ISSN: 2564-6850
e-ISSN: 2564-7032

TÜRK CERRAHİ DERNEĞİ
1929
www.turkcer.org.tr

Turkish Journal of Surgery

VOLUME 37
ISSUE 3
SEPTEMBER 2021

www.turkjsurg.com

Turkish
Journal of Surgery

VOLUME 37
ISSUE 3
SEPTEMBER 2021

Published by Turkish Surgical Society.

Owner/Editorial Manager
Seher Demirer
(Owner on behalf of the Turkish Surgical Society)

Print ISSN 2564-6850
Elektronic ISSN 2564-7032

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Publishing House

bilimsel tıp yayınevi
www.bilimseltipyayinevi.com

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Web : www.bilimseltipyayinevi.com

Publication Type: Periodical
Place of Printing: Korza Yayıncılık
Büyük Sanayi 1. Cadde No: 95/11 İskitler/Ankara
Phone: +90 (312) 342 22 08
Printing Date: 28 September 2021

Turkish
Journal of Surgery

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

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The journal is printed on an acid-free paper.

Turkish Journal of Surgery
Address: Koru Mah. Koru Sitesi, Ihlamur Cad. No: 26
06810 Çayyolu, Ankara, Turkey
Phone: +90 (312) 241 99 90
Fax: +90 (312) 241 99 91
E-mail: editor@turkjsurg.com

Publisher: Bilimsel Tıp Yayınevi
Address: Bükreş Sokak No: 3/20 Kavaklıdere, Ankara, Turkey
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2. Drafting the work or revising it critically for important intellectual content;
3. Final approval of the version to be published; AND
4. Agreement to be accountable for all aspects of the work, and ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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- Acknowledgment of the individuals who contributed to the preparation of the manuscript but who do not fulfill the authorship criteria.

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

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Table 1. Limitations for each manuscript type

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

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

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

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

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

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Publisher: Bilimsel Tıp Yayınevi

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FROM THE EDITOR'S DESK
Turk J Surg 2021; 37 (3): IX
10.47717/turkjsurg.2021.9904

Dear Readers of the Turkish Journal of Surgery,

The last three decades witnessed many exceptional improvements in surgery, especially in surgical technical advancements and in understanding the pathophysiological background of the diseases. If you take a look at the results of a large nationwide study from the USA, dating back to the 1970's, you can easily observe remarkable differences with the current status of surgery, in terms of mortality in major operations (1). Undoubtedly, one may link these significant changes to various factors, not only in the surgical field but also in anesthesia, postoperative care and diagnostic abilities. Yet, there is more to this than meets the eye. First of all, some major operations from the study of Luft et al., such as vagotomy, do not exist anymore in our routine practice (1). Throughout time, physicians were able to better understand the pathophysiology of diseases resulted by the disappearances of some frequent operations. Another major surgical evolution was, without a doubt, the introduction of minimally invasive surgery. The current laparoscopic and robotic surgery offer both the chance to operate more precisely and with less surgical trauma. We have not only abandoned some operations but also we now operate very "differently". The borders and principles minimally invasive surgery are still emerging, and there are still countless points to discuss about.

In this issue, you will have the chance to read an outstanding review article from Nösser et al. about their experience on minimally invasive liver surgery (2). The Department of Surgery of Charité-Universitätsmedizin is one of the leading surgical clinics in Europe. Moreover, this clinic has a worldwide-known reputation in liver surgery. The colleagues share, in their review, the technical details as well as the results of laparoscopic and robotic liver surgery. They also present a clear-cut comparison between both techniques. I am persuaded that you will benefit a lot from this inspiring review, especially to be aware of the limits of this novel complex surgery.

On behalf of the editorial team, I invite you to enjoy all of the interesting articles of the September 2021 issue.

Best wishes,

Kaya SARIBEYOĞLU
Editor,
Turkish Journal of Surgery

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2. *Nösser M, Feldbrügge L, Pratschke J. Minimally invasive liver surgery: the Charité experience. Turk J Surg 2021; 37 (3): 199-206.*

REVIEW
Turk J Surg 2021; 37 (3): 199-206

Minimally invasive liver surgery: the Charité experience

Maximilian Nösser, Linda Feldbrügge, Johann Pratschke

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ABSTRACT

Minimally invasive liver surgery (MILS) was established as last abdominal surgical specialty through the 1990s. With a shift from mainly benign to malignant indications, MILS was shown to be equal to open liver surgery in terms of oncological outcomes, with benefits in intraoperative blood loss, postoperative pain, postoperative complication rates, hospital length of stay and quality of life. With colorectal liver metastases and hepatocellular carcinoma as the most common indications, most liver resection can be performed minimally invasive nowadays, including patients with liver cirrhosis. Initially perceived limitations of laparoscopic liver surgery were weakened by gaining experience, technical progress and pioneering of new resection approaches. Lately robotic liver surgery was adopted to the field of MILS to further push the limits. To simplify first resections, technical variations of the minimally invasive approach can be utilized, and difficulty scores help to select resections suitable to the level of experience. We hereby give an overview of the establishing of a minimally invasive liver surgery program at our center.

Keywords: Minimally invasive liver surgery, laparoscopic liver surgery, robotic liver surgery, laparoscopy, liver, robotics

INTRODUCTION

Development of minimally invasive liver surgery

In the early 1950s, Caroli was one of the first to consider a role for laparoscopy in liver pathologies (1). Decades later, in the 1990s, different surgeons and centers around the world transferred their expertise from open liver surgery to minimally invasive liver surgery (MILS), and could show in a number of retrospective publications that it was equivalent to open surgery, and could even decrease perioperative blood loss, short term morbidity and mortality (2-4). In recent years, a few prospective, randomized controlled trials (RCT) have been added to the pile of evidence, confirming advantages of MILS over open surgery (5,6).

Adoption of MILS in different liver malignancies

In the beginning MILS was mainly performed for non-malignant liver lesions, due to initial concerns regarding oncological outcomes in comparison to open liver surgery (7,8). By now, the two most common indications for MILS are colorectal liver metastases (CRLM) and hepatocellular carcinomas (HCC), reflecting our experience (9,10). Based on a large number of retrospective studies on MILS for CRLM, two meta-analyses have shown MILS to be favorable to open liver resections for having significantly lower morbidity, reduced intraoperative blood loss and transfusion as well as a decreased length of stay in the hospital, but longer operation times (11,12). No differences were observed in disease recurrence or survival rates. The first RCT comparing open and laparoscopic liver resections for CRLM by Fretland et al. (OSLO-COMET) could demonstrate a significantly reduced rate of postoperative complications as well as a shorter length of stay (5). Rates of R0 resections were equal to open surgery. Contrary to prior findings operation times were similar in MILS and open surgery, possibly reflecting the overall learning curve.

Similarly to CRLM, MILS has been increasingly used for patients with HCC, who usually have underlying liver cirrhosis. Both retrospective studies and a small RCT have demonstrated advantages of laparoscopic techniques over open surgery, such as fewer postoperative complications, especially liver failure (13). Intrahepatic cholangiocarcinomas (iCC) were slower to be elected for MILS, due to initial concerns

Cite this article as: Nösser M, Feldbrügge L, Pratschke J. Minimally invasive liver surgery: the Charité experience. Turk J Surg 2021; 37 (3): 199-206.

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Received: 03.07.2021
Accepted: 12.08.2021
Available Online Date: 28.09.2021

DOI: 10.47717/turkjsurg.2021.1011

about the radicality of hilar lymphadenectomy in the laparoscopic approach, which we presented to be feasible in one of the largest report on MILS for iCC (14).

Standardization and future challenges

By 2021, MILS has become the standard in the field of liver surgery in many centers including ours. Conventional open liver surgery has not been replaced completely, as it is currently still used in cases of large tumors and complex vascular and biliary reconstructions. However, we and others have gained vast experience in MILS, and continue to extend boundaries and indications, along with the constant development of further technical advances, such as robotic surgery. At this point, it is becoming ever more important to move from experimental, individual approaches at different centers around the world to a standardization in surgical techniques and training.

After the first guideline meetings beginning with the pioneering conference in Louisville, USA in 2008, leading laparoscopic liver surgeons founded the International Laparoscopic Liver Society (ILLS) in 2016, with the superior intention to introduce international technical as well as reporting standards (15,16).

To meaningfully compare results from different studies, especially those of retrospective design and including eras of learning curves, a classification of surgical difficulty is needed. In the first international guideline conference in Louisville, USA in 2008, the extent of the hepatic resection was divided into three categories of complexity, defining posterolateral segments (4a, 7, 8) to be the most difficult along with hemihepatectomies as well as trisectionectomies (category III), while resections of anterolateral segments (4b, 5, 6) as well as left lateral sectionectomy (2,3) were classified to be less complex in the laparoscopic approach (category II), biopsies and small wedge resections (category I) were rated as the least difficult ones (15). Consecutively the Difficulty Scoring System was introduced and later extended by the Iwate criteria to calculate the complexity of the resection by preoperative parameters (17,18). The Iwate criteria include the high scoring aspects of segment of tumor location and extent of resection as well as tumor size, preoperative liver function defined by Child-Pugh-Score (A and B), proximity to major vessels as well as the laparoscopic approach. The main intention of the Iwate criteria was matching the skill level of the surgeon with the complexity of the planned resection to structure the training of laparoscopic liver surgeons and therefore improve safety for the patients.

