Scientific Research Project body of Adnan Menderes University. A total of 40 volunteer general surgery residents and specialists participated in the study.

Participants were informed about the objective of the study, and their written consent was obtained. Surgeons who did not wish to participate were excluded from the study. All the research participants watched the educational video, which was approximately six minutes in lengt hand explained laparoscopic appendectomy surgery, the way it is performed, the trap points and tricks of surgery, and complications; the surgery was demonstrated later. The advantages of the operation and definitions of the instruments and trocar parts were described in the first portion of the video. Brief anatomical information was then provided. Next, the surgical technique was described step by step. Complications were also discussed in the video. Finally, the surgery was shown. However, before the participants watched the video, they were asked to complete two forms: the "participant information form" questionnaire, with the intent of obtaining demographic and occupational information from all participants, consisting of 11 questions; and the "information measurement form" (IMF) questionnaire, with the intent of measuring the participants' level of knowledge, consisting of 20 questions. The questionnaires were administered in person. The IMF questionnaire contained 20 questions, ranging from the number of trochars to insufflation pressure and complications, and was evaluated with 5 points for each correct answer and 0 points for each wrong answer (Table 1). The total scores were found to be between 0 and 100. After completing these questionnaires, the participants watched the video; they paused the video when they wanted to ask a question, then continued watching. At the end of the video, the IMF questionnaire was administered again to evaluate the participants' level of knowledge. Furthermore, to evaluate the contribution of the video to the education of the surgeons, an "attitude evaluation form" questionnaire containing 9 questions and an "education evaluation form" questionnaire containing 23 questions were conducted. The respondents were asked to provide scores between 1 and 5 (1: not good at all, 2: not good, 3: medium, 4: good, 5: very good). Also, the amount of time they watched the video, the number of times they paused the video, and the number of questions asked were recorded. At the end of the study, CDs of the educational video were given to the participants so that they could watch it whenever they wanted.

Statistical Analysis

The resulting data were analyzed using the Statistical Package for the Social Sciences program (SPSS Inc.; version 17, Chicago, IL, USA). Descriptive statistics (mean, standard deviation, median value, minimum, maximum, number, and percentile) were identified for categorical and continuous variables in the study. The homogeneity of variance, which is a precondition of parametric tests, was also controlled using Levene's test. The assumption of normality was controlled using the Shapiro-Wilk test. To evaluate the differences between the two groups, provided that they satisfied the preconditions of the parametric test, Student's t-test was applied; otherwise, the Mann-Whitney U test was used. If the differences between two dependent groups satisfied the preconditions of parametric tests, they were evaluated by the matched-pair t-test; otherwise, they were evaluated using the Wilcoxon test. In cases where the relationship between two continuous variables did not satisfy the Pearson correlation coefficient or the preconditions of parametric tests, the data were evaluated using the Spearman correlation coefficient. The test was performed

Table 1. Information measurement form

General surgery laparoscopic appendectomy education information measurement form

Subject: Laparoscopic appendectomy video presentation

Your profile: a. Assistan b. Specialist

Questions

- 1. What is the number of trocar in laparoscopic appendectomy?
- Please describe the trocar entry places in laparoscopic appendectomy?
- 3. What are the trocar diameters in laparoscopic appendectomy?
- 4. What is the degree of laparoscope used?
- 5. How much mmHg is the pressure?
- 6. How is the position of the patient?
- 7. How is the anesthesia that applied to the patient?
- 8. Which probes should be attached to patient?
- 9. How appendix is detected with laparoscopic method?
- 10. What is the position of surgeon and assistant in laparoscopic appendectomy?
- 11. What is the critical opinion of laparoscopic appendiceal?
- 12. Is the group of patient is present that laparoscopic appendectomy is useful for?
- 13. Provided that your answer is yes in the twelfth question, then please describe these groups.
- 14. How is appendix's meso separated in laparoscopic appendectomy?
- 15. How is appendix's root separated in laparoscopic appendectomy?
- 16. How appendix is taken out of batin after laparoscopic appendectomy?
- 17. Which organs are under risk at surgery place?
- 18. Which advantages does laparoscopic appendectomy have as compared to open appendectomy?
- 19. What are the reasons for short passing?
- 20. What are the complications?

using retest reliability coefficients and intra-class correlation coefficients. The relationships between categorical variables were analyzed using Fisher's exact test and the chi-square test. In cases where the expected frequency was less than 20%, to include these frequencies in the analysis, the evaluation was conducted by the Monte Carlo simulation method. P<0.05 was considered as statistically significant.

RESULTS

Participants

A total of 40 people were included in the study; 80% of these individuals were male, while 20% were female. With respect to their educational status, 75% of the participants were residents, while 25% were specialists. The average age was 31.08 (min: 27; max: 40) years. Their average period of service was 4.2 (min: 1; max: 12) years.

Laparoscopic Surgery Education

All the participants stated that they had received training in laparoscopic appendectomy during their residency education. While 17.5% of the participants stated that they had performed advanced laparoscopic processes as well as appendectomy and cholecystectomy during the period of residency training, 82.5% stated that they had not attempted any advanced laparoscopic procedures during that time. While the scores of the IMF questionnaire administered before watching the educational video were lower, the scores increased after the video was watched. When the scores of the resident and specialist groups and the genders were compared, it was found that all the scores after watching the video significantly increased (p=0.001). When the scores of all questions included in the attitude evaluation form were compared for the residents and specialists, no statistical difference was determined between the two groups (p:0.584). It was found that the education provided after the questionnaires were administered increased the level of awareness (p=0.306); however, participants recommended this training to their colleagues (p=0.306) and felt that this type of education should continue (p:0.584). Also, the answers provided in this form implied that the video could have been produced more professionally.

The average video watching durations of the participants were found to be 7.11 ± 2.25 minutes for specialists and 6.10 ± 1.11 minutes for residents. A statistical significance was identified between the time that elapsed while the participants watched the video and the scoring of the education evaluation form (p<0.01). It was found that as the elapsed time increased, the education evaluation scores also increased. In addition, regarding the scores of the education evaluation forms, a statistically

Table 2. Respondents demographic data N (frequency) Percent (%) Sexuality Male 32 80.0 8 20.0 **Female Educational status** 75.0 Assistant 30 Specialist 10 25.0 **Educational institution** 32.5 University 13 27 67.5 Education and research hospital Have you applied the method of laparoscopic appendectomy? Have you received an education with the subject of laparoscopic appendectomy in the education period before graduation? 100.0 No 40 Have you received an education of laparoscopic process under a different title except for laparoscopic appendectomy approach? Yes 17.5 82.5 No 33 40 100.0 Total

significant difference was found between the evaluations of the residents and specialists (p=0.011). It was observed that residents gave higher scores when evaluating the video. The frequency values of the education evaluation form are given in Table 2, 3.

DISCUSSION

Currently, laparoscopy is replacing conventional surgery for many methods, and its widespread importance in daily use is rapidly increasing (9). However, this progress has some disadvantages. If surgery residents are inexperienced, especially in advanced laparoscopy surgeries, they should receive good training in this field (6). Many methods are available to provide this training. Although highly developed and very workable three-dimensional simulation devices are available in this field, their greatest disadvantages are that they are very expensive and are not accessible in every center (10). Additionally, simple and easy-to-operate laparoscopic educational devices are being manufactured. Chen et al. (11) reported that great progress could be achieved in laparoscopic training with simple training boxes that they made themselves. It was revealed in another study by Munz et al. (8) that there was no significant difference between groups operating with laparoscopic simulator devices and simple laparoscopic boxes in practice. It is stated in the literature that similar inexpensive education boxes could contribute to laparoscopic education; however, we considered that a contribution to laparoscopic education could also be provided by conducting questionnaires measuring the laparoscopic education level of surgeons, and after determining this level, identifying the missing aspects of the surgeons' knowledge, asking them to watch educational videos, and then re-measuring their levels of knowledge. We applied this educational method specifically for appendectomy, which is among the most common emergency operations.

While the educational box method is usually highly preferred in laparoscopic education, educational videos have been used in many centers, even in the "problem-based teaching" programs of medical school students (12, 13). In this method, participants can note their mistakes and make efforts to correct them; by continuously watching new educational videos, they remember key points and information. We primarily intended to measure the participants' level of knowledge with the IMF questionnaire. Before and after watching the video, the participants were asked two questions with very different answers: "How is the appendix detected by laparoscopic methods"? and "What is the laparoscopic appendiceal critical opinion"? These questions, which were generally answered incorrectly by both specialists and resident surgeons before watching the video, were generally answered correctly after watching the video. It was observed that almost all the other questions were answered correctly to a certain extent after the participants watched the video. As a result, we suggest that the educational video had a positive effect on the IMF questionnaire. Although we claim that no statistically significant difference was observed between residents and specialists with respect to the attitude evaluation form, the educational video helped to increase the participants' awareness of laparoscopy, as previously implied by the answers of the participants, and increased their levels of decision-making and skill; in

			Not good at all	Not good	Medium	Good	Very goo
Was the education arrangement date (timing) appropriate for you?	Assistan	n %	1 50.0	4 80.0	1 20.0	19 82.6	5 100.0
	Specialist	n %	1 50.0	1 20.0	4 80.0	4 17.4	0 0.0
Was the device required for watching the education video sufficient?	Assistan	n %	1 100.0	0 0.0	4 66.7	14 70.0	11 91.7
	Specialist	n %	0 0.0	1 100.0	2 33.3	6 30.0	1 8.3
Was the duration of the education video enough?	Assistan	n %	0 0.0	0 0.0	1 100.0	14 77.8	15 71.4
	Specialist	n %	0 0.0	0 0.0	0 0.0	4 22.2	6 28.6
Did the content of education comply with education's aim and was it sufficient?	Assistan	n %	0 0.0	1 100.0	4 80.0	13 86.7	12 63.2
	Specialist	n %	0 0.0	0 0.0	1 20.0	2 13.3	7 36.8
Was the education place appropriate for the education?	Assistan	n %	1 100.0	0 0.0	4 66.7	17 77.3	8 88.9
	Specialist	n %	0 0.0	2 100.0	2 33.3	5 22.7	1 11.1
Does the theoretical information displayed at the educational video comprise	Assistan	n %	0 0.0 0	0 0.0 0	0 0.0 4	18 90.0 2	12 75.0 4
study objectives?	Specialist	n %	0.0	0.0	100.0	10.0	25.0
Was the surgery images displayed at the educational video sufficient?	Assistan	n %	0 0.0	2 100.0	8 72.7	7 53.8	13 92.9
	Specialist	n %	0 0.0	0 0.0	3 27.3	6 46.2	1 7.1
Did the points that need to be paid attention emphasize?	Assistan	n %	0 0.0	1 100.0	1 50.0	14 77.8	14 73.7
	Specialist	n %	0 0.0	0 0.0	1 50.0	4 22.2	5 26.3
Did the subject discuss with appropriate methods and techniques?	Assistan	n %	1 100.0	0 0.0	0 0.0	13 72.2	16 80.0
	Specialist	n %	0 0.0	0 0.0	1 100.0	5 27.8	4 20.0
Was time used effectively and efficiently during education?	Assistan	n %	1 100.0	2 100.0	3 75.0	12 66.7	12 80.0
	Specialist	n %	0 0.0	0 0.0	1 25.0	6 33.3	3 20.0
Nas the issue clear understandable and appropriate to your level?	Assistan	n %	0 0.0	1 100.0	2 50.0	15 71.4	12 85.7
	Specialist	n %	0 0.0	0.0	2 50.0	6 28.6	2 14.3
Did you feel need to ask questions to observer educator while watching the educational film?	Assistan	n %	0 0.0	2 66.7	6 60.0	13 76.5	9 90.0
	Specialist	n %	0 0.0	1 33.3	4 40.0	4 23.5	1 10.0
Did the observer educator answer your questions?	Assistan	n %	0 0.0	0 0.0	3 75.0	10 62.5	17 85.0
	Specialist	n %	0 0.0	0 0.0	1 25.0	6 37.5	3 15.0
Was any resource recommended to develop your information?	Assistan	n %	0 0.0	0 0.0	1 50.0	9 56.3	20 95.2
	Specialist	n %	1 100.0	0 0.0	1 50.0	7 43.8	1 4.8

Table 3. Education evaluation form (Continu	ıe)						
Was the presentation sufficient visually and aurally?	Assistan	n %	0 0.0	0 0.0	0 0.0	19 86.4	11 73.3
	Specialist	n %	0 0.0	0 0.0	3 100.0	3 13.6	4 26.7
Did education contribute to your professional development positively?	Assistan	n %	0 0.0	0 0.0	1 33.3	10 62.5	19 95.0
	Specialist	n %	1 100.0	0 0.0	2 66.7	6 37.5	1 5.0
Did education contribute to your personal development positively?	Assistan	n %	1 100.0	2 66.7	2 66.7	15 78.9	10 71.4
	Specialist	n %	0 0.0	1 33.3	1 33.3	4 21.1	4 28.6
Did education bring new knowledge and skills?	Assistan	n %	0 0.0	1 100.0	0 0.0	16 80.0	13 76.5
	Specialist	n %	0 0.0	0 0.0	2 100.0	4 20.0	4 23.5
Did education increase your motivation?	Assistan	n %	0 0.0	0 0.0	2 66.7	14 87.5	14 73.7
	Specialist	n %	0 0.0	2 100.0	1 33.3	2 12.5	5 26.3
Did education bring new knowledge and skills that you can apply at your institution?	Assistan	n %	1 100.0	0 0.0	3 42.9	14 77.8	12 85.7
	Specialist	n %	0 0.0	0 0.0	4 57.1	4 22.2	2 14.3
Did education bring new knowledge and skills that you can share with your collegues?	Assistan	n %	0 0.0	1 100.0	4 50.0	13 76.5	12 85.7
	Specialist	n %	0 0.0	0 0.0	4 50.0	4 23.5	2 14.3
Did education increase your interest on the issue?	Assistan	n %	0 0.0	0 0.0	4 80.0	18 81.8	8 61.5
	Specialist	n %	0 0.0	0 0.0	1 20.0	4 18.2	5 38.5
How would you overview the education?	Assistan	n %	0 0.0	1 100.0	0 0.0	18 75.0	11 84.6
	Specialist	n %	0 0.0	0 0.0	2 100.0	6 25.0	2 15.4

contrast, we were informed that the educational video could be produced more professionally. Although we achieved our goal of increasing the participants' awareness and decision-making levels, our video was simple and plain; as we were criticized regarding this issue, we believe that more expensive three-dimensional films should be produced with the intent of increasing surgeons' interest and participation.

Educational videos are currently widely used as a means of communication in conventional surgery. However, few laparoscopic surgery programs have been evaluated by questionnaires to measure surgeons' levels of knowledge and provide corresponding education. Levi et al. (14) stated that in their study performed with two groups, in which an educational box was compared with a video, the two groups gained no advantages over each other with respect to education. In our study, the other parameters we evaluated in the video group were video watching time and the number of repetitions. When we compared resident and specialist surgeons, we found a statistically significant difference between elapsed time while watching the video and educa-

tion evaluation form score (p<0.01). It was observed that as the elapsed time increased, the education evaluation score also increased. Residents gave higher education evaluation scores after watching the film (p=0.011). When we reviewed the education evaluation form and questionnaire, we found that the video was useful for laparoscopic education and helped increase the participants' decision-making skills; however, a more professionally produced educational video would provide a greater contribution to surgeons' education.

CONCLUSION

Good education is currently required for advanced laparoscopy, which is rapidly replacing conventional surgery, and many methods exist to provide this education. Among these, educational videos can both identify levels of knowledge and fill knowledge gaps on this issue, while increasing levels of awareness and decision-making ability. Inexpensive professional educational films produced on this subject are a source of knowledge that all surgeons can draw upon throughout their careers and use when making decisions.



Video: Laparoscopic appendectomy education video

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Adnan Menderes University (Number of 2014/477).

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

Peer-review: Externally peer-reviewed.

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

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An unusual cause of hypercalcemic crisis: Water-clear cell double parathyroid adenoma

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ABSTRACT

Objective: To evaluate the clinical characteristics of a patient operated for water-clear cell adenoma and to discuss these in the light of relevant literature.

Material and Methods: PubMed and Google Scholar were searched to identify articles related to water-clear cell adenoma using the following keywords: parathyroid tissue, parathyroid gland, parathyroid cells, parathyroid adenoma, parathyroid hyperplasia, water-clear-cell, and water clear cell. The search included case reports, review articles, and original articles that had been published between January 1990 and November 2014 without any restrictions on language. All articles that contained information on the study population and treatment related data were identified and retrieved. In addition, an evaluation was of a case of a 47-year-old male patient with PHC who was treated at our clinic was conducted.

Results: A total of 19 patients, including our new case, (age range: 18 to 81 years, mean±SD: 57.47±16.31 years) were included in the analysis. Eleven patients were female. Information about adenoma location was available from studies involving 17 patients and they indicated the following distribution of locations: left inferior (n=10), right superior (n=4). When preoperative imaging methods were examined, a false negative result was given by ultrasonography in 28.5% of patients and only 57.1% were positive on scintigraphy. Concomitant thyroid papillary carcinoma was determined in 1 patient. The mean tissue dimensions were 3.47±1.73 cm (range, 0.8-6.8 cm).

Conclusion: Water-clear cell adenoma, which shows similar clinical characteristics to other parathyroid adenomas, is an uncommon cause of hyperparathyroidism.

Keywords: Double water-clear cell adenoma, hyperparathyroidism, hypercalcemic crisis

INTRODUCTION

Primary hyperparathyroidism is one of the most encountered endocrine pathologies, with an incidence of 21.6/100,000. In the etiology, the leading cause is solitary adenoma (87%-91%), generally originating from chief cells (1). Adenoma originating from more than one gland is a rarer event and comprises 2%-15% of all adenomas (2). The rare form (1%) of water-clear cell hyperplasia (WCCH) of hyperparathyroidism was first described by Albright et al. (3) in 1934. As adenoma in the etiology is even more uncommon, only 19 cases have been reported since 1994, and of those cases, adenoma was in both parathyroid glands in only one case (1, 2, 4-20).

Hypercalcemic crisis, which was first described by Hannas in 1939, is a severe and life-threatening condition of severe hypercalcemia progressing to associated failure of various systems (21). Of the known cases, the case reported here is the first of hypercalcemic crisis caused by water-cell clear adenoma (WCCA). In previous reports related to WCCA, the histopathological features of the disease have generally been the focus. The aim of this study was to present the preoperative and postoperative periods of the disease and to evaluate the clinical characteristics. Defining the clinical characteristics of these kinds of rare cases can be considered useful for clinicians.

In this case report, we present a patient who was successfully treated for double WCCA, and the case is discussed in comparison with the 19 cases reported in literature.

MATERIAL AND METHODS

A new case of WCCA with hyperparathyroidism is presented in this study and it was aimed to evaluate the preoperative clinical features and postoperative follow-up period in a comparison with other reports in literature of patients operated on for WCCA. Therefore, between January 2016 and March 2016, two of the authors scanned the PubMed and Google Scholar databases for publications between January 1, 1990 and March 21 2016 using the key words (Parathyroid tissue* OR Parathyroid gland* OR Parathyroid cells*) AND (Parathyroid adenoma* OR Adenoma*) AND (Water-clear-cell* OR water clear cell*) (Field: All Fields) (Figure 1). A total of 17 publications were determined, containing 19 patients with the demographic and technical data such as year of publication, patient age, gender, radiological and operative findings, and

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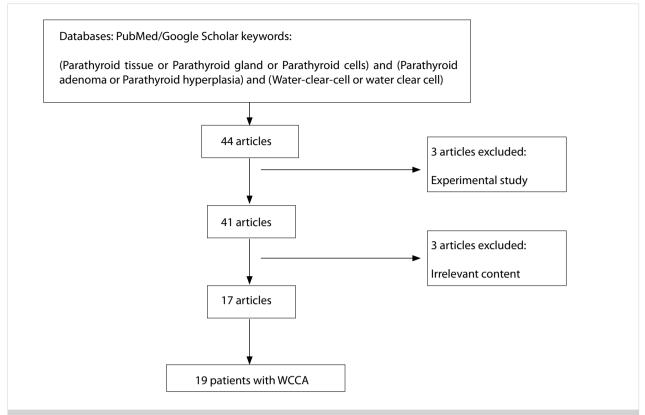


Figure 1. Flow chart of the patient selection and exclusion criteria

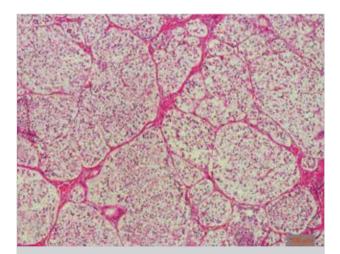


Figure 2. Histological appearance of the water-clear cell parathyroid adenoma. The cells show minimal nuclear pleomorphism and have uniformly foamy cytoplasm (hematoxylin and eosin, original magnification: 100×.)

preoperative diagnostic methods. 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.

RESULTS

Case Report

A 47-year-old male patient was referred to our clinic when hyperparathyroid was determined during investigations for repeated kidney stone etiology. There was no multiple endocrine neoplasia or familial hyperparathyroidism, and no concomitant disease was determined except for kidney stone. Clinically, the patient had complaints of abdominal pain, nausea, vomiting, and lethargy. In the biochemical analyses, test results were determined as serum calcium of 16.6 mg/dL (reference range 8.5-10.1 mg/dL) and an intact parathyroid hormone level (iPTH) of 744 pg/mL (reference range 11-67 pg/mL). Therefore, to bring the hypercalcemia under control, treatments were applied of hydration, subcutaneous calcitonin, and parenteral biphosphonate (Zoledronic acid: Zometa® ampoule Novartis, Stein, Switzerland). When the Ca level receded to 10.7, ultrasonography (USG) was performed and a well-defined, separated lesion was determined in the inferior pole of both thyroid glands; on the right side in the inferior posterior lobe, 2.2×1.1×0.7 cm in size, and on the left side, 1.6×1.0×0.7 cm in size. However, the lesions determined on USG could not be observed on Technetium-99m-sestamibi (MIBI) examination.

The patient was admitted for surgery with an initial diagnosis of double parathyroid adenoma. During the operation, lesions were excised from the inferior pole of both thyroid lobes, which were clearly separated between the thyroid gland and the intermediary planes, 2.5×1.1×0.7 cm in size on the right side and 1.6×1.0×0.7 cm on the left. These lesions were consistent with bilateral parathyroid adenoma. As the lesions were determined as adenoma in the intraoperative "frozen" section examination, the upper parathyroid glands were explored and biopsy and frozen section examination were applied. With the report of normal parathyroid tissue, the procedure was completed.

In the postoperative histopathological examination, both lesions were seen to be consistent with WCCA (Figure 2). In the

48th month postoperatively, the PTH level had recovered to 43.6 pg/m L and Ca to 9 mg/dL.

Literature Review

Using PubMed and Google Scholar, English-language medical literature published between January 1990 and March 2016 was searched. A total of 17 reports concerning 19 cases of WCCA with hyperparathyroidism meeting the aforementioned criteria were included in this review. The patients were aged from 18 to 81 years (mean, 57.47±16.31 years); 11 were female (57.9%) and 8 were male (42.1%).

Double adenoma was seen in only 1 patient. Except for 2 articles, all other publications included a single patient. In 1 patient, there was concomitant multiple endocrine neoplasia type 1 (MEN-1); in 1 patient, neurofibromatosis type 1 (NF-1); and in all others, it was found to be sporadic. The most common adenoma localization was the left inferior parathyroid gland (n=10), followed by the right lobe upper pole (n=4) (4, 12). In 1 patient, the lesion was reported to be located in the left thyroid lobe (8). Prior to the current patient, more than one adenoma was seen in only 1 patient, and these were located in the upper pole (9). In the 14 patients with available preoperative imaging data, USG and scintigraphy showed lesions in 6 patients, and in 1 patient, where both imaging methods had a negative result, the diagnosis was seen to have been made clinically. In 4 patients with negative scintigraphy results, diagnosis was made from USG, and 2 patients were diagnosed from scintigraphy. Apart from parathyroidectomy, total or subtotal thyroidectomy was performed in 3 patients (8, 9, 14). In 1 patient, thyroid papillary carcinoma was seen concomitant to the adenoma (14). The mean tissue size was 0.47±1.73 kg/ m², (range, 0.8-6.8). No postoperative recurrence was seen in any patient, including the patient who underwent surgery for double adenoma. The clinicopathological characteristics of the 19 patients are summarized in Table 1.

DISCUSSION

Primary hyperparathyroidism is one of the most frequently encountered clinical events within endocrine diseases. The disease generally originates from chief or oxyphilic cells, and has been rarely (1%) determined to originate from the hyperplasia seen in water-clear cells. Following the first case of WCCA reported in 1994, to the best of our knowledge, there have only been 19 cases in literature (1, 2, 4-20).

Multiple parathyroid adenomas constitute 2%-15% of all adenomas (9). According to the criteria defined by Harness et al. (22) to be able to make a diagnosis of multiple parathyroid adenoma, I) in the operation, there must be more than 1 and fewer than 4 involvements of the parathyroid gland, II) at least 1 of the parathyroid glands must be normal, III) there must not be multiple endocrine neoplasia or familial hyperparathyroidism, and IV) postoperatively permanent normocalcemia must be able to be obtained in the patient. In the current case, as a lesion consistent with adenoma was determined on preoperative USG with localization in both inferior parathyroid glands, surgery was planned preoperatively for the exploration of the four parathyroid glands.

In a report by Kuhel et al. (9), despite an appearance consistent with adenoma only in the right upper pole localization on

preoperative imaging, bilateral parathyroid exploration was conducted as potential persistent hyperparathyroidism was considered and adenoma were determined in both superior poles. All the other patients in the literature were operated on for single parathyroid gland involvement, and postoperative hypercalcemia was not observed in any case. When the current case was included, the rate of 1% bilateral WCCA was decreased. However, as the number of patients is extremely low, it would not be correct to comment on this subject.

Although the origin of water-clear cells is not fully known, it has been suggested that with ageing of the Golgi vesicles or of the granular endoplasmic reticulum cisterns, there is a change in water-clear cells (6, 14, 23, 24). When the age at which the disease was observed was examined, only one patient was 18 years old and the mean age of the patients was 57.47 years (12). As six of the patients were aged over 70 years, it was considered consistent with a relationship between the disease and increased age (7, 14, 16, 17, 19). When the current case was evaluated, although the rate of female patients of 55% (n=11) was slightly low compared to literature, the addition of new patients will clarify this in the future. According to the hypothesis of Kanda et al. (10), although WCCAs reach large sizes, this does not cause severe increases in calcium levels. In the current case, the preoperative serum calcium was 16.6 mg/dL and a need for preoperative hydration and medical treatment was felt. Hypercalcemic crisis, which is seen in <1%-2% of primary hyperparathyroid patients, may cause severe and lifethreatening problems in the central nervous system, cardiac, gastrointestinal, and renal functions. Generally, serum calcium levels are >3.5 mmol/L (25, 26) or 14 mg/dL (27). Despite there being no clear data in literature correlating to the increased tissue weight or volume of the removed gland of multiple parathyroid adenomas with severe hypercalcemia, it has been emphasized that factors such as accompanying dehydration, reduced calcium excretion, and immobilization could increase the risk of hypercalcemic crisis (28).

There are no previous reports in literature of any patient with WCCA being treated for hypercalcemia and no patient was seen to have calcium levels as high as those observed in the current patient. The total weight of the tissue of the removed parathyroids in the current patient was 2.8 g. Kuhel et al. (9) reported that the total removed tissue weight in the patient operated for double adenoma was 2.2 g and the preoperative calcium level was 3.3 mmol/L, which was an increase of approximately 25% over normal. Lower calcium levels in patients with a greater weight of tissue and the relatively high calcium levels in the 2 cases with double adenoma with low tissue weight suggest that there could be a relationship between the number of adenoma and calcium level.

In studies related to the efficacy of USG and scintigraphy in showing adenoma localization, it has been reported that Technetium 99 m sestamibi scintigraphy (MIBI) has low levels of success in the determination of lesions with a low PTH level and the diagnostic value of USG is higher in this type of lesions (29). When the preoperative imaging methods were examined, it was seen that of the 28.5% of patients where USG gave false negative results, only 57.1% were positive on scintigraphy. Khorasani et al. (29) reported that in atypical lesions such as cystic adenoma, USG provided better results for adenoma

Study	Years	Age/gender (years)/ (F/M)	Concomitant clinico- pathological situation	Preoperative calcium	Preoperative PTH	Preoperative imaging method	TISSUE size	Treatment method		Adenoma localisation
Kovasc et al. (4)	1994	48/M	MEN-1	11.8 mg/dL	435 mlU/mL	NA	NA	Total parathyroidectomy	Single	LI
Roth et al. (5)	1995	48/M		11.8 mg/dL	4.5 mIU/mL	NA	NA	Р	Single	NA
Grenko et al. (6)	1995	40/M		11.3 mg/dL	945 pg/mL	USG (-)/ MIBI (-)	5.0 cm (7.6 g)	Р	Single	RS
Begueret et al. (7)	1999	73/M		13.8 mg/dL	207 pg/mL		2.8 cm	Р	Single	Lİ
Dundar et al. (8)	2001	43/F		13.3 mg/dL	1667 pg/mL	USG (+)/ Scinti (-)	6 cm	Near total thyroidectomy	Single	Intrathyroid L lobe
Kuhel et al. (9)	2001	56/F		3.3 mmol/L	52 ng/L	USG (+)/ MIBI (-)	2.8 cm (1.7g) 1.5 cm (0.5)	P+ right lobectomy and isthmectomy	Double	RS/LS
Kanda et al. (10)	2004	52/F		11.7 mg/dL	672 pg/mL	USG(+)/ TITc (+) MR (+)	6.8 cm (15.4 g)	Р	Single	LI
Prasad et al. (11)	2004	40/F		12.4 mg/dL	346 pg/mL	ND	3.0 cm (4.2 g)	Р	Single	LI
Kodoma et al. (12)	2007	18/F	NF1	11.6 mg/dL	356 pg/mL	USG (+)/ TITc (+)	5.0 cm (21.7 g)	Р	Single	RS
Liang et al. (13)	2010	59/F		11.8 mg/dL	265 pg/mL	USG (-)/ MIBI (+)	4.5 cm 13.3 g	Р	Single	RS
Bai et al. (14)	2012	81/M		NA	22.2 pmol/L	USG (-)/ MIBI (+)	4.0 cm (6.91 g)	Р	Single	RS
Bai et al. (14)	2012	55/M		NA	15.9 pmol/L	USG (-)/ MIBI (-)	1.4 cm 0.27 g	P+BTT (Papillery ca)	Single	LS
Papanicolau- Sengos et al. (15)	2013	64/M		NA	NA	NA	4.7 cm	Р	Single	Ц
Piggott et al. (16)	2013	74/F		3.13 mmol/L	488.9 ng/L	USG (+)/ MIBI (+)	5.5 cm (13 g)	Р	Single	LI
Ezzat et al. (17)	2013	73/M		3.24 mmol/L	30.8 pmol/L	USG (+)/ MIBI (+)	3.7 cm (8 g)	Р	Single	Ц
Ezzat et al. (17)	2013	74/F		2.9 mmol/L	11.8 pmol/L	USG (+)/ MIBI (-)	1.6 cm (0.9 g)	Р	Single	Ц
Murakami et al. (18)	2014	59/F		11.9 mg/dL	72.3 pg/dL	USG (+)/ MIBI (-)/ CT (+)	0.8 cm (0.5 g)	Р	Single	LI
Chou et al (19)	2014	81/F	Pancreatitis	12 mg/dL	450 pg/mL	USG (+)/ MIBI (+)	3.8 cm	Р	Single	NA
Tassone et al. (20)	2014	54/F		12.4mg/dL	130 ng/L	USG (+)/ MIBI (+)	2.8 cm	Р	Single	Ц
Current Study	2016	47/M		16.6mg/dL	744 pg/mL	USG (+)/ MIBI (-)	2.5 cm (1.9 g)/ 1.6 cm (0.9 g)	Р	Double	R inf/L inf

localization than scintigraphy, which is consistent with the observation of USG being more effective in showing adenoma localization than scintigraphy in patients with WCCA in the current patient population.

Classically, in WCCH, there is firstly upper parathyroid gland involvement and hypertrophy in the inferior glands emerges later (9). However, in studies related to parathyroid adenoma localization, it has been reported that majority of cases originate

in the inferior glands (30). Of the patients for whom complete data were available, it was observed that WCCA behaved like adenoma rather than WCCH with respect to localization. While inferior parathyroidal tissues were involved in 11 patients, upper pole localization was seen in 5 patients and intrathyroidal localization was seen in 1 patient.

CONCLUSION

WCCA causing hyperparathyroidism is an extremely rare event. Although localization is determined less effectively compared with other types of adenoma, USG seems to be relatively effective. Moderate level hypercalcemia has been previously reported in literature, but it should be kept in mind that as reported for the first time in the current case, there could be a cause of hypercalcemia at a level requiring treatment.

From the behavior and localization, although it is thought to be adenoma rather than WCCH, as the number of patients increases in the future, clearer information will be able to be obtained.

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

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

Peer-review: Externally peer-reviewed.

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

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Emergency cases following elective colonoscopy: latrogenic colonic perforation

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ABSTRACT

Objective: Our aim in this study was to present the cases of our patients who contracted colonic perforation during elective colonoscopy and became emergency cases; we also discuss treatment modalities along with literature reports on the subject.

Material and Methods: Cases of patients who contracted iatrogenic colonic perforation following endoscopy of the colorectal system between January 2009 and December 2015 at Kartal Koşuyolu Yüksek İhtisas Training and Research Hospital's Endoscopy Unit were reviewed retrospectively.

Results: Within the duration of the study, 5.586 patients underwent colonoscopies at our hospital; 7 (0.12%) of these patients contracted iatrogenic colonic perforation. Three (42.8%) of these patients were male, four (57.2%) were female, and their mean age was 69 years (46 to 84). Six (85.7%) patients were diagnosed intraoperationally, while one (14.3%) patient was diagnosed 12 hours after the procedure. The perforation area was the sigmoid colon in six patients and the ascending colon in one patient; all patients underwent surgery. Four patients were discharged with no complications. One of the remaining three patients had enterocutaneous fistula, one had acute renal failure, and one died of sepsis.

Conclusion: The progress of perforation due to colonoscopy varies according to the underlying diseases, the mechanism of perforation formation, the treatment modality used, and the experience of the physicians treating the patient. Special attention should be paid to senior and comorbid patients receiving therapeutic procedures during colonoscopy.

Keywords: Colon, colonoscopic perforation, endoscopy

INTRODUCTION

Colonoscopy is commonly used in the diagnosis, treatment, and follow-up of colorectal diseases. It is generally acknowledged to be a safe procedure. The most frequent colonoscopy-related complication is post-polypectomy bleeding. The number of patients necessitating surgical intervention related to bleeding is very low (1). Colonoscopy-related colonic perforation is seen less than bleeding; however, it is still a significant complication that can lead to morbidity and mortality (2). The prevalence of post-colonoscopic perforation is 0.03% to 0.8% in diagnostic colonoscopy procedures, while it varies between 0.3% and 3% in therapeutic colonoscopies (3). There is still no consensus on the optimal treatment of iatrogenic colonic perforations because there are no prospective randomized and controlled studies in the literature. In this study, we present the cases of our patients who contracted colonic perforation during elective colonoscopy and who were transformed into emergency cases, along with their treatment modalities.

dedinent

The Patients

MATERIAL AND METHOD

The cases of patients who contracted iatrogenic colonic perforation following endoscopy of the colorectal system between January 2009 and December 2015 at Kartal Koşuyolu Yüksek İhtisas Training and Research Hospital's Endoscopy Unit were reviewed retrospectively. The study was made according to Helsinki Declaration.

The total numbers of diagnostic and interventional colonoscopy and sigmoidoscopy procedures along with the total number of polypectomy and biopsy procedures conducted within the scope of interventional colonoscopy were determined within the designated timeframe of the study.

Endoscopic investigations are performed by gastroenterology surgery specialists and sub-specialty residents with gastroenterology specialists at the endoscopy unit of our hospital. All the patients signed detailed informed consent forms before the procedure. Patients who recently experienced myocardial

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Tab	Table 1. Clinical and demographic characteristics of the patients									
	Age	Sex	Comorbidities	ASA	Procedure	Indication for procedure	Diverticulosis			
1	71	K	HT, DM	2	Colonoscopy	Anemia	Yes			
2	70	K	MVR, HT, DM	3	Colonoscopy	Anemia	Yes			
3	46	K		1	Colonoscopy	Hematochezia	No - polipectomy			
4	74	K	HT, DM, AF	3	Colonoscopy	Constipation	Yes			
5	65	E		1	Colonoscopy	Change in bowel habits	Yes			
6	84	Е	COPD, DM, HT	3	Colonoscopy	Anemia	No			
7	68	Е	CABG, HT	3	Colonoscopy	Change in bowel habits	Yes			

HT: hypertension; DM: diabetes mellitus; MVR: mitral valve replacement; AF: atrial fibrillation; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease



Figure 1. The perforated site was the sigmoid colon

infarction, had poor performance statuses, were diagnosed with serious arrhythmia, had acute phase diverticulitis, and who had coagulation disorders requiring biopsy or polypectomy did not receive the procedure.

The detailed clinical and demographic characteristics and colonoscopy reports of the patients diagnosed with perforation were investigated. The age, sex, additional disease, previous history of abdominal surgery, colonoscopy indication, American Society of Anesthesiologists (ASA) scoring, perforation area, presence of diverticulum, polypectomy, diagnosis and treatment method of the perforation, period of surgery for patients who underwent surgery, surgical technique, duration of hospitalization, and postoperative complications of the patients were reviewed.

The Procedure

Standard colon preparation was conducted using 500 mg Sennoside (XM solution, Yenişehir Lab, İstanbul, Turkey) and 118 ml sodium dihydrogen/disodium phosphate enema (B.T. Enema, Yenişehir Lab, İstanbul, Turkey). Propofol (1%, Fresenius Kabi, İstanbul, Turkey) and fentanyl citrate (0.5 mg/10 mL, VEM, İstanbul, Turkey) were used for premedication. A Fujinon 530 WL4 590 WL4 (Fujinon, Willich, Germany) Olympus 160 VR video-colonoscopy tool, polypectomy noose,

and coagulation catheters (Olympus, Japan) were utilized during the procedure.

Statistical Analysis

Statistical Package for the Social Sciences version 21.0 (IBM Corp.; Armonk, NY, USA) computer software was used for the bio-statistical analyses.

RESULTS

Within the duration of the study, 5,586 patients underwent colonoscopies at our hospital; 7 (0.12%) of these patients contracted iatrogenic colonic perforation. Three (42.8%) of these patients were male, four (57.2%) were female, and their mean age was 69 years (46-84). Colonoscopic indications of the patients with perforations included investigation of the etiology of anemia in three (42.8%) patients, constipation and changes in intestinal habits in three (42.8%) patients, and rectal bleeding in one (14.3%) patient. None of the patients had a history of previous abdominal surgery. Six (85.7%) of these patients underwent diagnostic colonoscopy, while one underwent therapeutic colonoscopy. Polypectomy was performed as the therapeutic procedure. The clinical and demographic data of the patients are summarized in Table 1.

While six (85.7%) patients were diagnosed during the procedure (Figure 1), one (14.3%) was diagnosed 12 hours after the procedure was completed. The case of the patient who was diagnosed 12 hours after the procedure was evaluated to be delayed diagnosis. The X-ray results for the patients observed to have perforation areas during the procedure showed pneumoperitonium (Figure 2). In the delayed case, however, computerized tomography was used to diagnose the patient. The perforation area was the sigmoid colon in six patients and the ascending colon in one patient. Five of the patients with sigmoid colon perforations had diverticulum perforations. The patient with the ascending colon perforation had a polypectomy-related perforation.

All the patients diagnosed with colonoscopy-related iatrogenic colonic perforation received laparotomies: primary repair was performed in six patients, while the Hartmann procedure was performed in the delayed diagnosis patient. Four patients (57.2%) were discharged with no postoperative complications. The patient with perforation in the ascending colon had leakage following primary repair. The patient was re-operated, and a right hemicolectomy and ile-

Та	Table 2. Diagnosis and treatment									
	Time of diagnosis	Perforation area	Time between colonoscopy and operation	Surgical intervention	Complications	Length of stay	Results and follow-up			
1	During colonoscopy	Sigmoid	<12 h	Primary suture repair		7	Discharged			
2	During colonoscopy	Sigmoid	<12 h	Primary suture repair	ARF	18	Discharged			
3	During colonoscopy	Ascending colon	<12 h	Primary suture repair	Leak (reoperation)	20	Discharged-stoma closure in 6 months			
4	Follow-up after colonoscopy	Sigmoid	>12 h	Hartman's colostomy		7	Discharged-stoma closure in 6 months			
5	During colonoscopy	Sigmoid	<12 h	Primary suture repair		7	Discharged			
6	During colonoscopy	Sigmoid	<12 h	Primary suture repair		8	Discharged			
7	During colonoscopy	Sigmoid	<12 h	Primary suture repair	Acute COPD exacerbation, pneumonia, sepsis	8	Exitus			
AR	F: acute renal failure; COPD: o	chronic obstructi	ve pulmonary diseas	e						



Figure 2. X-ray demonstrating bilateral subdiaphragmatic free air

ostomy were performed. This patient's ileostomy was closed about six months after the procedure without any problems. One patient contracted acute renal failure and required dialysis. The patient's renal functions improved during followup, and the patient did not require dialysis after discharge. One patient, however, died on the postoperative 8th day because of serious comorbidity and complications. The mean duration of hospitalization for the cases was 10.7 (7 to 20) days. The diagnoses, treatments, and follow-up results of the patients are summarized in Table 2.

DISCUSSION

Colonoscopy is commonly used as a diagnostic and therapeutic tool in colorectal diseases. The number of patients receiving this procedure is increasing; consequently, the number of complications related to this procedure has increased. Perforations seen during colonoscopy are rare; however, they are serious complications that generally necessitate surgical inter-

vention with a high morbidity-mortality rate (2, 3). Although their frequencies vary according to the center where they are performed, complications are seen at a rate of 0.03% to 0.8% in diagnostic colonoscopies and 0.3% to 3% in therapeutic colonoscopies (4, 5).

In a study conducted by Iqbal et al. (6), the authors found that the number of perforations was higher in the rectosigmoid corner and the sigmoid colon (52%). The results of the same study indicated that the perforation rates of the other segments of the colon were 17% (cecum), 14% (ascending colon), 7% (transverse colon), 8% (descending colon), and 1% (rectum). The authors also determined that the perforation areas were between 0.1 and 6.0 cm (mean: 1.7 cm) in size. Electrocautery injuries result in small perforations, while mechanical injuries cause large perforations. In our series, most of the perforations (85.7%) were seen in the sigmoid colon.

Colonoscopy-related perforations occur by three different mechanisms: mechanical trauma, pneumatic trauma, and post-therapeutic trauma. The factors that increase the risk of perforation during colonoscopy are old age, dramatic comorbidity, inflammatory intestinal disease, diverticulosis, steroid use, malignity, previous necrosis, invasive procedures, and insufficient experience of the endoscopist. Moreover, a previous history of abdominal surgery that causes a decrease in colonic and rectosigmoid movements, radiation, and adhesions result in acute intestinal angling; this increases the risk of perforation by increasing the difficulty of the colonoscopic procedure (7-9).

Findings and symptoms can be seen during the perforation, can be delayed, or can be asymptomatic according to the size and location of the perforation. Furthermore, breakthrough pain or failure to achieve sufficient distention in the lumen despite pushing air by colonoscopy may suggest perforation (6, 8). When patients are suspected to have perforations, standing direct abdominal radiography or lung radiography and left lateral decubitus abdominal radiography are initially performed. If the results of these radiographs are normal or a

strong suspicion of perforation exists, abdominal computerized tomography (CT) with water-soluble contrast should be performed. CT aids in the diagnosis of free air, micro-punctures and/or abscesses (6). Cho et al. (10) showed that all patients had subdiaphragmatic free air following perforation. Six of our cases were diagnosed during colonoscopy, and their diagnoses were confirmed by standing direct abdominal radiography. Additional radiological imaging methods were unnecessary. Therefore, we believe that X-ray is an inexpensive and beneficial method to ascertain the existence of subdiaphragmatic free air.

There are three treatment modalities pertaining to postcolonoscopic perforations: conservative, endoscopic, and surgical. The fact that patients only have subdiaphragmatic free air is not an indication for surgical repair. Most patients with no peritoneal irritation or abdominal sepsis symptoms can be followed up with intravenous antibiotics treatment, suspension of oral intake, and serial abdominal examinations (11, 12). Conservative treatment results in shorter hospitalization and a low rate of morbidity in appropriate patients. Igbal et al. (6) reported that of the 10 patients they treated and whose relatives refused surgical treatment, only one died. It has been suggested that small localized perforations with a subclinical progress can be completely closed without any problems. It was later observed in laparotomies performed for other reasons that the perforation areas closed in patients with subclinical perforations who had localized abdominal sensitivity and short-term fever (13). In our series, surgical procedures were performed as the primary treatment because the six patients who were diagnosed during colonoscopy had wide areas of perforation and the one patient who had delayed diagnosis manifested with acute abdomen.

Immediate surgical intervention is not necessary. Intraoperative findings determine the type of surgery to be performed in patients necessitating surgery. In cases where surgical intraabdominal contamination is limited, primary repair or post-resection primary anastomosis can be performed. Stoma can be considered in cases of intensive contamination. The number of laparoscopic colonic repairs for colorectal perforations has increased recently with developments in minimally invasive surgical procedures (11, 14). Zhang et al. (15) reported in their study that laparoscopic repair is a safe and feasible repair method. In our series, we performed primary repair in six out of seven laparotomy cases and performed the Hartmann procedure on the patient who had a delayed diagnosis. However, the patient who underwent primary repair of the ascending colon perforation was ascertained to have intestinal leakage in the postoperative period. This patient was re-operated and underwent a right hemicolectomy and end ileostomy.

Physicians have started to use endoscopic clips for the treatment of iatrogenic colonic perforations, which are increasing with the increasing number of endoscopic mucosal resections and submucosal dissection procedures. In a study conducted by Kim et al. (16), the authors ascertained 27 iatrogenic colonic perforation cases (0.02% incidence) out of 115,285 colonoscopy procedures. Endoscopic clips were used to repair perforations in 16 of these patients, with success in 13 patients.

CONCLUSION

latrogenic colorectal perforations are rarely seen in endoscopy; however, they are among the most dangerous complications. Perforation management remains difficult and alarming for many endoscopists. The progress of colonoscopy-related perforations depends on the underlying diseases, mechanism of perforation, treatment modality performed, and experience of the treating physicians. Special attention should be paid to senior and comorbid patients receiving therapeutic procedures during colonoscopy.

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

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

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Evaluation of perioperative nutritional status with subjective global assessment method in patients undergoing gastrointestinal cancer surgery

Aylin Erdim, Ahmet Özdemir Aktan

ABSTRACT

Objective: This study was designed to evaluate the perioperative nutritional status of patients undergoing surgery for gastrointestinal cancer using Subjective Global Assessment and surgeon behavior on nutritional support.

Material and Methods: We recruited 100 patients undergoing surgery for gastrointestinal cancer in one university and two state teaching hospitals. Subjective Global Assessment was administered to evaluate preoperative and post-operative nutritional status. Fifty-two patients in the state hospitals (Group 1) and 48 in the university hospital were assessed. Anthropometric and biochemical measurements were performed. Changes in preoperative Subjective Global Assessment scores and scores at the time of discharge and types of nutritional support were compared. Subjective Global Assessment-B was regarded as moderate and Subjective Global Assessment-C as heavy malnutrition.

Results: Ten patients had Subjective Global Assessment-B and 29 had Subjective Global Assessment-C malnutrition in Group 1 and nine had Subjective Global Assessment-B and 31 had Subjective Global Assessment-C malnutrition in Group 2 during preoperative assessment. Respective numbers in postoperative assessment were 12 for Subjective Global Assessment-B and 30 for Subjective Global Assessment-C in Group 1 and 14 for Subjective Global Assessment-B and 26 for Subjective Global Assessment-C in Group 2. There was no difference between two groups. Nutritional methods according to Subjective Global Assessment evaluation in pre- and postoperative periods were not different between the groups.

Conclusion: This study demonstrated that the malnutrition rate is high among patients scheduled for gastrointestinal cancer surgery and the number of surgeons were inadequate to provide perioperative nutritional support. Both university and state hospitals had similar shortcomings. Subjective Global Assessment is an easy and reliable test and if utilized will be helpful to detect patients requiring nutritional support.

Keywords: Gastrointestinal cancer, malnutrition, perioperative nutrition, subjective global assessment

INTRODUCTION

An organism should maintain its physiological and metabolic functions to sustain healthy life. Adequate and balanced nutrition is a priority for the regular maintenance of these functions. An organism becomes more sensitive to malnutrition particularly during times of illness (1, 2). In surgical patients, malnutrition rates vary between 22% and 54% due to various parameters such as age, sex, and current illness (3). Increased incidence of infections, liquid-electrolyte disturbances, and decline in functional status may accompany malnutrition (4-6). Operated patients with malnutrition are at increased risk of mortality and have higher complication rates and prolonged hospital stays; this condition also prolongs the period of rehabilitation and recovery. Thus, surgical patients should be screened for nutritional status and perioperative nutritional support should be provided for patients with malnutrition (4, 7, 8). In a study by Hill et al. (9), it was determined that 40% of medical patients and 50% of surgical patients had malnutrition and that these rates increased as hospital stays lengthened. Research on what type of nutrition should be recommended is still proceeding (6, 10, 11).

Assessment of patients' nutritional status should be conducted by a multidisciplinary team. This team should include doctors, nurses, dietitians, and social workers. Nurses are among health personnel who mostly contact and communicate with patients, and therefore, nurses have an important role in terms of detecting patients who need nutritional support (12, 13). Various methods are used for determining the level of malnutrition. Subjective Global Assessment (SGA) is based on patient history and physical examination findings. SGA is easy to use and has high accuracy rates, which increase its clinical utilization. SGA was developed to assess physiological symptoms of malnutrition or conditions related to malnutrition and to assess functional capacity (Appendix) (1, 2, 5, 12, 14). Patients with gastrointestinal (GIS) cancer frequently have nausea, vomiting, lack of appetite, and malabsorption; therefore, malnutrition is more common among such patients who will be undergoing surgery.

The current study aimed to assess nutritional status in the perioperative period using the SGA method in patients undergoing GIS cancer surgery at a university hospital and two state training and research hospital are surgery at a university hospital and two states training and research hospital are surgery at a university hospital and two states training and research hospital are surgery at a university hospital and two states training and research hospital are surgery at a university hospital and two states training and research hospital are surgery at a university hospital and two states training and research hospital are surgery at a university hospital and two states training and research hospital are surgery at a university hospital and two states training and research hospital are surgery at a university hospital and two states training and research hospital are surgery at a university hospital and two states training and research hospital are surgery at a university hospital and two states training and research hospital are surgery at a university hospital and two states training and research hospital are surgery at a surge

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©Copyright 2017 by Turkish Surgical Association Available online at www.turkjsurg.com pitals and to determine malnutrition rates and the proportion of patients with malnutrition who will benefit with nutritional support. It was also investigated whether there were differences with regard to patient profiles and nutritional behavior of patients between the university hospital and other training and research hospitals.

This study was based on the hypothesis that surgeons could not provide adequate nutritional support for patients during the perioperative period.

MATERIAL AND METHODS

The study was conducted in 2007 at the Marmara University Hospital General Surgery Service, Göztepe Training and Research Hospital 4th Surgical Service, and Lütfi Kırdar Kartal Training and Research Hospital Surgical Service. Patients undergoing GIS surgery were recruited. Nutritional status of the patients during the perioperative period was assessed using SGA and patients receiving nutritional support were noted (Appendix).

To conduct the subjective assessment, patient medical history was noted and physical findings were investigated based on the form presented in Appendix. In the history section, the assessment was conducted according to the titles that investigate the change in body weight within the last 6 months (<5%, 5-10%, or >10% loss), change in nutritional intake, GIS symptoms (e.g., lack of appetite, nausea, vomiting, and diarrhea), and functional capacity. As a result of the assessment, each feature is scored as A (normal or good nutrition), B (mild-moderate malnutrition), or C (severe malnutrition). In terms of physical examination, loss of subcutaneous fat tissue over the mid-axillary line of the lateral chest walls (axillary skinfold thickness=AST) and triceps (triceps

skinfold thickness=TST), loss of muscle mass (over the deltoid and quadriceps areas), and presence of edema (ankles, sacral region, or ascites) were assessed and each feature was scored as 0=normal, l+=mild, 2+=moderate, and 3+=severe. After scoring history and physical examination data, patients were classified by researcher who conducted the assessment as follows: good nutritional status (A), mild-to-moderate impairment in nutritional status (B), and severe impairment in nutritional status (C). In order to standardize the assessment, SGA was conducted and scored by the same researcher on the first day of hospitalization at the surgical service and on the day of discharge (after 5-10 days). According to this assessment procedure, patients who had a score of SGA-A were accepted to have adequate nutritional status.

After receiving permission from the Marmara University School of Medicine Ethics Committee to carry out the study, approval for conducting the study at the Göztepe Training and Research Hospital and the Lütfi Kırdar Training and Research Hospital was obtained from the Provincial Directorate of Health. Patients who were undergoing surgery for colon or stomach cancer, who were aged between 18 and 65 years, who were at least elementary school graduates, who had no barriers to communication, who did not undergo GIS surgery 6 months prior to treatment, who did not have additional malignities to stomach or colon cancer, and who agreed to participate were included in the study. Patients not meeting these criteria were excluded from the study.

After obtaining consent from all study patients, nutritional status in the pre- and post-operative period was determined using SGA. According to this assessment, SGA-B and SGA-C patients were accepted to have malnutrition.

Descriptive patient		(Group	1) (n=52)	(Group	2) (n=48)	
characteristics		n	%	n	%	р
Mean age (min-maximu	um)	49	(39-65)	54	(37-65)	0.080
Height (cm)		167	(154-185)	162	(155-188)	0.190
Body weight at hospita	lization (kg)	61	(48-78)	59	(45-82)	0.125
Gender	Female	23	44	23	48	0.712
	Male	29	56	25	52	
Marital status	Married	44	85	45	94	0.145
	Single	8	15	3	6	
Educational status	Elementary school	13	25	14	29	0.877
	Middle school	29	56	26	54	
	Higher education	10	19	8	17	
Employment status	Unemployed	21	40	21	44	0.733
	Employed	31	60	27	56	
Health insurance	Present	47	90	46	96	0.286
	None	5	10	2	4	
Smoking status	Smoking	27	52	29	60	0.393
	Not smoking	25	48	19	40	
Previous operations	Yes	14	27	7	15	0.130

The personal characteristics [such as age, height, body weight, body mass index (BMI), marital status, educational and employment status, health insurance, and smoking status] of the patients were also recorded. Loss of weight in the past 6 months was also questioned. On the day of discharge, SGA was repeated by the researcher. Patients were also assessed for provided nutritional support and malnutrition.

Statistical Analysis

significance level

Data was evaluated using the Statistical Package for the Social

Table 2. Comparison anthropometric measurements and biochemical parameters affecting nutritional status

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Anthropometric measurements and biochemical parameters	(Group 1) (n=52)	(Group 2) (n=48)	р
Loss of body weight (kg)	7.7±2.8	8.5±2.1	0.197
Body mass index (BMI) (kg/m²)	21.7±2.2	19.0±1.8	0.001
Triceps skinfold thickness (TST) (mm)	17.0±4.2	15.5±2.9	0.03
Middle upper arm circumference (MUAC) (cm)	26.9±1.3	26.3±1.3	0.15
Middle upper arm muscle circumference (MUAMC) (cm)	22±2.7	21±2.5	0.001
Total Protein (g/dL)	5.9±0.8	5.7±0.5	0.07
Albumin (g/dL)	4.05±0.6	3.7±0.4	0.001
Prealbumin (g/dL)	0.2±0.01	0.16±0.01	0.289
Hemotocrit (Hct) %	36.7±3.5	35±3.0	0.02
Hemoglobin (Hgb) (g/dL)	9.6±1.2	8.7±1.0	0.02
*Data was interpreted according to	means, ±SD, n	umber (n) and (0.05

Sciences version 17.0 (SPSS Inc.; Chicago, IL, USA) software. Values of p<0.05 were accepted to be statistically significant. Independent groups were analyzed using the chi-square test and the Mann-Whitney U test, while dependent groups were compared using the student t test.

RESULTS

A total of 52 patients were recruited from training and research hospitals (Group 1), while 48 patients were recruited from the university hospital (Group 2). Descriptive characteristics of the patients are presented in Table 1. It was found that the two groups were similar and that there were no significant differences between them. Examination of anthropometric measurements and biochemical parameters that determined patients' preoperative nutritional status revealed that patients in Group 1 had significantly better nutritional parameters than patients in Group 2 (Table 2). Mean loss of weight in the past 6 months was 7.7 \pm 2.8 kg in Group 1 and 8.5 \pm 2.1 in Group 2 (p>0.05). It was determined that patients in Group 1 had a mean BMI of 21.7 \pm 2.2 kg/m², while patients in Group 2 had a mean BMI of 19.0 \pm 1.8 kg/m² (p<0.001).

It was found that patients in Group 1 had a mean TST of 17.02 \pm 4.2 mm, whereas patients in Group 2 had a mean TST of 15.5 \pm 2.9 mm (p<0.05). Examination of mid-upper arm circumference (MUAC) showed that patients in Group 1 had a mean MUAC of 26.9 \pm 1.3 cm, whereas patients in Group 2 had a mean MUAC of 26.3 \pm 1.3 cm (p<0.05). It was determined that patients in Group 1 had a mean mid-upper arm muscle circumference (MUAMC) of 22 \pm 2.7 cm, whereas patients in Group 2 had a mean MUAMC of 21 \pm 2.5 cm and that the difference between the two groups was highly significant (p<0.001).

Examination of albumin values revealed that patients in Group 1 had a mean value of 4.05 ± 0.6 g/dL, whereas patients in Group 2 had a mean value of 3.7 ± 0.4 g/dL (p<0.001). Patients in Group

Table 3. Comparison of the distribution of pre- and post-operative nutrition types according to the localization of disease in Group 1 and Group 2

Preoperative nutrition type		(Group 1) (n=52)		(0	Group 2) (n=48))
	SGA-A n	SGA-B n	SGA-C n	SGA-A n	SGA-B n	SGA-C n
Enteral	2	3	9	4	1	6
Parenteral	-	1	2	1	3	10
Enteral+parenteral	-	-	2	-	4	11
Nutrition via oral route	11	6	16	3	1	4
Total	13	10	29	8	9	31
Postoperative nutrition type		(Group 1) (n=52)		(0	Group 2) (n=48))
	SGA-A n	SGA-B n	SGA-C n	SGA-A n	SGA-B n	SGA-C n
Enteral	2	2	4	4	2	3
Parenteral	7	6	10	3	6	8
Enteral+parenteral	1	3	12	1	5	14
Nutrition via oral route	-	1	2	-	1	1
Total	10	12	30	8	14	26
SGA-A: well nourished; SGA-B: moderate	tely (or suspected of b	peing) malnourished: SO	GA-C: severly malnour	ished		

1 had a mean prealbumin value of 0.2 ± 0.01 g/dL and patients in Group 2 had a mean value of 0.16 ± 0.01 g/dL (p>0.05).

It was found that patients in Group 1 had a mean hematocrit (Hct) value of 36.7±3.5% and patients in Group 2 had a mean value of 35±3.0% (p<0.05). Patients in Group 1 had a mean hemoglobin (Hgb) value of 9.6±1.2 g/dL, whereas patients in Group 2 had a mean value of 8.7±1.0 g/dL (p<0.05). Among patients in Group 1, 12 of 15 patients with stomach cancer (80%), 16 of 18 with colon cancer (88.9%), 11 of 19 with rectal cancer (57.9%), and 39 of 52 in total (75%) were determined to have malnutrition during preoperative assessment. In Group 2, 8 of 10 patients with stomach cancer (80%), 19 of 22 with colon cancer (86.3%), 13 of 16 with rectum cancer (81.2%), and 40 of 48 in total (83.3%) had malnutrition. There was no difference in malnutrition rates between the two groups.

Examination of postoperative values revealed that 35 of 52 patients in Group 1 (67.3%) and 19 of 48 patients in Group 2 (39.6%) had malnutrition. Examination of nutrition types according to preoperative SGA values showed that 2 of 13 patients at SGA-A level in Group 1 received enteral, parenteral, or enteral+parenteral nutritional support (15.4%), whereas 4 of 10 patients at SGA-B level (40%) and 13 of 29 patients at SGA-C level (44.8%) received nutritional support. In Group 2, 62.5% of SGA-A patients, 88.9% of SGA-B patients, and 87.1% of SGA-C patients received nutritional support (Table 3). It was determined that there was no significant difference between the groups. The adequacy of nutritional support provided for the patients was not investigated. Examination of nutrition types according to postoperative SGA values revealed that all 10 patients at SGA-A level in Group 1 (100%), 11 patients out of 12 at SGA-B level (91.6%), and 28 patients out of 30 at SGA-C level (93.3%) received nutritional support. In Group 2, all 8 patients at SGA-A level (100%), 13 patients out of 14 at SGA-B level (92.8%), and 25 patients out of 26 at SGA-C level (96.2%) received nutritional support (Table 3). There was no significant difference between the groups.

DISCUSSION

In the current study, which assessed preoperative nutritional status of patients undergoing GIS surgery using the SGA method and examined the rate of nutritional support provided, 52 patients operated in training and research hospitals (Group 1) and 48 patients in the general surgery clinic of a university hospital (Group 2) were compared. Although the demographic characteristics of the two groups were similar, patients staying at the university hospital had significantly worse anthropometric measures. A number of values, notably BMI and Hgb and Hct values were lower in patients undergoing surgery at the university hospital. Because university hospitals have better equipment and medical staff, these patients may have been referred to this hospital in particular. However, due to increased patient complaints and law suits in recent years, doctors tend to avoid problematic patients and may refer these patients to a university hospital clinic. Such a difference between two institutions both of which provide tertiary healthcare services indicates that defensive medicine is more commonly practiced at training and research hospitals.

In preoperative assessment, 39 patients out of 52 in Group 1 (75%) and 40 patients out of 48 in Group 2 (83.3%) were found

to have malnutrition. There was no difference in malnutrition rates between the two groups. However, high malnutrition rates indicate that patients who present with GIS cancers in our country are diagnosed late due to various reasons and that a large group of patients need nutritional support during treatment. An even more surprising finding of the current study is that 29 patients out of 39 with malnutrition in Group 1 and 31 of 40 patients with malnutrition in Group 2 had severe malnutrition (SGA-C). These findings demonstrated that patients undergoing surgery for malignant disease need nutritional support at extreme levels. The research hospitals were public hospitals, and therefore, they have a specific patient profile. Among 100 patients in both groups, 82 were elementary and middle school graduates. In these patients, late diagnosis has a negative impact on nutritional status. In patients undergoing surgery for GIS malignity, in particular, nutritional status has a key role in surgical outcomes (14). Thus, the purpose of determining preoperative nutritional status is to detect high-risk patients and provide an appropriate nutritional regime. Numerous studies have shown that SGA gives accurate results in detecting malnutrition and that it is as reliable as other methods.

Although malnutrition rates are very high in patients undergoing GIS surgery for malignant disease, nutritional support provided for these patients was well below expected rates. In preoperative assessment, 20 SGA-C patients in both groups did not receive any type of nutritional support prior to surgery. One-third of 60 patients with severe malnutrition in both groups did not receive any nutritional support. Adequacy of nutritional support provided for other patients was not investigated. Postoperative nutritional support was better compared with the preoperative period; however, it was found that 3 SGA-C patients in both groups did not receive any nutritional support. Pre- and postoperative nutritional support practices did not differ between the general surgery clinic of the university hospital and the two training and research hospitals. One of the reasons of inadequate nutritional support may be that none of the study hospitals had nutrition units. There are also recent studies indicating that this problem is still continuing (15). It was concluded that nutritional support was rarely provided in the preoperative period. According to the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines, surgery may be postponed in patients under risk for malnutrition or in patients predicted to experience inadequate oral intake, although there is no present malnutrition; further, enteral nutritional support is recommended 10-14 days prior to surgery (16, 17). In a study that recruited patients with GIS cancer and malnutrition, nutritional support provided 7-10 days prior to surgery and continued after the surgery reduced complication rates compared with postoperative standard intravenous liquid administration (18). Gencosmanoglu et al. (19) reported that enteral feeding via a nasojejunal tube during the early postoperative period in patients with stomach cancer who underwent total gastrectomy surgery has low morbidity rates and is easy to use. In the literature, it has been reported that parenteral feeding may be an effective alternative if malnutrition is present and enteral feeding cannot be tolerated or if GIS cannot function (20).

CONCLUSION

The current study determined that malnutrition rates were very high in patients undergoing GIS surgery for malignant diseases and that surgeons could not provide adequate nu-

tritional support for patients with severe malnutrition during the preoperative period. Nutritional practices were found to be similar in state teaching hospitals and in the university hospital. Because SGA is a simple and easy-to-use method, its routine administration during the preoperative period would help identify patients who need nutritional support.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Marmara University Institute of Health Science and İstanbul provincial health directorate.