Not even two decades after LLS was first established, robotic liver surgery became a part of the MILS spectrum with first scientific reports in 2008 with the intention to further improve surgical accuracy, enable more complex resections and also to reduce fatigue of the surgeon (19,20). Robotic liver surgery has not been implemented outside of few specialized centers around the world. Currently, several promising studies about the safety, feasibility and potential advantages are being published.

Establishment of a laparoscopic liver surgery program

At the Department for Surgery of the Charité – Universitätsmedizin Berlin, the first laparoscopic liver resection was a wedge resection of a single CRLM in segment 6, performed in 2008. In the following five years, another 20 minor resections were performed in a highly selected group of patients. From 2015 on, we focused efforts to form a structured program for MILS to further increase the quality and the number of cases per year.10 The number of laparoscopic liver resections rose from 16 (2014) to 95 (2017), while the share of major resections (≥3 segments) increased from 14.3% to 48.4% in the same time. Despite the escalating surgical difficulty, the rate of severe complications (Clavien-Dindo ≥IIIa) remained similar. Robotic liver surgery was added in 2018, framed in a prospective, post-marketing observational study in collaboration with Intuitive (Intuitive Surgical Inc., Sunnycale, CA, USA), in order to assess the quality and the value of the new technique in standardized, scientific way during implementation. An overview of the numbers of laparoscopic and robotic liver resections at our center since 2014 is displayed in Figure 1. In the following sections, we address some technical challenges, and discuss the strategies we adopted in the years of implementing MILS.

Aspects of Technical Difficulty In Minimally Invasive Liver Surgery

Tumor location

The "classic laparoscopic segments" were originally defined as anterolateral segments 2, 3, 4b, 5, 6 (15). They seemed to be accessible through the laparoscopic approach from very early on, especially as the surgical strategy of laparoscopic liver resections shifted from the `anterior´ or `ventral´ approach in open surgery to a `caudal approach´ in MILS, which exposes the hilar plate and the vena cava as leading structures in the best possible way during primarily anatomical resection (18). With a growing experience in MILS, posterosuperior segments were increasingly also resected minimally invasively, which are regarded more difficult to access in the Iwate criteria. The `caudal approach´ was later augmented by the `diamond technique´, when posterosuperior segments were addressed through parenchyma-sparing resections (21). By now MILS of posterosuperior segments is the approach of choice independent from the indication at our center (22).

Extent of resection

In the early stages of MILS, predominantly minor resections were performed, starting with left lateral sectionectomies in the 1990s as well as simple anatomical segmentectomies (2,23). With the intention of foremost oncological radicality with clear margins, consequently resection of 3 or more segments – defined as major resections – were performed, with the principle of keeping

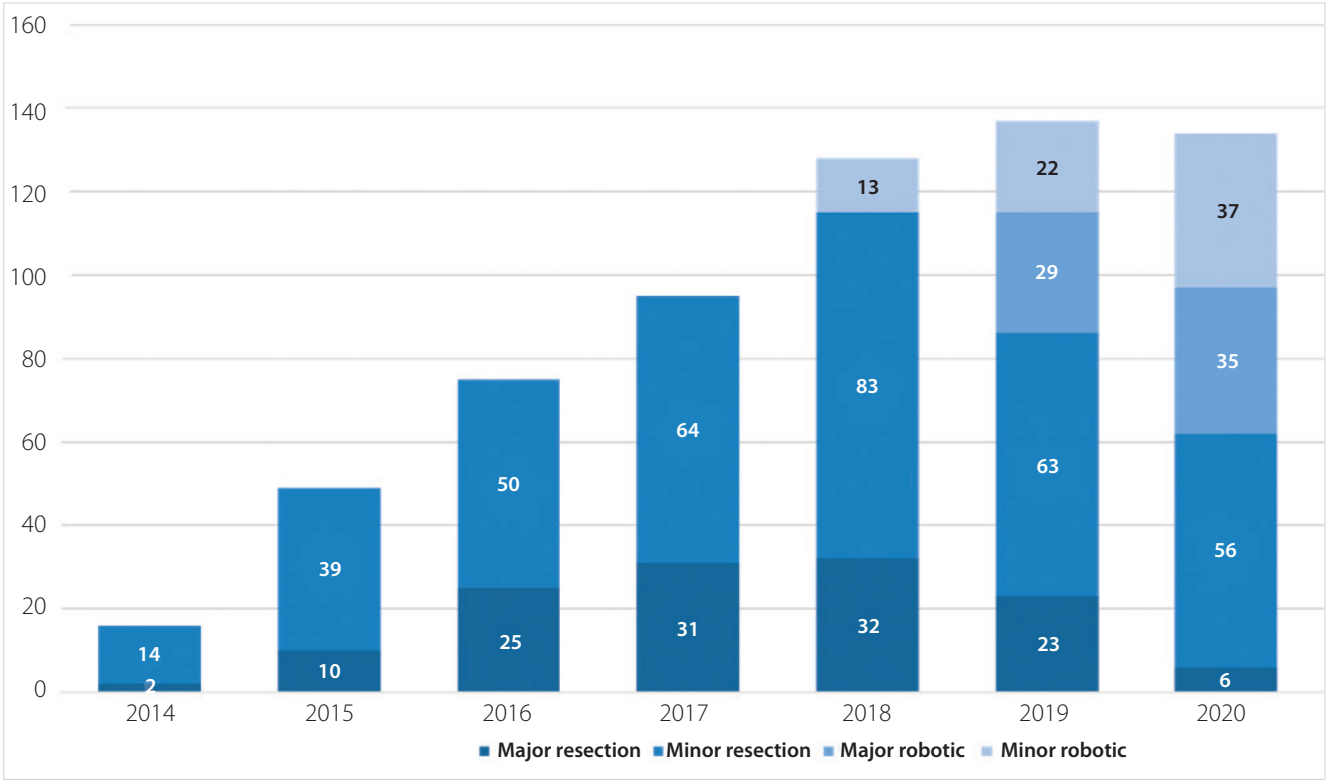

Figure 1. Development of minimally invasive liver surgery at the Charité, Department for Surgery between 2014 -2020.

the volume of the remnant liver as big as possible. Within the last five years, the percentage of major resections performed minimally invasively at our center nearly doubled (Figure 1), so that MILS also became the standard procedure for left (segments 2-4) or right (segments 5-8) anatomical hepatectomies (also hemihepatectomy) at our center as well as most specialized centers across the world, with even economic advantages (24,25). If indicated e.g. for iCC, even extended left or right hepatectomy can be performed minimally invasive today (14).

Tumor size

Tumor lesions sized below 3 cm commonly do not affect the difficulty of the planned resection, as indicated by the Iwate criteria (18). MILS for large lesions (5-10 cm) and also giant lesions (>10 cm) was shown to be possible in retrospective analysis, although giant tumors had greater blood loss and prolonged operative times compared to large lesions, but the evidence is overall limited (26). Tumor perforation through shear forces, lesions size-related deviation from regular trocar placement and specimen recovery has to be taken under consideration along with the surgeon's own experiences prior to choosing MILS for large hepatic lesions.

Technical variations

Previously standardized laparoscopic techniques (multi-incision, hand-assisted and hybrid-laparoscopy) were adopted by laparoscopic liver surgeons, with individual preferences in different countries (15). In terms of difficulty, the Iwate criteria postulated a reduced complexity when hand-assisted or hybrid approaches were chosen rather than a pure laparoscopic approach (18). Within our laparoscopic liver surgery program, we investigated the different approaches from very early on. At our center we applied hand-assisted procedures (n= 187, 65.2%) significantly more than multi-incision laparoscopic approaches (n= 100, 34.8%) between 2013 and 2018, with a decreasing use of hand-assisted surgery over time. For malignant lesions as well as for major resections hand-assisted laparoscopy was used significantly more in those earlier years. We found no differences in operative time and major postoperative complications (27). In our experience the application of hand-assisted laparoscopic liver resections is valuable especially in the establishing phase of a laparoscopic liver surgery program, but can be decreased once the necessary experience in pure laparoscopic resections is achieved. We therefore left the hand-assisted approach in the last few years (10).

Liver cirrhosis

One of the main aspects of liver surgery for HCC in general is the mostly underlying liver cirrhosis, which can lead to severe postoperative complications, including hepatic insufficiency with formation of ascites and also liver failure, resulting in a contraindication of liver resections for patients with HCC and Child-

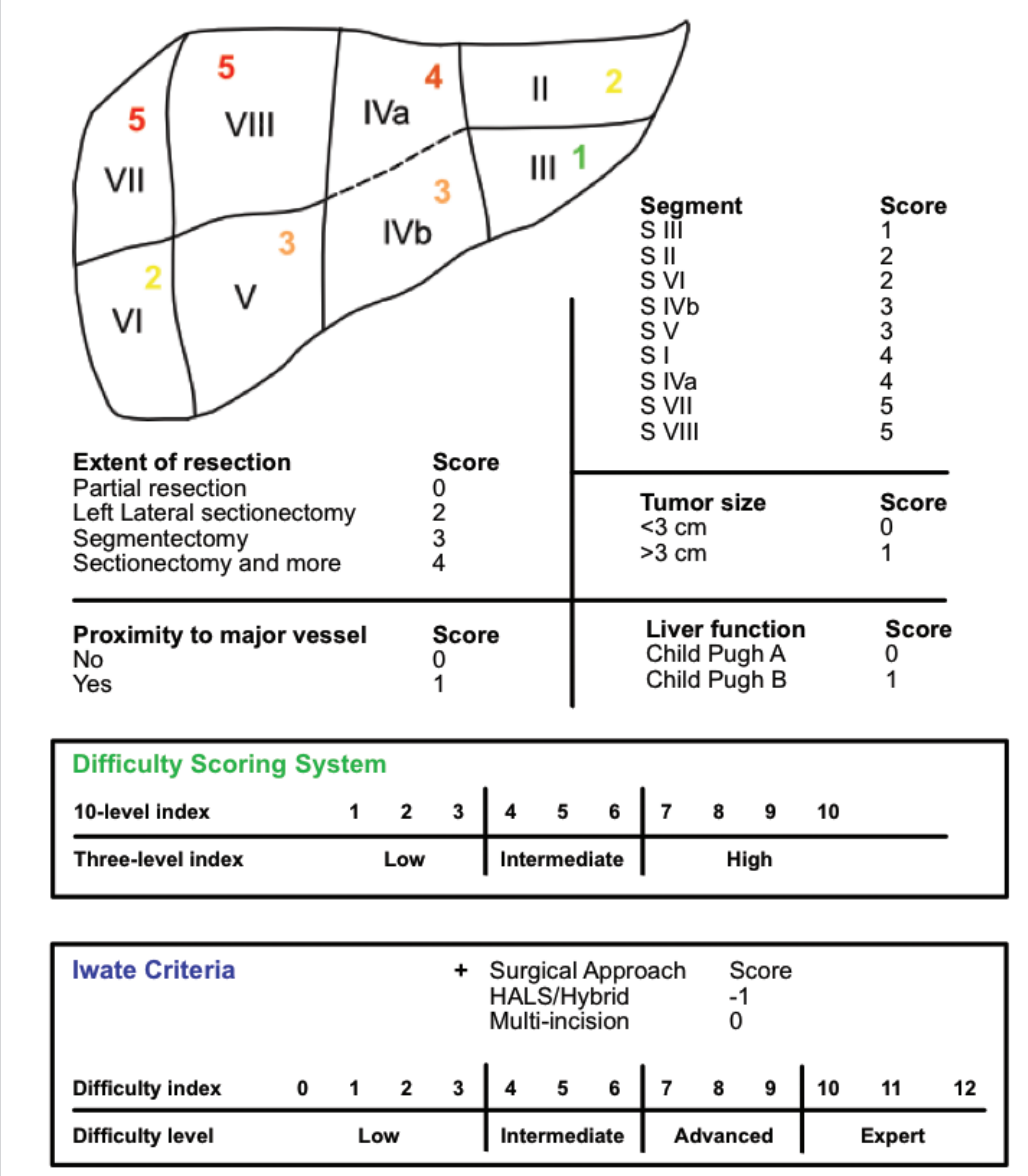

Figure 2. MILS difficulty scores: Difficulty scoring system (DSS) with five categories. Iwate criteria with the same categories as the DSS adding the type of laparoscopic approach (17,18).

Pugh C cirrhosis, as well as for lower grade cirrhosis under circumstances likes multinodular lesions and portal vein invasion (28). Between 2010 and 2015, we performed 21 laparoscopic liver resections for HCC lesions in Child-Pugh A cirrhosis (29). For all patients preoperatively an assessment of the functional reserve of the liver was performed by using a 13C-labelled methacetin breath test (LiMAx) which was developed at our center (30). All patients had impaired liver function due to their LiMAx scores, and furthermore, a small number of patients (n= 3) were below the previously chosen cutoff for open liver resections (31). With no cases of conversion and no mortality, 19% developed minor complications (Clavien-Dindo I-II), while only one patient (4.8%) developed a Clavien-Dindo IIIa complications. No severe complication (Clavien-Dindo ≥IIIb) occured. Therefore, laparoscopic approaches became the standard for liver resections in cirrhosis at our center (32). Preoperative assessment of the hepatic function by serum levels of laboratory values (bilirubin, albumin, liver enzymes, international normalized ratio - INR) is always obligatory prior to hepatic resection, in our experience additional assessment of the complex hepatic metabolism, e.g. through LiMAx, is distinctly helpful in order to avoid postoperative liver function related complications, especially in patients with liver cirrhosis. In a meta-analysis, Witowski et al. stated significantly reduced overall morbidity of pure laparoscopic HCC resections in com-

parison to open surgery, with no differences in mortality rate or survival (33). Sotiropoulos et al. found in another meta-analysis that the laparoscopic approach was associated with significantly lower blood loss and reduced need for blood transfusion, successful achievement of R0 resections as well as lower morbidity and lower 30-day mortality rates (34). Their results make the initiation of a prospective randomized trial on open versus laparoscopic liver resection for HCC in cirrhosis quite unlikely.

Learning laparoscopic liver surgery

While laparoscopic liver surgery was growing during the 1990s, experienced liver surgeons predominantly adapted their knowledge from open liver surgery procedures as well as from already well-established laparoscopic surgery programs in order to successfully promote the growth of the field. For the next generation of young liver surgeons, the International Laparoscopic Liver Society (ILLS) suggested to develop a structured surgical education program to increase the safety of patients, synergistic with the Iwate criteria as a tool to select a certain procedure based on the skill level (18). Based on data from all laparoscopic liver surgery procedures, which were performed at our center in 2017 and 2018, we suggested substeps for a curriculum for a two-year fellowship, which were submitted to the ILLS council and was further validated in a survey by 61 experienced liver surgeons from across the world (35). Complex surgical procedures were divided into 22 substeps, which can be separately executed by the laparoscopic liver surgeon fellow under observation of experienced laparoscopic liver surgeons, according to the fellow´s level of training. Objective of the survey was to determine the difficulty of the various steps and how often certain substeps had to be executed by the fellow to perform the substeps without further observation. We concluded that basic skills (positioning of the patient, trocar placement, definition of resection margins based on ultrasound, etc.) as well as most fundamental skills (Pringle maneuver, parenchymal dissection with Iwate difficulty low and intermediate, etc.) can be successfully taught in centers with more 150 cases in two years. Advanced skills (dissection of the hepatic artery, portal vein and hepatic vein, dissection of the bile duct and hilar plate, etc.) can also be taught within 150 cases in two years, while a few advanced skills (hilar lymphadenectomy, parenchymal dissection with Iwate difficulty expert) are too rare to successfully be taught within two years. In addition, certain fundamental and advanced skills are too rare in centers with less than 100 laparoscopic liver resections in two years to comprehensively teach them to fellows. Therefore, a comprehensive training of laparoscopic liver surgeons is most suitable in highly specialized centers with more than 200 cases in two years.

Limitations of laparoscopic liver surgery

There are numerous limitations to the laparoscopic approach for liver resections. Previous abdominal surgeries – dependent on the type of procedure and the number of previous surgeries –often lead surgeons to favor open surgery because of abdominal adhesions, which frequently require time-consuming adhesiolysis.

Halls et al. could show previous open liver resection to be a risk factor for intraoperative complications in laparoscopic liver resections in a multi-center retrospective analysis, while previous laparoscopic and conventional open surgery in general and previous laparoscopic liver resections were not identified as risk factors (36). In an analysis of 319 laparoscopic liver resections between 2015 and 2018 at our center, 44% of the patients had a history of previous abdominal surgery. We found postoperative complications with a Clavien-Dindo grade of >3a to be similar in both groups (37). In our experience previous abdominal surgery should not be a general contra-indication for laparoscopic liver resection, but the choice of the procedure has to be well selected by an experienced laparoscopic liver surgeon. Another leading limitation is the reconstruction of the biliary tract. Performing a hepaticojejunostomy is a critical step even in open surgery and is reserved for liver surgeons with the highest experience. First reports of fully laparoscopic biliary reconstruction were made not long ago with a limited number of cases with respect to the rare indication (38-40). As expected, operating times were significantly longer than in the conventional open surgery groups, whereas rates of severe complications (Clavien-Dindo >III) were not different. With respect to these achievements, we do not expect further studies on laparoscopic biliary reconstruction in the near future nor the extensive implementation of this laparoscopic procedure in liver surgery programs across the world. The main reason is the growing interest and application of robotic minimally invasive surgery in our field.

Pushing the Boundaries – Implementation of Robotic Liver Surgery

Robotic liver surgery

The initial idea behind robotic surgery –which was created in the late 1960s– was to separate surgical expertise and the patient, in order to perform the highest standard of medical care far away from hospitals, e.g. for traumatic injury suffered in military foreign assignments, rather than bringing differently specialized surgeons into battlefield scenarios. This was one of the reasons the development of a robotic surgical device was financially supported by the US department of defense as one of the most important governmental institutions in the United States (41).