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

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1. Weight change Overall loss in past 6 months: amount: kg % loss: % loss:	
	•
Change in past 2 weeks: decrease,	
increase,	
no change	
2. Dietary intake change	
a. No change	
b. Change duration: weeks	
type: suboptimal liquid diet full liquid diet	
hypocaloric liquids starvation	
3. Gastrointestinal symptoms (that persisted for >2 weeks)	
a. None	
b. There is nausea vomiting anorexia diarrhea	
4. Functional capacity	
a. No dysfunction	
b. Dysfunctionduration weeks	
c. Working suboptimally ambulatory bedridden	
5. Disease and its relation to nutritional requirements	
a. Primary diagnosis	
b. Metabolic demand (stress): No stress Low stress	
Moderate stress High stress	
B. Physical (for each trait specify: 0=normal, 1+=mild, 2+=moderate, 3+=severe)	
a. Loss of subcutaneous fat triceps and chest:	
b. Muscle wasting (quadriceps, deltoid ve temporal):	
c. Ankle edema and sacral edema:	
d. Ascites:	
e. Skin and tongue lesions with food deficiencies:	
C. SGA rating (select one)	
a. Well-nourished A	
b. Moderately malnourished B	
c. Severely malnourished C	

Appendix. Subjective Global Assessment (SGA) of nutritional status Destky et al. (12) J Parenteral Enteral Nutr 1987; 11: 8. DOI: 10.5152/turkjsurg.2017.3583

Comparison of open appendectomy and laparoscopic appendectomy with laparoscopic intracorporeal knotting and glove endobag techniques: A prospective observational study

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ABSTRACT

Objective: Despite the recent increase in the use of laparoscopic appendectomy procedures to treat acute appendicitis, laparoscopic appendectomy is not necessarily the best treatment modality. The aim of this study is to examine the value of laparoscopic intracorporeal knotting and glove endobag in terms of various parameters and in terms of reducing the costs related to laparoscopic appendectomy procedures.

Material and Methods: Seventy-two acute appendicitis patients who underwent laparoscopic appendectomy and open appendectomy surgery were enrolled in the study and were evaluated prospectively. The patients were divided into two groups: group 1 was treated with laparoscopic appendectomy using laparoscopic intracorpreal knotting and glove endobag (n=36) and group 2 was treated with open appendectomy (n=36). The two groups were statistically compared in terms of preoperative symptoms and signs, laboratory and imaging findings, operation time and technique, pain score, gas and stool outputs, duration of hospital stay, return to normal activity, and complications.

Results: No statistically significant differences were found between the groups in relation to gender, age, body mass index, or pre-operation findings, which included loss of appetite, vomiting, time when pain started, displacement of pain, defense, rebound, imaging methods, and laboratory and pathology examinations (p>0.05). Moreover, there were no differences between the groups with respect to drain usage, hospital stay time, or complications (p>0.05). In contrast, a statistically significant difference was found between the groups in terms of operation time, pain scores, gas-stool outputs, and return to normal activity in the laparoscopic appendectomy group (p=0.001).

Conclusion: Laparoscopic appendectomy can be performed in a facile, safe, and cost-effective manner with laparoscopic intracorporeal knotting and glove endobag. By using these techniques, the use of expensive instruments can be avoided when performing laparoscopic appendectomy.

Keywords: Acute appendicitis, laparoscopic appendectomy, laparoscopic intracorporeal knotting, glove endobag

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INTRODUCTION

Acute appendicitis is one of the most common causes of acute abdomen in all ages. It occurs more frequently in men than in women (male/female: 1.3/1); the mean and median ages related to this pathology are 31.3 and 22 years, respectively (1-3). Open appendectomy (OA), which was first described by McBurney (4) in 1894, is the most frequently performed emergency abdominal operation in the world. However, the use of the laparoscopic appendectomy (LA) procedure has rapidly increased since it was first described by Semm in 1984 (5). Although LA is commonly performed for acute appendicitis, it is not always the best treatment choice. Many studies comparing LA and OA with respect to treatment and follow-up have been conducted. These studies have reported less postoperative surgical-site infection, decreased need for analgesics, much greater visualization, rapid healing, shorter hospital stay times, and earlier return to normal activity (RTNA) rates associated with LA (6-10). However, because of the high costs related to endostaplers, endoclips, and knottings, LA is not the most efficient operation technique (11, 12).

Our aim in this study is to prospectively compare OA and LA performed with laparoscopic intracorporeal knotting and glove endobag; we also wish to demonstrate that the latter is a facile and effective alternative LA procedure.

MATERIAL AND METHODS

Methodology and Ethics

This study was conducted in the Surgery Department at Kars Harakani State Hospital during the period from May 2014 to April 2015. A total of 72 patients who were treated for acute appendicitis were eligible for the study. These 72 patients were divided into two groups: the LA group (group 1) (n=36) and the OA group (group 2) (n=36). All the patients were evaluated in terms of age; gender; perioperative symptoms

and signs, such as physical examination results and laboratory and imaging findings; operation time and technique; postoperative pain scores determined by the visual analog scale (VAS); gas-stool outputs; hospital stay time; postoperative complications; and RTNA. The diagnosis of acute appendicitis was made on the basis of physical examination and laboratory and imaging findings (Figure 1). The patients who were diagnosed with acute appendicitis were operated on within 12 hours. Consent forms were obtained from the patients. Approval for the study protocol was obtained from the Ethical Committee of our center.

Inclusion Criteria

Patients who were willing to provide written informed consent, were between the ages of 17 and 65 years, had an international normalizing ratio (INR) <1.5, a prothrombin time (PT) <15 seconds, partial thromboplastin (APTT) in the normal range, and platelet counts >50,000/mm³, and showed clinical suspicion of acute appendicitis (defense, rebound), with supporting appendicitis findings, such as those taken from imaging and laboratory results, were included in the study.

Exclusion Criteria

Patients who were not willing to provide informed consent, were younger than 16 or older than 65 years of age, and had

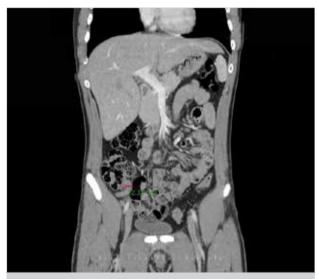


Figure 1. Acute appendicitis with computed tomography



abnormal hemodynamic parameters, perforated appendicitis, ovarian cyst rupture, tub ovarian abscess, multiple organ failure, congestive heart failure, chronic obstructive pulmonary disease, systemic connective tissue diseases, or rheumatism were excluded from the study.

Surgical Procedure

All the patients were administered first-generation cephalosporin for antibiotic prophylaxis, while some patients also received second-generation cephalosporin and metronidazole. The operation time was defined as the time of induction of anesthesia to the point of extubation. All operations were performed by two surgeons. Following the operation, an intramuscular injection of 75 mg of diclofenac sodium was administered to the patients and continued at 8 hour-intervals. Every patient began receiving liquid foods 6-8 hours after the operation.

Open Appendectomy

To access the appendix, McBurney's incision was used on all patients. The appendix was located after entering the abdominal cavity. First, the mesoappendix was divided with 3/0 silk knots, and the base of the appendix was then ligated with 2/0 silk before the appendectomy specimen was removed from the abdominal cavity (Figure 2a). The appendix stump was not buried in any of the patients. A drain was placed in patients with gangrenous appendicitis and to control hemostasis.

Laparoscopic Appendectomy

The North American three-port technique was used on all patients. Prior to inserting the trocar, a Foley catheter was inserted into the bladder. A 10 mm trocar was then inserted under the umbilicus using the open technique. Pneumoperitoneum was applied with carbon dioxide (CO₂), and intraabdominal pressure was fixed at 10-12 mmHg. Next, a 5 mm trocar was inserted into the suprapubic area before applying a 10 mm trocar to the left iliac fossa under direct vision (Figure 2b). The possibility of hemorrhaging or organ injury occurring in connection with the trocar was controlled prior to performing the appendectomy. After the appendix became visible, it was lifted from the mesoappendix. A 10 mm bipolar vessel sealer (LigaSure; Valleylabs, Tyco, USA) was used for the mesoappendix dissection. Once the base of the appendix was revealed, it was ligated with 2/0 silk (10-12 cm) using the intracorporeal knotting technique (Figure 3). The appendectomy specimen



Figure 2. a, b. Intraoperative open appendectomy (a), Laparoscopic appendectomy trocar sites (b)



Figure 3. Preparation of the glove endobag

was then removed with a 10 mm trocar using a sterile glove endobag. In one patient who had suppurate appendicitis, the appendectomy area was washed with physiological serum (0.9% sodium chloride) and then aspirated. Irrigation was not performed for any other patients. A drain was only used in patients with gangrenous appendicitis and to control hemostasis.

Preparation of Glove Endobag and Removal of Specimen

A number 7 wrist-size sterile glove was cut to approximately 7-9 cm; then, the glove was ligated 0.5 cm from the distal with 2/0 silk. The sterile glove endobag was washed with physiological serum and inserted into the abdominal cavity using a 10 mm trocar in the left iliac fossa. The appendectomy specimen was removed with a 10 mm trocar using the glove endobag (Figure 4). No other endobag instruments were used on any patients in our study.

Anesthesia Protocol

Before the patients entered the operation room, they were administered 2 mg of midazolam. The patients were monitored, with control measures taken for heart rate and rhythm, noninvasive arterial blood pressure, peripheral arterial oxygen saturation (SpO₂), and end-tidal CO₂ (EtCO₂). To induce anesthesia, 2-2.5 mg/kg of propofol, 2 mg/kg of fentanyl, and 0.6 mg/kg of rocuronium were administered to the patients. After intubation, the respiratory parameters (ETCO₂ 30-35 mmHg, 50% FiO₂ and air mixture, tidal volume 6-7 Ml/kg, respiratory rate 12-14/minute) were regulated before the patients were connected to the mechanical ventilator support. Anesthesia was maintained using 1%-2% sevoflurane and 0.1 mg/kg rocuronium. Heart rate and rhythm, noninvasive arterial blood pressure, SpO₂, and EtCO₂ were evaluated at five-minute intervals during the operation. Near the end of the operation, 1 g of paracetamol was administered to the patient for 15 minutes by IV infusion for postoperative analgesia. Atropine and neostigmine were administered to all patients for decurarization before extubation.

Assessment of Pain

The patients' levels of pain were evaluated at the 6th, 24th, and 36th hours using the VAS. Pain scores were numbered from 1 to 10, with 1 indicating no pain and 10 indicating the highest level of pain, requiring significant analgesic intervention.



Figure 4. Laparoscopic intracorporeal knotting

Statistical Analysis

The data were analyzed using the Statistical Package for the Social Sciences version 20.0 for Windows (IBM Corp.; Armonk, NY, USA). The Shapiro-Wilk test was used for the number of units in cases of normal distribution of variables. When measuring the differences between the groups, the Mann-Whitney U test was used when normal distribution was absent. Because the number of units was higher than 20, standardized z values were given for the Mann-Whitney U test. Chi-square analysis was performed to measure the relationship between the nominal variables of the groups examined. To interpret the results, the p-value for the level of statistical significance was set at 0.05. In cases where p<0.05, the variables did not show normal distribution, whereas in cases where p>0.05, the variables showed normal distribution. In cases where 2×2 tables did not have a sufficient volume of expected values in the cells, Fisher's exact test was used. Pearson's chi-square test was applied with the aid of Monte Carlo simulations in the RxC tables. The significance level was set at 0.05; if p<0.05, the difference was significant, whereas if p>0.05, the difference was not significant.

RESULTS

Of a total of 84 patients, 72 were enrolled in the study; 12 patients were excluded for failing to meet the inclusion criteria. The patients were divided into the following two groups: the LA group (group 1) (n=36) and the OA group (group 2) (n=36). The mean age for the LA group was 29.2 (± 10) (17-57) years, and that for the OA group was 30.1 (± 11.4) (19-61) years (p=0.142). The LA group included 17 females and 19 males, while the OA group included 11 females and 25 males. The body mass indices (BMI) were 24 (± 3) , 4 (18.4-32.9) kg/m² and 24 (± 3) , 4 (18.2-31) kg/m² in group 1 and group 2, respectively (p>0.05) (Table 1, 2).

The total follow-up time was 15,586 days; the mean follow-up time was 216 days. In the LA and OA groups, the mean follow-up times were 277 and 161 days, respectively (p<0.05). LA was performed commonly in the first half of the study. In the LA group, 97.2% of the cases had loss of appetite, 88.9% had nausea, 88.9% had vomiting, 30.6% had displacement of pain, 100% had defense, and 86.1% had rebound. In the OA group, 86.1% of the cases had loss of appetite, 66.7% had nausea, 36.1% had vomiting, 33.3% had displacement of pain, 100% had defense, and 94.4% had rebound. The most common

				Groups	5				
		L	A	O/	4	To	tal	Chi-square t	est (χ²)
		n	%	n	%	n	%	$\chi^{\mathbf{z}}$	р
Gender	Female	17	47.2	11	30.6	28	38.9	Fisher's exact	0.227
	Male	19	52.8	25	69.4	44	61.1		
Loss of appetite	No	1	2.8	5	13.9	6	8.3	Fisher's exact	0.199
	Yes	35	97.2	31	86.1	66	91.7		
Nausea	No	4	11.1	12	33.3	16	22.2	3.938	0.047
	Yes	32	88.9	24	66.7	56	77.8		
Vomiting	No	20	55.6	23	63.9	43	59.7	0.231	0.631
	Yes	16	44.4	13	36.1	29	40.3		
Displacement	No	25	69.4	24	66.7	49	68.1	0	1.00
of pain	Yes	11	30.6	12	33.3	23	31.9		
Defense	No	0	0	0	0	0	0	-	-
	Yes	36	100	36	100	72	100		
Rebound	No	5	13.9	2	5.6	7	9.7	Fisher's exact	0.429
	Yes	31	86.1	34	94.4	65	90.3		
Drain usage	No	30	83.3	28	77.8	58	80.6	0.089	0.766
	Yes	6	16.7	8	22.2	14	19.4		
Intraoperative	No	3	8.3	2	5.6	5	6.9	Fisher's exact	1.00
appendicitis	Yes	33	91.7	34	94.4	67	93.1		
Pathology result	No	4	11.1	2	5.6	6	8.3	Fisher's exact	0.674

34

28

8

13

23

94.4

77.8

22.2

36.1

63.9

66

57

15

32

40

91.7

79.2

20.8

44.4

55.6

1.406

1.00

0.236

symptom was anorexia, while the most frequent finding was defense.

32

29

7

19

17

LA: laparoscopic appendectomy; OA: open appendectomy; USG: ultrasonography; CT: computed tomography

88.9

80.6

19.4

52.8

47.2

Yes

Appendicitis no

Appendicitis yes

Appendicitis no

Appendicitis yes

appendicitis

USG

CT

In the LA and OA groups, the mean fever temperatures were 37.5 (±0.5) °C (36.2°C-38.8°C) and 37.3°C (±0.7) (36°C-39°C), respectively. There were more cases of fever and nausea in the LA group than in the OA group; a statistically significant difference was found between the two groups in terms of nausea and fever (p=0.035 and p=0.047, respectively). The durations of primary pain were 37.9 (±28) (8-120) minutes in the LA group and 45.4 (±38) (6-168) minutes in the OA group. In the LA group, the preoperative mean white blood cell (WBC) count, neutrophil, lymphocyte, and neutrophil lymphocyte rate (NLR) and platelet distribution width (PDW) were 12300 (±4445.6) (4800 to 20000) K/uL, 9197 (±4109) (2970-16800) K/uL, 1626.5 (±755.3) (158-3200) K/uL, 6.9 (±3.8) (1.42-18.99) and 14.6 (±2.5) (11-19.3), respectively. In the OA group, the preoperative mean WBC, neutrophil, lymphocyte, NLR, and PDW were 12051.7 (±4698.2) (5000-22100) K/uL, 9053.8 (±4553.9) (2720-18200) K/uL, 1477.2 (±33.54) (170-3950) K/ uL, 9.2 (±8.5) (1.37-50.29), and 15 (±39.06) (11-19.3), respectively. There were no statistically significant differences between the two groups in terms of WBC count, neutrophil, lymphocyte, NLR, or PDW (p>0.05). Neither ultrasonography (USG) nor contrast-enhanced computed tomography (CT) was used on any of the patients for diagnosis of acute appendicitis (Table 1-3).

The mean operation time (76.7 (± 17.5) minutes) of the LA group was higher than that of the OA group (60.1 (±21.8) minutes); a statistically significant difference was found between the two groups with respect to this parameter (p=0.001). A drain was used in patients with gangrenous appendicitis, suspected hemorrhaging, or pelvic fluid (6 patients (8.3%) in the LA group and 8 patients (11.1%) in the OA group. No statistically significant differences were found between the two groups in terms of the use of drains (p>0.05) (Table 1, 2).

The mean diameter and length of the appendectomy specimens according to the pathologic examination results were 1 (±0.4) and 5.9 (±2) cm, respectively; the diameter and length of the appendectomy specimens in the OA group were 1 (\pm 0.4) and 5.9 (\pm 2) cm, respectively. The diameter of the appendectomy specimens in the OA group was longer

Aziret et al. Effectiveness of laparoscopic intracorporeal knotting and glove endobag appendectomy

				Gro	up			Mann-Whi	tney U Test
		n	Mean	Median	Min	Max	SD	Z	р
Age	LA OA Total	36 36 72	29.2 30.1 31.7	26.5 31 30	17 19 17	57 61 61	10.6 11.4 11.2	-1.436	0.14
BMI (kg/m²)	LA OA Total	36 36 72	24 24.4 24.2	24 25.2 24.3	18.4 18.2 18.2	32.9 31 32.9	3.4 3 3.2	-1.076	0.28
Time pain started (hours)	LA OA Total	36 36 72	37.9 45.4 41.6	24 48 24	8 6 6	120 168 168	28 38 33.3	-0.571	0.56
Fever (°C)	LA OA Total	35 36 71	37.5 37.3 37.4	37.5 37.1 37.3	36.2 36 36	38.8 39 39	0.5 0.7 0.6	-2.105	0.03
Lymphocyte	LA OA Total	36 36 72	1626.5 1477.2 1551.8	1605 1265 1425	158 170 158	3200 3950 3950	755.3 1015.8 891.9	-1.2	0.23
NLR	LA OA Total	36 36 72	6.9 9.2 8.1	6.5 7.5 6.9	1.42 1.37 1.37	18.99 50.29 50.29	3.8 8.5 6.6	-1.098	0.27
PDW	LA OA Total	36 34 70	14.6 15 14.8	14 14.9 14.7	10.8 11 10.8	21.5 19.3 21.5	2.5 1.9 2.2	-1.424	0.15
Operation time (minutes)	LA OA Total	36 36 72	76.4 60.1 68.3	75 55 63.5	45 35 35	120 140 140	17.5 21.8 21.3	-4.149	0.00
Pain (6 th hour)	LA OA Total	36 36 72	3.6 5.4 4.5	3 5 5	2 2 2	7 9 9	1.4 1.6 1.8	-4.296	0.00
Pain (24 th hour)	LA OA Total	36 36 72	2.1 3.7 2.9	2 3 3	0 1 0	6 7 7	1.2 1.5 1.6	-4.599	0.00
Pain (36 th hour)	LA OA Total	36 36 72	1.5 2.6 2.1	1 2 2	0 1 0	4 6 6	0.9 1.2 1.2	-4.476	0.00
Gas output (hours)	LA OA Total	36 36 72	19.6 28.3 23.9	16 30.5 22	6 10 6	42 49 49	8.1 9.8 9.9	-3.633	0.00
Diameter of appendix (cm)	LA OA Total	36 36 72	3.2 1.2 2.2	1.5 1 1	0.4 0.4 0.4	11.5 2.5 11.5	3.5 0.5 2.7	-1.333	0.18
Length of appendix (cm)	LA OA Total	36 36 72	5.9 6.6 6.2	5.8 6.3 6	2.5 3.5 2.5	10 10 10	2 1.9 1.9	-1.564	0.11
Return to normal activity (days)	LA OA Total	36 36 72	3.1 3.3 3.2	3 3 3	2 1 1	8 6 8	1.3 1.1 1.2	-1.146	0.25
Beginning of work (days)	LA OA Total	36 36 72	10.8 15.5 13.2	10 15 12	1 6 1	25 35 35	4.6 6.1 5.8	-3.443	0.00
Follow-up period (days)	LA OA Total	36 36 72	277 161 216	211 159 212	65 15 15	424 424 424	67 86 85	-2.405	0.00

LA: laparoscopic appendectomy; OA: open appendectomy; BMI: body mass index; PDW: platelet distribution width; NLR: neutrophil lymphocyte rate; SD: standard deviation; Min: minimum; Max: maximum

Table 3. Comparison of preoperative and postoperative results between LA and OA

				Grou	ıp			Independent T-Test	
		n	Mean	Median	Min	Max	SD	t	р
WBC	LA	36	12300	12550	4800	20000	4445.6	0.23	0.818
	OA	36	12051.7	11600	5000	22100	4698.2		
	Total	72	12175.8	11850	4800	22100	4543		
Neutrophil	LA	36	9197.9	9825	2970	16800	4109	0.141	0.888
	OA	36	9053.8	8065	2720	18200	4553.9		
	Total	72	9125.8	8680	2720	18200	4307.1		
Stool output (hours)	LA	36	41	38.5	20	78	14.9	-5.782	0.001
	OA	36	64.2	66	24	96	19		
	Total	72	52.6	50	20	96	20.6		

LA: laparoscopic appendectomy; OA: open appendectomy; WBC: white blood cell; SD: standard deviation; Min: minimum; Max: maximum

than that in the LA group (p=0.031) (Table 2). In a total of five patients (three LA and two OA), the appearance of appendicitis was not found macroscopically, and we were unable to detect any pathology that could explain this clinical presentation. However, because we were unable to conduct microscopic evaluations, we still performed appendectomies on these patients. Vermicular appendix was found in four of these five patients, and our negative appendectomy rate was 8.3% (6/72) (Table 1).

The mean VAS pain scores were found to be significantly lower in the LA patients; the mean 6th, 24th, and 36th hour pain scores of the patients in this group were 3.6 (\pm 1.4), 2.1 (\pm 1.2), and 1.5 (± 0.9), respectively, while those in the OA group were 5.4 (\pm 1.6), 3.7 (\pm 1.5) and 2.6 (\pm 1.2), respectively. A statistically significant difference was observed between the two groups in terms of pain scores (p=0.001) (Table 2). The timing of gas and stool outputs was determined during postoperative follow-up; it was found that gas and stool output occurred earlier in the LA group, which had mean gas and stool output times of 19.6 (±8.1) hours and 41 (±14.9) hours, respectively. In the OA group, the mean gas and stool output times were 28.3 (\pm 45.4) hours and 64.2 (\pm 19) hours, respectively. A statistically significant difference was observed between the LA and OA groups in terms of gas and stool output times (p = 0.001) (Table 2, 3). The hospitalization times were also significantly longer in the OA group. In the LA and OA groups, the mean hospitalization times were 3.1 (\pm 1.3) days and 3.3 (\pm 1.1) days, respectively. In the LA group, the mean RTNA was shorter than that in the OA group; a statistically significant difference was detected between the two groups with respect to this parameter (p=0.001) (Table 2).

There were no cases of mortality in the study. Surgical-site infection was observed in a total of six patients among the two groups, occurring in five patients (13.9%) in the OA group and in one patient (1.3%) in the LA group. In these patients, wound cultures were taken, prophylactic antibiotics were started, and surgical-site care was administered until complete healing occurred. In a total of two patients (2.7%), incisional hernia was observed in the left trocar-site on the 3rd and 5th postoperative days. These patients were taken to the operating room, where the trocar-site incisional hernias were primer-repaired under

sedoanalgesia. Trocar-site incisional hernias were found in these two patients only.

Among both groups, a major complication was observed in a total of one patient in the OA group. A partial pulmonary embolism was observed in one patient, who was admitted to the emergency room with breathlessness after the postoperative 15th day. The 46-year-old female patient presented with weakness but did not have any comorbidities. Findings from her pathological specimen revealed gangrenous appendicitis. The patient was hospitalized at the pulmonary disease clinic, where she was started on anticoagulant and bronchodilator therapy. She was discharged uneventfully with low-molecular-weight heparin. No incidences of intraabdominal abscess, hemorrhage, or appendectomy stump leakage were found in either the LA or the OA group (Table 4).

DISCUSSION

Acute appendicitis is the most common cause of acute abdomen, and appendectomies are the most commonly performed emergency abdominal surgery in adults (1). The appendectomy risk for males and females during their lifetime are 12% and 23%, respectively, and approximately 7% of all people will undergo an appendectomy for acute appendicitis at some point in their lifetime (1, 2). The annual appendectomy rate for acute appendicitis is 10/10000 (2, 3).

Open appendectomy has remained the gold standard for more than a century since McBurney's incision was described in 1894 (4). After Semm et al. (5) performed the first LA, the path for a much wider application of minimally invasive surgery was opened. LA was revealed to be an effective procedure that could be performed in a short time. Over the years, many studies have compared OA and LA (6-10). In a prospective randomized study conducted by Hansen et al. (6) on the effectiveness of LA, it was found that LA resulted in less wound infection, decreased analgesic need, and earlier RTNA but had a longer operation time. In a meta-analysis conducted by Temple et al. (7), it was shown that LA had an early RTNA but had longer operation and hospital stay times. In addition, Korndorffer (8) and Reiertsen (9) reported lower misdiagnosis rates, decreased analgesic need, and less wound infection with LA. However, LA does have some drawbacks, such as in-

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				Groups					
		LA		OA		Total		Chi-square test (χ^2)	
		n	%	n	%	n	%	χ^2	р
Surgical-site infection	No	35	97.2	31	86.1	66	91.7	Fisher's exact	0.199
	Yes	1	2.8	5	13.9	6	8.3		
Incisional hernia	No	34	94.4	36	100	70	97.2	Fisher's exact	0.493
	Yes	2	5.6	0	0	2	2.8		
Stump leakage	No	36	100	36	100	72	100	-	-
	Yes	0	0	0	0	0	0		
Partial pulmonary	No	36	100	35	97.2	71	98.6	Fisher's exact	1
embolism	Yes	0	0	1	2.8	1	1.4		

creased rate of intraabdominal abscess and the requirement for costly instruments, such as endostaplers, endoclips, and endoloops (10-15). In the present study, we aimed to decrease the costs associated with LA by using intracorporeal knotting and glove-endoloop. In addition, we sought to compare LA and OA in terms of pre/intra/postoperative technique, time of return of gastrointestinal functions, and complications.

An endostapler, extracorporeal sliding knots, endoloops, endoclips, and endobags are usually used to remove the appendix during LA. These devices are costly and are not always accessible; however, the operation cannot be performed without the use of these instruments. In a prospective study on LA conducted by Hanssen (11), the appendix stump was ligated with polymeric clips (Hem-o-lok); this technique was found to be a feasible, safe, and economic alternative to ligation of the appendicular stump during LA. Beldi et al. (12) used a stapler in 60.5% of patients and an endoloop in 39.5% of patients for appendix stump ligation in their study; they reported surgicalsite infection rates of 0.7% and 1.7% in the stapler group and endoloop group, respectively. In studies conducted by Moreno (13) and by Delibegović et al. (14), for Gea extracorporeal knotting, endoloops and Hem-o-lok plastic clips were used for the appendix stump ligation. Delibegović and Matović (14) reported that the operation time was 47.1 (±6.7) minutes in the endoloop group and 38.7 (±5.0) minutes in the non-absorbable Hem-o-lok clip group. In a study conducted by Ay (15) on the effects of the intracorporeal knotting technique for appendix stump ligation, they found that the median operation time was (range 26 to 100) minutes. Furthermore, in a study with 141 cases conducted by Katsuno et al. (16) on the use of a laparoscopic stapler or 2/0 or 0/0 PolySorb for appendix stump ligation in complicated appendicitis, it was found that the mean operation time was 116.7 minutes and the mean duration of hospital stay was 8.9 days. In the present study, the appendix stump was ligated with 2/0 non-absorbable silk, and we removed the appendectomy specimen from the abdominal cavity with an intraoperatively prepared glove endobag. As a result, the operation cost was reduced and LA could be easily and effectively performed with intracorporeal knotting and glove endobag. Despite the increased operation time in the LA group compared to the OA group, our operation times were found to be similar to those in the abovementioned studies (Table 2).

Surgical-site infection can be seen after appendectomy. Deep surgical-site infection is more common in patients who undergo LA than in patients who undergo OA. In a study on LA conducted by Ay (15), 10.7% surgical-site infection and 7.1% small bowel obstruction rates were reported. In a study on LA conducted by Katsuno (16), 6.4% surgical-site infection, 4.3% intraabdominal abscess, and 2.1% small bowel obstruction rates were reported. In our study, the surgical-site infection rates were found to be 13.9% and 2.8% in the OA and LA groups, respectively. There were no statistically significant differences between the groups in terms of surgical-site infection. However, in one patient, a partial pulmonary embolism was observed. The patient was discharged uneventfully after undergoing treatment and follow-up (Table 3).

The length of hospital stay and RTNA are important indicators of patient recovery; many studies have shown that the length of hospital stay and RTNA are shorter in patients who underwent LA than in those who underwent OA (17-20). In a study on LA conducted by Shaikh et al. (17), the hospital stay time and RTNA were found to be 1.7 and 12.6 days, respectively. Additionally, in a meta-analysis consisting of prospective randomized studies conducted by Li et al. (18), it was reported that the length of hospital stay was less than 0.6 days and the RTNA was earlier than 4.5 days in patients who underwent LA. In our study, because the patients generally lived far from the center, the length of hospital stay was longer than that found in the literature. We observed that the LA group had shorter hospital stay times and earlier RTNA. A statistically significant difference was found between the groups in terms of RTNA (p=0.001) (Table 2).

Postoperative pain is an important problem following surgery and is directly related to quality of life. Postoperative pain levels and need for analgesics can be determined through VAS scores (18). Many studies have reported that patients who underwent LA had less postoperative pain and decreased need for analgesics (18-20). In a study on LA conducted by Cipe (19) involving 241 cases, it was found that the mean VAS scores were 4 (versus 4.6 in OA) and 2.9 (versus 3.4 in OA) at the 4th and 24th hours, respectively. Similar to the results found in the literature, we found that the VAS scores in the LA group were lower and that the OA group had greater postoperative analgesic requirements. The

mean VAS scores of the LA group in our study were 3.6 (versus 5.4 in OA), 2.1 (versus 3.7 in OA), and 1.5 (versus 2.6 in OA) at the 4th, 24th, and 36th hours, respectively. In addition, a statistically significant difference was found between the groups in terms of postoperative pain (p=0.001) (Table 2).

Laparotomy and anesthesia can inhibit intestinal motility. The paralytic period occurs even in cases of minor surgery and usually ends spontaneously within 0 to 24 hours in the small intestine, within 24 to 48 hours in the stomach, and within 48 to 72 hours in the colon after major abdominal surgery (21). The etiopathogenesis is not clear for decreased motility: however, it is thought to be related to the anesthetic agents used, manipulation of the intestine, increased sympathetic tone, and administration of opioids after surgery (22). However, some simple preventive methods can be used, such as intestinal manipulation limitations and a meticulous approach to tissue by the surgeon during the surgery (23). The PubMed database was searched to discover the relationship between gas-stool outputs and LA. Unfortunately, supporting clinical studies could not be accessed. In our study, the LA group had shorter gas-stool output times; the mean gas and stool output times for LA were 19.6 hours (versus 28.3 hours in OA) and 41 hours (versus 64.2 in OA), respectively. A statistically significant difference was found between the groups in terms of postoperative pain (p=0.001) (Table 2, 3). We believe that these results may be associated with less manual manipulation, early feeding, and decreased need for analgesics.

There were some limitations to our study. First, our patients generally resided in rural areas. Secondly, the average altitude of the region where the study was conducted is 1768 meters, and in winter, the temperature sometimes decreases to -39 °C; the region is covered with snow for more than 120 days. These geographical conditions may have affected the patients' hospital visits and discharge times. Finally, in our study, because USG and CT could not be performed on every patient, comparisons were limited.

CONCLUSION

In the present study, we found less postoperative pain, decreased need for analgesics, and earlier gas-stool outputs, discharge rates, and RTNA in patients who underwent LA compared to those who underwent OA. In addition, through the use of laparoscopic intracorporeal knotting and glove endobag, the costs associated with the LA procedure can be reduced. As a result, we believe that LA is an effective surgical method for appendectomy.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethic committee of Health Science University Adana Training and Research Hospital.

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

Peer-review: Externally peer-reviewed.

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

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Is it possible to reduce the surgical mortality and morbidity of peptic ulcer perforations?

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ABSTRACT

Objective: Peptic ulcer perforation is a life-threatening situation requiring urgent surgical treatment. A novel vision in peptic ulcer perforation is necessary to fill the gaps created by antiulcer medication, aging of the patients, and presentation of resistant cases in our era. In this study, we aimed to share our findings regarding the effects of various risk factors and operative techniques on the mortality and morbidity of patients with peptic ulcer perforation.

Material and Methods: Data from 112 patients presenting at our Training and Research Hospital Emergency Surgery Department between January 2010 and December 2015 who were diagnosed with PUP through physical examination and laboratory and radiological tests and operated at the hospital have been retrospectively analyzed. Patients were divided into three groups based on morbidity (Group 1), mortality (Group 2), and no complication (Group 3).

Results: Of the 112 patients included in the study, morbidity was observed in 21 (18.8%), mortality in 11 (9.8%), and no complication was observed in 80 (71.4%), who were discharged with cure. The differences between group for the average values of the perforation diameter and American Society of Anesthesiologists, Acute Physiology and Chronic Health Evaluation II, and Mannheim Peritonitis Index scores were statistically significant (p<0.001 for each). The average values for the group with mortality were significantly higher than those of the other groups.

Conclusion: In this study where we investigated risk factors for increased morbidity and mortality in PUPs, there was statistically significant difference between the average values for age, body mass index, perforation diameter, and Acute Physiology and Chronic Health Evaluation II and Mannheim Peritonitis Index scores among the three groups, whereas the amount of subdiaphragmatic free air did not differ.

Keywords: Mortality, perforation, peptic ulcer perforation, risk factors

INTRODUCTION

With regard to creating a novel vision for former diseases, our memorizations should be updated. Some diseases and their outcomes, which have been previously very well known, are nowadays almost always presented as unexpected cases because of new technologies and evolvements in medicine due to resistant events. Thus, antiulcer medication and presentation of elderly patients have changed in peptic ulcer perforation (PUP) and, transforming the patient profiles with PUP in our era. Therefore, a novel vision to avoid gaps is necessary to evaluate the patients with PUPsas surgeons are coming across newer patient profiles in last decades. Peptic ulcers are focal defects in the stomach and the duodenum extending below the mucosa or deeper (1, 2). They can be acute or chronic; the etiology of the condition is the disruption of balance between gastric acid effect and mucosal defense mechanisms (2, 3). Although medical treatments such as H2 receptor antagonists, proton pump inhibitors, and *Helicobacter pylori* eradication through antibacterial drugs, have decreased the number of surgeries in non-complicated peptic ulcer cases, the number of patients presenting to the emergency clinics with peptic ulcer perforation has not decreased (1-5).

Peptic ulcer perforation is still an important health problem, despite the decreasing incidence of peptic ulcer disease. The aim of this study was to investigate factors affecting the mortality and morbidity of PUPs and specifically determine approaches to decrease mortality.

MATERIAL AND METHODS

The data from 112 patients operated with the diagnosis of PUP at our Training and Research Hospital between January 2010 and December 2015 were retrospectively analyzed. Patient age, gender, weight, height, American Society of Anesthesiologists (ASA) score, symptoms, time interval between symptom onset and surgery, accompanying diseases, length of hospital stay, operative technique, laboratory findings, site and diameter of perforation, Acute Physiology and Chronic Health Evaluation (APACHE) II and Mannheim Peritonitis Index (MPI) scores, preoperative shock state, morbidity, and mortality were recorded. MPI (Table 1) and APACHE II scores were calculated for all patients. Patient age, chronic health status, rectal temperature, mean arterial blood pressure, heart rate, respiratory rate, arterial pH, partial oxygen pressure, serum sodium, serum potassium, serum creatinine, hematocrit, white blood cell count, and Glasgow coma score were recorded for determining the APACHE II score.

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©Copyright 2017 by Turkish Surgical Association Available online at www.turkjsurg.com All patients were operated with the open technique. After the aspiration of the intraabdominal free fluid, the intraperitoneal cavity was irrigated with at least 1000 mL of isotonic saline and aspirated. The surgical procedure was determined by the operating surgeon and either one of omental patch with Gra-

Table 1. Mannheim peritonitis index Risk factor Weighting if present 5 Age >50 years 5 Female sex Organ failure 4 Malignancy Preoperative duration of peritonitis >24 h Origin of sepsis not colonic 4 Diffuse generalized peritonitis 6 Exudate Clear 0 Cloudy, purulent 6 Fecal 12 Definitions of organ failure Kidney Cratine level >177µmol/L Urea level>167 mmol/L Oliguria <20 mL/h Lung PO₂<50 mmHg PCO₂>50 mmHg Shock Hypodynamic or hyperdynamic Intestinal obstruction Paralysis >24 h or complete mechanical obstruction PO²: PCO²

ham's procedure, bilateral truncal vagotomy with pyloroplasty or, antrectomy and gastroenterostomy was applied. Patients were divided into three groups based on morbidity (Group 1), mortality (Group 2), and no complication (Group 3).

Written informed consent of the included patients and local ethics committee approval were obtained.

Statistical Analysis

Statistical Package for Social Sciences software version 15.0 (SPSS Inc.; Chicago, IL, USA) was used for statistical analysis. Descriptive statistics were presented with number and percentage for categorical variables and mean, standard deviation, minimum, maximum, and median values for numerical variables. Comparisons between more than two independent groups were made using the one-way Anova test for normal distribution of numerical values and the Kruskal-Wallis test when normal distribution was not present. Subgroup analyses were carried out with the Tukey test for parametric tests and the Mann-Whitney U test for non-parametric tests and interpreted using the Bonferroni correction. The ratio of categorical variables between groups was tested using the chi square analysis. Risk factors for morbidity and mortality were evaluated using Cox regression analysis. Statistical significance level was accepted as p<0.05.

RESULTS

Of the 112 patients included in the study, morbidity was observed in 21 (18.8%) and mortality in 11 (9.8%). Eighty (71.4%) patients were discharged with cure, free of complications. Ninety-seven (86.6%) of 112 patients were male and 15 (13.4%) were female. No significant difference in the gender distribution of the groups was detected (p=0.252). There was statistically significant difference between the mean age of the groups (p<0.001). The mean age of the group with mortality was significantly higher than the that of the morbidity and no complication groups, and the mean age of the morbidity group was significantly higher than that of the no complication group. The demographic data and subgroup analyses are presented in Table 2-4.

Table 2. Demographics							
	Non-cor	nplicated	Morb	idity	Morta	lity	р
Gender Male	71	71 (88.8)		18 (85.7)		8 (72.7)	
Female	9 (11.3)	3 (14	3 (14.3)		3)	
	Mean±SD	Median	Mean±SD	Median	Mean±SD	Median	
Age	30.7±12.8	29	53.0±16.6	60	70.2±15.1	73	<0.001
Weight	67.5±14.0	66	80.8±11.6	82	82.1±4.6	83	<0.001
Height	175.6±7.6	175	169.0±6.6	169	167.6±7.6	169	<0.001
BMI	22.0±5.2	21.2	28.5±4.9	28.1	29.4±2.9	30.1	<0.001
Time from onset of symptoms	1.5±1.3	1	3.0±2.0	2	4.6±1.6	4	<0.001
Duriation of hospital stay (days) 5.3±1.1	5	11.7±11.3	7	9.2±6.2	10	<0.001
Perforation diameter (mm)	5.8±3.4	5	10.0±7.6	5	18.2±8.4	15	<0.001
ASA	1.1±0.3	1	2.1±0.9	2	3.6±0.9	4	<0.001
APACHE II score	2.0±2.5	1	4.5±3.2	5	10.2±5.3	9	<0.001
MPI score	2.4±3.6	0	9.2±6.5	6	18.5±6.4	17	<0.001
BMI: body mass index; ASA: America	an Society of Anesth	esiologists; APAC	HE: acute physiology	and chronic heal	th evaluation; MPI: M	lannheim perito	onitis index

The mean body mass index (BMI) of the patients were significantly different among groups (p<0.001). The average BMI in the mortality and morbidity groups was significantly higher than that in the no complication group.

Table 3. Subgroup analyses of demographics

5 1	,	3 1	
No	n-complicated vs Morbidity	Non-complicated vs Mortality	Morbidity vs Mortality
	р	р	р
Age	<0.001	<0.001	0.003
Weight	<0.001	<0.001	0.842
Height	0.001	0.003	0.875
BMI	<0.001	<0.001	0.858
Time from onset of symptoms	<0.001	<0.001	0.013
Duriation of hospita stay (days)	l <0.001	0.110	0.857
Perforation diameter (mm)	0.001	<0.001	0.003
ASA	<0.001	< 0.001	<0.001
APACHE II score	0.001	<0.001	0.001
MPI score	<0.001	<0.001	0.001

BMI: body mass index; ASA: American Society of Anesthesiologists; APACHE: acute physiology and chronic health evaluation; MPI: Mannheim peritonitis index

There was significant difference between groups with regard to time interval between symptom onset and surgery (p<0.001). The time interval was significantly higher in the mortality group than in the morbidity and no complication groups, and significantly higher in the morbidity group than in the no complication group. Statistically significant difference was observed in duration of hospital stay (p<0,001). The average duration of hospital stay in the group with morbidity was significantly longer than that in the no complication group.

The differences between the average values of the diameter of perforation and ASA, APACHE II and MPI scores among groups were statistically significant (p<0.001 for each). The average values for the group with mortality were significantly higher than those for the morbidity and no complication groups. Likewise, the average values for the morbidity group were significantly higher than those for the no complication group. In 98 (87.5%) patients, subdiaphragmatic free air was detected in the initial erect abdominal X-ray. There was no statistically significant difference between the rate of presence of free air between the groups. The white blood cell (WBC) count was 17.045±13.517 for Group 1, 13.347±6.434 for Group 2 and 14.608±3.857 for Group 3. No statistically significant difference was detected between the groups (p=0.734). The laboratory findings and subgroup analyses of the groups are displayed in Table 5, 6.

The presence of accompanying diseases showed a statistically significant difference between groups for all but ischemic

Table 4. Subgroup analyses of findings

		Non-con	nplicated	Mor	bidity	Mor	tality	
		n	%	n	%	n	%	р
Accompanying disease	2	9	11.3	12	57.1	9	81.8	<0.001
	DM	2	2.5	1	4.8	3	27.3	0.014
	HT	7	8.8	8	38.1	6	54.5	<0.001
	CRF	0	0.0	1	4.8	2	18.2	0.005
	ARF	0	0.0	2	9.5	3	27.3	0.001
	CHF	0	0.0	0	0.0	5	45.5	<0.001
	IHD	0	0.0	1	4.8	1	9.1	0.081
	COPD	0	0.0	3	14.3	1	9.1	0.008
	GI hemorrhage	1	1.3	0	0.0	1	9.1	0.214
	Cancer	0	0.0	3	14.3	0	0.0	0.011
Surgical procedure	Graham's raphe omentoplasty	78	97.5	14	66.7	5	45.5	<0.001
	Graham's procedure+additional procedures	2	2.5	5	23.8	5	45.5	
	Other	0	0.0	2	9.5	1	9.1	
Site of perforation	Duodenum 1st segment	51	63.8	9	42.9	6	54.5	0.001
	Prepyloricareal	29	36.3	7	33.3	5	45.5	
	Other	0	0.0	5	23.8	0	0.0	
Free air	70	87.5	18	85.7	10	90.9	0.899	
Shock state	3	3.8	7	33.3	11	100	<0.001	

DM: diabetes mellitus; HT: hypertension; CRF: chronic renal failure; ARF: acute renal failure; CHF: congestive heart failure; IHD: ischemic heart disease; COPD: chronic obstructive pulmonary disease; GI: gastrointestinal

Table 5. Laboratory findings

lable 5. Laborato	ory findings						
	Non-comp	licated	Morbi	dity	Mortalit	у	
	Mean±SD	Median	Mean±SD	Median	Mean±SD	Median	р
Glucose	130.9±41.8	121	133.6±52.6	123	136.8±38.4	137	0.783
Urea	33.0±13.6	32.2	59.6±33.4	52.7	108.0±43.1	90.4	<0.001
Creatinine	1.0±1.3	0.78	1.4±1.0	1.14	2.4±1.7	2.1	<0.001
AST	25.8±14.6	22	31.0±21.1	26	36.8±21.1	28	0.013
ALT	18.6±8.9	17	30.3±48.3	18	16.1±6.9	14	0.547
GGT	20.7±15.6	17	41.5±24.1	34	29.5±18.0	26	<0.001
LDH	233.8±139.3	194	242.3±91.2	234	318.1±106.2	323	0.009
ALP	75.2±39.3	67	101.8±55.2	83	89.6±23.8	89	0.001
Total protein	7.5±0.4	7.4	7.1±0.9	7.1	5.4±0.7	5.44	<0.001
Albumin	4.0±0.4	3.9	3.6±0.5	3.8	2.6±0.5	2.6	<0.001
Calcium	9.3±0.5	9.42	9.0±0.5	9.04	8.5±0.9	8.31	<0.001
Sodium	136.2±3.0	136	135.0±3.7	134	136.2±6.2	133	0.192
Potassium	4.1±0.4	4.075	4.2±0.3	4.22	4.9±0.9	4.8	0.007
CRP	26.0±50.2	4.4	60.2±97.5	15.58	174.6±190.1	95	<0.001
Amilase	83.8±70.6	65.1	77.9±33.6	80.4	117.9±104.9	100.9	0.460
WBC	13.6±4.2	13.4	11.6±3.9	11.7	13.0±6.4	11.7	0.222
HGB	14.7±2.0	14.6	13.9±2.2	14.2	12.2±3.3	11.3	0.026
HCT	44.2±5.6	44.55	43.0±5.3	42.8	37.1±10.4	34.5	0.150
PLT	257.0±69.5	242	281.6±70.1	272	333.4±209.7	289	0.250

AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: gamma glutamyl transferase; LDH: lactate dehydrogenase; ALP: alkaline phosphatase; CRP: C reactive protein; WBC: white blood cells; HGB: hemoblobin; HCT: hematocrit; PLT: platelet

Table 6. Subgroup analyses of laboratory findings

	Non-complicated vs morbidity	Non-complicated vs mortality	Morbidity vs mortality
	р	р	р
Urea	<0.001	<0.001	0.002
Creatinine	0.039	<0.001	0.047
AST	0.186	0.004	0.190
GGT	<0.001	0.097	0.147
LDH	0.140	0.006	0.031
ALP	0.001	0.027	0.984
Total protein	0.285	<0.001	<0.001
Albumin	0.012	<0.001	<0.001
Calcium	0.005	<0.001	0.057
Potassium	0.199	0.004	0.025
CRP	0.002	<0.001	0.007
HGB	0.127	0.015	0.226

AST: aspartate aminotransferase; GGT: gamma glutamyl transferase; LDH: lactate dehydrogenase; ALP: alkaline phosphatase; CRP: C reactive protein; HGB: hemoblobin

heart disease and gastrointestinal hemorrhage. The presence of accompanying diseases was most frequent in the mortality group, with chronic obstructive pulmonary disease (COPD) being the most common accompanying condition.

The preferred surgical approach showed a statistically significant difference between the groups. In the morbidity and mortality groups, additional procedures to the Graham's procedure were applied. The distribution of the site of perforation was significantly different among groups (p=0.001). In the morbidity group, hemorrhage from other sites was more common. State of shock was another variable showing statistically significant difference in distribution. All patients in the mortality group were in shock state.

In the model developed for determining factors affecting morbidity with single variables (age, BMI, ASA score, accompanying diseases, perforation diameter, MPI score, urea, GGT, ALP, calcium, and WBC) the most significant variables were BMI, GGT, and ALP (Table 7, 8). In the multivariate regression analysis for factors affecting morbidity, age was determined to be a significant parameter using the enter and backward method (Table 9).

In the model developed for determining factors affecting mortality with single variables; age, BMI, ASA score, accompanying diseases, perforation diameter, MPI score, APACHE II score, urea, creatinine, total plasma protein, albumin, calcium, potassium, CRP, hemoglobin, hematocrit levels and platelet counts were determined to be significant predictors (Table 10). In the multivariate regression analysis for factors affecting mortality, age and APACHE II score were determined to be significant parameters using the enter and backward method (Table 11).

Table 7. Univariate log	jistic regre	ession ana	lysis for m	orbidity
	p OR 95 % C.I.			6 C.I.
Age	<0.001	1.046	1.020	1.073
Gender (female)	0.894	1.097	0.280	4.296
BMI	<0.001	1.219	1.095	1.358
ASA	0.002	2.022	1.288	3.174
Accompanying disease	0.001	5.407	1.976	14.794
Perforation diameter	0.088	1.059	0.992	1.130
APACHE II score	0.122	1.091	0.977	1.218
MPI score	0.006	1.095	1.026	1.168
Free air	0.784	0.825	0.209	3.264
Shock state	0.064	2.750	0.942	8.027
Glucose	0.853	1.001	0.990	1.012
Urea	0.034	1.014	1.001	1.027
Creatinine	0.515	1.103	0.822	1.480
AST	0.349	1.012	0.987	1.037
ALT	0.195	1.023	0.988	1.059
GGT	0.002	1.053	1.019	1.088
LDH	0.957	1.000	0.996	1.004
ALP	0.033	1.011	1.001	1.022
Total protein	0.681	0.890	0.510	1.553
Albumin	0.138	0.564	0.264	1.201
Calcium	0.070	0.481	0.218	1.061
Sodium	0.143	0.895	0.771	1.038
Potassium	0.875	0.929	0.371	2.324
CRP	0.477	1.002	0.997	1.006
Amilase	0.559	0.997	0.989	1.006
WBC	0.073	0.897	0.797	1.010
HGB	0.348	0.910	0.748	1.108
HCT	0.827	0.992	0.922	1.067
PLT	0.500	1.002	0.997	1.006

BMI: body mass index; ASA: American Society of Anesthesiologists; APACHE: acute physiology and chronic health evaluation; MPI: Mannheim peritonitis index: AST: aspartate aminotransferase: ALT: alanine aminotransferase: GGT: Gamma glutamyl transferase; LDH: lactate dehydrogenase; ALP: alkaline phosphatase; CRP: C reactive protein; WBC: white blood cells; HGB: hemoblobin; HCT: hematocrit; PLT: platelet

Table 8. Most significant variables for morbidity

	р	OR	95.0% C.I.	
ВМІ	0.001	1.223	1.085	1.379
GGT	0.003	1.045	1.015	1.076
ALP	0.075	1.015	0.999	1.031

BMI: body mass index: GGT: gamma glutamyl transferase: ALP: alkaline phosphatase

DISCUSSION

Perforation is the second most common complication of peptic ulcer disease following hemorrhage, with an incidence ranging from 3.77 to 14 in 100,000 (6-10). High rates of morbidity (20%-

Table 9. Multivariate logistic regression analysis for morbidity

		р	OR	95.0%	o C.I.		
Enter	Gender	0.702	0.728	0.143	3.705		
method	Age	0.017	1.050	1.009	1.092		
	Time from onset of symptoms	0.969	0.993	0.706	1.396		
	MPI score	0.158	1.117	0.958	1.302		
	APACHE II score	0.133	0.840	0.670	1.055		
	Perforation diameter	0.442	0.964	0.877	1.059		
	Free air	0.526	0.598	0.122	2.925		
Backward method	Age	<0.001	1.046	1.020	1.073		
Model: gend	Model: gender, age, time fromonset of symptoms, MPI score, APACHE II score,						

perforationdiameter, freeair

MPI: Mannheim peritonitis index; APACHE: acute physiology and chronic health evaluation

50%) and mortality (3%-40%) have been reported for patients surgically treated for PUP (11-14). There are many studies about the risk factors for these high mortality and morbidity rates. In our study, there were statistically significant differences between groups with regard to the average values for age, BMI, perforation diameter, APACHE II score, and MPI score (p<0.001).

The diagnosis of PUP is most often made using the initial plain abdominal X-ray (15-17). In our study, 98 (87.5%) patients were diagnosed using the initial plain abdominal X-ray. The presence of subdiaphragmatic free air did not have a statistically significant relationship with mortality or morbidity. Wakayama et al. (18) reported WBC counts below 9500/mm³ was a significant predictor of mortalityHowever, no significant effect of WBC count on mortality or morbidity was observed in our study.

Ninety-seven (86.6%) of the 112 patients included in the study were male and 15 (13.4%) were female. Most (71.4%-94.5%) of the patients with PUP are reported to be male (19-23). However, Sonnenberg (24) has displayed in his study that the ratio of females is increasing and has claimed that female gender is a risk factor for postoperative morbidity. On the contrary, Nomani et al. (25) reported the negative effect of male gender on mortality and morbidity. In our study, no prognostic value of gender was detected. Testini et al. (26) have reported that patients aged 65 years or more have significantly higher rates of mortality compared with younger patients and explained this finding with the increased incidence of accompanying diseases in the elderly patients. Similarly, in our study, older age was determined to have a significant effect on mortality and morbidity. In the study of Kim et al. (2), it was determined that the presence of accompanying diseases did not have a significant effect on postoperative mortality and morbidity. On the other hand, numerous studies have shown that the presence of accompanying diseases has a significant effect on postoperative mortality and morbidity. In these studies, pulmonary diseases, hypertension (HT), diabetes mellitus (DM), and cardiac diseases were found to be of importance with varying frequency (5, 27, 28). In our study, the presence of DM, HT, renal failure, heart failure, COPD, and malignancies was observed to be related with a significantly increased risk of postoperative mortality and morbidity.

Table 10. Univariate logistic regression analysis for mortality				
	p OR		95 %	6 C.I.
Age	<0.001	1.125	1.058	1.197
Gender (female)	0.169	2.781	0.648	11.945
BMI	0.004	1.254	1.074	1.465
ASA	<0.001	10.203	3.505	29.699
Accompanying disease	0.001	17.143	3.441	85.401
Perforation diameter	< 0.001	1.212	1.107	1.326
APACHE II score	<0.001	1.625	1.286	2.053
MPI score	< 0.001	1.366	1.181	1.580
Freeair	0.720	1.477	0.174	12.512
Glucose	0.696	1.003	0.990	1.016
Urea	<0.001	1.051	1.027	1.076
Creatinine	0.043	1.474	1.012	2.147
AST	0.090	1.023	0.996	1.050
ALT	0.352	0.960	0.882	1.046
GGT	0.474	1.010	0.983	1.037
LDH	0.083	1.003	1.000	1.007
ALP	0.514	1.004	0.992	1.017
Total protein	<0.001	0.033	0.006	0.174
Albumin	<0.001	0.011	0.001	0.096
Calcium	0.001	0.130	0.039	0.434
Sodium	0.836	1.019	0.856	1.212
Potassium	<0.001	7.524	2.549	22.207
CRP	0.001	1.010	1.004	1.016
Amilase	0.136	1.005	0.998	1.011
WBC	0.871	0.988	0.857	1.140
HGB	0.004	0.703	0.552	0.894
НСТ	0.003	0.876	0.802	0.955
PLT	0.039	1.006	1.000	1.012

BMI: body mass index; ASA: American Society of Anesthesiologists; APACHE: acute physiology and chronic health evaluation; MPI: Mannheim peritonitis index; AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: gamma glutamyl transferase; LDH: lactate dehydrogenase; ALP: alkaline phosphatase; CRP: C reactive protein; WBC: white blood cells; HGB: hemoblobin; HCT: hematocrit; PLT: platelet

There are many scoring systems for predicting risk of morbidity and mortality in PUP, with ASA and Boey scoring methods being the most commonly used ones (29-32). However, ASA score is used as an overall surgical risk score rather than just for predicting the risks of PUP. Also in many studies, high MPI and APACHE II scores were found to be related with increased mortality and morbidity. Some studies have only investigated the effects of preoperative shock state on morbidity and mortality, concluding it to be an important risk factor (26, 33-35) We used the ASA, MPI, and APACHE II scoring methods as variables in our study. According to the statistical analysis, we concluded that all three scoring methods could be used to predict the risk of mortality and morbidity.

Table 11. Multivariate logistic regression analysis for mortality OR р 95.0% C.I. Enter Gender 0.236 10.320 0.217 490.9 method Age 0.172 1.063 0.974 1.161 Time from onset of 0.125 1.875 0.840 4.186 symptoms MPI score 0.530 1.090 0.832 1.428 **APACHE II score** 0.159 1.489 0.855 2.594 Perforation diameter 0.197 1.101 0.952 1.273 Free air 0.080 79.742 0.589 10793.3 0.035 1.079 Backward Age 1.006 1.159 method Time from onset of 1.593 0.069 0.965 2.629 symptoms APACHE II score 0.026 1.506 1.051 2.157 Model: Gender, age, time from onset of symptoms, MPI score, APACHE II score, perforation diameter, free air MPI: Mannheim peritonitis index; APACHE: acute physiology and chronic health

Nomani et al. (25) have reported a worse prognosis in patients with a perforation diameter greater than 5 mm. Consistent with the literature, we found that a large perforation diameter significantly increases morbidity and mortality (26-36). Duration of postoperative hospital stay of patients operated for PUP ranges between 7 and 12.5 days (37-39). In our study, the mean duration of hospital stay was 11.7±11.3 days in the morbidity group and 5.3±1.1 days in the no complication group. The duration of postoperative hospital stay in the morbidity group was significantly longer than that in the no complication group (p<0.001). In their study with 2668 patients, Buck et al. (40) have calculated a two-fold risk of mortality for underweight patients operated for PUP, and determined that being obese has no positive or negative effect on mortality. In our study, for patients with an increased BMI, mortality and morbidity were also significantly increased in both univariate and multivariate analysis (p<0.001).

CONCLUSION

evaluation

Peptic ulcer perforation continues to be an important cause of mortality and morbidity. We think that a novel vision to avoid gaps is necessary to evaluate the patients with PUPsas surgeons are coming across new types of patient profile in last decades. Mortality and morbidity are increased in patients with older age and higher BMI, perforation diameter, and APACHE II and MPI scores. We hypothesize that through closer follow-up of these patients, rates of mortality and morbidity can be decreased.

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

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

Peer-review: Externally peer-reviewed.

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

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Clinicopathological analysis of appendiceal mucinous tumors: A single-center experience

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ABSTRACT

Objective: Appendiceal mucinous tumors can be encountered in four different types. The clinical approach varies according to these types and the severity of the present disease. We aimed to share clinical, radiological, and pathological features and surgical options of the patients diagnosed with mucinous tumors at our center.

Material and Methods: Between August 2009 and March 2016, 757 patients underwent appendectomy for presumed diagnosis of acute appendicitis at the Department of Surgery, Kahramanmaraş Sütçü İmam University School of Medicine, Kahramanmaraş, Turkey. Among them, demographic, clinical, and histopathological characteristics of patients who diagnosed with appendiceal mucinous tumors were retrospectively analyzed. This study was approved by our faculty's human ethics committee.

Results: Incidence of mucinous tumor was 1.71%. Mean age of a total of 13 cases including 6 women and 7 men was 52.4±21.6 years (Range: 25-83 years). On preoperative diagnosis, acute appendicitis was detected in 8 patients, perforated appendicitis and periappendiceal abscess in two patients, and suspicious cecal mass in two patients. One patient had an operation for uterine leiomyoma. On histopathological examination, four patients were diagnosed with simple mucinous cyst, four with mucinous cystadenoma, three with mucosal hyperplasia, and two with mucinous cystadenocarcinoma. Mean duration of hospital stay was 5.1±4.7 days. One patient died from septic shock on first day, one from respiratory failure on 14th day, and one from cardiac arrest on 20th day. The average follow-up duration for the other 10 patients was 44 months (ranging from 1 to 78 months). No recurrence or death occurred in these patients over the course of follow-up.

Conclusion: Intraoperative clinical diagnosis of appendiceal mucinous tumors is rarely seen. Close histopathological and cytological examination of the specimen is required to separate malignant tumors from benign ones. The treatment varies depending on different types and the severity of the disease.

Keywords: Appendiceal mucinous tumors, cystadenoma, cystadenocarcinoma, mucocele, mucosal hyperplasia

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INTRODUCTION

Appendiceal mucocele is a pathological process occurring due to mucosal inflammatory or neoplastic diseases that result in the formation of an enlarged appendix and thinned appendicular wall caused by abnormal accumulation of mucus in the appendicular lumen, depending on any obstructive etiologic agent. It is at least two times more common in women than in men, and is only observed in 0.2%-0.7% of all appendectomy specimens (1-3). Although it is one of the most common primary epithelial tumors in the appendix, it is a rare clinical condition compared with other pathologies. This disease has unpredictable biological behavior in consideration of its outcomes. There is a large body of literature showing that mucocele is an important pathological condition as spontaneous or iatrogenic ruptures lead to pseudomyxoma peritoneum (PP) syndrome, of which a complete treatment algorithm has not been established so far. Four different types of formations widely accepted in the literature are retention cysts, mucosal hyperplasia, cystadenoma, and cystadenocarcinoma. Although clinical presentation of mucocele is nonspecific, it is incidentally detected during appendectomies, which are mostly performed for acute appendicitis. Cystadenoma and cystadenocarcinoma have more clinical significance because spontaneous or iatrogenic rupture of these can lead to PP syndrome. Opting for open laparotomy in the presence of a mucocele detected during laparoscopic procedures is extremely important to ensure that all spaces in the peritoneal cavity are explored and that the appendix wall remains intact and does not lead to PP syndrome, which is considered to be malignant and develops as a result of rupture (4). Understanding the clinical and pathological profile of patients with appendiceal mucocele can help the clinicians in better diagnosis and management of this rare condition. Therefore, in this retrospective study, besides the clinical, radiological, and pathological profile of the patients with mucocele, we also aimed to focus on the surgical management of appendiceal mucinous tumors according to different types.

MATERIAL AND METHODS

Data for this study were obtained through retrospective analysis of files of patients who underwent appendectomy at the Department of Surgery, Kahramanmaraş Sütçü İmam University School of Medi-

Table	Table 1. Preoperative characteristics of the patients						
Age	Sex	Admittion type	Main complaint	Radiologic Tools USG/CT/MRI	WBC	CRP	Presumed diagnosis
83	М	Emergency	Abdominal pain	-/-/-	Normal	Elevated	Acute appendicitis
34	М	Emergency	Abdominal pain	+/+/-	Normal	Normal	Acute appendicitis
72	F	Electively	Abdominal pain	-/-/+	Normal	Non available	Incidentally
80	М	Emergency	Abdominal pain	-/-/-	Elevated	Elevated	Acute appendicitis
61	F	Emergency	Abdominal pain	+/+/-	Elevated	Elevated	Perforated appendicitis
33	М	Emergency	Abdominal pain	-/-/-	Non available	Non available	Acute appendicitis
49	F	Emergency	Abdominal pain	-/-/-	Normal	Elevated	Acute appendicitis
81	F	Emergency	Abdominal pain	-/-/-	Normal	Elevated	Perforated appendicitis
60	М	Electively	Abdominal mass	-/+/-	Normal	Non available	Abdominal mass
41	М	Emergency	Rectal bleeding	-/+/-	Normal	Non available	Abdominal mass
37	F	Emergency	Abdominal pain	-/-/-	Elevated	Elevated	Acute appendicitis
25	F	Emergency	Abdominal pain	-/-/-	Elevated	Non available	Acute appendicitis
25	М	Emergency	Abdominal pain	-/-/-	Elevated	Non available	Acute appendicitis
F: fema	ıle; M: m	ale; WBC: white blood	d cells; CRP: C-reactive pr	otein; USG: ultrasonog	raphy; CT: computed	l tomography; MR: magne	etic resonance imagining



Figure 1. Computed tomography image of a giant mucocele

cine, Kahramanmaraş, Turkey. On April 20th, 2016, ethics committee approval was obtained from our faculty for this study. A total of 13 patients whose histopathological reports were compatible with primary appendiceal mucinous tumor from among 757 appendectomy cases between August 2009 and March 2016 were included in the study. Demographic data including patients age, gender, preoperative complaints, radiological assessments, inflammatory parameters, surgical procedure, histopathological examination of specimens, associated gynecological and colorectal pathologies, duration of hospitalization, information regarding recurrence or death, and records of causes of death were analyzed.

RESULTS

Mucinous tumor was detected in 13 of a total of 757 appendectomy specimens. Incidence of mucinous tumor was 1.71%. Mean age of a total of 13 cases including six women (46%) and seven men (54%) was 52.4±21.6 years (Range: 25-83 years). Eleven patients were first admitted to emergency service and

the other two electively presented at the outpatient clinic. Eleven patients (84.5%) complained of abdominal pain as the most common symptom; abdominal mass was detected in one patient (7.75%) and lower gastrointestinal system bleeding was seen in one patient (7.75%). Computed tomography (CT) was performed in two patients (Figure 1), magnetic resonance imaging (MRI) in one patient, and CT and ultrasonography (USG) in two patients. Although data on WBC count of one patient were not retrieved from the medical records, leukocytosis was present in five (42%) and normocytosis in seven (58%) of 12 patients. Data on CRP level of six patients were not extracted from the medical records, and there was an increase in this value in six (86%) out of the remaining seven patients.