For this purpose, the technical foundation has to be on the highest possible level, incorporating attributions like three-dimensional visualization, a range of motion that is comparable to the surgeon´s motions in conventional open surgery and a

haptic feedback to feel tissue during surgery. The currently most common robotic device is the daVinci® system (Intuitive Surgical, Inc., Sunnycale, CA, USA) or its variations. The first daVinci® system was available in Europe in 1999. With the technical attributions of the system, which were originally designated for a different dedication, laparoscopic surgeons quickly discovered the potential of robotic surgery, furthermore because a potential gain in the surgeon´s ergonomics, reduced fatigue over the time of a surgical procedures as well as a stable camera position. The first experience with robotic surgery in a liver-associated procedure was performed in 2001 in Italy with a preclinical study on minimally invasive cholecystectomy, back then with the ZEUS robotic system (Computer Motion Inc, Goleta, CA, USA) (42). First clinical reports on robotic liver surgery were published in the late 2000s about left lateral sectionectomies, unsurprisingly the same choice of segment combinations as in the first reports on laparoscopic liver resections in the mid 1990s (19,20,23).

We started a robotic liver surgery program in 2018 in association with a single-center, prospective, post-marketing observational study (DRKS00017229) using the daVinci® Xi (Intuitive Surgical, Sunnycale, CA, USA). The development of the utilization of robotic liver surgery is displayed in Figure 1. In summary, the numbers of robotic liver surgery increased to a 5-fold case load in two years. While minor resections were still performed laparoscopically to a large extent, major resections were dominantly allocated to the robotic approach. Last year we performed more robotic than laparoscopic resections for the first time, with an even share of major and minor robotic resections.

In a meta-analysis of 26 retrospective studies with 2630 patients undergoing robotic versus laparoscopic liver resection, there was no difference in intraoperative blood transfusion, conversion and R0 resection rates, as well as no difference in postoperative complications, hospital length of stay and 30-day and 90-day mortality (43). In a recently published retrospective, single-center study comparing difficulty of robotic (n= 91) versus laparoscopic (n= 92) liver resections, Chong et al. could show equal conversion and complication rates, equal hospital length of stay and rates of free resections margins in the general comparison. While operative times were prolonged in the robotic group, significantly more major resections were performed in the robotic group with a significantly higher difficulty rated by the Difficulty scoring system (44). It has therefore been shown, that for more difficult resections the surgeons´ preference might tend towards the robotic approach, emphasizing the status of robotic surgery within MILS.

At our center, we found 59% out of 126 patients undergoing robotic surgery within the first three years to have previous abdominal surgery in their patient history. Duration of surgery, conversion rates and postoperative complications were not significantly different between patients with and without previous abdominal surgery, with the exception of prior liver resections, which led to longer durations of surgery in only the univariate analysis (45). In our opinion, previous abdominal surgeries are no limitation nor contra-indication of robotic liver resection.

Postulated advantages of robotic liver resections overlap with certain advantages of laparoscopic liver surgery, e.g. less postoperative complications and pain, shorter hospital stays and consecutively a higher quality of life after surgery, because of minimally invasive approaches in both procedures. The quality of oncologic outcomes has been questioned and tested repeatedly during the development of MILS. A central point especially in the resection of iCC is the hilar lymphadenectomy (LAD). While hilar LAD used to be considered a contra-indication for MILS in the past, it has been shown to be safe and technically possible in the laparoscopic approach, consistence with the experience of our center (14,46). Nevertheless, due to the 10-fold magnification of the daVinci® system robotic hilar LAD seems to be not only feasible but might also be superior to the laparoscopic hilar LAD (47). The miniaturization of the movements by the surgeon and the reduction of a natural tremor are other major advantages, especially when it comes to suturing. Therefore, the robotic approach seems to be suitable to perform biliary reconstruction in an easier way than in the laparoscopic procedure, which has been shown for resection of the pancreatic head with hepaticojejunostomy before (48). It also could pave the way for hepatic vessel reconstructions, e.g. in cases with portal vein resection.

A major disadvantage in the field of robotic surgery is the lack of established devices for the parenchymal dissection. While for laparoscopic resections all devices from open liver resections were adapted over time, for robotic liver resections extensively used ultrasound dissector are not available due to physical reasons, besides non-angulated devices like the Harmonic Ace Curved Shears (Ethicon, Somverille, NJ, USA), which we use for superficial parenchymal dissection (49). Beyond that, longer transition times of instruments are critical in case of especially severe intraoperative bleeding. We therefore extend the robotic procedure with a laparoscopic trocar for application of clips or staples during the parenchymal dissection, accepting higher expenditure per surgery for safety reasons.

CONCLUSION

Minimally invasive liver surgery grew rapidly over nearly three decades, with a major impact on standardization and safety through international meetings and foundation of an international society. Minimally invasive approaches has become the standard of care for patients undergoing liver resection across the world, including our own center at the Charité. Advantages over open surgery was shown independent of indications, tumor location and extent of the resection with a positive impact on intraoperative blood loss, postoperative pain, hospital length of stay and quality of life. Robotic liver surgery was

adopted not long ago and will be the most discussed topic in MILS over the next years.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - P.J.; Design - P.J., N.M., F.L.; Supervision - P.J.; Literature Review - N.M., P.J., F.L.; Writing Manuscript - N.M.; Critical Reviews - P.J., F.L.

Conflict of Interest: The authors declare that they have no conflict of interest.

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

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DERLEME-ÖZET
Turk J Surg 2021; 37 (3): 199-206

Karaciğerin minimal invaziv cerrahisi: Charité deneyimi

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ÖZET

Minimal invazif karaciğer cerrahisi (MİKC), 1990'lı yıllarda karın cerrahisi uzmanlığının gelişen en son parçasıdır. Önceleri ağırlıklı olarak benign endikasyonlardan malign endikasyonlara olan değişim ile MİKC'nin, intraoperatif kan kaybı, postoperatif ağrı, postoperatif komplikasyon oranı, hastanede kalış süresi ve hayat kalitesi bakımından sağladığı yararlar ile onkolojik sonuçlar açısından açık karaciğer cerrahisine eşdeğer olduğu gösterilmiştir. Kolorektal karaciğer metastazları ve hepatosellüler karsinom endikasyonlarda başı çekerken, günümüzde karaciğer sirozu olan hastalarda dahi birçok karaciğer rezeksiyonu minimal invazif yöntemlerle yapılmaktadır. Laparoskopik karaciğer cerrahisi ile ilgili erken dönemde düşünülen sınırlılıklar, kazanılan deneyimler, teknik alanda ilerlemeler ve yeni rezeksiyon yaklaşımları sonucunda etkisini kaybetmeye başlamıştır. Son yıllarda, sınırları iyice zorlamak adına robotik karaciğer cerrahisi de MİKC alanına uygulanmıştır. İlk rezeksiyonları basitleştirmek için minimal invazif yaklaşımın teknik varyasyonları kullanılabilmekte ve tecrübe seviyesine uygun rezeksiyonların seçiminde zorluk skorları da yardımcı olmaktadır. Bu çalışmanın amacı, merkezimizde başlattığımız minimal invazif karaciğer cerrahisi programının bir özetini sunmaktır.

Anahtar Kelimeler: Minimal invaziv karaciğer cerrahisi, laparoskopik karaciğer cerrahisi, robotik karaciğer cerrahisi, laparoskopi, karaciğer, robotik

DOİ: 10.47717/turkjsurg.2021.1011

ORIGINAL ARTICLE
Turk J Surg 2021; 37 (3): 207-214

Extreme living donation: A single center simultaneous and sequential living liver-kidney donor experience with long-term outcomes under literature review

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ABSTRACT

Objective: Living liver and kidney donor surgeries are major surgical procedures applied to healthy people with mortality and morbidity risks not providing any direct therapeutic advantage to the donor. In this study, we aimed to share our simultaneous and sequential living liver-kidney donor experience under literature review in this worldwide rare practice.

Material and Methods: Between January 2007 and February 2018, a total of 1109 living donor nephrectomies and 867 living liver donor hepatectomies were performed with no mortality to living-related donors. Eight donors who were simultaneous or sequential living liver-kidney donors in this time period were retrospectively reviewed and presented with their minimum 2- year follow-up.

Results: Of the 8 donors, 3 of them were simultaneous and 5 of them were sequential liver-kidney donation. All of them were close relatives. Mean age was 39 (26-61) years and mean BMI was 25.7 (17.7-40). In 3 donors, right lobe, in 4 donors, left lateral sector, and in 1 donor, left lobe hepatectomy were performed. Median hospital stay was 9 (7-13) days. Two donors experienced early and late postoperative complications (Grade 3b and Grade 1). No mortality and no other long-term complication occurred.

Conclusion: Expansion of the donor pool by utilizing grafts from living donors is a globally-accepted proposition since it provides safety and successful outcomes. Simultaneous or sequential liver and kidney donation from the same donor seems to be a reasonable option for combined liver-kidney transplant recipients in special circumstances with acceptable outcomes.