In preoperative diagnosis, acute appendicitis was detected in eight patients, perforated appendicitis and periappendiceal abscess in two patients, and suspicious cecal mass in two patients. One patient underwent an operation for uterine leiomyoma (Table 1). Periappendiceal mucin deposits were detected in four patients intraoperatively. Right hemicolectomy was performed in the same session for two of these patients whose histopathological examination was indicated cystadenocarcinoma and for other two in the early period after appendectomy. Partial cecum resection together with appendectomy was performed for one patient with giant benign mucinous cystadenoma depending on frozen section examination (Figure 2). Seven patients underwent wide mesoappendix excision along with appendectomy. On pathological examination, epithelial cells were identified in the mucin deposits of only one patient out of four patients in which periappendiceal mucin deposits were detected. Except for a patient who had been operated for uterine leiomyoma with a diameter of 10 cm and whose appendiceal mucocele was incidentally detected during surgery, any accompanying ovarian or colorectal pathology was not detected in any other patients. Macroscopic examination of 12 patients' appendix from pathology records showed that average diameter of the appendix was 23.5 mm (ranging from

Table 2. Postopera	ative charac	cteristics of the pa	tients						
Type of Surgery	Appendix length/size (mm)	Extraappendiceal mucine, epithelial cells	Associated pathology	Pathologic examination	Hospital stay (day)	Follow-up (day, month)	Recurrence	Mortality	Cause of mortality
Appendectomy	80/10			Muc. cyst	14	14 d	Died	Yes	Respiratory failure
Appendectomy	40/15			Muc. cyst	1	50 mo	No		
Appendectomy	35/30		Uterine leiomyoma	Muc. cyst	3	51 mo	No		
Appendectomy	50/15			Muc. cyst	11	20 d	Died	Yes	Cardiac failure
Appendectomy+ partial cecal resection	140/50			Muc. cystadenoma	5	20 d	No		
Appendectomy	60/30			Muc. cystadenoma	3	50 d	No		
Right hemicolectomy	40/15	Mucine (+), epithelial cells (-)		Muc. cystadenoma	13	6 mo	No		
Right hemicolectomy	50/10	Mucine (+), epithelial cells (-)		Muc. cystadenoma	1	1 d	Died	Yes	Septic shock
Right hemicolectomy	120/30	Mucine (+), epithelial cells (+)		Muc. cystadenocar- cinoma	4	49 mo	No		
Right hemicolectomy		Mucine (+), epithelial cells (-)		Muc. cystadenocar- cinoma	8	50 mo	No		
Appendectomy	40/5			Mucosal hyperplasia	1	78 mo	No		
Appendectomy	60/5			Mucosal hyperplasia	2	76 mo	No		
Appendectomy	70/10			Mucosal hyperplasia	1	78 mo	No		
Muc: mucinous; d: day; mo	o: month; mm: m	ilimeter							

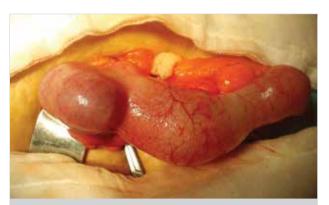


Figure 2. Perioperative view of a giant mucocele

5 mm to 50 mm) and average length was 62 mm (ranging from 35 mm to 140 mm). Information on the average length and diameter of one patient's appendix was not obtained from the pathological records. As a result of histopathological examinations, four patients were diagnosed with simple mucinous cyst, four with mucinous cystadenoma, three with mucosal hyperplasia, and two with mucinous cystadenocarcinoma. Average length of hospital stay was 5.2 days. One patient died from septic shock, one from respiratory failure, and one from

cardiac arrest on days 1, 14 and 20, respectively. The mean follow-up duration for the other 10 patients was 13.21±9.27 days (Range: 20-2340 days). No recurrence occurred in these 10 patients over the course of follow-up (Table 2).

DISCUSSION

The mucocele of the appendix was first described as a pathological entity in 1842 by Karel Rokitansky (5). It is characterized by the obstructive dilatation of the organ lumen with accumulation of mucoid material. Although being one of the most common primary epithelial tumors in the appendix, it is a rare clinical condition compared with other pathologies. It is found in 0.2% to 0.7% of the appendectomies (6, 7). In our study, the incidence of mucinous tumors was much higher than that reported in the literature, with a rate of 1.71%.

Appendiceal mucinous tumors consist of a rare disease that is generally diagnosed clinically during the operation. However, closer histopathological and cytological examination of the specimen may be required to distinguish malignant tumors from benign ones (8). There are four different types of formations that cause the mucocele of the appendix according to the World Health Organization: simple mucocele or retention mucocele, mucosal hyperplasia (5%-25%), mucinous

cystadenoma (63%-84%), mucinous cystadenocarcinoma (11%-20%) (7-10). Simple mucocele is a condition characterized by the presence of normal epithelial cells and the accumulation of mucinous material in the lumen depending on the occlusion of the appendiceal lumen in the presence of a fecaloid or other obstructive etiological factors. Dilation is expected to be up to 1 cm. However, the diameter is usually greater than 1 cm in mucosal hyperplasia (mucocele), with the hyperplasia in epithelial cells. Villous adenomatous changes and, to some degree, cellular atypia have occurred in the epithelial cells of mucinous cystadenoma which is the most often encountered form in the literature. Cystadenocarcinoma is the most prognostically dangerous form of appendiceal mucinous neoplasms and a malignant tumor derived from the peritoneal glandular stromal cells or epithelial cells. (11). We observed simple mucocele in four patients (30.7%), mucosal hyperplasia in three (23.2%), mucinous cystadenoma in four (30.7%), and mucinous cystadenocarcinoma in two (15.4%). Incidence of mucinous cystadenoma was higher than that of other types.

The clinical presentation of mucocele of the appendix is usually non-specific. Abdominal pain is the most common symptom of symptomatic patients. Other symptoms include abdominal mass, weight loss, nausea, vomiting, changes in bowel habits, unexplained anemia, obstipation, and lower gastrointestinal system bleeding (12). A large number of patients often admit to emergency service with one or more of these symptoms. In our study, while 11 patients were admitted to emergency service, other two patients admitted electively to the outpatient clinic. Abdominal pain, one of the most common symptoms, was present in 11 patients (84.5%), abdominal mass in one (7.75%), and lower gastrointestinal system bleeding in one (7.75%). Appendiceal mucocele may present as spontaneous rupture of mucocele along with acute appendicitis, leading to PP syndrome. This PP syndrome following the rupture may manifest through nonspecific symptoms such as abdominal hernia and ovarian mass.

Laboratory investigation of patients with appendiceal mucinous tumors shows that leukocytosis and an increase in CRP values for these tumors are not as high as those in acute appendicitis. Leukocytosis was present in five (42%) and normocytosis (58%) in seven of 12 patients with measured values. Data on CRP (C-reactive protein) value of six patients could not be obtained from the medical records, but there was an increase in this value for six (86%) out of the remaining seven patients.

Preoperative diagnosis is thought to be an important factor for the determination of surgical management and the extension of surgery, but preoperative diagnosis is generally difficult (8). Although a mucocele may be diagnosed preoperatively with abdominal USG, CT, or MRI, diagnosis is generally made intraoperatively due to macroscopic appearance and a final diagnosis can only be reached after histopathological examination of the specimen (8, 13, 14). However, preoperative diagnosis is possible as a preliminary diagnosis when cystic dilation of the appendix, mural calcification of the appendix wall, luminal diameter greater than 15 mm, and lack of appendicolith are observed on imaging studies (13). In this study, CT was performed in two patients, MRI in

one patient, and CT and USG in two patients. The mucocele can be seen as a well-encapsulated, thin-walled, round cystic mass with abdominal CT, and also calcification can be seen in about half of the cases. Abdominal USG reveals an encapsulated cystic lesion associated with the cecal wall. An image is formed in varying echoes depending on the density of mucin within the cyst. Multiple echogenic layers give it an onion skin appearance in some patients, suggesting that this appearance is pathognomonic for mucocele. Nodular appearance in the cyst wall may increase the likelihood of developing cystadenocarcinoma. Although malignancy is rarely seen in a diameter of 2 cm or less, the possibility of developing malignancy increases if the diameter is 6 cm or larger. Macroscopic examination of 12 patients' appendix from pathology records showed that the average diameter was 23.5 mm (ranging from 5 mm to 50 mm), and the average length was 62 mm (varying from 35 mm to 140 mm). The average diameter of the appendix of malignancy-detected patients was 30 mm and the average length was 120 mm. Abdominal ascites is a non-specific finding in PP syndrome. Mucin deposits may localize in natural spaces, liver, and spleen within the abdominal cavity. In this study, epithelial cells were identified in the mucin deposits of only one out of four patients with a detection of periappendiceal mucin deposits.

The key principle in the surgical treatment of appendiceal mucinous toumors is the necessity of excising largely all mesoappendix including appendix and its lymph nodes, which can vary by associated benign or malignant pathology (8). To determine the surgical extension, the base of the appendix should be checked during surgery. Positive margins and difficulties in closing the appendiceal stump, call for a more extensive surgery such as cecectomy. When the luminal diameter of the appendix is larger than 2 cm, in case of extension beyond the appendix such as lymph node metastasis and PP syndrome, and in case of cystadenocarcinoma based on frozen section examination, right hemicolectomy should be the choice for extensive surgery (13). Switching to open surgery on detection of mucocele during laparoscopic approaches is extremely important in order to explore all spaces in the peritoneal cavity and assure that the appendix wall remains intact and does not develop PP syndrome, which is considered to be malignant as a result of a rupture that may occur (4, 5). However, the experience of the surgical team in laparoscopy is the principal determining factor for proceeding laparoscopically (8, 13).

In this study, periappendiceal mucin deposits were detected in four patients intraoperatively. Right hemicolectomy was performed in the same session for two of these patients whose histopathological examination was reported as cystadenocarcinoma and for other two, in the early period after appendectomy. Partial cecum resection together with appendectomy was performed for one patient with giant benign mucinous cystadenoma based on the result of frozen section examination. Seven patients underwent wide mesoappendix excision along with appendectomy. The root of the appendix should be examined and excised carefully. While examining the abdominal cavities, if any mucin deposit is noticed, sufficient amount of sample should be sent for cytological examination and intra-abdominal parts should be washed with plenty of physiological saline solution.

Rupture of mucocele and discharge of mucus and epithelial cells in the abdominal and peritoneal cavity are associated with poor prognosis due to the risk of PP syndrome or appendiceal mucinous carcinomatosis. Treatment is more complicated in PP syndrome where diffuse mucin deposits and mucinous implants are found on omental and peritoneal surfaces and in the abdominal cavity. The basic principle of the surgery in case of PP is that as much tumor as possible should be removed from the relevant region since development of symptomatic recurrences including remote and nodal metastases may take years because of the slow progression of the disease (14). Removal of all microscopic foci and omentum is required. Also in female patients, routine appendectomy and bilateral salpingo-oophorectomy along with hysterectomy are required. Results of R0 and R1 resections are better than those of R2 when compared in terms of survival (14, 15). In these patient groups, hyperthermic intraperitoneal chemotherapy together with cytoreductive surgery is a standard practice at many centers (16, 17). Repetitive operations should be performed in case of any recurrences.

CONCLUSION

As a consequence, preoperative diagnosis of mucocele of the appendix is difficult, so when a mass like appearance is seen on imaging studies, it should be kept in mind that with a high possibility it is a kind of mucocele and carries a risk of perforation which can cause PP. Further, it should be kept in mind that solid organ tumors may accompany mucocele, and PP risk lasts for a long term postoperatively. Therefore, it is reasonable to explore thoroughly during operation and periodically follow-up patients after discharge. The sufficient and required treatment for mucocele is simple appendectomy with negative margins, but cecum resection or a right hemicolectomy may be necessary depending on the size and location. During the surgery, maximum care should be taken to avoid intraperitoneal rupture of a mucocele because of the risk of PP.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Kahramanmaraş Sütçü İmam University (Date: 04/20/2016, decision no: 131/10).

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

Peer-review: Externally peer-reviewed.

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

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Clinicopathological features of gastroenteropancreatic neuroendocrine tumors: A retrospective evaluation of 42 cases

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ABSTRACT

Objective: Neuroendocrine tumors arise from neuroendocrine cells in any part of the body; approximately two thirds of these tumors are located in the gastrointestinal tract and pancreas. Although gastroenteropancreatic neuroendocrine tumors are known as rare neoplasms, their prevalence has recently increased due to advanced diagnostic methods and increased awareness of the disorder. In the present study, we aimed to review patients who were treated and followed up for gastroenteropancreatic neuroendocrine tumors at our clinic in terms of clinical picture, pathological findings, and prognosis.

Material and Methods: Data from 42 patients diagnosed with gastroenteropancreatic neuroendocrine tumors who were treated and followed up at our Training and Research Hospital from August 2011 to December 2015 were retrospectively evaluated.

Results: A total of 42 patients aged 17-81 years (mean age 46.9 years) were enrolled in the study. The most common symptom was abdominal pain, which was seen in 31 (73.8%) patients. gastroenteropancreatic neuroendocrine tumors were detected in the stomach (n=5, 35.7%), appendix (n=11, 26.2%), rectum (n=6, 14.3%), pancreas (n=4, 9.5%), ileum and colon (n=2, 4.8%), and duodenum and jejunum (n=1, 2.4%). Local excision was performed in seven (16.7%) patients. Nine (21.4%) patients underwent gastric wedge resections, either by a laparoscopic procedure (n=3) or by open surgery (n=6). Total gastrectomy and laparoscopic subtotal gastrectomy were performed on three (7.1%) patients and two patients (4.8%), respectively. After the surgical procedures, the patients were followed up for a mean period of 36 months (15-57 months); the one-year and three-year survival rates were determined to be 100% and 97.6%, respectively.

Conclusion: Management of gastroenteropancreatic neuroendocrine tumors requires accumulation of knowledge and experience to establish a standardized approach. Therefore, we believe that collecting regular national data from these cases in every country will contribute to understanding the details of this entity worldwide.

Keywords: Chromogranin A, endoscopy, gastroenteropancreatic neuroendocrine tumor, ki-67 antigen, mitosis, synaptophysin

INTRODUCTION

Neuroendocrine tumors (NETs) arise from neuroendocrine cells in any part of the body; approximately two thirds of these tumors are located in the gastrointestinal tract and pancreas (1, 2). Although gastroenteropancreatic neuroendocrine tumors (GEP-NETs) are known as rare neoplasms, their prevalence has recently increased due to advanced diagnostic methods and increased awareness of the disorder (3). The incidence of GEP-NETs was reported to be 3.65/100,000 according to the Surveillance, Epidemiology, and End Results database program (4). Because NETs may be located in various parts of the body and secrete different hormones, clinical findings may show differences with regard to mass effects on surrounding structures and the types of hormones secreted. However, most NETs are nonfunctional and present with non-specific symptoms such as abdominal pain and gastrointestinal bleeding.

According to the World Health Organization (WHO) 2010 classification (Table 1), GEP-NETs are classified as NET Grade 1 (G1) and NET Grade 2 (G2) (well-differentiated endocrine tumors in the WHO 2000 classification) and NEC Grade 3 (G3) (poorly differentiated endocrine carcinoma in the WHO 2000 classification) (5, 6). The WHO 2010 classification takes into account the mitotic rate (usually expressed as mitoses per 10 high power microscopic fields or per 2 mm) and/or Ki67 index (the percentage of neoplastic cells immunolabeled for the proliferation marker Ki67) when grading GEP-NETs. Tumors with a Ki67 index of <2% or a mitotic rate of <2/10 hpf are classified as G1, those with a Ki67 index of 3%-20% or a mitotic rate of >20/10 hpf are classified as G2, and those with a Ki67 index of >20% or a mitotic rate of >20/10 hpf are classified as G3 (7, 8).

In the present study, patients who were treated and followed up for GEP-NET at our clinic were reviewed in terms of clinical picture, pathological findings, and prognosis.

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Table 1. WHO 2	010 classification of GEP-NETs		
Grade	Equivalent staging in WHO 2000 classification	Ki 67 index	Mitotic rate
NET Grade 1	Well-differentiated endocrine tumors	<2%	<2/10 hpf
NET Grade 2		3-20%	2-10/10 hpf
NEC Grade 3	Poorly differentiated endocrine carcinoma	>20%	>20/10 hpf
WHO: World Health	Organization; GEP-NETS: gastroenteropancreatic neuroendocrine tum	ors; NET: neuroendocrine tumor	

MATERIAL AND METHODS

Data from 42 patients diagnosed with GEP-NET who were treated and followed up at our Training and Research Hospital from August 2011 to December 2015 were retrospectively evaluated. We excluded patients from whom we did not obtain sufficient data, who could not be followed up, or who refused to participate in the study. The variables of age, gender, symptoms and signs, diagnostic methods, pathological findings, tumor features with regard to the WHO 2010 classification for GEP-NETs and the TNM staging system, and treatment and follow-up outcomes were recorded. The WHO 2010 classification for GEP-NETs was used as the grading system. Cancer staging was performed according to the TNM staging system for the involved organ or anatomical region for each tumor.

This research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects". Written informed consent was obtained from the patients who participated in this study.

RESULTS

A total of 42 patients (20 male, 22 female) aged 17-81 years (mean age 46.9 years) were enrolled in the study. The most common symptom was abdominal pain, which was seen in 31 (73.8%) patients. While two (4.3%) patients presented with hypoglycemic attack, one (2.4%) patient presented to the emergency department with blood in their vomit. One patient described recent constipation, while two patients presented to our outpatient clinic with weight loss and abdominal mass, respectively. While insulinoma was determined in two patients, the remaining patients (n=40, 95.2%) were determined to have hormonally nonfunctional GEP-NETs. Diagnosis was mostly made by endoscopy among the various diagnostic procedures used. Half the patients (n=21) were diagnosed through endoscopy, and endoscopic ultrasonography (EUS) was used in two patients. Computed tomography (CT) was performed on 13 (31%) patients. Eight (61.5%) of those provided a diagnosis of NET, while five (38.5%) had no diagnostic yield. Nine (21.4%) patients underwent positron emission tomography CT (PET-CT); there were no findings in two of those patients.

Gastroenteropancreatic neuroendocrine tumors were detected in the stomach (n=15, 35.7%), appendix (n=11, 26.2%), rectum (n=6, 14.3%), pancreas (n=4, 9.5%), ileum and colon (n=2, 4.8%), and duodenum and jejunum (n=1, 2.4%). A local excision was performed in seven (16.7%) patients. Nine (21.4%) patients underwent gastric wedge resections, either by a laparoscopic procedure (n=3) or by open surgery (n=6). Total gastrectomy and laparoscopic subtotal gastrectomy were

performed in three (7.1%) patients and two patients (4.8%), respectively. Diagnosis of 11 (26.2%) patients was made after pathological examination of appendectomy specimens; therefore, their treatments were recorded as appendectomy. Distal pancreatectomy was performed in four (9.5%) patients, segmental ileal resection in two (4.8%) patients, low anterior resection in one (2.4%) patient, and segmental jejunal resection in one (2.4%) patient. Two patients were assumed to be inoperable due to distant metastases; therefore, they did not undergo surgery.

A range of tumor sizes between 2 and 105 mm was detected (mean size 9.7 mm) according to the pathology reports. Twenty-six (61.9%) patients presented with stage 1, 12 (28.6%) patients with stage 2, 2 (4.8%) patients with stage 3, and 2 (4.8%) patients with stage 4 tumors based on the TNM staging system. Ki-67 indices ≤2% were detected in 28 (66.7%) patients, between 2% and 20% in 13 (31%) patients, and >20% in 1 patient. Thirty-eight (90.5%) patients had a mitotic rate of <2/10, and 4 (9.5%) patients had a mitotic rate of 3 to 20/10. Twenty-eight (66.66%) patients were classified as NET G1, 13 (30.95%) were NET G2, and 1 (2.38%) was NEC G3 according to the WHO 2010 classification.

Staining for chromogranin A, for synaptophysin, and for neuron-specific enolase was positive in 26 (78.8%), 28 (90.3%), and 3 (7.1%) patients, respectively. Both chromogranin A and synaptophysin were found to be positive in one of two patients with metastasis; only synaptophysin was positive in the other patient in our study. These results are summarized in Table 2. After the surgical procedures, the patients were followed up for a mean period of 36 months (15-57 months); the one-year and three-year survival rates were determined to be 100% and 97.6%, respectively.

DISCUSSION

Neuroendocrine tumors are classified as functional and nonfunctional. Over 90% of patients are reported to have nonfunctional tumors (9); most nonfunctional GEP-NETs are found to present fairly late, with symptoms of mass effect or distant metastases (10). Functional GEP-NETs cause some symptoms due to excessive production of hormones or peptides. Various typical symptoms can be seen related to carcinoid syndrome, Zollinger-Ellison syndrome, Whipple's triad, Verner-Morrison syndrome, insulinoma, and glucagonoma (11). However, Modlin et al. (12) advocated that categorizing these tumors as functional or nonfunctional is an archaic clinical concept because they are indistinguishable at the cellular, biological, and morphological levels.

Ninety-five per cent of NETs were determined to be nonfunctional in our study; the most common symptom was ab-

Table 2. Clinicopathological features of the patients

	Stomach n=15	Duodenum n=1	Jejunum n=1	lleum n=2	Colon n=2	Appendix n=11	Rectum n=6	Pancreas n=4	Total n=42
Stage (TNM)									
Stage 1	6	1	1	1	2	10	3	2	26
Stage 2	6	-	-	-	-	1	3	2	12
Stage 3	1	-	-	1	-	-	-	-	2
Stage 4	2	-	-	-	-	-	-	-	2
Grade (WHO 2010)									
G1	7	1	1	1	2	9	5	2	28
G2	8	-	-	1	-	2	1	1	13
G3	-	-	-	-	-	-	-	1	1
Diagnosis									
Endoscopy	14	1	-	-	2	-	4	-	-
EUS	2	-	-	-	-	-	-	-	-
СТ	1	-	1	2	-	-	-	4	-
PET-CT	3	-	-	-	-	-	2	2	-
Incidental		-	-	-	-	11	-	-	-
Treatment									
Laparoscopic gastric wedge resection	3	-	-	-	-	-	-	-	-
Open gastric wedge resection	6	-	-	-	-	-	-	-	-
Total gastrectomy	3	-	-	-	-	-	-	-	-
Laparoscopic subtotal gastrectomy	2	-	-	-	-	-	-	-	-
Appendectomy	-	-	-	-	-	11	-	-	-
Distal pancreatectomy	-	-	-	2	-	-	-	4	-
Segmental ileal resection	-	-	1	-	-	-	-	-	-
Segmental jejunal resection	-	-	-	-	-	-	-	-	-
Low anterior resection	-	-	-	-	-	-	1	-	-
Endoscopic local excision	-	1	-	-	2		4		-
Pathology									
Chromogranin A	10/11	1/1	1/1	2/2	1/2	5/6	3/6	3/4	26/33
Synaptophysin	10/11	1/1	1/1	2/2	1/2	5/5	5/5	3/4	28/31

 $WHO: World\ Health\ Organization;\ G:\ grade;\ EUS:\ endoscopic\ ultrasonography;\ CT:\ computed\ tomography;\ PET-CT:\ positron\ emission\ tomography-computed\ tomography$

dominal pain, which was seen in three fourths of patients. The rate of distant metastasis was found to be less than 5%, and the pathological mean tumor size was measured as 9.7 mm. Therefore, although the prevalence of nonfunctional tumors is consistent with the literature, we cannot say this is true for the clinical picture because neither mass effect nor distant metastases were main features in the diagnosis of our cases. Zhang et al. (9) found that most patients (29.17%) presented with non-specific symptoms, such as abdominal or back pain.

Neuroendocrine tumors are diagnosed and staged by CT, MRI, PET, US, endoscopy, and EUS. Functional imaging methods (somatostatin receptor scintigraphy, PET) are applicable because these tumors secrete hormones and peptides and express somatostatin receptors (13). The most accurate diagnostic method can differ according to tumor location. CT, MRI, and PET should be used for staging and follow-up of response to treatment accord-

ing to the North American Neuroendocrine Tumor Society Guidelines (14). Our cases were mostly diagnosed through endoscopy. Though the other imaging methods were also used as diagnostic tools, they were mainly preferred for staging and follow-up. In addition, the GEP-NETs of 11 patients were incidentally detected by pathological examination of appendectomy specimens.

In two different studies, GEP-NETs were mostly located in the rectum (17.7%-58.93%), whereas the stomach (35.7%), appendix (26.2%), and rectum (14.3%) were the most frequently involved anatomic sites in our study. We consider that the distribution of GEP-NETs may differ between various countries (9, 15). A multidisciplinary approach is required in the treatment of GEP-NETs. It is advocated that surgery should be performed as a primary treatment as much as possible (16). It was reported that curative resections of primary tumor and locoregional lymph nodes provided 5-year and 10-year sur-

vival rates of 100% in stage 1 and 2 tumors and a 5-year survival rate of 95% and a 10-year survival rate of 80% in stage 3 tumors (17). The other therapeutic options are transcatheter arterial embolization, chemotherapy, somatostatin analogs, and novel therapies such as tyrosine kinase and angiogenesis inhibitors (9, 10).

We performed surgical procedures on almost all patients (95.2%). Only two (4.8%) patients were found to be unsuitable for surgery because one had an unresectable tumor and one presented with liver metastases. These patients were referred to the medical oncology clinic. The patient with an unresectable tumor died 28 months after diagnosis.

The WHO 2010 classification based on Ki-67 index and mitotic rate is currently used to grade GEP-NETs. In our series, 66.66% and 30.95% of patients were found to have G1 and G2 tumors, respectively. Although these tumors were assumed to be well-differentiated endocrine tumors in the WHO 2000 classification, NETs should be considered as potentially malignant lesions (18). The most commonly used immunohistochemical markers in pathological examination to identify NETs are chromogranin A and synaptophysin. Immunoreactivity of chromogranin A is more common in well-differentiated NETs, while that of synaptophysin is common in both well-differentiated NETs and poorly differentiated NECs (19, 20). In our study, positive immunohistochemical stainings for chromogranin A and synaptophysin were found with rates of 78.8% and 90.3%, respectively. Both these markers were found to be positive in one of two patients showing metastasis in our study; only synaptophysin was positive in the other patient.

The mean follow-up period was 36 months in our study, and the one-year and three-year survival rates were 100% and 97.6%, respectively. Wang et al. (21) reported 178 patients with a mean follow-up period of 8.6 years and with one-year, three-year, and five-year survival rates of 74.4%, 66.7%, and 54.5%, respectively. However, the mean tumor size in their study was larger than ours (3.9 cm versus 9.7 mm), and NEC G3 tumors were detected more frequently in their patients than in our study (30.2% versus 2.38%).

CONCLUSION

As a heterogeneous disorder, GEP-NETs can be located in various anatomic sites in the abdomen, resulting in a wide range of clinical pictures and requiring further awareness of relevant clinicians. A review of the literature revealed that management of GEP-NETs requires accumulation of knowledge and experience to establish a standardized approach. Therefore, we believe that collecting regular national data from these cases in every country will increase understanding of the details of this entity worldwide.

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

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

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

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The effects of sleeve gastrectomy on shoe size one year after surgery

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ABSTRACT

Objective: The aim of this study is to evaluate the effects of sleeve gastrectomy on shoe size one year after the procedure. To our knowledge, no study has yet been conducted addressing this issue.

Material and Methods: Patients who were prepared for sleeve gastrectomy were eligible for the study, and all data and preoperative shoe sizes were recorded in our prospective database. At the 12th month of follow-up, each patient's excess weight loss % was calculated, and their shoe sizes were recorded by verbal report. Arbitrary or half-size changes were not taken into consideration. The probability of a change in shoe size and the effects of age, sex, preoperative body mass index, and 12th month excess weight loss % on this change were investigated. p<0.05 was regarded as statistically significant.

Results: The subjects of the study were 212 patients who completed their 12-month follow-ups after sleeve gastrectomy between January 2012 and February 2016. The mean shoe size was 41.5; this decreased to 40.5 one year after sleeve gastrectomy (p<0.001). In patients with body mass index (BMI)>50, both the mean decrease (p=0.008) and the percentage of at least two size decreases (p=0.009) were significantly higher than those in patients with BMI<40. Age, sex, and excess weight loss % did not have any significant effects on shoe size.

Conclusion: Sleeve gastrectomy was clearly associated with decrease in shoe size after 12 months. Only preoperative body mass index was found to be directly associated with this decrease.

Keywords: Bariatric surgery, sleeve gastrectomy, shoe size

INTRODUCTION

New evidence strongly suggests that bariatric surgery extends the lifespan of morbidly obese patients; therefore, the number of bariatric operations performed worldwide is increasing (1-7). The introduction of sleeve gastrectomy (SG) to the armamentarium of bariatric surgeons during the last decade probably effected this exponential increase due to its technical ease, physiological nature, and comparable mid-term results (8-10). SG is arguably becoming the new gold standard bariatric procedure, and the demand for this procedure is continually increasing (9, 7). Depending on the definition of "ideal body weight" and the timing of preoperative weight measurement, the expected excess weight loss (EWL) % one year after SG is reported to be between 60 and 100 (8, 11, 12). This considerable reduction in body weight, in addition to increasing life quality and expectancy, is expected to necessitate the purchase of a new wardrobe, as is known by the entire bariatric community. Observational experience also suggests that a decrease in shoe size can occur following a bariatric procedure, although this has never been scientifically investigated.

The main aim of this study is to prospectively evaluate changes in shoe size one year following SG. To our knowledge, our study represents the first report that addresses this issue.

MATERIAL AND METHODS

All patients prepared for SG were eligible for the study. The demographics, preoperative and operative data, postoperative complications, and follow-up results of the patients were recorded in our prospective database. Preoperative shoe size and body mass index (BMI, kg/m²) were recorded once the surgery was scheduled. European shoe sizing was used.

All operations were performed by the same team using a standard technique. Briefly, special care was taken to excise the antrum, starting 2 to 3 centimeters from the pylorus; wide excision of the fundus was also enforced. Our procedure also involved purse string inversion of the upper corner and full thickness, as well as continuous suturing of the entire staple line after the 36 F bougie was withdrawn. All patients were seen at the clinic three months and one year after surgery and then at yearly intervals. The 12th month postoperative follow-up visit was the endpoint for this study; the patient's shoe size and weight in kilograms were recorded again, and the EWL % was calculated. The change in shoe size was estab-

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Table 1. Preoperative versus 12-month postoperative shoe sizes					
	Preoperative shoe size (mean, median, SD)	12-month postoperative shoe size (mean, median, SD)	Preoperative versus 12-month postoperative shoe size		
All patients (n: 212)	(41.5, 41, 2.7)	(40.5, 40, 2.7)	p<0.001		
Male (n: 85)	(44.2, 44, 1.8)	(43.2, 43, 1.75)	p<0.001		
Female (n: 127)	(39.7, 40, 1.5)	(38.6, 39, 1.4)	p<0.001		
Age 40 years< (n: 84)	(41.4, 41, 2.8)	(40.5, 40, 2.8)	p<0.001		
Age 40 years> (n: 128)	(41.5, 41, 2.58)	(40.5, 40, 2.6)	p<0.001		
BMI<40 (n: 55)	(40.3, 40, 2.3)	(39.5, 39, 2.4)	p<0.001		
40 <bmi<50 (n:="" 105)<="" td=""><td>(41.6, 41, 2.7)</td><td>(40.6, 40, 2.8)</td><td>p<0.001</td></bmi<50>	(41.6, 41, 2.7)	(40.6, 40, 2.8)	p<0.001		
BMI>50 (n: 52)	(42.6, 42.5, 2.8)	(41.3, 42, 2.7)	p<0.001		
EWL %<75 (n: 70)	(42.04, 42, 2.5)	(40.97, 40.5, 2.5)	p<0.001		
75 <ewl %<100="" (n:="" 84)<="" td=""><td>(41.9, 41, 2.8)</td><td>(40.9, 40, 2.8)</td><td>p<0.001</td></ewl>	(41.9, 41, 2.8)	(40.9, 40, 2.8)	p<0.001		
EWL %>100 (n: 58)	(40.2, 40, 2.4)	(39.3, 39, 2.6)	p<0.001		
BMI: body mass index; EWL: exces	ss weight loss; SD: standard deviation				

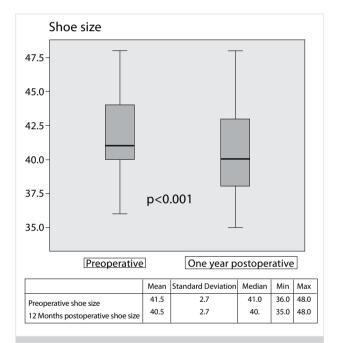


Figure 1. Preoperative and 12-month postoperative shoe sizes

lished by a direct verbal report obtained from each patient. Half-size or similar arbitrary reductions that did not result in at least one shoe size change were not taken into consideration (i.e., any patient declaring a half-size reduction was recorded as "no change," a size reduction of 1.5 was recorded as a size change of 1, and a size reduction of 2.5 was recorded as a size change of 2). The EWL % was calculated by accepting the ideal body weight as equivalent to a BMI of 25 Kg/m².

The effect of age on the probability of shoe size change was calculated by comparing the shoe size decreases in patients older and younger than 40 years of age. The effect of preoperative BMI on shoe size change was evaluated by comparing the decreases in three consecutive preoperative BMI groups, which were defined as <40, 40 to 50, and >50 Kg/m². The probable association between shoe size change and EWL % was

assessed by comparing the reduction figures in three consecutive groups of EWL %, defined as <75, 75 to 100, and >100.

This study was conducted in accordance with the ethical standards set out in the Helsinki Declaration.

Statistical Analysis

All statistical analysis was performed using the Statistical Package for the Social Sciences software for MacOS X 21 (SPSS Inc.; Chicago, IL, USA). The normal distribution of numeric values was checked with the Kolmogorov-Smirnov test. Numeric variables, such as the difference in shoe size one year after SG, were evaluated by the Wilcoxon test. Decreases in the consecutive BMI and EWL % groups were evaluated by the Kruskal-Wallis test. Shoe size change categories in the consecutive BMI groups and the effects of age and sex on shoe size decrease were evaluated by x2 tests. p values (type one error) smaller than 0.05 were accepted as significant.

RESULTS

Between January 2012 and February 2016, among 382 patients who underwent SGs at our institution, 212 completed their 12th month follow-up; these patients are the subject of the present study. No mortality, conversion, leaks, or major complications were observed in these 212 patients. The mean preoperative BMI and age were 45 (min: 33, max: 70) and 37 (min: 14, max: 63), respectively. Of the patients, 60% were female and 40% were male (n: 127/85). The mean preoperative shoe size was 41.5 (Figure 1). The mean EWL % 12 months after surgery was 87% (min: 30, max: 172, ±24). The mean shoe size one year after surgery was 40.5, and this decrease from 41.5 was found to be highly significant (p<0.001, Figure 1, Table 1). The distributions of shoe size change in both sexes are shown in Figure 2. The decreases in shoe size at 12 months following SG were similar in both women and men (p=0.356). Patients older than 40 years of age (n: 84) had almost the same decrease in shoe size as patients younger than 40 years (p=0.99). Only preoperative BMI was found to be associated with decrease in shoe size. This asso-

Kg/m²	SHOE	SIZ	Œ	
	No change	Minimum one size change	Minimum two size changes	Total
BMI<40	n: 16 (29.1%)	n: 33 (60.0%)	n: 6 (10.9%)	55
40 <bmi<50< td=""><td>n: 24 (22.8%)</td><td>n: 64 (61.0%)</td><td>n:17 (16.2%)</td><td>105</td></bmi<50<>	n: 24 (22.8%)	n: 64 (61.0%)	n:17 (16.2%)	105
BMI>50	n: 8 (15.4%)	n: 26 (50.0%)	n: 18 (34.6%)	52
All BMIs	n: 48 (22.6%)	n: 123 (57.5%)	n: 41 (19.9%)	212

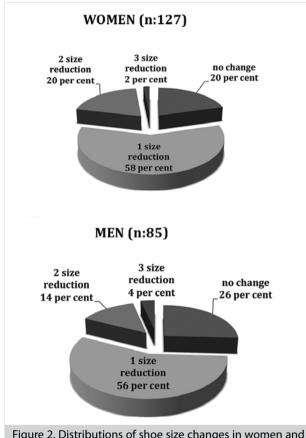


Figure 2. Distributions of shoe size changes in women and men 304

ciation was statistically significant for super obesity. Patients with BMI>50 had a significantly high shoe size decrease compared to patients with BMI<40 (p=0.008). The shoe size change categories according to the BMI groups are summarized in Table 2. In contrast to patients with BMI>50, who had a 34.6% rate of at least 2 size changes, patients with BMI<40 had a rate of 10.9% (p=0.009). EWL % at one year, regardless of increase or decrease, was not associated with decrease in shoe size (p=0.46).

DISCUSSION

Currently, obesity is a pandemic; morbid obesity, which is also endemic, is the second most common preventable cause of death, only following smoking (13, 14). It is also known that in both men and women, there has been a constant increase in

average shoe size, especially during the last five decades; according to the College of Podiatry of the United Kingdom, this phenomenon is thought to be related to the ongoing increase in the obesity pandemic (15).

If becoming obese has an association with an increase in shoe size, hypothetically, the reverse could also be true; also, it is reasonable to assume that weight loss surgery may result in a smaller shoe size. We, as bariatric surgeons, actually observed a relevant trend, which is why we undertook the present study. Our results actually confirm this hypothesis and provide scientific documentation that weight loss surgery achieves a significant decrease in shoe size. Furthermore, this is especially true in super obese patients, further suggesting a direct relationship between obesity and shoe size. One year after SG, 80% of women and 75% of men experienced at least one size decrease compared to their preoperative shoe sizes, which was found to be highly significant (p<0.001, Table 1, Figure 1, 2). It is also noteworthy that almost one fifth of the patients had a decrease of at least two sizes. The extents of decrease in shoe size were similar in both sexes; this is also true for patients older than 40 years of age compared to younger patients. Interestingly, the extent of EWL % one year after SG also had no effect on the decreasing trend; however, this is not surprising. It is known that the EWL % is higher in patients with lower BMI, as these patients have less weight to lose (11). It is also shown in the present study that in this group of patients (BMI <40), the decrease in shoe size is significantly less than in patients with BMI >50.

According to our results, postoperative shoe size decrease is mainly dependent on the patient's weight before surgery rather than how much of the patient's excess weight was lost. We are aware of the limitations of verbal reports of shoe size change compared to direct foot size measurements; however, this would be especially true if we wished to show that the patients' feet decreased in size in accordance with the decrease in shoe size. As our main aim was simply to assess the probability of changes in shoe size, more detailed and complicated measurements of three-dimensional foot size are irrelevant to the present study. Furthermore, as no half-size or arbitrary decreases were taken into account, our reduction rates actually reflected a minimum rate, which is still highly significant when compared to preoperative shoe size.

The mechanics, physics, and chemistry behind the decrease in foot or shoe size are beyond the scope of this article. Decrease

in foot adipose tissue, decreased lymphedema, increased venous drainage, and correction of the arch height may all have effects; however, the fact remains that almost 80% of people who undergo SG will buy shoes at least one size smaller one year after SG. Super obesity is associated with significantly higher rates of shoe size decrease compared to lower BMIs, and almost 35% of patients with a BMI>50 will experience at least two size decreases.

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

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

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Laparoscopic surgery in distal pancreatic tumors

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ABSTRACT

Objective: Laparoscopic distal pancreatectomy is increasingly being used in the surgical treatment of corpus and distal pancreatic tumors. In this study, patients who underwent laparoscopic or open distal pancreatectomy for benign or malignant causes were evaluated in terms of tumor characteristics and perioperative outcomes.

Material and Methods: We retrospectively reviewed data from a total of 27 distal pancreatectomy cases performed for benign or malignant causes in the General Surgery Department between January 2013 and December 2015. Groups were compared according to the demographic characteristics of patients, operation type (laparoscopic or open, with splenectomy or spleen preservation), operation time, surgical site infection (superficial, deep wound infection, or intra-abdominal abscess), pancreatic fistula development, and histopathological examination results.

Results: Both groups were similar in terms of age, sex, and body mass index (p=0.42). Tumor diameter was similar (p=0.18). The total number of resected lymph nodes was similar in both groups (p=0.6). Pancreatic fistula developed in one patient in each group. Mean hospital stay duration and the amount of intraoperative bleeding were similar in both groups. The laparoscopy group had a markedly lower overall morbidity rate (p=0.08). There was no mortality observed in the study subjects.

Conclusion: Laparoscopic distal pancreatectomy can be safely performed as a minimally invasive procedure in experienced centers and in selected cases without increasing perioperative complication rates, particularly in benign cases. Although oncological outcomes are acceptable for malignant cases, future prospective controlled studies are necessary for more reliable evaluation.

Keywords: Laparoscopy, pancreas, oncology

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INTRODUCTION

Today, minimally invasive surgery is being performed safely and effectively to treat a range of conditions. Advantages of minimally invasive techniques include short hospital stays, early return to work, and reduced scar formation (1, 2). In comparison to other fields of surgery, minimally invasive surgical interventions are lacking in the field of pancreatic surgery. This lack of innovation may be due to the anatomical location of pancreas, difficulties in surgical technique, and concerns about poor oncological outcomes.

The first laparoscopic distal pancreatic surgery was performed by Gagner and Pomp (3) in 1996. Since that time, additional laparoscopic approaches for pancreatic pathologies have emerged. Several studies have emphasized the advantages of laparoscopic approaches over open surgery, particularly with regard to short-term outcomes (4, 5). Laparoscopic distal pancreatectomy is increasingly used in the surgical treatment of corpus and distal pancreatic tumors. Due to concerns of worsening oncological outcomes, laparoscopic pancreatectomy is generally performed in benign disease (6). Nonetheless, this procedure is performed in select malignant cases in conjunction with splenectomy (7, 8).

In this study, patients who underwent laparoscopic or open distal pancreatectomy for benign or malignant causes were evaluated in terms of tumor characteristics and perioperative outcomes.

MATERIAL AND METHODS

In this study, we retrospectively reviewed data from a total of 27 distal pancreatectomy cases performed for benign or malignant causes in the General Surgery Department between January 2013 and December 2015 by scanning the archived data forms. Patients were divided into two groups based on whether the operation technique was laparoscopic or open surgery (Group 1: open surgery and Group 2: laparoscopic surgery). Cases where the operation was initiated as laparoscopic surgery but required conver-

sion to open surgery were evaluated separately. Groups were compared according to the demographic characteristics of patients, operation type (laparoscopic or open, with splenectomy or spleen preservation), operation time, surgical site infection (superficial, deep wound infection, or intra-abdominal abscess), pancreatic fistula development, and histopathological examination results. The rate of conversion to open surgery was determined. Pancreatic fistulae were evaluated according to the International Study Group of Pancreatic Fistula classification established by Bassi et al (9). This study was conducted in accordance with the ethical standards set out in the Helsinki Declaration. Informed consent was taken from all patients.

Statistical Analysis

Data were analyzed in collaboration with a biostatistician, using a Student's t-test for parametric data, Mann-Whitney U test for non-parametric data, and the Fischer's exact chi-square test for cross tables. p<0.05 and a 95% confidence interval was considered statistically significant.

RESULTS

Table 1 summarizes the demographic features, perioperative findings, and histopathological results of the patients who underwent open or laparoscopic surgery. Open surgery was performed in 14 patients, whereas laparoscopic distal pancreatectomy was performed on 10 patients. Both groups were similar in terms of age, sex, and body mass index (BMI) (p=0.42). Tumor diameter was similar (p=0.18) in both groups; mean tumor diameter was 5.6 cm in the open surgery group and 3.9 cm in the laparoscopy group. The total number of resected lymph nodes was similar in both groups (p=0.6). The average number of resected lymph nodes was 12.46 in the open surgery group and 10.38 in the laparoscopy group. Proximal and surrounding surgical border positivity occurred at similar rates in both groups. Spleen-preserving pancreatectomy was performed in two patients in the open surgery group and three patients in the laparoscopy group; there was no significant difference between the groups with regard to the rate of spleen preservation. Two patients in the open surgery group developed surgical site infection, while no patient in the laparoscopy group experienced surgical site infection. Two patients developed intra-abdominal abscess in the open surgery group, while no patient in the laparoscopy group developed abscess. Pancreatic fistula developed in one patient in each group. The fistula observed in the open surgery group was classified as Grade B, while the fistula observed in the laparoscopy group was classified as Grade A. Mean hospital stay duration and the amount of intra-operative bleeding were similar in both groups. The laparoscopy group had a markedly lower overall morbidity rate (p=0.08). There was no mortality observed in the study subjects.

In three patients, the operation was initiated as a laparoscopic surgery but later converted to open surgery. Table 2 shows the demographic features, perioperative findings, and histopathological properties of these cases. Causes of conversion to open surgery were as follows: dissection was difficult due to a previous pancreatitis episode in one patient; one patient had adhesions and splenic vessel invasion related to malignancy; and another patient had a tumor localized to the body of pancreas, which was in close proximity to the portal confluence and therefore presented difficulty in dissection of the area.

Table 1. Demographic features, perioperative findings, and histopathological results in patients operated with open or laparoscopic surgical approach

	Group 1 Gr (open) (lapa		р
n (=number of patients)	14	10	
Age	57.7 (17-74)	50.7 (19-86)	0.32
Sex			
-female	13	7	0.27
-male	1	3	
BMI (kg/m²)	26.2	27	0.61
Tumor location			
-body	7	3	0.42
-tail	7	7	
Histopathology			
-benign	8	8	0.39
-malignant	6	2	
Tumor diameter (cm)	5.6	3.9	0.18
Total lymph nodes	12.46 (2-33)	10.38 (4-23)	0.6
Surgical border positivity			
-proximal	0	1	0.41
-surrounding	2	0	0.49
Splenectomy			
-present	12	7	0.62
-absent	2	3	
Surgical site infection			
-present	2	0	0.49
-absent	12	10	
Intra-abdominal abscess			
-present	2	0	0.49
-absent	12	10	
Pancreatic fistula			
-present	1	1	1
-absent	13	9	
Operation time (minute)	227.5	221.5	0.83
Intraoperative bleeding (mL)	125	128	0.95
Morbidity (patient)	7 (50%)	1 (10%)	0.08
Hospital stay length (days)	7.1	5.6	0.11
BMI: body mass index			

DISCUSSION

Minimally invasive surgery is preferred in many circumstances due to reduced hospitalization time, accelerated functional recovery, reduced scar formation, and rates of perioperative complication comparable to or better than standard surgical procedures (1, 2). In the field of pancreatic surgery, minimally invasive surgery was first performed by Gagner and Pomp (3) in 1996. For all the popularity of

Table 2. Demographic features, perioperative findings, and histopathological findings in patients who required conversion to open surgery from laparoscopic surgery

	Patients who required conversion to open surgery
n (=number of patients)	3
Sex	
-female	2
-male	1
BMI (kg/m²)	26.1 (20-29.3)
Tumor location	
-body	2
-tail	1
Histopathology	
-benign	1
-malignant	2
Tumor diameter (cm)	4.3 (1.5-6)
Total number of lymph nodes	10 (4-16)
Surgical border positivity	
-proximal	0
-surrounding	0
Splenectomy	
-present	2
-absent	1
Wound site infection	
-present	0
-absent	3
Intra-abdominal abscess	
-present	0
-absent	3
Pancreatic fistula	
-present	1
-absent	2
Operation time (minute)	230 (210-240)
Intraoperative bleeding (mL)	266.6 (100-500)
Morbidity (patient)	1 (33%)
Hospital stay length (days)	6.3 (4-8)
BMI: body mass index	

laparoscopic techniques in other fields of surgery, there has been less progress in laparoscopic pancreatic surgery. The reasons for this include the challenging anatomical structure of the pancreas and ethical concerns specific to surgical oncology (2).

Laparoscopic distal pancreatectomy has gained popularity within the recent years as a minimally invasive procedure. It is performed for tumors of the body and tail of the pancreas, and is generally preferred for benign cases (7). Nevertheless,

it can also be performed in select malignant cases in conjunction with splenectomy (10).

Study results supporting the use of laparoscopic pancreatic surgery are often based on retrospective data, and it is difficult to conduct comparative prospective studies on this subject. Nevertheless, Riccive et al. (5) compared 41 cases of laparoscopic distal pancreatectomy conducted to treat benign diseases with 40 cases treated by open surgery and evaluated both quality of life outcomes and cost efficacy. They reported no difference between these two groups with regard to postoperative complication rates, pancreatic fistula development, or bleeding. Length of hospital stay was significantly shorter in non-complicated cases. One of the primary advantages of laparoscopic surgery is shorter hospital stay; however, the study conducted by Ricci et al. (5) did not observe a reduction in the length of hospitalization among patients who underwent laparoscopic procedures, possibly because of the high rate of morbidity associated with all types of pancreatic surgeries. Another advantage of laparoscopic surgery is earlier initiation of oral intake, and Riccive et al. (5) observed that patients who underwent laparoscopic procedures were able to tolerate oral intake at earlier time points. Quality of life metrics were also notably improved among the patients who underwent laparoscopic procedures relative to those who underwent open surgery. Laparoscopic surgery was also found to be more cost effective. In the present study, we found that the length of hospitalization remarkably was shorter in the laparoscopic surgery group, although this difference did not meet the criteria for statistical significance (p=0.11). This is consistent with previous studies. In a review conducted by Postlewait et al. (11), evaluating distal pancreatectomy operations performed on malignant cases, laparoscopic distal pancreatectomy was associated with oncologic results comparable to open surgery. Shakyan et al. (12) evaluated outcomes in 196 patients in their cohort study and Adam et al. (4) evaluated short-term outcomes in 1733 cases of distal pancreatectomy. Both studies concluded that laparoscopic distal pancreatectomy can be safely performed with regard to oncological principles. According to these two studies, although bleeding and wound site complications are less common with laparoscopic surgery, there was no significant difference in the overall rate of complications between the two types of surgeries. Nevertheless, long-term prospective studies on this topic are lacking. In the present study, none of the malignant cases exhibited surgical border positivity in pathological results, and the number of resected lymph nodes was similar between the two study groups. As a result, we conclude that laparoscopic distal pancreatectomy may be expected to produce oncological results comparable to open pancreatic surgery. Nonetheless, evaluation of oncological outcomes from a larger number of cases would provide additional evidence for these conclusions. The major advantages of laparoscopy include reduced hospital stay, lower rates of surgical site infection, reduced scar formation, and adaptability to a wide variety of conditions (13, 14).

Consistent with reports in the literature, our data demonstrates that perioperative findings and complications are comparable between laparoscopic procedures and open surgery (p>0.05).

Postoperative fistula development is the most significant complication of pancreatic surgery. In one multi-center cohort study published in 2015, Sahakyan et al. (12) retrospectively evaluated data from 196 cases and reported postoperative morbidity rates of 32%-40% and postoperative pancreatic fistula rates of 11%-27.9%. Majority of these cases were benign; among malignant cases, the rates of morbidity and postoperative fistula development were substantially greater (31.9% and 25.1%, respectively). In the present study, pancreatic fistula occurred in 7.1% of patients in the open surgery group and 8.3% of patients in laparoscopic surgery group; there was no significant difference between the groups (p=1.00). The laparoscopy group contained fewer malignant cases, which may have contributed to the lower rate of pancreatic fistula development among those patients. Taken together, our results are consistent with the literature in supporting the conclusion that the laparoscopic techniques do not increase the risk of pancreatic fistula development.

In a study evaluating 1733 patients, Adam et al. (4) reported a rate of conversion from laparoscopy to open surgery of 23%. Various studies report this rate at 8%-28% (15). Majority of these cases are malignant disease or other conditions in which dissection is particularly challenging. In our study, three patients (23%) required conversion to open surgery. The causes for conversion to open surgery in our patients were as follows: difficult dissection due to previous pancreatitis episode; adhesions and splenic vessel invasion related to malignancy; and tumor localization to the body of the pancreas, which was in close proximity to portal confluence.

The primary limitations of our study are the retrospective approach, the relatively low number of patients, and the absence of qualitative measurements of quality of life. Large-scale prospective studies are required to evaluate the potential for laparoscopic surgery approaches in malignant cases. An important aim for these studies should be to determine oncological outcomes in malignant cases with long-term follow-up and to demonstrate that laparoscopic surgery is not associated with additional risk for cases of malignancy.

CONCLUSION

Laparoscopic distal pancreatectomy can be safely performed as a minimally invasive procedure at experienced centers and in selected cases without increasing perioperative complication rates, particularly in benign cases. Although oncological outcomes are acceptable for malignant cases, future prospective controlled studies are necessary for more reliable evaluation.

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

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

Peer-review: Externally peer-reviewed.

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

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Central hepatectomy: A valuable option to avoid posthepatectomy liver insufficiency in patients requiring extensive liver resection

Mehmet Fatih Can, Murat Urkan, Emin Lapsekili, Rahman Senocak, Ümit Alakus

Despite being uncommon, posthepatectomy liver failure (PLF) is a dreadful complication following extended hepatectomy or liver trisectionectomy. It has been reported that liver insufficiency may occur in as high as 12% of posthepatectomy patients, especially in those who have a concomitant chronic liver disease, hepatosteatosis or history of receiving long-course (>6 cycles) chemotherapy (1). Central hepatectomy or mesohepatectomy, defined as en-bloc anatomical resection of liver segments 4-5 and 8, is a valuable option in patients with central large or multiple liver lesions to minimize PLF caused by the loss of a considerable portion of functional liver parenchyma following extensive resections (2). The purpose of this video-based article is to share key procedural components to be adhered to when performing central hepatectomy.

In order to render a final video reflecting our technique of central hepatectomy, we reviewed raw operation videos recorded in our surgical video collection. Every important step of the procedure was assessed visually to determine if it had been performed the same way in each case. The step was considered an integral part of our approach and reproducible if it had taken place in the majority of operations. The final video is composed of video clips demonstrating those standardized certain steps. Informed consent was obtained from all patients.

All extended anatomical hepatic resections in our department are performed through a shortened modified Makuuchi incision. The right and left triangular ligaments are divided. The right and left hepatic veins are partly exposed, but not encircled with umbilical tape. Following preparation for the Pringle maneuver, parenchymal transection starts without preceding hilar dissection. The Pringle maneuver is applied intermittently (15 min occlusion and 5 min release) during transection. Parenchyme splitting is initiated just right to the falciform ligament between the left lateral (liver segments 2-3) and left medial (liver segment 4) sections, during which inflow structures of liver segment 4 arising off of the hilar plate are ligated and divided (Video). The transection on this plane is continued down to the vena cava - middle hepatic vein junction. The middle hepatic vein is secured by passing a tape around it (Video). Thereafter the attention is turned to the hilar and cystic plates again. The cystic duct is ligated and transected, and the Callot triangle is exposed. This allows for the surgeon to utilize intraparenchymal Glissonian approach when exposing the right anterior sector plate structures. The whole plate of the right anterior section is exposed en-bloc and divided by using a linear stapler (Video). This step is followed by parenchymal transection between the right anterior and posterior sections. During this transection, the split line is on the left-side of the right hepatic vein and proceeds cephalad. The resection is completed after ligation and division of the middle hepatic vein (Figure 1). It is our practice to utilize the White test to check for bile leaks at the end of the procedure. In our series, postoperative bile leak occurred in 20 percent of patients, of whom one required endoscopic stent placement. No other significant morbidities, including PLF, were detected postoperatively. The median length of hospital stay was 7 (5-13) days.

In summary, central hepatectomy or mesohepatectomy, which relies on preservation of at least one more liver segment as compared to anatomical trisectionectomy, is a good alternative for curative treatment of patients who have large or multiple liver masses with median bi-sectoral involvement. With the last ten consecutive patients having been operated on using this technique, our approach seems safe, feasible and reproducible, resulting in low morbidity rates without occurrence of posthepatectomy liver failure.

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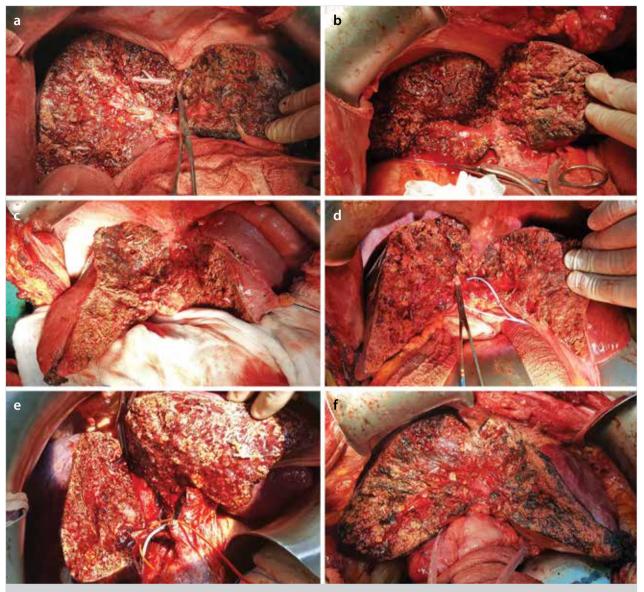


Figure 1. a-f. Views of surgical field (a-f) obtained immediately after the resection has been completed by means of the technique described herein

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - M.F.C.; Design - M.U.; Supervision - M.F.C., R.Ş.; Resource - E.L., Ü.A.; Materials - M.U.; Data Collection and/or Processing - Ü.A.; Analysis and/or Interpretation - R.Ş., M.F.C.; Literature Search - M.F.C.; Writing Manuscript - M.U., R.Ş.; Critical Reviews - Ü.A., E.L.

Conflict of Interest: No conflict of interest was declared by the authors.

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Video: Central hepatectomy - surgical technique

- Skrzypczyk C, Truant S, Duhamel A, Langlois C, Boleslawski E, Koriche D, et al. Relevance of the ISGLS definition of posthepatectomy liver failure in early prediction of poor outcome after liver resection: study on 680 hepatectomies. Ann Surg 2014; 260: 865-870. [CrossRef]
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Splenic hamartoma is a rare cause of abdominal pain: Case report and literature review

Tevfik Eker¹, Akın Fırat Kocaay¹, Yusuf Sevim², Atıl Çakmak¹

ABSTRACT

Hamartoma is a rare benign tumor of the spleen. It is often asymptomatic and diagnosed incidentally. In this study, we report the case of a 51-year-old female patient who was admitted to our department for intermittent epigastric pain since the last 6 months and left upper quadrant fullness. She was diagnosed with splenic hamartoma histopathologically after splenectomy. Although splenic hamartoma is very rare, it must be included in the differential diagnosis of splenic mass-forming lesions.

Keywords: Splenic mass, hamartoma, splenectomy

INTRODUCTION

Splenic hamartoma (SH), which was first described in 1861 by Rokitansky, is a rare benign lesion of the spleen (1). Splenic hamartoma occurs equally in men and women (2). It is often asymptomatic and diagnosed incidentally (2, 3). Splenic hamartoma is generally a single lesion, with rare occurrence of multiple lesions. The size of SH ranges from a few millimeters to centimeters, with a median size of 5 cm. A 20 cm SH was reported in the literature (4). A minority of patients with large hamartomas have symptoms such as non-specific abdominal pain, thrombocytopenia, splenomegaly, fever, and night sweats (3, 4). In this study, we report the case of a 51-year-old female patient diagnosed with SH histopathologically.

CASE PRESENTATION

A 51-year-old female patient was admitted to our department for intermittent epigastric pain of 6 months' duration and left upper quadrant fullness. Physical examination was unremarkable, and blood tests revealed mild thrombocytopenia (140×10^9 /L). Abdominal ultrasonography (US) showed a 1-cm mass in liver segment 7 and a splenic mass 5×6 cm in size. Further investigation with abdominal and dynamic liver computed tomography (CT) scans were performed. Computed tomography analysis suspected a hemangioma for the liver mass and revealed intraparenchymal hypodense splenic lesion (7 cm in size) with late phase enhancement after the administration of contrast material (Figure 1).

Splenectomy was performed for diagnosis and treatment. The patient was discharged from the hospital on the postoperative 8^{th} day without any complications. Pathological examination revealed round, well-circumscribed, $8.5 \times 6 \times 6$ cm in size, and unencapsulated bulging hamartoma containing fibrotic areas inside the tumor.

DISCUSSION

Splenic hamartomas are rare benign lesions originating from the red or white pulp of the spleen. More than 80% of the cases are asymptomatic, and SHs are normally an incidental finding during imaging, surgery, or autopsy (1, 2). They can occur in any age group and equally in men and women (2). It tends to be larger in women probably because of female sex hormones (5). Approximately 20% of the patients are presented with non-specific symptoms. The main complaints of these patients are abdominal pain and digestion problems. In physical examination, spleen can be palpated below the costal margin or splenic mass can be palpated (5, 6). Splenic rupture caused by hamartomas has been reported only in a few patients in the literature (7).

Recently, Wang et al. (6) reviewed the features of the SH in US, colored Doppler US, CT, and magnetic resonance imaging (MRI) for radiological diagnosis. According to this study, SHs were generally detected as a hypoechoic solid mass in US, and they showed an inc-reased blood flow due to hypervascularity in Doppler US. On CT, SHs appeared as isodense or hypodense solid masses, and cystic and calcified areas in splenic lesions were found to be characteristic for the SHs. On MRI, it was isointense on T1-weighted images and was heterogeneously hyperintense on T2-weighted images (6).

The use of the fine-needle aspiration biopsy (FNAB) and cytological examination in splenic lesions are disputable. Although performing FNAB with US is helpful for diagnosis, FNAB by itself is not sufficient for definitive diagnosis (2, 8).

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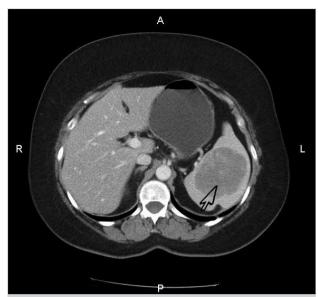


Figure 1. Contrast-enhanced computed tomography scan showing a solid mass (7 cm in diameter) in the center of the spleen

The open and laparoscopic procedures can be applied with lower mortality for diagnosis and treatment of SHs (9). Total or partial splenectomy can be performed safely for these patients. Although the use of partial splenectomy is not preferred in surgical practice today, it is significant for preserving the immunological functions of the spleen (10). The laparoscopic methods are preferred for partial splenectomy and smaller lesions, whereas total splenectomy or open surgical procedures are preferred for larger and multiple lesions (9).

In postoperative histopathological examinations, well-circumscribed single mass or multiple lesions are observed. Larger masses may cause pressure on normal splenic parenchyma. They may be divided into the red pulp type (disorganized splenic sinus), white pulp type (lymphoid tissue), mixed type (red and white pulp), and fibrous type (10). The structures of both pulps are found to be mixed in most SHs. The characteristic histological aspect is randomly located endothelial cells and vascular channels. Immunohistochemically, the lining cells of the vascular channels of the hamartoma are positive for the endothelial markers CD8, CD31, CD34, von Willebrand factor antigen, and vimentin (1).

Splenic hamartoma must be distinguished from splenic malignant lesions such as lymphangioma, hemangioblastoma, and

angiosarcoma. In addition, in radiological differential diagnosis, inflammatory myofibroblast tumors; lymphoma; the rare splenic metastasis of malignant melanoma; and breast, lung and colorectal cancers should be considered (5, 6).

CONCLUSION

Splenic hamartoma is a benign vascular proliferative lesion. Because this tumor is very rare, it must be included in the differential diagnosis of splenic mass-forming lesions.

Informed Consent: Data was evaluated retrospectively after the required current treatment was completed, so the informed consent was not received.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - T.E.; Design - T.E.; Supervision - A.Ç.; Materials - A.Ç.; Data Collection and/or Processing - A.F.K.; Analysis and/or Interpretation - Y.S.; Literature Review - T.E.; Writer - T.E.; Critical Review - Y.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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Giant multicystic malignant pheochromocytoma

Erdal Uysal¹, Türkay Kırdak², Ahmet Orhan Gürer¹, Mehmet Ali İkidağ³

ABSTRACT

Pheochromocytoma is a rare tumor originating from the embryonic neural crest and secreting high levels of catecholamines. The average tumor size is approximately 7 cm, and the average weight is approximately 200 g in the previous publications. Sometimes these tumors may be bigger. In this report, a case of multicystic malignant pheochromocytoma with a huge size is presented, which is seldom reported in the past. A 37-year-old male patient was referred to our hospital for etiological investigation of his recently diagnosed hypertension. Contrast-enhanced computed tomography (CT) examination was performed for further evaluation of the lesion and surrounding tissues. The lesion was 18×8×13 cm in size. It had lobulated margins, large cystic components, and peripheral and septal contrast enhancement. The levels of metanephrine, normetanephrine, adrenaline, noradrenaline, vanilmandelic acid, and dopamine were significantly elevated. The patient was prepared for surgery. In the pathological evaluation, the mass weighed 1018 g and was 18×8×13 cm in size. He was diagnosed with malignant pheochromocytoma. After eight months, a CT examination showed a recurrent mass, liver metastasis, and distant metastasis. The patient received chemotherapy and radiotherapy. Multicystic malignant pheochromocytoma may reach huge sizes without causing any symptoms.

Keywords: Giant, malignant, pheochromocytoma

INTRODUCTION

Pheochromocytoma is a rare tumor originating from the embryonic neural crest and secreting high levels of catecholamines (1). Though it may remain silent, it usually causes clinical symptoms such as headache, palpitation, and hypertension due to these secretions. Asymptomatic cases may have a late diagnosis. The average tumor size is approximately 7 cm, and the average weight is approximately 200 g in the previous publications (2). Sometimes these tumors may be bigger (1, 3-8). In this report, a case of multicystic malignant pheochromocytoma with a huge size is presented, which is seldom reported in the past.

CASE PRESENTATION

A 37-year-old male patient was referred to our hospital for etiological investigation of his recently diagnosed hypertension. In his physical examination, a bulky mass was palpated in the left upper quadrant. Blood electrolyte and glucose levels, haemogram, and other biochemical parameters were unremarkable. Ultrasound examination showed a huge multicystic mass lesion in the left adrenal gland, next to the left kidney. Contrast-enhanced computed tomography (CT) was performed for further evaluation of the lesion and surrounding tissues. The lesion was 18 cm×8 cm×13 cm in size. It had lobulated margins, large cystic components and peripheral and septal contrast enhancement. The tail of the pancreas and spleen was anteriorly displaced, and the left kidney was inferiorly displaced. The left adrenal gland was not visible apart from this lesion. Minimally abdominal free fluid was noted; the right adrenal gland was normal, and there was no finding of distant metastasis. There was no evidence of invasion and lymphadenopathy (Figure 1).