Keywords: Simultaneous living liver-kidney donation, living donor hepatectomy, living donor nephrectomy, complications

INTRODUCTION

During the last three-four decades, liver and kidney transplantations have become the most effective treatment options for end stage liver and kidney failure starting with the first case reported by Margreiter et al. in 1984. In addition, combined liver-kidney transplantation is well-established as a definitive therapy with the potential to provide complete recovery for certain liver-kidney diseases (1). The gap is still high between organs from deceased donors and number of patients awaiting organs all over the world. Transplantation from living donors provides an alternative way to solve the problem and save the patient's life. Transplanting multiple grafts from a single living donor might be a potentially useful strategy for a group of patients especially for pediatric or lower-risk recipients in western countries but might be the only chance for a recipient in a region with insufficient deceased donor support. This rare practice is a topic of both clinical and ethical interest, but there is not too much published data in the literature. In addition, most of the publications focus on the recipient outcomes and there are few studies focusing on donor outcomes (1-4). As an experienced liver and kidney transplant center in a region with insufficient deceased donor support, we aimed to share our combined and sequential living liver-kidney donors' experience under literature review. According to our English literature search and knowledge, this is the only center with the highest number of case experience in the literature till the end of 2020.

Cite this article as: Yankol Y, Karataş C, Kanmaz T, Koçak B, Kalayoğlu M, Acarlı K. Extreme living donation: A single center simultaneous and sequential living liver-kidney donor experience with long-term outcomes under literature review. Turk J Surg 2021; 37 (3): 207-214.

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Received: 06.06.2021
Accepted: 12.08.2021
Available Online Date: 28.09.2021

DOI: 10.47717/turkjsurg.2021.5387

MATERIAL and METHODS

Between January 2007 and February 2018, a total of 1109 living donor nephrectomies and 867 living liver donor hepatectomies were performed with no mortality to living-related donors. After committee approval from the Institutional Ethical Review Board (09.30.2019), our center data reviewed and eight donors who were simultaneous or sequential living liver-kidney donors were found in this time-period. Eight cases were retrospectively reviewed and presented with their at least 3- year follow-up. In addition, their recipients' results were reviewed. Hand assistant donor nephrectomy was the standard procedure for living donor nephrectomy in our center. Open living donor hepatectomy performed to all living liver donors. Complications were scored with the modified Dindo-Clavien classification of surgical complications and adapted donor morbidity classifications (5,6).

Living liver donor (7) and living kidney donor (8) selection criteria, donor evaluation, surgical techniques and post-operative follow-up plans have been described separately in our previous publications. Donors were both approved by multidisciplinary living liver donor and living kidney donor institutional donor committees. All donors were the only suitable donor candidates for the recipients. Candidates were informed on all procedures, surgical complication risks of living donation and expected outcomes of the recipient with their family member. In addition, they were informed that they could stop the evaluation at any time. In addition, timing for living kidney donation was also discussed with them, and all agreed to the simultaneous or any time sequential kidney donation after living liver donation. Simultaneous or sequential donation was mostly decided according to recipient health condition. Open living donor hepatectomy and nephrectomy performed when donation was simultaneous. When the donation was sequential, hand-assisted laparoscopic donor nephrectomy was performed for kidney donation following open living donor hepatectomy.

RESULTS

Of the 8 donors, 6 (75%) were females and 2 (25%) males. Mean age was 39 years (range 26-61) and mean BMI was 25.7 (range 17.7-40). Of the 8 donors, 6 (75%) were parents, 1 (12.5%) was the grandparent and 1 (12.5%) was the cousin. Of the 8 donors, 3 (37.5%) were performed right lobe donor hepatectomy (RLH), 4 (50%) were performed left lateral sector hepatectomy (LLH) and 1 (12.5%) was performed left lobe donor hepatectomy (LDH). Six (75%) of them donated the left kidney and 2 (25%) of them donated the right kidney. Of the 8 donors, 3 (37.5%) of them were simultaneous donation and 5 (62.5%) of them early sequential kidney donation between 4 to 11 days after living liver hepatectomy. Median hospital stay was 9 days with a range of 7 to 13 days (Table 1). Median follow-up was 6 years (3-11.5 years). Of the 8 donors, only 2 (25%) donors experienced early and late postoperative complications during the at least three-year follow-up period. One of them was a simultaneous left lobe liver and left kidney donor to his grandson, and he was re-operated due to bleeding from left donor nephrectomy area 8 hours after the first surgery (Grade 3b). He was discharged without any problems on postoperative 9th day. The other donor's complication was a small wound infection treated with local drainage and antibiotic treatment (Grade 1). No other long-term complication and problem occurred in 8 donors during their at least three-year follow-up period (Table 1).

Table 1. Memorial Şişli Hospital simultaneous and sequential liver kidney donor experience

	Age	Sex	Liver graft	K	Sim/Seq-(d)	H-stay (d)	Donor Compl.	F-up year	Recipient Relation	Rec. Age	Recipient Primary Disease	Recipient Complication
1	33	F	Right	R	Sim	7	No	10.5	Cousin	49	Crn. HCV/ CKD	No
2	61	M	Left	L	Sim	9	Bleeding	8.5	Grand-father	1	PHO Type 1	Graft lost-(Chr Rej-K)
3	35	F	LLS	R	Sim	7	No	6	Mother	2	PHO Type 1	MOF -6 day
4	26	M	LLS	L	Seq-4 day	7	No	5	Father	2.5	PHO Type 1	No
5	33	F	LLS	L	Seq-5 day	10	No	4	Mother	7.5	Caroli/ ARPKD	No
6	35	F	LLS	L	Seq-25 day	8-1	No	2	Mother	9	PHO Type 1	No
7	47	F	Right	L	Seq-18 day	11-2	No	2	Mother	22	PHO Type 1	No
8	45	F	Right	L	Seq-11 day	11	Wound infection	2	Mother	14	PHO Type 1	Biliary Leak (ERCP stent)

K: Side of kidney, Sim: Simultaneous, Seq: Sequential, d: Day, H-stay: Length of hospital stay, Compl: Complication, Rec: Recipient, LLS: Left lateral sectorectomy, PHO: Primary hyperoxaluria, ARPKD: Autosomal recessive polycystic kidney disease, Crn. HCV: Chronic hepatitis C infection, CKD: Chronic kidney disease, Chr Rej: Chronic rejection.

Recipients and Complications

Of the 8 recipients, 6 (75%) of them were pediatric patients (age range, 1-14 years) and 2 (25%) of them were adult patients (22 and 47 years). Most of the recipients' (6 recipients, 75%) primary disease was primary hyperoxaluria type 1. One of the pediatric recipients (aged 2 years) died due to multiple organ failure (MOF) in the early postoperative period (day 6). One of the pediatric recipients (aged 1 year) lost his transplanted kidney due to chronic rejection 14 months after transplantation, and he was re-transplanted from another related living kidney donor.

DISCUSSION

The gap is still increasing between deceased donors and organ failure patients. Living donor liver and kidney transplantation has become a worldwide solution to decrease the waiting list mortality. Over the past two decades, while living donor transplant attempts continued in Western countries, significant progress was achieved in eastern countries especially in living donor liver transplantation, where religious and cultural beliefs do not allow deceased donation to significantly contribute to the donor pool (9). Although living donor transplantation is a potentially life-saving operation for the recipient, with similar outcomes to deceased donor transplantation, living donor surgeries are major surgical procedures with morbidity and mortality risks, which is applied to healthy people. In addition, donor surgery does not provide any direct therapeutic advantage to the donor. The donor undertakes these risks to save the life of a loved one. Risk concerning the living donor in liver and kidney transplantation can be justified only when the recipient enjoys reasonable and visible positive results (2,9).

Living donor liver transplantation (LDLT) only makes sense if we can provide a safe donation environment with a low complication profile. Donor safety and complications continue to be major problems in LDLT. A worldwide survey including 11,553 living liver donors reported a donor risk of estimated mortality of 0.2%, transplant rate of 0.04%, and overall morbidity of 24% (10). For LDLT centers, the aim of zero donor mortality with donor complication rate <20%, Clavien-Dindo grade 1/2 and <5% Clavien-Dindo grade 3/4 complications have been considered acceptable (11). We reported our center living liver donation complication rates in our previous publication with no mortality in 939 living liver donor hepatectomies. Of the 939 donors, in 890 donors' followed-up at least 1-year overall early and late complication rate was 19.5%, including 2.9% life- threatening and nearly life- threatening complications. Right donors hepatectomy complication rate (23.3%) was higher than left donor (14.3%) and left lateral sector donor hepatectomy (11.5%) (7). In addition, long-term medical and psychosocial outcomes in living liver donors is always one of the hot topics in the field. There is growing international consensus that the long-term impact of living liver donation demands greater attention in both research and clinical arenas (12). Muzaale et al. (13) from the US have found in their long-term mortality risk comprehensive analysis that cumulative mortality in a US national cohort of living donors was similar to that in national samples of living kidney donors and healthy community residents at 2,5,9 and 11 years post donation. In addition, they reported that risk did not vary by type of donated graft. These findings suggest no decrease in longevity in the first decade after living liver donation (13). It is clear that greater experience and knowledge of LDLT will allow reduced donor and recipient morbidity.

According to the OPTN data from US, perioperative mortality after living donor nephrectomy is approximately 3 per 10,000 cases (0.03 %), and major and minor perioperative complications affect approximately 3% to 6% and 22% of the donors. Living kidney donation does not appear to increase long-term mortality compared with control groups, nor does appear to increase end-stage renal disease risk (14). Laparoscopic donor nephrectomy (LDN) has replaced open nephrectomy quickly after the initial report by Ratner et al. (15). LDN has been shown to be a safe and advantageous approach for procuring kidneys from living donors, not only because of better cosmetics, but also because of reduced morbidity and a short recovery. Like in our center nowadays, LDN is the worldwide accepted technique for living donor nephrectomy (8). Jacobs et al. (16) have reported emotional and financial experiences of kidney donors over the past 50 years. They examined long-term medical and psychosocial outcomes of 2455 living kidney donors, who had donated 5 to 48 years earlier at three US transplant center by mailing questionnaires. They concluded that most living kidney donors viewed their overall donation experience positively, however almost 10% of them reported at least one negative consequence related to donation. Recipient graft failure was associated with poor psychosocial outcome, defined as one or more of these consequences addition to some financial disadvantages (16).

First combined liver-kidney transplantation from a deceased donor was reported by Margreiter et al. in 1984 (17). Over the time, first simultaneous liver-kidney transplantation from the same living donor was reported by Haberal et al. from Turkey in 1992 (18). The recipient was a 23-year-old female with end-stage liver and kidney disease. The donor was her mother and donated her left lateral sector of the liver and right kidney. The donor was discharged on the 7th day with normal liver and kidney functions without complication. The recipient died due to sepsis after the 15th postoperative day. First successful living related combined living donor right liver lobe and kidney transplantation was reported by Marujo et al. from Brazil in 1999 (19). The recipient was a 53-year-old male, and the donor was his 26-year-old son. However, the donor's postoperative course was complicated by transient moderate hepatic insufficiency, he was discharged on postoperative 10th day from the hospital and fully recovered af-

ter 2 months from the donation. In addition, the recipient was discharged from the hospital on postoperative 18th day.

Transplanting multiple grafts from a single living donor is not a common worldwide practice. It might be a potentially useful strategy for a group of patients especially for pediatric or lower-risk recipients in western countries. On the other hand, it might be the only chance for a recipient in a region with insufficient deceased donor support. In addition, most of the reports focus on recipient outcomes, and most of the recipients are pediatric primary hyperoxaluria type 1 patients (20-32). No donor mortality and no life-treating complications were reported in these cases and case series. No additional mortality and life-treating complications were reported for adult recipients' donors (2, 18, 20, 25, 32) (Table 2).

There are few studies focusing on donor outcomes (1-4). Most of them are single-center series and only one of them is a registry-based cohort study with all living multi-organ donation from US reported by Henderson et al. (1) In this study, data from Scientific Registry of Transplant Recipients (SRTR) between March 1994 and June 2017 was analyzed. The study population consisted of 101 living multi-organ donors and their 133 recipients. Of the 101 donors, 52 of them were simultaneous living multi-organ donors and 49 of them were sequential multi-organ donors. Of the 52 simultaneous living multi-organ donors, there were no simultaneous liver-kidney donors (48 donated kidney-pancreas and 4 donated liver-intestine). No death and no intraoperative complication were reported. Of the 49 sequential multi-organ donors, 36 of them donated liver and kidney (21 donated a kidney than liver lobe and 15 donated liver lobe than a kidney). In addition, 5 donated lung-lobe and a kidney, 3 donated liver lobe and intestine, 4 donated a kidney and pancreas, 1 donated lung lobe and live lobe. No donor death reported related to donation and no intraoperative complication reported. One liver-kidney donor's death not related to donation reported 2.5 year after last donation. This report has the highest number of sequential liver- kidney donors in the English literature according to our knowledge (1).

Although Kitajima et al. (20) from Japan reported a single-center experience with 3 sequential liver-kidney donors in 2017, the report primarily focused on the recipient's outcomes with limited additional information about the donors' outcomes. They reported no donor mortality and no serious donor complication. In 2017, Unek et al. (2) from Turkey reported their single-center experiences with 6 donors focusing on donor long-term outcomes. This is the highest single-center case number in the English literature till our report according to our literature search and knowledge. Of the 6 donors, 5 of them were simultaneous liver-kidney donation and 1 of them sequential kidney donation 11 days after liver donation for an adult recipient. Of the 6 donors, 4 of them donated right liver lobe, 1 donated left liver lobe and 1 donated liver left lateral sector. They reported no mortality and early postoperative ileus resolved with medical treatment as only early and late morbidity. Nair et al.(3) from the US in 2020 reported their experience with 5 sequential liver kidney donors. First 3 of them donated left liver lobe and 2 of them donatde liver left lateral sector. Their kidney donation intervals for these 5 donors were between 10 months to 6 years. They reported no mortality. They concluded that sequential liver-kidney donation can be safely performed when left-sided liver graft is utilized to maximize donor safety. According to our English literature search and knowledge, our case series seems to have the highest case number. Here, we reported 8 simultaneous and short-term sequential liver-kidney donors which focused on the donor outcomes with the literature review. Of the 8 donors, 3 of them were simultaneous liver- kidney donation (1 right liver lobe, 1 left liver lobe and 1 liver left lateral sector) and 5 of them sequential liver kidney donation with the 4 to 11day intervals (2 right liver lobe and 6 liver left lateral sector). Six of our recipients were pediatric and 2 of them were adult. Of the 8 donors, 2 of them experienced morbidity (Grade 3 and 1) with no mortality. In regions with insufficient deceased donor support like Turkey, living donors are the only chance for saving lives and this responsibility push the transplant providers to expand the limits for living donation.

Since the donor is healthy, the safety of the donor is of paramount importance. In addition, minimally invasive approaches are important for functional and cosmetic demands of the donors. Minimizing incision is an alternative, which has been reported in the literature with same outcomes (33,34). In the last two decades, pure laparoscopic or laparoscopic hand assistant donor nephrectomy has been established as the gold standard (28). Beginning with donor left lateral sector hepatectomy in 2002 by Cherqui et al. (35), laparoscopic and other minimally invasive approaches are being used today for living liver donation. This seems feasible and safe when performed by a surgeon who is highly experienced in both laparoscopic and hepatobiliary surgery and with an experienced transplant team (36-38). According to recent consensus guidelines, living donor laparoscopic left lateral sector hepatectomy adult to child liver transplantation may be regarded as standard procedures, but it is still limited to few highly specialized centers. First laparoscopic living liver donor hepatectomy cases from Turkey were reported by Karatas et al. including some of our authors in 2019 (39). In 2018, Gautier et al. from Russia reported the first case of laparoscopic left lateral sector hepatectomy and nephrectomy in the same donor. The donor was discharged on postoperative day 5 without any complications (4). In addition, in 2019, Angelico et al. from Italy reported two sequential laparoscopic living liver hepatectomy and living donor nephrectomy in the same donor. Both cases first underwent laparoscopic left lat-

Table 2. English literature review of simultaneous and sequential liver kidney donation

	Year	Number of cases	Liver Graft	Kidney Graft	Sim/Seq-(m,y)	Donor Death	Recipient Relation	Recipient Age	Recipient Prim. Disease Liver/Kidney
Haberal M et al. (18)	1992	1 (Turkey)	LLS	R-Op	Sim.	None	Mother	23 y	Crn. HBV/NS
Kitajima et al. (20) Sato S et al. (29) Nakamura M et al. (26) Motoyoshil et al. (27)	1996 2014	13 (Japan)	LLS (8)- Left (5)	L (5) NA (8)	Seq- 1.5 month to 4 year	None	Mother (7) Father (5) Sibling (1)	Ped (11) Adult (2)	PHO Type 1 (7) Caroli/ARPKD (2) Cong. L fibr/ARPKD (1) Cong. Cholestas/NA (1) Biliary Atresia/Jeune Synd (1) Alagille Synd./Aplastic KD (1)
Marujo WC et al. (19)	1999	1 (Brazil)	Right	NA	Sim.	None	Child	53 y	Cirrhosis/CKD
Unek T et al. (2) Astarcioglu L et al. (25)	2001 2009	6 (Turkey)	LLS(4) -Op Left(1)-Op Right(1) Op	R	Sim. (5) Seq .(1) – 11 d	None	Mother 2 Sibling 2 Child 1 Spouse 1	9 y	PHO Type 1 (5) Crn. HBV/CKD (1)
Pacheco-Moreira et al. (32)	2005	1 (Brazil)	Right	NA	Seq- 20 y	None	Sibling	Adult	Crn. HCV/NS
Rosenblatt GS et al. (30)	2006	1 (USA)	LLS-Op	L	Seq	None	Mother	1.5 y	PHO Type 1
Moray G, Haberal M et al. (22)	2002-2013	1 (Turkey)	NA	NA	Seq.-4 m	None	Relative	10 y	PHO Type 1
Mor E et al. (24)	2013	2 (Israel)	Right Right	L L	Seq-4.5m Seq-20 d	None	Father (2)	17 y 17 y	PHO Type 1 (2)
Kotb et al. (21)	2010 2014	4 (Egypt)	LLS 4 -Op	NA	Sim.	None	Mother (1) Siblings (1) NA (2)	Ped (4)	PHO Type 1 (4)
Khorsandi et al. (31)	2016	2 (UK)	LLS- Op	NA	Seq-6 m	None	NA	1 y/2 y	PHO Type 1 (2)
Henderson et al. (1) (US SRTR data)	1994-2017	36 (US)	NA	NA	Seq- NA	None	NA (All type)*	NA	NA
Angelico R et al. (28)	2008-2018	5 (Italy)	LLS (Lap) LLS (Lap) LLS 3 -Op	L (Lap) R(Lap) NA -3	Seq. 8 m Seq. 4 m Seq- NA	None	Mother 1 Father 1 NA-3	1.5 y 3 y Ped (3)	PHO Type 1 (5)
Ozer A et al. (23)	2017-2018	4 (Turkey)	LLS(3 Right(1)-	NA- Lap(3)	Sim. (1) Seq. (3)-4m	None	Mother (2) Father (2)	Ped (3) Adult (1)	PHO Type 1 (4)
Gautier et al. (4)	2019	1 (Russia)	LLS (Lap)	L (Lap)	Sim.	None	Mother	2 y	Cong. L fibrosis/ARPKD
Nair A et al. (3)	2020	5 (US)	Left 3 LLS 2	L 4 R 1	Seq- 11 month to 9 year	None	NA	NA	NA