Twenty-four hour urine catecholamine levels were studied. The levels of metanephrine, normetanephrine, adrenaline, noradrenaline, vanilmandelic acid, and dopamine were significantly elevated. The 24 h urine levels of metanephrine, normetanephrine, vanilmandelic acid, homovanillate, epinephrine, norepinephrine, and dopamine were 2195 mg/24 h (0–320 mg/24 h), 3707 mg/24 h (0–390 mg/24 h), 33 mg/24 h (1.7–6.5 mg/24 h), 23 mg/24 h (2–7.4 mg/24 h), 65 mg/24 h (1–27 mg/24 h), 154 mg/24 h (1–97 mg/24 h), and 1719 mg/24 h (1–500 mg/24 h), respectively. Blood cortisol level was normal. Blood parathyroid hormone and calcitonin levels were normal. Family history was negative with regards to multiple endocrine neoplasia (MEN) syndrome. The diagnosis of a possibly malignant pheochromocytoma was made. The patient was prepared for surgery; median incision was performed for exploration. The lesion had a close relation to the left lobe of the liver, left kidney, and tail of the pancreas, but there was no invasion. The mass was totally resected. Perioperative or postoperative complication did not develop. The patient was discharged from the hospital

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Figure 1. Large pheochromocytoma on computed tomography (coronal section)

on the seventh postoperative day. In the pathological evaluation, the mass weighted 1018 g and was $18 \times 8 \times 13$ cm in size. It showed a high mitotic index and capsular and vascular invasion, and the abdominal fluid sample showed atypical cells leading to the diagnosis of malignant pheochromocytoma. Postoperative 131-l-metaiodobenzylguanidine (MIBG) was administered for treatment. After eight months, a CT examination showed a recurrent mass, which was 12 cm, in the left adrenal gland. There were two liver metastases; one was 9 cm and the other was 1.5 cm in size. Additionally, he had multiple para-aortic, perirenal, and perisplenic enlarged lymph nodes and a small metastatic nodule in the right adrenal gland. There were distant metastases in both lungs and multiple bones, including the lumbosacral vertebrae and right iliac bone on CT. The patient received chemotherapy and radiotherapy. Our patient died eleven months after surgery.

DISCUSSION

Most pheochromocytomas are benign and approximately 10% have malignant behavior (1). With increasing size, the probability of malignancy becomes higher; in lesions over 6 cm, the ratio of benign-to-malignant tumors is 1:8 (9). The average tumor size is approximately 7 cm (2). There are only few reports of huge multicystic malignant pheochromocytoma above 18 cm, and to our knowledge, the pheochromocytoma in this case is the largest one reported from our country (1, 3-8). Seven giant pheochromocytomas larger than 16 cm in current literature have been documented (Table 1). Classical symptoms of pheochromocytoma include headache, palpitation, and hypertension. Some cases may not show any symptoms. The sole reason for the admission of our patient was hypertension. In our case, the lack of prominent symptoms may have resulted in the tumor reaching huge sizes and the late diagnosis.

Histopathologically, it is not always possible to distinguish benign lesions from malignant ones that do not have an ac-

Table 1. Pheochromocytomas reported to be larger than 16 cm						
Author/ year	Sex/ age	Country	Size (cm)	Lap/ open	Recur- rence	Survival
Grissom et al. (4)	F/54	USA	45×25	Open	Unknown	Unknown
Costa et al. (5)	M/46	Brazil	30	Open	No	Died
Suga et al. (3)	M/48	Japan	21×13	Open	No	Yes
Melegh et al. (6)	M/55	Hungary	20	Open	Unknown	Unknown
Ambati et al. (1)	F/77	Canada	19×12×18	Open	No	Yes
Pan et al. (7)	M/46	USA	18×14×13	Open	No	Yes
Current case	M/37	Turkey	18×13	Open	Yes	Died
Costa et al. (5)	F/43	Brazil	18	Open	Yes	Yes
Daughtry et al. (8)	/ M/53	USA	17	Open	Unknown	Unknown
F: female; M: male; Lap: laparoscopic						

companying metastatic lesion or invasion. The presence of capsular and vascular invasion, distant metastasis, high mitotic index and proliferative activity, intra-abdominal malignantfree fluid, and postopererative local recurrence are features of malignancy. Immunohistochemical analysis may be necessary to support the diagnosis. The role of the laparoscopic approach for large tumors is still controversial. In a study, lesion sizes of 12 cm to 14 cm have been cited as the upper limit for laparoscopic adrenalectomy (10). In our case, considering the large size of the tumor and possible malignancy with local invasion, we preferred traditional open surgery. There are not enough studies on the prognosis and survival of malignant pheochromocytoma because of its lower incidence. Malignant pheochromocytoma usually has a poor prognosis and resistance to chemotherapy and radiotherapy. The administration of 131-I-MIBG and long-acting octreotide in patients who are somatostatin receptor positive can be used in the treatment of malignant pheochromocytoma. In patients with metastatic pheochromocytoma, long-term survival is possible; the overall five-year survival; however, is less than 50%.

When the cases in Table 1 were evaluated, the largest pheochromocytoma in the world was reported to be 45 cm. All patients were operated with the open method. Two cases were benign and six were malignant. One case was uncertain. Mortality and recurrence developed in two malignant cases.

CONCLUSION

Multicystic malignant pheochromocytoma may reach huge sizes without causing any symptoms.

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - E.U., T.K., A.O.G., M.A.İ.; Design - E.U., T.K., A.O.G., M.A.İ.; Supervision - E.U., T.K., A.O.G., M.A.İ.; Funding - E.U., T.K.; Materials - E.U., T.K., M.A.İ.; Data Collection and/or Processing - E.U., T.K., M.A.İ.; Analysis and/or Interpretation - E.U., T.K., A.O.G., M.A.İ.; Literature Review - E.U., T.K., A.O.G.; Writer - E.U., T.K., M.A.İ.; Critical Review - E.U., T.K., A.O.G.

Conflict of Interest: No conflict of interest was declared by the authors.

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A rare soft tissue tumor located in the trunk: Ossifying fibromyxoid tumor

Yelda Dere¹, Serkan Yaşar Çelik¹, Özgür İlhan Çelik¹, Özcan Dere²

ABSTRACT

Ossifying fibromyxoid tumor (OFMT), a rare soft tissue tumor, is generally located in the extremities with a distinct morphology characterized by bland, small cells lying in a fibromyxoid stroma and a peripheral rim of the lamellar bone. These tumors mostly express Leu-7, neuron specific enolase in addition to S-100 and vimentin. Some tumors may have malignant cytological features with aggressive behavior but even in classical morphology, recurrence or metastasis can be detected. Thus, the outcome of the tumor remains a mystery and depends on the different results detected during the follow up. Herein, we report a case of OFMT regarding this entity in the differential diagnosis of subcutaneous masses.

Keywords: Ossifying fibromyxoid tumor, trunk, subcutaneous mass, soft tissue

INTRODUCTION

Ossifying fibromyxoid tumor (OFMT) is a rare soft tissue neoplasm first described by Enzinger in 1989 with uncertain differentiation (1). It is usually a well-defined, small, subcutaneous mass located in the extremities and is slightly more common in men (2). The tumor is characterized by small, round to ovoid cells forming cords and trabeculae in a fibromyxoid matrix. One of the main characteristics of this lesion is the partial rim of metaplastic woven bone surrounding the tumor (3). Despite the classical form, many cytological features such as high mitotic activity and increased cellularity associated with aggressive behavior were described in the literature (4). Herein, we report a case of OFMT, which is subcutaneously located in the trunk and is to be kept in the mind of clinicians and pathologists because of the rarity.

CASE PRESENTATION

A 43-year-old female patient presented with a palpable mass in the trunk. On physical examination, a small, firm, 2-cm sized mass was revealed over the 5th rib near the epigastric region. There were no abnormalities in the laboratory tests and the tumor was excised with a written consent form taken from the patient.

The specimen was a nodular, gray-white solid mass with fibrotic and lipomatous areas. Gritty areas were detected and the cut surface showed a well-defined, tan-white 1.8-cm sized lesion. Once the tumor was decalcified, two cut surfaces were processed for microscopic examination. In the hematoxylin eosin stained microscopic slides, a small, nodular, and lobulated mass with small ovoid cells surrounded by a fibrous capsule was detected (Figure 1). The tumor was moderately cellular and generally the tumoral cells were scattered in a myxoid stroma. The cells of the tumor were generally round shaped with bland cytological features. However, some cells had fusiform shaped nuclei with inconspicuous nucleoli (Figure 2). The nuclei of the tumoral cells were pale with inconspicious nucleoli. The cytoplasms were clear and scant with an eosinophilic appearance. No granulomas or giant cells and lipoblasts were detected. The mitotic rate was measured as <1/10 HPF. The general view of the fibromyxoid matrix was moderately cellular admixed with fibrotic and myxoid areas; however, the matrix was confusing in some foci, showing high vasculature. Perivascular hyalinization was detected in most of the stroma. The stroma was positively stained with PAS.

Many different slides were prepared from different blocks and in only one slide, a partial rim of metaplastic lamellar bone surrounding the tumor was detected (Figure 3). In the immunohistochemical study, vascular structures were positive for CD34 and CD31 but the tumoral cells were negative. However, the tumoral cells showed diffuse positivity of S-100, vimentin, and GFAP, which form the characteristic immune profile of the lesion (Figure 4). The main differential diagnosis was chondroid syringoma, which is also known as mixed tumor. But no ductal epithelial component was detected. Moreover, extraskeletal myxoid chondrosarcoma was considered in the differential diagnosis; however, due to the absence of a cell population with vacuolated cytoplasm and chon-

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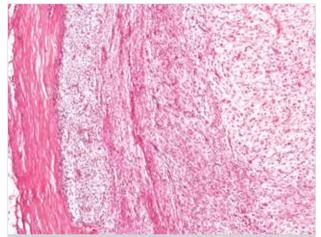


Figure 1. A small, nodular mass with small ovoid cells scattered in a fibromyxoid matrix, HE, $\times 100$

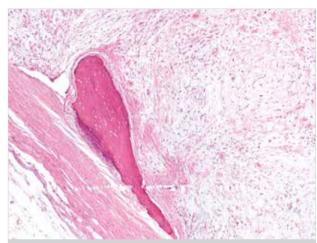


Figure 3. Partial rim of lamellar bone surrounding the tumor, $HE, \times 200$

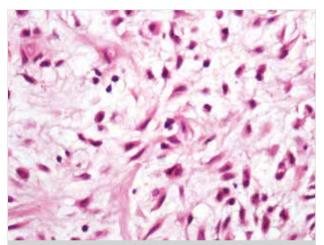


Figure 2. Nests or cords of uniform cells with bland cytological features and inconspicuous nucleoli, HE, \times 400

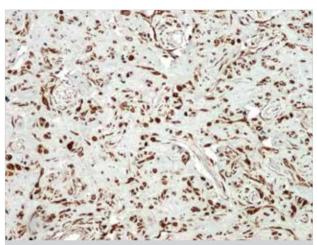


Figure 4. S-100 positivity, DAB, ×200

dromyxoid matrix, this entity was excluded. With these uniform cells, which are positive for vimentin and S-100 in a fibromyxoid stroma in addition to the peripheral rim of the metaplastic bone, the case was diagnosed as OFMT.

The treatment procedure was local excision with intact surgical margins and no additional therapy was provided. The patient was under follow up for 9 months and is disease free.

DISCUSSION

Ossifying fibromyxoid tumor, firstly described by Enzinger as associated with uncertain differentiation, is usually a small, nodular mass located in the subcutaneous tissue of the extremities (5). Ossifying fibromyxoid tumor is generally observed in adult men with a mean age of 50 years (3). Most cases arise in the lower extremities but different localizations such as head and neck and retroperitoneum were reported (1, 6). Despite the classical form of small subcutaneous nodules, OFMTs can reach larger sizes or invade deep soft tissue parts including the bone (7).

The most common presentation is a palpable, well-defined, slowly growing mass; however, many aggressive forms such as those that metastasize to the lungs or those invading the spine were reported in the literature (8, 9).

The tumor comprises small, ovoid cells forming cords, nests, or trabeculae in a fibrous or fibromyxoid stroma. In high power examination, cytologically bland round cells with scattered fusiform shaped nuclei can be observed in a highly vascularized stroma showing perivascular hyalinization (3, 10). The stroma shows PAS positivity and a peripheral rim of lamellar bone, which partially surrounds the tumor, can be detected in about 80% of cases (3). We detected the partial rim of the bone in only one block. Immunohistochemically, OFMTs show a positivity of S-100, vimentin, Leu-7, neuron specific enolase (NSE), and glial fibrillar acidic protein (GFAP) (3). Our case was diffusely positive with S-100, vimentin, and GFAP but the lesional cells were negative for CD34 and CD31. Leu-7 and NSE were not performed due to technical reasons in our laboratory.

The main differential diagnosis is chondroid syringoma, which is also known as a benign mixed tumor of the skin, and comprises of bland tumor cell nodules surrounded by a hyaline myxoid stroma commonly admixed with calcifications as well as ossifications. Ductal/epithelial component arising due to immunoreactivity with cytokeratins can help differentiate these lesions. Myxoma of the nerve sheath is another entity considered in the differential diagnosis; however, no peripheral metaplastic bone formation is seen in this tumor. Extraosseous osteosarcomas are large masses located in deep soft

tissue parts with highly atypical, pleomorphic cells. Malignant peripheral nerve sheath tumor is a more aggressive tumor generally located in deep counterparts of the soft tissue. Extraskeletal myxoid chondrosarcoma, a malignant soft tissue tumor must also be excluded by detecting tumor cells with more vacuolated cytoplasm and chondromyxoid stroma (4).

The major prognostic features were cellularity, mitotic rate, and nuclear grade in a 3 step classification by Folpe and Weiss (4) grouping OFMT in a) typical form with low cellularity, mitotic rate <2/50 HPF, and low nuclear grade; b) malignant form with high cellularity and nuclear grade, mitotic rate >2/50 HPF; and c) atypical with intermediate grade between a and b. This classification is important because of the high risk of recurrence and metastasis in malignant OFMTs. In the atypical forms, the rate of local recurrence was stated as 13% in the study by Folpe et al. (4) and was reported to recur even after 11 years. In the same study, the metastasis was found as 60% of malignant OFMTs whereas 4% and 6% of typical and atypical OFMTs respectively (4). According to this classification, our case can be counted as an typical form of OFMT. In typical OFMTs, complete excision with intact surgical margins is accepted to be optimal but long term follow up of the case is needed because of the potential of different biological behavior (8, 9).

The outcome of this tumor remains controversial and depends on the presence of tumors having the same morphology but showing different biological behavior. For example, Yoshida et al. reported a case with aggressive behavior, which caused death of the patient lacking malignant features (9). Binesh et al. (8) described a case showing the classical morphological features of a typical OFMT but metastasized to the lungs. Because of the reports describing tumors with a typical morphological appearance and clinically malignant outcomes, patients should be under close follow-up for recurrence or aggressive behavior.

CONCLUSION

Ossifying fibromyxoid tumors are rare tumors usually associated with benign behavior but the rarity of the lesion may lead the pathologists to misdiagnose. In our opinion, OFMT deserves to be remembered in the differential diagnosis of subcutaneous masses with these unique features.

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - Y.D., Ö.D.; Design - Y.D., S.Y.Ç.; Supervision - Ö.D., Ö.İ.Ç.; Funding - Y.D.; Materials - Y.D., Ö.D.; Data Collection and/or Processing - S.Y.Ç., Ö.D.; Analysis and/or Interpretation - Y.D., Ö.İ.Ç., S.Y.Ç., Ö.D.; Literature Review - Y.D., Ö.İ.Ç.; Writer - Y.D., Ö.D.; Critical Review - Ö.İ.Ç., S.Y.Ç.; Other - Y.D.

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Invasive papillary breast carcinoma, solid variant with neuroendocrine differentiation

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ABSTRACT

Invasive papillary carcinoma, solid variant is a rarely observed breast tumor. It is encountered in patients of advanced ages and has a good prognosis. After the physical examination, mammography, and ultrasonography examinations, modified radical mastectomy were applied to the 72-year-old patient, who came to our hospital complaining of a mass in the left breast. During the macroscopic analysis, a well-limited, necrotic, and bleeding tumor with a diameter of 7 cm was found in the left breast, covering almost the whole area. The case was diagnosed as invasive papillary carcinoma, solid variant with neuroendocrine differentiation, which has been reported in the literature as a result of the histopathological and immunohistochemical analysis.

Keywords: Breast carcinoma, papillary carcinoma, solid variant

INTRODUCTION

Papillary carcinoma, which constitutes 1–2% of the breast cancers observed in women, has usually a good prognosis with low grade nuclear features (1). Almost half of the papillary carcinomas develop from the center of the breast. It is observed as a round and well-limited mass on mammography. There can be a cystic area in most of the papillary carcinomas, but this is not necessary; there may be a minimum cyst formation or it may never be seen. Papillary carcinomas are divided into two categories such as invasive and noninvasive. There are no papillary structures in the histopathological appearance of the papillary carcinoma; it is called solid papillary carcinoma. Solid papillary breast carcinoma is encountered at more advanced ages than other breast carcinoma cases; the average age range is 63–71 years. Invasive papillary carcinoma, solid variant is a rarely seen breast tumor with a good prognosis. The average size of the tumors is 2–3 cm. Big tumors can fill the whole breast. Fibroadenoma, benign cystic lesions, mucinous, and medullary carcinoma must be considered in the differential diagnosis (2). In this case, we diagnosed invasive papillary carcinoma, solid variant with neuroendocrine differentiation in the 72-year-old patient, who had a mass with a 7 cm diameter in the left breast.

CASE PRESENTATION

The 72-year-old female patient presented to our hospital with the complaint of a mass, pain in her left breast, and bloody nipple discharge, which had been noticed for 2 months. A mass was detected during the examination, which was fixed in the breast and filled almost all of it. An approximately 7-cm hypoechoic lesion was found on ultrasonography, which was filling the left breast and a 28×16 mm lymph node was detected in the left axillary tail. An approximately 7 cm nodular radioopacity was found in her mammography, which was filling the left breast, and a 28×16 mm lymph node was detected in the left axillary tail.

Modified radical mastectomy was applied to the left breast of the patient. Fine needle aspiration or trucut biopsy was not performed preoperatively. Macroscopically, a $7 \times 5 \times 5$ cm sized, properly-limited, necrotic and locally bleeding tumor was found on the incision site of the $19 \times 9 \times 6$ cm mastectomy material, which covered the upper and lower inner quadrants and reached the outer quadrants, and 10 lymph nodes were removed from the axilla. The tumor was seen in some areas during the microscopic analysis; these tumors had invasion to the surrounding tissue (Figure 1), formed solid islands, lobules and nests, had an oval nucleus, showed a slight pleomorphism, and comprised of noticeable cells with local nucleoli (Figure 2).

Wide necrosis areas and bleeding was observed within the tumor. A metastatic axillary lymph node was found. In the immunohistochemical analysis, the epithelial membrane antigen, pancytokeratin, was diffuse positive and cytokeratin-18 was positive (Figure 3), NSE was focal positive (Figure 4). E-cadherin was weak positive, S-100 protein, synaptophysin, vimentin, and cytokeratin-5 were negative. Smooth muscle actin and myoepithelial cells were not detected. Estrogen and progesterone receptor was positively stained, whereas cerbB2 was negatively stained. Ki67 proliferation index was around 10%. With PAB and mucicarmine stains, mucin accumulation was not observed on histochemical analysis. As a result of all

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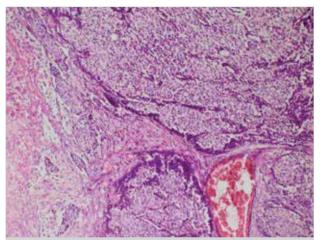


Figure 1. Invasion of the surrounding tissue (H & E: \times 10)

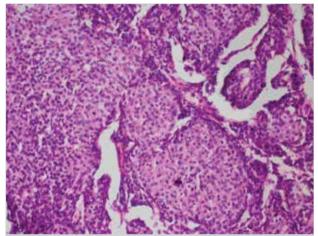


Figure 2. Round tumor with oval nucleus and slight pleomorphism, forming solid islands, lobules, and nests (H & $\text{E:} \times 20$)

these morphological and immunohistochemical findings, the case was evaluated as invasive papillary carcinoma, solid variant with neuroendocrine differentiation.

DISCUSSION

Papillary carcinoma constitutes 1–2% of the breast carcinomas in women (1). Solid variant forms less than 1% of the breast carcinomas. Similar to our case, it is mostly seen in postmenopausal women and is frequent in the 7th decade (3, 4).

Approximately 50% of the papillary carcinomas develop from the central part of the breast; nipple changes are observed in one-third of the patients (2, 3). Our patient also presented with bloody nipple discharge and a mass.

Papillary carcinomas may histopathologically show papillary, micropapillary, cribriform, reticular, and solid appearance. Solid variant is mostly well-limited and frequently multinodular (2). In the histopathological appearance of the solid papillary carcinoma, the tumor comprises of cellular islands, ductal structures, and intensive fibrous connective tissues between them. The cellular islands seem noninvasive because they are well-limited, but generally, no peripheral myoepithelial cell layers are observed with immunohistochemical staining (5). The cellular proliferations in the tumor nodule are homogenous and adjacent to each other; there are no cribriform or

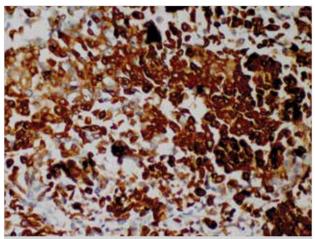


Figure 3. Positive staining with CK18 in tumor cells (×40)

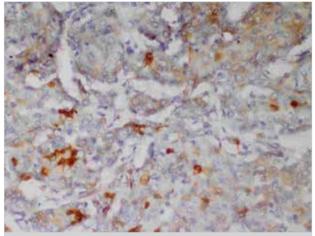


Figure 4. NSE positivity (×40)

papillary patterns (6). The cells are small and have hyperchromatic nuclei. Signet ring cell forms can also be observed and the number of mitoses is generally low (7).

Papillary carcinomas may exist in at least half of the neuro-endocrine differentiation cases. NSE, chromogranin, and/or synaptophysin stainings are detected. In our case, neuroendocrine differentiation was present and focal NSE staining was observed (8). Similar to our case, estrogen and progesterone receptor are positive and HER2 is negative in the solid papillary carcinoma (6). Moreover, CK8 and CK18 are positive (9, 10). In our case, CK18 was stained diffuse-strong positively. Microscopic diagnosis of the invasive papillary carcinoma is difficult. Nonexistence of the myoepithelium layer and the muscle and adipose tissue invasion of the tumor in its periphery are important for the diagnosis (2). Invasive or in situ differentiation cannot be made with the needle biopsy or the cytology materials; this differentiation can only be made within the excision material (2).

Intraductal papilloma and generalized ductal hyperplasia must also be considered in the differential diagnosis. Myoepithelial cells exist in benign papillary lesions but not in the papillary carcinoma. Immunohistochemically, high-molecular-weight keratin negativity distinguishes the solid papillary carcinoma from proliferative lesions (11). Medullary carcinoma and mucinous carcinoma are the tumors, which must also be considered in the differential diagnosis.

Prognosis of papillary carcinoma is better when compared to invasive ductal carcinoma (12).

Patients with axillary lymph node metastasis at the rate of 20–32% have been reported (13). A metastatic axillary lymph node was found in our case. Solid papillary carcinoma and cystic papillary carcinoma result in local recurrences with similar frequencies, but those with solid papillary carcinoma were more likely to have axillary lymph node and systemic metastasis and to die of metastatic carcinoma (2).

Prognosis with lumpectomy is perfect in invasive or noninvasive carcinomas. The relapse risk is high in multifocal masses. According to the study results of Nassar et al. (4), hormonal and/or chemotherapy application to invasive solid papillary carcinoma patients without paying attention to lymph node involvement was considered appropriate. Modified radical mastectomy was conducted in our case. According to the American Joint Committee on Cancer 2010, the patient was pT3N1 (stage IIIA). Because of the good general status of the patient, oncologists decided to give chemotherapy treatment regardless of old age and chemotherapy was applied after 2 months. She is alive with no recurrence at 25 months.

CONCLUSION

Invasive papillary carcinoma, solid variant is seen in women at advanced ages and has a good prognosis. It must be considered during the differential diagnosis of benign and malign breast tumors. Invasive or in situ differentiation cannot be made with the needle biopsy or the cytology materials; this diagnosis can only be made within the excision material.

Informed Consent: Written patient consent could not be obtained for the patient and their relatives could not be reached.

Peer-review: Externally peer-reviewed.

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A rare case of non-surgical vocal cord paralysis: Vocal cord hematoma

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ABSTRACT

Although vocal cord paralysis (VCP) following thyroidectomy is primarily associated with surgical trauma, it is not the sole etiology. Vocal cord paralysis following thyroidectomy can be caused by a vocal cord hematoma with an incidence of 1.4% due to direct injury during orotracheal intubation. In this article, we present a case of VCP caused by vocal cord hematoma. A 32-year-old male patient who has been receiving propylthiouracil treatment for toxic multinodular goiter since 10 years was admitted to our hospital to be operated because of persisting complaints. The patient was hospitalized for sutureless thyroidectomy after he became euthyroid. Preoperative fiberoptic laryngoscopy performed by the ear, nose, and throat department revealed bilaterally motile vocal folds and a completely open airway. Patient underwent sutureless total thyroidectomy with a vessel sealing device (LigasureTM LF1212, Covidien, CO), and a minivac drainage system was placed in the thyroid lodge. On the morning of the first postoperative day, 50 mL of serosanguinous fluid was drained. The patient's voice was normal, and there was no ecchymosis. Postoperative fiberoptic laryngoscopy revealed a hematoma near the right vocal fold and paralysis of the right vocal fold; however, the airway was open. It should be kept in mind that VCP is not solely due to surgery but can also result from intubation, as observed in this case.

Keywords: Vocal cord hematoma, vocal cord paralysis, hematoma, thyroidectomy

INTRODUCTION

Thyroid surgery is one of the most popular surgeries worldwide. Postoperative hematoma after total thyroidectomy is a major but unpredictable complication. However, it can be diagnosed by follow-up after surgery even in unsuspected cases. Although it is generally asymptomatic, patients with postoperative hematoma can suffer from a range of symptoms from ecchymosis to life-threating dyspnea (1, 2).

Vocal cord paralysis (VCP) following thyroidectomy is another major complication, and its incidence has been varied (1, 2). Although VCP following thyroidectomy is primarily associated with surgical trauma, it is not the sole etiology. Vocal cord paralysis can result from nerve damage, such as transection (complete or partial), excessive traction, direct handling, contusion, crush, thermal injury, clamping, incorrect ligature, and compromised blood supply. In addition, neurological diseases, tuberculosis, aortic aneurysms, lung and mediastinal malignancies, esophageal malignancies, metastatic tumors, and post-anesthesia complications can cause VCP (1, 2). According to a review by Jeannon et al. (3) that includes 27 articles and evaluates over 25,000 patients, the average rate of temporary VCP is 9.8% (1.4%–38.4%), whereas the average rate of permanent VCP is 2.3% (0%–18.6%). Vocal cord paralysis following thyroidectomy can result from a vocal cord hematoma with an incidence of 1.4%, due to direct injury during orotracheal intubation (incidence: 4.5%)(4, 5). In this article, a case with VCP resulting from vocal cord hematoma is presented.

CASE PRESENTATION

A 32-year-old male patient who has been receiving propylthiouracil treatment for toxic multinodular goiter since 10 years was admitted to our hospital because of persisting complaints of restlessness, fatigue, tremor, and heat intolerance. He was hospitalized for sutureless thyroidectomy after he became euthyroid. Preoperative fiberoptic laryngoscopy performed by the ear, nose, and throat department revealed bilaterally mobile vocal folds and a completely open airway. The patient underwent sutureless total thyroidectomy with a vessel sealing device (Ligasure™ LF1212, Covidien, CO) and a minivac drainage system was placed in the thyroid lodge (6). During operation, there was no loss of signal by intraoperative nerve monitoring (NIM-Response 3.0, Medtronic, FL). On the morning of the first postoperative day, 50 mL of serosanguinous fluid was drained. The drain was removed; his voice was normal and there were no ecchymosis. Postoperative fiberoptic laryngoscopy revealed a hematoma near the right vocal fold (Figure 1) and paralysis on the right vocal fold; however, the airway was open. The patient was discharged within 24 h after surgery. As a routine procedure, the patient was called for a follow-up on the tenth postoperative

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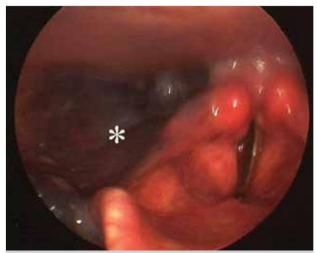


Figure 1. Early postoperative image of vocal folds.

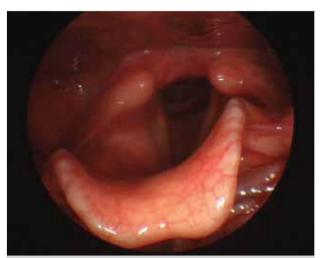


Figure 2. Sixth postoperative week image of vocal folds revealing that the previous hematoma on the right vocal fold had degraded.

day and at the sixth week, with the advice of application to the emergency department in case of any respiratory problems.

The patient did not apply to the emergency department or our clinic before the sixth postoperative week. Fiberoptic laryngoscopy on the sixth postoperative week revealed degraded hematoma and bilaterally mobile vocal folds (Figure 2). The same ear, nose, and throat doctor performed all fiberoptic laryngoscopies.

DISCUSSION

Unilateral vocal cord palsy (UVCP) is a complication of thyroid-ectomy; however, it is not solely caused by recurrent laryngeal nerve injury. According to a study by Spataro et al. (7), UVCP occurs in 46.3%–55.6% of patients. Regarding postoperative UVCPs, 14.9%–15.7% of all cases are due to thyroid surgery and 1.9% are due to parathyroid surgery. While malignancy is responsible for 17.8%–18.4% of UVCPs, direct invasion of thyroid cancer is responsible for 1.5%. Of all UVCPs, 5.8%–6.2% are due to intubation, 3.2%–6.1% are due to trauma, and 13.2%–18.5% are idiopathic (7, 8). In this case, there was no nerve injury causing VCP; however, a hematoma caused dur-

ing intubation resulted in VCP. Fifty percent of UVCPs are asymptomatic, as seen in this patient (9).

Vocal cord hematoma generally appears on the left vocal fold; this is typically related to right-sided insertion of the orotracheal tube and left-handed hold of the laryngoscope (10). However, this patient presented with a hematoma on the right side. The possible reasons for the right vocal fold injury are left handedness, inexperience, and prolonged intubation (4). Reasons for right-sided VCP in this case were not revealed even after discussing the case with the anesthesiology team.

It is hard to predict the development of a hematoma after surgery (11). Hematomas are the most limiting complications of short-stay thyroidectomy; however, this patient was discharged within 24 h after surgery.

CONCLUSION

It should be kept in mind that VCP does not solely result from surgery but can also result from intubation, as seen in this case.

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

Peer-review: Externally peer-reviewed.

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Myxoglobulosis in the appendix

Cengiz Koçak¹, Akile Zengin², İbrahim Girgin³, Fatma Ferda Kartufan⁴, Mehmet Hüseyin Metineren¹

ABSTRACT

Myxoglobulosis is a specific type of mucocele consisting of mucoid material. It is characterized by opaque, transparent globules that resemble "fish eggs" or "frogspawns". It is generally diagnosed incidentally during an appendectomy or an autopsy. In this paper, we aim to present the case of a 58-year-old male patient who was referred to our hospital because of abdominal pain and loss of appetite. The patient underwent an appendectomy. Opaque intraluminal globules were found in the appendectomy material. The globules resembled pearls and they were 2-3 mm in diameter. After histopathological examinations, the patient was diagnosed with myxoglobulosis accompanied with acute appendicitis. According to our research, this is the first case of myxoglobulosis in our country.

Keywords: Acute appendicitis, myxoglobulosis, appendectomy

INTRODUCTION

Myxoglobulosis or caviar appendix is a special type of mucocele. It is characterized by the presence of opaque globules. Globules are made up of mucoid material and they form clusters that resemble "fish eggs" or "frogspawns." The first case of myxoglobulosis was described by Latham in 1897, who found the condition in a postmortem examination, as reported in the manuscript of Probstein and Lassar (1). In 1914, the term "myxoglobulosis" was used by von Hansemann, who analyzed opaque globules varying in diameter from 0.1 to 1.0 cm (2), and it was described as a variant of mucocele. The etiology and pathogenesis of myxoglobulosis are still uncertain. Probstein and Lassar (1) have reported that the probable etiological factors are bacteria and necrotic epithelial debris, which may cause nidus formation for the deposition of mucin. Lubin and Berle (2) have reported that the core of the globules represent a mass of mucin by the granulation tissue that originated from the appendiceal wall and then these globules are disintegrated by mechanical contractions. Li et al. (3) have reported that the globules occur as a formation of mucin by the granulation tissue capsule and then these globules are extruded into the lumen by mechanical forces.

In this case report, we present an extremely rare case of appendiceal myxoglobulosis. According to our studies, this case is the first report of myxoglobulosis in our country.

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CASE PRESENTATION

The procedures of this case were performed in accordance with the Declaration of Helsinki. The patient was instructed and then informed consent was received. A 58-year-old male patient was referred to the Gediz State Hospital in July 2012 with complaints of nausea and abdominal pain in the right lower abdomen. His historical and anamnestic data were not unusual, but he had a history of smoking for 46 years and had been diagnosed with chronic obstructive pulmonary disease. Physical examination revealed that he had rebound tenderness. His blood cell count tests showed that the number of white blood cells had slightly increased. Based on these findings, the patient was diagnosed with acute appendicitis. After spinal anesthesia was performed, the patient underwent an appendectomy. During the operation, the appendix was enlarged and distended. Then, the appendix was removed and appendectomy material was sent to our pathology laboratory for histopathological examination.

Macroscopic examination results revealed that the appendectomy specimen was 7 cm in length and 1 cm in thickness. In the area that was cut, the appendiceal lumen was dilated and filled with numerous opaque, whitish pearl-like globules 2-3 mm in diameter (Figure 1). The accumulation of these globules resembled fish eggs (Figure 2). Biopsy samples were examined histopathologically. On microscopic examination of samples stained by hematoxylin and eosin (H&E), the globules which consisted of eosinophilic laminations of mucin surrounding an amorphous granular core were observed. The diffusion of inflammatory infiltration consisting of polymorphonuclear leucocytes and mononuclear cells were observed in the entire layer of the appendiceal wall. Furthermore, hemorrhage was evidently observed in the wall. Globules were positively stained with Alcian Blue (Figure 3, 4). Considering all these histo-



Figure 1. Numerous pearl-like globules in the dilated appendix lumen



Figure 2. Macroscopic appearance of the globules resembling "fish eggs"

pathological findings, our case was diagnosed as myxoglobulosis accompanied with acute appendicitis.

DISCUSSION

The incidence of the appendiceal mucocele is estimated to be 0.2%-0.3% of the appendectomy specimens, with myxoglobulosis constituting 0.35%-0.8% of mucoceles (4-6). There are patients with myxoglobulosis who clinically exist in a manner similar to those with a mucocele of the appendix. The disorder occurs most commonly in the sixth or seventh decade of life. Patients are generally asymptomatic, and myxoglobulosis is found by chance during autopsies or laparotomies for other reasons. Sometimes, right lower abdominal pain and acute appendicitis is observed in patients with myxoglobulosis (7). To our knowledge, this case is the first report of myxoglobulosis in our country. The development of myxoglobulosis requires obstruction to the proximal appendiceal lumen with continued production of mucin distally. The causes of the proximal appendiceal obstruction include fecalith, epithelial hyperplasia, post-inflammatory fibrosis, cystadenoma, cystadenocarcinoma, carcinoid, and endometriosis. The characteristic feature is the presence of opaque, pearl-like globules in the appendiceal lumen. The most frequent complication is peritonitis or pseudomyxoma peritonei (8, 9). In the literature, the number of reported cases of myxoglobulosis is extremely rare. Recently, Aroukatos et al. (10) reported that a case of myxoglobulosis of the appendix is associated with a ruptured diverticulum. Falah et al. (11) have reported a case of appendiceal myxoglobulosis associated with peritonitis due to

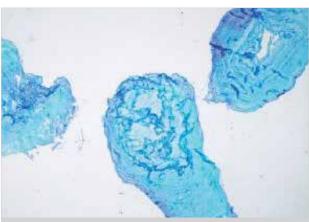


Figure 3. Alcian Blue positive staining of the globules (Alcian Blue pH 2.5×20)

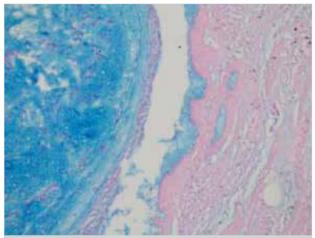


Figure 4. Alcian Blue positive staining of the globules and adjacent appendiceal luminal mucosa (Alcian Blue pH 2.5×40)

perforated peptic ulcer. Padhy et al. (12) have reported a case of myxoglobulosis of the appendix. Routine histopathological examination is essential to diagnose myxoglobulosis.

CONCLUSION

In this paper, we have reported a rare case of myxoglobulosis, which was incidentally found in a patient with peritonitis due to acute appendicitis.

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

Peer-review: Externally peer-reviewed.

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Single-incision laparoscopic adrenalectomy in a patient with acute hypokalemic paralysis due to primary hyperaldosteronism

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ABSTRACT

Acute hypokalemic paralysis is a relatively rare cause of acute weakness. It may resolve spontaneously; however, it may be a potential life-threatening condition. Hypertension may be considered the most important finding in combination with hypokalemic paralysis for raising the suspicion of primary hyperaldosteronism (PHA). A 55-year-old hypertensive Mexican woman was admitted to the Emergency Unit with a sudden onset of generalized paralysis. An endocrinological workup and an abdominal magnetic resonance imaging revealed PHA with a 1.5 cm left adrenal tumor. After preoperative medication, left adrenalectomy was performed with single-incision laparoscopic surgery (SILS). The duration of the surgery was 45 min, and no postoperative complication was encountered. The patient was discharged after 24 h. Hypokalemic paralysis may be due to different conditions, but it may raise the suspicion of PHA in combination with a history of generally mild hypertension. Laparoscopic adrenalectomy is the preferred operation for unilateral adrenal adenomas that cause PHA. Single-incision laparoscopic surgery is a step-forward technique that improves the cosmesis, decreases access-related morbidity, and increases the postoperative recovery. We report a case with acute hypokalemic paralysis due to PHA and treated with SILS.

Keywords: Hypokalemic paralysis, hypokalemia, single-incision laparoscopic surgery

INTRODUCTION

Primary hyperaldosteronism (PHA) involves the hypersecretion of the mineralocorticoid aldosterone due to adrenal gland pathology (mostly unilateral adrenal adenoma). It increases the excretion of potassium and hydrogen ions via urine; mild retention of sodium and water in the body; and results in hypokalemia, mild hypertension, and metabolic alkalosis. Hypokalemic weakness either presents in the form of persistent or acute paralysis, a common symptom of PHA. Hypokalemia is generally well tolerated in otherwise healthy people, but it can be life-threatening when severe (1). Hypokalemic paralysis (HP) may be due to different conditions, but it may raise the suspicion of PHA in combination with hypertension.

Hypokalemic paralysis may either be periodic or not and can be classified as hypokalemic periodic paralysis (HPP) and hypokalemic nonperiodic paralysis (HNP) (2). Lin et al. (2) previously termed non-hypokalemic periodic paralysis instead of HNP, but we prefer the second term for nomenclature because Williams et al. (3) have used it recently. The acute shift of potassium into cells is the main etiological factor in HPP, while hypokalemia and paralysis are generally caused by excessive excretion and depletion of potassium in HNP (2). We have to mention that sometimes HP may be the first manifestation of HPP without any periodic attacks, while HNP may have episodes of HP. Very recently, Hiraga et al. (4) have employed the term acquired non-thyrotoxic hypokalemic paralysis (ANHP) in place of HNP. From our point of view, this is the best term which meets all criteria, and also thyrotoxic hypokalemic paralysis (THP) is better than thyrotoxic hypokalemic periodic paralysis. There is a growing interest in minimal invasive surgical techniques. The number of procedures utilizing surgical methods such as single-incision laparoscopic surgery (SILS) and natural orifice transluminal endoscopic surgery (NOTES) is gradually increasing. Laparoscopic implementations are preferred as an alternative method to open surgeries because the complication rate and post-operative pain are low, better cosmetic results are obtained, and patients return to their everyday life earlier (5). Single-port or SILS is a current development in minimal invasive surgery. This approach is based on inserting all laparoscopic equipment from a single incision on the abdominal wall. After single incision, the operation is performed by entering from the fascial plans under the single port made for this method or under the same skin incision.

Herein, we report a case with acute HP due to PHA with a left adrenal adenoma and treated with SILS.

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CASE PRESENTATION

A 55-year-old Mexican woman was admitted to the Emergency Unit with a sudden onset of general paralysis during her holiday trip to Turkey. No predisposing factors for paralysis were pres-

ent. She had no previous attack before and there was no known family history of periodic paralysis. On physical examination, her blood pressure was 160/90 mm - Hg, and her pulse was 86 bpm and regular. Her weight was normal with a body mass index of 22.2 kg/m^2 . Her muscle strength was found to be 4/5 in distal, 3/5 in proximal upper extremities, bilaterally. The deep tendon reflexes were hypoactive. In her medical history, she had a serious hypertensive attack and a multi-drug antihypertensive regimen was administered (olmesartan/hctz: $40/12.5 \text{ mg} 1\times 1$ and amlodipine $10 \text{ mg} 1\times 1$ in a day).

On laboratory examination, serious hypokalemia was diagnosed (potassium level: 1.35 mEg/L). She had signs of grade I hypertensive retinopathy and grade I diffuse euthyroid enlargement. There was no pathological finding in the cranial computed tomography (CT). Normal calcium, phosphorous, and magnesium levels were found, while there were high creatine phosphokinase levels (1029 U/L) and metabolic alkalosis. Thyroid function tests were in normal limits. Hypokalemia was attributed as the reason of paralysis. Then, the patient was hospitalized and transferred to the Endocrinology Department. After obtaining the patient's informed consent, intravenous (IV) potassium replacement therapy was started and totally 600 mEq of KCl was administered in 48 h. Her potassium level increased to 2.7 mEg/L. Magnetic resonance imaging examination was performed to observe the adrenal glands, and an adenoma with a diameter of 1.5 cm was found in her left side (Figure 1). The aldosterone/ plasma renin activity ratio (A/PRA) was 200. For confirmation of hyperaldosteronism, the salt loading test was performed (Table 1). During the test, the basal A/PRA ratio was 323, and it decreased to only 23.75 after salt loading. In normal subjects, it must decrease to below 10. The patient was diagnosed with PHA (Conn syndrome) based on the left adrenal mass observed in MRI images and hormone levels. An operation on the left adrenal mass by the laparoscopic method was planned. Spironolactone (Aldactone; 100 mg 1×1), olmesartanHCl (Olmetec; 20 mg 1×1), and potassium citrate + carbonate (Kalinor; 8 mg 2×1) effervescent tablets were started in the preoperative period.

Surgical technique: The surgical team had previously conducted more than 200 laparoscopic donor nephrectomies and more than 50 laparoscopic adrenalectomies. After the anesthetic induction, the patient was positioned in a right semilateral position. A 2.5 cm incision was made to the left lateral side of the umbilicus and a 3-channel single port was placed through this incision with an open technique (SILS port, Covidien). Pneumoperitoneum was obtained through carbon dioxide insufflation by ensuring 14 mm-Hg pressure from the channel on port. Two 5 mm laparoscopic trocars and a 10 mm camera with 30° angle were placed through the ports (Figure 2). The splenic flexure of the colon and the spleen was mobilized with the help of an ultrasonic dissector. During the procedure, an endoscopic retractor or a loop retractor was not required. The left main adrenal vein was clipped and cut with the help of an ultrasonic dissector. The left adrenal gland was completely mobilized with the help of an ultrasonic dissector and extracted by the simultane-

Table 1. The list of the hormone and electrolyte levels during illness and wellness periods

Date	State	Α	PRA	A/PRA	K	Na
Day 1	Before K Infusion	-	-	-	1.35	142
Day 2	During K Infusion	44	0.22	200	2.22	148
Day 4	Before salt loading test	48.5	0.15	323	2.62	145
Day 4	After salt loading test	38	1.6	23.75	-	-
Day 15	Before operation after SPNL	65	13.7	4.7	4.64	134
Day 16	After operation	6.4	1.8	3.56	4.79	135
A: aldosterone; PRA: plasma renin activity; SPNL: spironolactone						

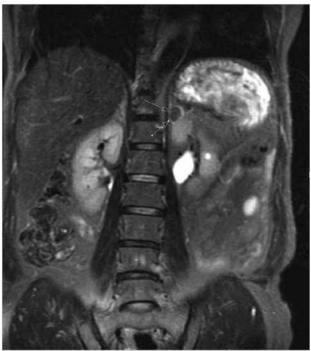


Figure 1. Magnetic resonance imaging examination revealed an adenoma with a diameter of 1.5 cm in the left adrenal gland

ous removal of the endobag and SILS port. No drain was inserted. The fascia was closed using polypropylene sutures (number-0), and the procedure was completed by closing the skin using the 3/0 polypropylene suture (Ethicon). The operation time was 45 min.

No complications occurred during the postoperative followup period. After 6 h, she was able to eat. Postoperative analgesia was ensured through a single dose of 100 mg of diclofenac sodium. She was normotensive and normokalemic without any medication after the operation. The list of preoperative and postoperative hormone and electrolyte levels are given in Table 1. She was discharged after 24 h, and her satisfaction with postoperative pain and the incision was high. Pathological evaluation demonstrated an adrenal adenoma.

DISCUSSION

Hypokalemia is generally well tolerated in otherwise healthy people, but it can be life-threatening when severe. On the



Figure 2. Left adrenalectomy performed with the single-incision laparoscopic surgery procedure

other hand, the clinical symptoms of PHA are often absent or non-specific. Spontaneous hypokalemia in a patient with a generally mild hypertension is a strong indicator for PHA. Hypokalemia can be defined as a serum potassium level below 3.5 mEq/L. The major outcomes of severe hypokalemia result from its effects on nerves and muscles, including the heart muscle (6). When severe hypokalemia develops in which serum potassium levels are less than 2.5 mEg/L, generalized weakness and dangerous ventricular tachyarrhythmias may occur. An acute decrease of serum potassium levels may be more arrhythmogenic than chronic hypokalemia (7, 8). Although there are extensive potential causes in the differential diagnosis of hypokalemia, the etiological factors for acute HP are less (9). Treatment of hypokalemia immediately with potassium supplementation provides rapid improvement of clinical symptoms. Spironolactone is a preferable drug in the postoperative period for maintaining normokalemia. The goal of the therapy will be to normalize serum potassium levels and treatment of the underlying disease. Surgical treatment of primary aldosteronism is the definitive therapy of HP induced by Conn's syndrome; therefore, the serious events that hypertension and paralysis trigger will be prevented (7). After surgery, our patient was cured for both hypertension and HP.

The first laparoscopic appendectomy was performed by Semm in 1983, and the first laparoscopic cholecystectomy was performed by Mouret in 1987. Subsequently, the frequency of advanced laparoscopic surgeries has increased. For the last 30 years, laparoscopic implementations have been successfully applied in the treatment of many diseases and in many branches. Single-incision laparoscopic surgery implementation is a recent method. Many operations, such as cholecystectomy, adrenalectomy, laparoscopic total extraperitonal inguinal hernia treatment, right hemicolectomy, left hemicolectomy, rectum operations, sleeve gastrectomy, gastrojejunostomy, and nephrectomy have been performed through a single incision. The literature includes some cases of SILS adrenalectomy (10). During single-port or single-incision surgery, the surgeon may have to cross handle tools to ensure correct angles, which may cause the operations to last longer in the first cases. Within the last few years, devices have been developed for SILS and have become more flexible; the development of lockable models has also allowed operations to be conducted more easily.

We believe that SILS adrenalectomy can easily be applied in weak patients and small diameter tumors. Generally, adrenal glands cannot be entirely removed from the abdomen through 5 mm incisions in classical adrenalectomy; therefore, the incision may have to be extended. On the other hand, in SILS adrenalectomy, the adrenal adenoma is removed via an alternative incision to the port without any need to extend the present incision. Single-incision laparoscopic surgery procedures have recently become more common worldwide and undoubtedly suppressed standard laparoscopy. In particular, with respect to cosmetic purposes, SILS is seen as an alternative to conventional methods. However, the results of prospective randomized studies should be undertaken, evaluating prospective pain, complications associated with port location, cosmetic outcomes, length of hospital stay, and patient satisfaction. Single-incision laparoscopic surgery adrenalectomy is a safe procedure for the removal of a benign adrenal lesion when performed by an experienced surgeon.

CONCLUSION

We report a case with acute HP due to PHA and treated with SILS. Hypokalemic paralysis may be due to different conditions, but it may raise the suspicion of PHA in combination with a history of generally mild hypertension. Laparoscopic adrenalectomy is the preferred operation for unilateral adrenal adenomas that cause PHA. Single-incision laparoscopic surgery is a step-forward technique that improves the cosmesis, decreases access-related morbidity, and increases the postoperative recovery.

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

Peer-review: Externally peer-reviewed.

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Pneumatosis cystoides intestinalis: A rare cause of intraabdominal free air

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ABSTRACT

Pneumatosis cystoides intestinalis is a rarely seen disease characterized by cysts filled with multiple gases in the wall of the small or large intestine. Many factors have been suggested in the etiology and pathogenesis, including peptic ulcer, pyloric stenosis, and endoscopic trauma. Because various clinical characteristics and symptoms are observed together, diagnosis is generally difficult. It may be a cause of free air observed on direct radiographs. Treatment is directed at the cause and although there is generally a good course, it can sometimes lead to severe complications. In this paper, we present the case of a 33-year old male being prepared for surgery for pyloric stenosis due to a peptic ulcer. In the preoperative tests, because acid was determined within the abdomen and free air below the diaphragm, pneumatosis cystoides intestinalis was considered in the differential diagnosis. Definitive diagnosis was made during the operation and surgical treatment was applied.

Keywords: Ascites, pyloric stenosis, intraabdominal free air, pneumatosis cystoides intestinalis

INTRODUCTION

Pneumatosis cystoides intestinalis (PCI) is a rarely seen disease that is characterized by cysts filled with multiple gases in the subserosa or submucosa of the small or large intestine. It may cause intra-abdominal free air (1). In 85% of the cases, PCI is seen secondary to another pathology. These secondary pathologies are pyloric stenosis, peptic ulcer, appendicitis, ischemic and inflammatory intestinal diseases, diverticular disease, sigmoid volvulus, obstructive pulmonary disease, connective tissue diseases, various parasitic diseases of the intestine, and surgical or endoscopic trauma (2). Because PCI is seen with many different clinical findings and symptoms, most cases are found incidentally. Therefore, when free air is seen in the abdomen, it should be considered in the differential diagnosis. Generally, treatment includes the removal of the concomitant secondary pathology and includes resection of the involved segment of the intestine. Although it can lead to serious complications, the course is generally good (3). In this paper, a case of PCI seen together with pyloric stenosis due to acid and a peptic ulcer is discussed.

CASE PRESENTATION

A 33-year-old male patient presented at our clinic with complaints of nausea, severe vomiting, epigastric pain, and swelling. Questioning revealed a 10-year history of dyspeptic complaints and that he had been diagnosed endoscopically with a duodenal ulcer 5 years previously. Although medical treatment was administered in the subsequent period, endoscopy and biopsy procedures were applied on further two occasions as the complaints continued. Despite a good appetite, the patient had lost 30 kg in weight over 10 years. He was cachectic in appearance and there was succussion splash and sensitivity in the epigastric region on physical examination. No pathology was determined in the laboratory tests. On the postero-anterior pulmonary radiograph, free air was determined below the right diaphragm (Figure 1).

In the esophago-gastro-duodenoscopy that was applied, a large amount of solid and liquid food remnants were seen in the stomach despite 12 h of fasting. Grade A esophagitis was determined, and loosening of the lower esophageal sphincter, antral gastritis, and pyloric stenosis to a degree that would not permit the passage of the endoscope were observed. The biopsy taken on the basis of an ulcer was reported as chronic gastritis. On the abdominal ultrasonography (USG) applied to the patient who did not have findings of acute abdomen, widespread free fluid was observed. On the computed tomography (CT) imaging of the whole abdomen, the stomach was full, there was increased thickness of the pyloric wall, and widespread free fluid was observed in the abdomen. In the parasynthesis applied under USG, acid-like fluid was aspirated. No pathological finding was determined on examination of this fluid. After 2 days of hydration and nasogastric decompression, the patient was admitted for surgery. When the abdomen was surgically entered, approximately 1 L of acid fluid was aspirated. In the subsequent exploration, the stomach was dilated and hypotonic to an advanced degree and scar tissue and stenosis in the pylorus were observed. As additional pathology, multiple cystic structures of varying sizes were noticed that were located subserosally involving a 20 cm colon segment starting from the splenic flexura towards the distal region (Figure 2). Additional to the distal subtotal gastrectomy because of the

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Figure 1. Free air seen under the right diaphragm on the posteroanterior chest radiography

pyloric stenosis, a resection of the colon segment where PCI was determined and end-to-end anastomosis were applied. In the postoperative follow-up, no complications developed and the patient was discharged on the 7th day.

The pathology examination of the excised material determined ulceration in the pylorus, gastritis in the antrum, intermittent smoothing of the mucosa in the colon segment, and air-filled cysts ranging from a few mm to a few cm on the serosal surface. At the postoperative 3-month follow-up examination, the patient had put on 10 kg in weight and none of the preoperative complaints remained.

DISCUSSION

Pneumatosis cystoides intestinalis is seen in the small intestine in 42% of cases, in the colon in 36%, and in both the colon and small intestine and extra-intestinal tissues such as the mesentery and omentum in 22% (4). In the current case, the air cysts were localized in the colon subserosa and mesentery. Pneumatosis cystoides intestinalis is seen most often in those aged 30-50 years and in males (5). The case presented here was that of a 33-year-old male. The incidence of PCI has been reported as 0.37% (6) and although the etiology is unknown, many hypotheses have been suggested. Pneumatosis cystoides intestinalis etiology may be classified as primary (idiopathic) or secondary. The form seen not together with any other intestinal or systemic disease is named "primary" (15%) and that seen together with another disease, "secondary" (85%) (7). These secondary factors are pyloric stenosis, peptic ulcer, appendicitis, ischemic and inflammatory intestinal diseases, diverticular disease, sigmoid volvulus, obstructive pulmonary diseases, connective tissue diseases, nephrotic syndrome, AIDS, transplantation, the use of some medications (chemotherapeutic agents, steroids, sorbitol, lactulose) various parasitic diseases of the intestine, hematological tumors, and surgical or endoscopic trauma (2). The current case was accepted as the secondary form as there was acid accompanied by pyloric stenosis associated with a peptic ulcer and more than one endoscopy and biopsy procedure had been applied.

There is no evident relationship between the severity of the clinical findings and involvement of the PCI disease (4). Pneumatosis cystoides intestinalis is generally asymptomatic,



Figure 2. Gas-filled cysts seen in the colon serosa

but depending on the localization, non-specific symptoms such as diarrhea, constipation, abdominal pain, distension, meterorism, tenesmus, and bloody or mucous stools or specific symptoms of gas-filled cysts such as invagination, volvulus, or mechanical obstruction may develop. In addition, pneumoperitoneum may result from ruptured cysts without any peritoneal irritation findings (8). When PCI is suspected, simple methods such as direct radiograph (two-thirds of the cases are diagnosed) and USG and advanced diagnostic techniques such as colonoscopy and CT, may be requested (3). Because PCI is seen with a wide range of clinical findings and symptoms, most cases are found incidentally. In the current case, sub-diaphragmatic free air was seen on the direct pulmonary radiograph taken during the preparation for surgery for pyloric stenosis. Because there were no findings of acute abdomen, PCI was considered and definitive diagnosis was made during the operation. Clinically, the presence of intra-abdominal free air with the rupture of subserosal cysts without peritoneal findings is known as "benign pneumoperitoneum" (4). When free air is seen in the abdomen radiologically, attention must be paid to the indications for surgical intervention and there must be good knowledge of the clinical and physical examination findings and the underlying disease of the patient.

The treatment of PCI depends on the spread of the disease and the underlying reason. The clinical findings are corrected. In patients with symptomatic but uncomplicated cases, good results have been reported with wide spectrum antibiotics, metronidazole, prednisone, normobaric or hyperbaric oxygen, somatostatin, and bismuth (3). Surgical treatment is useful in cases where the underlying reason for PCI is an obstructive gastrointestinal disease or an acute abdomen event such as perforation, which leads to peritonitis. In the current case, during the surgical intervention for pyloric stenosis, segmental colon resection and end-to-end anastomosis was applied to a segment of approximately 20 cm with PCI involvement seen in the colon. Recurrences have been reported after treatment (9). In the current case, where an intestinal segment with lesions was removed and pyloric stenosis was corrected, no recurrence was determined throughout a 14-month postoperative period.

Despite surgery, the mortality rates have been reported in complicated cases as 44% (4). In a case of mortality with PCI,

it seemed to be associated with the underlying reason or pathology rather than the PCI itself (10).

CONCLUSION

Pneumatosis cystoides intestinalis is rarely seen and several factors are held responsible in the etiology. Delayed treatment may be a reason for serious morbidity and mortality. When intra-abdominal free air is seen, intestinal perforation or bacterial infections, which can create gas should be considered in the differential diagnosis.

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Editorial comment on: 'Colonoscopic perforations: Single center experience and review of the literature'

Erdinc Kamer, Serkan Karaisli

Dear Editor,

We read the article on "Colonoscopic perforations: Single center experience and review of the literature" by Colak et al. (1) with great interest.

Colonoscopy is the most effective diagnostic method for colorectal lesions because it allows direct visualization of the colorectal mucosa, it is also the standard procedure for colorectal cancer screening (2). Since early recognition and removal of colorectal polyps are very important in the prevention of colorectal cancer, the use of colonoscopy has increased over the years. Although colonoscopy is a safe procedure, fatal complications such as perforation or bleeding may occur during the procedure. The authors presented their clinical experience on colonoscopic perforation, one of the most serious complications of colonoscopy, in the light of the literature. First, we believe that the addition of some parameters such as ASA score, body mass index, history of abdominal surgery, colonoscopy indications (polypectomy, screening, gastrointestinal symptoms), detected colorectal pathology, time to diagnosis (during colonoscopy, delayed), peritoneal findings, leukocytosis, management (operative, non-operative) and length of hospital stay (day) of the patients into Table 2 that described the demographic characteristics, localization, diagnosis and treatment of patients with colonoscopic perforation will enlighten readers.

In the material-methods section, the authors stated that they applied "radiological examination" for diagnosis, but they only presented X-ray results in the results part. We are of the opinion that clarifying whether abdominal computerized tomography (CT) was applied (especially in patients with peritoneal irritation findings) and describing CT findings (a CT imagemay be added) if available, will strengthen the article.

Although the title of the article is about colonoscopic perforation, the authors grouped perforations of colonoscopy and rectosigmoidoscopy (RSS) separately in their study (Table 1). We think that the RSS information will not provide an additional contribution to the readers. Likewise, perforation occuring during RSS leads to a question mark in the reader's mind. We also think that it would be useful to clarify the specialty of the endoscopist (surgeon or gastroenterologist) in case of colonoscopic perforation.

The authors declared that "ethics committee approval was not required due to the retrospective nature of the study" in the material-methods section. On the other hand, due to the current legislation and the scientific using of the information of the patients, it is necessary to obtain approval of the ethics committee in all studies that do not require the direct intervention of a physician such as all observational studies, survey studies, retrospective archive scans for file or image records. In this regard, we believe that it would be appropriate to correct the disclosure in order not to mislead the readers.

The authors did not specify the ASA scores of the study group, although they emphasized "the findings from our study showed that patients older than 65 years and those with ASA scores greater than 3 are at higher risk for colonic perforation following therapeutic endoscopy" in the results part. We believe that it is worthwhile authors' sharing their thoughts with the readers about how they have achieved this result.

Peer-review: Externally peer-reviewed.

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

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Authors' reply

Dear Editor,

Following is the authors' response to the contribution to and criticism of the article titled "Colonoscopic perforations: Single center experience and review of the literature".

As noted by the reader, colonoscopy is a very effective tool in the assessment of colorectal cancer and benign lesions. In addition to the parameters of duration of hospital stay, indication for colonoscopy, colonoscopy findings and time to surgery, all of which were elaborated in the text after Table 2, demographic and medical parameters that the reader have mentioned could be documented in Table 2.

X-ray is the initial radiological test in the evaluation of patients. Of the 13 perforations as a result of colonoscopy, nine were detected during the procedure. Therefore, erect abdominal X-ray and chest X-ray were sufficient to confirm the diagnosis and for preoperative evaluation. Additional radiological tests were not needed for these cases. For the other four patients, because of a recent history of colonoscopy, decision was made according to physical examination. Two patients with signs of acute abdomen underwent emergency surgery following the detection of free air in X-ray.

In addition to X-ray, abdominal CT was utilized for the patient who had polypectomy in the ascending colon and had mild tenderness only, as well as the patient with very poor status that refused surgery.

12 of the 13 cases of perforation occurred in the sigmoid colon, rectosigmoid junction or the rectum, which constitute the

area of investigation of rectosigmoidoscopy. Only one perforation was from the ascending colon. Although all cases of perforation were patients for whom colonoscopy was planned, no perforations developed for the young patients who underwent rectosigmoidoscopy for rectal hemorrhage. This shows that age and accompanying diseases are important risk factors for perforation.

Colonoscopies were performed by 27 endoscopists of which 24 were general surgeons and 3 were gastroenterologists. Perforations happened during the procedures of ten general surgeons and two gastroenterologists. The rate of perforation for the two groups did not differ significantly.

Perforations occurred in 12 diagnostic colonoscopies and one therapeutic colonoscopy. The mean age was 65.13 years for the diagnostic group and 45 for the therapeutic group. The ASA (American Society of Anesthesiologists) score was not stated in the article, however, the mean length of hospital stay being 15 days (from four to 45 days) suggests a high ASA score.

"Research ethics have become universal in their principles through international treaties. The standardization of regulations facilitates the internationalization of research on drugs. However, for observational studies (i.e. data collected either retrospectively or prospectively, without any therapeutic procedures or follow up in addition to how the patients would otherwise be managed) the modalities used for applying the main principles vary from one country to another." (1) In our country, according to the regulation on clinical research effective since 2014, for retrospective studies utilizing data collected from medical records, approval of the ethics committee is not mandatory. On the other hand, we agree with the reader that it would have been better to obtain ethics committee approval.

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Editorial comment on: 'Evaluation of the Alvarado scoring system in the management of acute appendicitis'

Erdinc Kamer, Turan Acar

Dear Editor,

We read the article titled "Evaluation of the Alvarado scoring system in the management of acute appendicitis" by Özsoy et al. (1) published in 2017 issue (2017; 33(3): 200-204.) of the Turkish Journal of Surgery with great interest.

Acute appendicitis (AA) is probably the most common surgical emergency throughout the world. It is important to make an accurate diagnosis of AA in order to reduce the negative appendectomy rate. Therefore, taking a good medical history, physical examination, imaging tests and scoring systems have a great value.

Özsoy et al. (1) aimed to show the value of Alvarado Score (AS) in AA and to suggest a "management algorithm" according to AS in their study. After reviewing this paper, we would like to emphasizeseveral issues. First of all, it is not understood whether the study design was prospective or retrospective. If this is a prospective study, it will be appropriate to define the randomization method between the groups. The authors divided patients into 3 groups according to their Alvarado score: AS 1-4 (Group 1), AS 5-7 (Group 2) andAS ≥8 (Group 3). However, when we reviewed the literature, we found that the groups were generally divided as AS 1-4, AS 5-6 and AS 7-10 (2). The authors should explain to readers how they have classified these patients.In addition, the reasons why 14.7% of the patients in Group1 underwent surgery despite the literature recommendation of discharge instead of surgery for this group should be clarified by the authors (2). Although the authors' main purpose was to suggest a "management algorithm" in light of their results, we could not find an algorithm in this paper.We believe that writing a "management algorithm" will be quite beneficial for the readers.

The efficiency of AS parameters for the diagnosis was given in Table 3. The reliability AS in the diagnosis for AAhas already been shown in various studies (2, 3). It is also controversial that only 3 of those parameters were found significant in this study. In our opinion, creating a new table comparing Group 1 with Group 3 and Group 2 with Group 3 by determining a cut-off value will contribute more to the literature than the existing table.

Furthermore, the authors recommended that imaging tests should not be used in patients with AS> 7 in the conclusion part, whereas the correlation between imaging tests and AS was not evaluated in the study and they did not even mention which imaging methods had beenperformed in the materialsmethods section. We believe that it is crucial to explain how they have reached such a conclusion.

Peer-review: Externally peer-reviewed.

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

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Authors' reply

Dear editor,

We would like to thank the author' evaluation for the manuscript.

This is a retrospective study. The demographic and clinical findings, histopathological characteristics were all retrieved from patient's files.

There are different studies about randomization of groups in the literature (1-5). In this study, the patients were divided into 3 groups according to AS values. We used Yüksel et al. (5) recommendations since it is a recent study. In our study, the optimum cut-off value for AS in AA diagnosis was found to be 7 according to ROC curve analysis. All patients with AS of >7 was found to have histopathological appendicitis.

The negative appendectomy rate was reported as 15-30% of the patients who were operated with a diagnosis of AA (6-9).

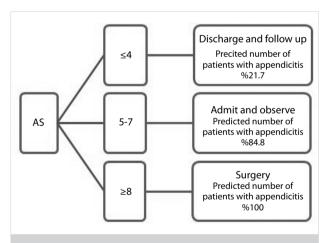


Figure 1. Clinical management strategy by the AS and probability of appendicitis

In our study, the negative appendectomy rate was 19.8%. The negative appendectomy rate was higher than the average in the groups with an AS of \leq 4. Based on our findings, we agree with the recommendations put forward in the literature. In short, patients with an AS of \leq 4 can be discharged and followed-up at home after informing the patient. Patients with an AS of 5-7 should be followed-up closely by using imaging methods since they probably have AA. We think that patients with an AS of \geq 8 can undergo an operation without imaging methods (Figure 1).

We agree with the suggestion of creating a new table comparing Group 1 with Group 3 and Group 2 with Group 3 by determining a cut-off value. However, the study is retrospective in nature. AS components were examined, but they were not effective for surgical decision making. The limitations of the study were explained in the discussion section. Sincerely,

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