LLS: Living liver left lateral sector donation, Left: Living liver left lobe donation, Right: Living liver right lobe donation, Sim.: Simultaneous living liver and kidney donation, Seq.: Sequential living liver kidney donation, R: Living right kidney donation, L: Living left kidney donation, KD: Kidney disease, Op: Open surgery, Chr: Chronic, L: Liver, ARPKD: Autosomal recessive polycystic kidney disease, PHO: Primary hyperoxaluria, d: Day, m: Month, Lap: Laparoscopic surgery, UK: United Kingdom, US: United States, Ped.: Pediatric.

eral sector hepatectomy and followed by laparoscopic donor nephrectomy. Intervals between the two surgeries were 4 and 8 months. No serious complications were reported with no morality (28). According to our literature review and supported by the literature reports, there were no cases of donor morbidity higher than Clavien-Dindo Grade 3 in the English language literature publications for simultaneous or sequential liver-kidney donors (1, 4). Minimally invasive approaches seem to be the close future of living liver donation.

Tong et al. have verified that the donors' well-being is depended on the recipients' well-being. Feeling of regret, sense of loss, or psychosocial complications were reported when the recipient died or had a poor outcome (16). Our clinical experience is similar to this conclusion. Most of the extreme donors reported in the literature were close relatives of the recipients, especially for pediatric recipients. Especially, these close relationships with recipients impact the decision made and motivate the donors during the extreme donation process. With good recipients' outcome, long-term psychosocial complications seems to be limited in this rare practice.

CONCLUSION

In conclusion, the expansion of the donor pool by utilizing grafts from living donors is a globally-accepted proposition in experience hands, since it provides safety and successful outcomes. Under the literature review and with the addition of our limited case experience, simultaneous or sequential liver and kidney donation from the same donor seems to be a reasonable option for combined liver-kidney transplant recipients in special circumstances. Right recipient indication and appropriate donor evaluation with right time decision making, experienced team and meticulous surgical technique with close early and long-term follow-up are mandatory during this extreme donation process for good outcomes.

Ethics Committee Approval: Committee approval was received from the Memorial Şişli Hospital Institutional Review Board (09/30/2019) 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).

Peer-review: Externally peer-reviewed.

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

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

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2021; 37 (3): 207-214

Canlı vericilikte uç nokta: Literatür irdemesi eşliğinde uzun dönem sonuçları ile eş zamanlı ve birbirini takip eden canlı karaciğer-böbrek verici tek merkez deneyimi

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ÖZET

Giriş ve Amaç: Canlı karaciğer ve böbrek verici ameliyatları tamamen sağlıklı bireylere uygulanan cerrahi işlemlerdir. Bu cerrahiler vericiye doğrudan bir faydası olmayan, ölüm ve komplikasyon riski taşıyan büyük bir işlemdir. Bu çalışmamızda dünya genelinde çok yaygın olmayan eş zamanlı veya birbirini takip eden canlı karaciğer ve böbrek verici ameliyatı deneyimimizi literatür irdemesi ile birlikte paylaştık.

Gereç ve Yöntem: Ocak 2007-Şubat 2018 tarihleri arasında merkezimizde, alıcısı ile yakınlık ilişkisi olan vericilere toplam 1109 canlı böbrek verici ameliyatı ve 867 canlı karaciğer verici ameliyatı verici kaybı yaşanmadan gerçekleştirilmiştir. Bunlardan eş zamanlı veya birbirini takip edecek şekilde canlı karaciğer ve böbrek verici ameliyatı olan 8 verici minimum 2 yıllık takipleri ile incelenmiştir.

Bulgular: Bu 8 vericiden 3 tanesi eş zamanlı ve 5 tanesi birbirini takip edecek şekilde canlı karaciğer ve böbrek verici ameliyatı olmuşlardır. Hepsi alıcının yakın akrabasıydı. Ortalama yaş 36 (26-61) ve ortalama BMI 25,7 kg/m (17,7-40) idi. Vericilerden 3'üne sağ lob verici hepetektomisi, 4'üne verici sol lateral sektör hepatektomisi ve 1'ine sol lob verici hepetektomisi gerçekleştirilmiştir. Median hastanede kalış süresi 9 (7-13) gündü. Vericilerden 2'sinde erken dönemde komplikasyon gelişmiştir (Dindo Grade 3b ve Grade 1). Verici ölümü ve başka bir geç dönem komplikasyonu gelişmiştir.

Sonuç: Verici havuzunun genişletilmesinde canlı vericilerin güvenli olarak başarılı sonuçlar ile kullanılması dünya genelinde kabul görmektedir. Aynı vericinin eş zamanlı veya takip eden ameliyatlar ile karaciğer ve böbrek vericisi olması özel durumlarda kombine karaciğer ve böbrek alıcıları için güvenli bir seçenek olabilmektedir.

Anahtar Kelimeler: Eş zamanlı canlı karaciğer-böbrek vericisi, canlı verici hepatektomisi, canlı verici nefrektomisi, komplikasyon

DOİ: 10.47717/turkjsurg.2021.5387

ORIGINAL ARTICLE
Turk J Surg 2021; 37 (3): 215-221

Comparison of laparoscopic percutaneous internal ring suturing method and open inguinal hernia repair in children under 3 months of age

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ABSTRACT

Objective: Laparoscopic inguinal hernia repair in younger infants has not been completely accepted worldwide. The aim of this study was to evaluate the safety and feasiblity of laparoscopic percutaneous internal ring suturing method in children aged younger than 3 months and compare the recurrence and complication rates with open repair; which may still be mentioned as the gold standard procedure.

Material and Methods: A total of 387 children underwent inguinal hernia repair in the clinic between 2016 and 2019. One hundred and forty of them were under 3 months old and divided into two groups; children who underwent laparoscopic percutaneous internal ring suturing (Group 1) and open surgery (Group 2). Selection of the surgical method was regardless of weight, sex or any patient characteristics other than surgeon's choice. Operation durations, complications and recurrences were compared between the two groups.

Results: A total of 140 patients underwent surgery due to inguinal hernia. Group 1 included 85 and Group 2 included 55 children. There were two recurrences in each group ($p > 0.05$). Operative durations were shorter in Group 1 for both; unilateral and bilateral repairs ($p < 0.0001$). There were no intraoperative complications in any group. There was one major postoperative complication in Group 2: iatrogenic undescended testis, and none was observed in Group 1. In the laparoscopic group, 47% of the children who were diagnosed to have unilateral hernia were revealed to have bilateral inguinal hernias (n= 31).

Conclusion: Laparoscopic percutaneous internal ring suturing method seems favourable in terms of operative time. It also has the advantage of detecting contralateral patent processus vaginalis or asymptomatic contralateral inguinal hernia.

Keywords: Infant, inguinal hernia, laparoscopy

INTRODUCTION

Inguinal hernia (IH) is one of the most common conditions which requires surgical intervention among children (1). The gold standard procedure has been open approach for years. Laparoscopic inguinal hernia repair has gained popularity recently but not totally accepted worldwide due to concerns as increased recurrence and complication risks, anaesthetic considerations and engaging the peritoneum. Its usage in younger infants and newborns have been under an even greater debate (2-4).

Two of the authors have preferred laparoscopic percutaneous internal ring suturing (PIRS) method regardless of age, weight or sex of children since 2016 among variable laparoscopic approaches. The reasons are ability to complete the procedure with only one transumbilical trochar, excellent cosmetic results, comparable complication and recurrence rates with open approach and not dealing with the cord and the vessels.

Even though open approach has been performed for many years, recurrence is still a concern; even a bigger one in newborns or younger infants (2,5). Open IH repair in small children is a technically demanding procedure which brings the increased risk of complications such as testicular atrophy in addition to recurrence (4,6). The studies with big data sets refer comparable results in terms of recurrence of open and laparoscopic IH repairs (7). Also, the fact that newborns have a higher possi-

Cite this article as: Ergün E, Yağız B, Kara YA, Abay AN, Balcı Ö, Eryılmaz S, et al. Comparison of laparoscopic percutaneous internal ring suturing method and open inguinal hernia repair in children under 3 months of age. Turk J Surg 2021; 37 (3): 215-221.

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Received: 07.04.2021
Accepted: 12.08.2021
Available Online Date: 28.09.2021

DOI: 10.47717/turkjsurg.2021.5157

bility to have bilateral hernia may render laparoscopic approach reasonable since laparoscopy through the hernia sac may rarely be possible due to the fragile and thin sac of newborns.

The aim of this study was to evaluate the safety and feasiblity of laparoscopic PIRS method in children younger than 3 months and compare the recurrence and complication rates with open repair; which may still be mentioned as the gold standard procedure.

MATERIAL and METHODS

The study was performed in adherence to Declaration of Helsinki. Written informed consent was obtained from all participants' parents. Institutional review board and local ethical committee approval was granted. A total of 387 children underwent inguinal hernia repair in our clinic between 2016 and 2019. Among these children, 140 of them were under 3 months old. Patients younger than 3 months were divided into two groups; children who underwent laparoscopic PIRS (Group 1) and open surgery (Group 2). Laparoscopic PIRS was performed by two surgeons and open repair was performed by the other two. Patient selection was regardless of weight, sex or any patient characteristics other than comorbidities that may be a contraindication to laparoscopic surgery which we have not encountered in our series. Exclusion criterias were; age older than 3 months, presence of co-morbidities which were regarded as a contraindication for laparoscopy, and patients with a previous inguinal surgery.

Surgical Technique

Laparoscopic PIRS method: The patient was placed in supine position under general anesthesia. Preference of endotracheal intubation or laryngeal mask ventilation was at the discretion of the anaesthesiologist. Following local anesthesia with lidocaine, 5mm umbilical trocar was placed by an open technique. Intraabdominal pressure was set between 6-8 mm CO_2 according to child's weight and age. A 5mm telescope with 30° angle was preferred. A 2 mm incision was made to the skin at the level of inguinal ring after inspection and a 22G angiocath needle was used to access preperitoneal space. A 3/0 or 4/0 non-absorbable monofilament suture was passed inside the needle to form a loop for ligation. Lateral-superior corner of the inguinal ring was the starting point and first half-round was created dissecting the peritoneum and encircling the internal ring including the peritoneum over the vas deferens and the spermatic vessels. Once the peritoneum over the vas deferens was dissected and passed, the loop was pushed into the peritoneal cavity and another suture starting from the same point but travelling counter-clockwise direction around the internal ring meeting with the first suture was introduced. The second needle and suture were also pushed in to the peritoneal cavity and, first needle and suture within is caught by the loop of the second suture. Then the first needle was withdrawn leaving its suture caught in the loop the second suture and first suture is taken out by the help of the second suture. Finally, the suture encircling the internal ring was tied outside, leaving the knot in the extraperitoneal space.

Open Technique: The patientis were placed in supine position, and external ring was exposed by dissecting medially along the Poupart's ligament by a standard inguinal transverse incision. The hernia sac was separated from the testicular vessels and vas deferens by using fine tissue forceps, and the hernia sac was dissected until the preperitoneal fat tissue was exposed. After confirming the absence of any sliding organs, the hernia sac was twisted and double suture-ligated with 3/0 or 4/0 absorbable suture. Fascia and other layers were closed with absorbable sutures.

Statistical Analysis

Statistical evaluation was conducted on SPSS for Windows 11.5 (Chicago, IL). Categorical variables between the groups were compared by Chi Square test, normally distributed nominal variables were compared with independent t-test, non normally distributed variables were compared with Mann-Whitney U test. p value was set as <0.05 as a statistical significance indicator.

RESULTS

Laparoscopic PIRS procedure was performed in 85 children and open repair in 55. Male to female ratio of the study group was 5 (117 males and 23 females). Mean age of the children was 53 days (range; 14-90 days) and mean weight was 4.3 kg (3-5.4). Detailed data on patient characteristics is given in Table 1. The preference of the surgical method was at the discretion of the surgeons; one team performed laparoscopic surgery and the other preferred open approach regardless of patient characteristics unless refused by the parents or contraindicated due to co-morbidites.

Although the rate of bilaterality was found lower on preoperative evaluation (28/140; 20%), the rate was increased to 42% (59/140) due to incidental repair of contralateral patent processus vaginalis (cPPV) in the laparoscopy group. In one patient with incarcerated hernia, the procedure was converted to open to perform resection of the necrotic intestines (Conversion rate: 1/85; 1%).

DISCUSSION

Laparoscopic IH repair in children has gained worldwide popularity recently. One of the most popular laparoscopic techniques in children is PIRS, described by Patkowski et al., which was accepted and underwent many modifications by many others (4,8). Despite the popularity of this method, open surgery is still the first choice in many centers. Laparoscopic repair has evolved significantly with many modifications, and results are comparable to each other without demonstrating any significant advantage (4,8-14).

Although there are studies on laparoscopic IH repair in younger infants and neonates, very few performed percutaneous techniques (2-4,6,15-17). Zenitani et al. have reported comparable re-

Table 1. Patient Characteristics and Operative Data

	Group 1 (Laparoscopic PIRS)		Group 2 (Open repair)	p
N	85		55	
Male/Female	73/12		44/11	
Side	Preoperative: Right: 42 Left: 24 Bilateral: 19	Postoperative: Right: 22 Left: 13 Bilateral: 50	Right: 30 Left: 16 Bilateral: 9	
Intraoperative complication	None		None	
Intraoperative finding	Amyand's hernia (n=1) Ischemic intestine (n=1)		Amyand's hernia (n= 1)	
Operative time Unilateral Bilateral	 Mean: 24 ± 4.14 minutes (17-34) Mean: 33 ± 3.70 minutes (29-44)		 Mean: 42 ± 5.27 minutes (35-58) Mean: 65 ± 8.55 minutes (51-79)	 p< 0.0001 p< 0.0001
Conversion to open surgery	n= 1 (necrotic intestines)		-	
Major postoperative complications	n= 0		n= 1 iatrogenic undescended testis	
Recurrence	n= 2 (1 and 11 months after the surgery) (both repaired laparoscopically)		n= 2 (1 week and 3 months after the surgery) (both repaired laparoscopically)	p> 0.05

sults with open surgery in terms of safety and efficacy in infants younger than 6 months in their series of 120 patients and reduced incidence of metachronous contralateral inguinal hernia (MCIH) (16). They have reported the recurrence rate as 0.83% (n= 1/120) without any major complications. Patkowski et al. have stated no recurrences and only one minor intraoperative complication in their study with 25 infants (15). Shibuya et al. have presented their study on percutaneous IH repair in extremely low birth weight infants with 17 children versus 22 who underwent open surgery and showed one recurrence (5.9%) and one postoperative vomiting during postoperative period which may be attributed to general anaesthesia (17). Our study with 85 children under 3 months of age revealed a recurrence rate of 2.3%. Studies on other laparoscopic IH repair methods in younger infants and newborns present recurrence rates between 1-4% (1-4,6,18). Considering the fact that IH repair in newborns and infants has higher recurrence risk, our results seem comparable with the literature but tend to be higher than the mentioned studies on percutaneous method (0.83%, 0%, 5.9% and 2.3% respectively). When we compared the results with the open group, the recurrence rates were not statistically significant (p= 0.65). Even though low weight, prematurity and young age are considered as predisposing risk factors for recurrence, Choi et al. have revealed the opposite and found higher recurrence rates in older children (4% vs. 1%) (1). The recurrence rates were not statistically significant but they attributed it to the relatively small sample size.

Open herniorrhaphy is a technically challenging procedure, especially in small male infants due to fragile and thin hernia sac and vulnerable vas deferens with puny vessels. Very high percentage of complications and recurrences after IH repair have been reported either by open or laparoscopic approach in male patients (19, 20). Miyake et al. have reported 9 recurrences in total of 2067 children and all of the children who suffered from recurrence were boys and Amano et al. have presented only 6 recurrences in 2028 cases and only one of them was a girl (19,20). Very thin and fragile hernia sac and delicate dissection of vas deferens and vessels from the sac may be very difficult and challenging. In a study, vas deferens or epididymis has been found in 0.53% of excised hernia sacs (21). Also, as neonates and younger infants are more prone to incarceration, surgery may become more complicated and troublesome due to edematous and fragile peritoneum (16). All of these factors contribute to the increased risk of complications such as iatrogenic undescended testis and testicular atrophy secondary to a complicated surgery which is already technically demanding (6,21,22). Recurrence rates of open surgery have been reported between 0.8-3.8% in younger infants (23). On the other hand, since no dissection is needed in the PIRS procedure; it may be safer and easier in children with history of incarcerated inguinal hernia. In the present series, there were not any major postoperative complications such as testicular atrophy or morbidity that required additional surgeries such as hydrocele, ascended or atrophic testis in the laparoscopic PIRS group. In the open surgery group, one child suffered from iatrogenic undescended testis and underwent additional surgery at one year of age (1.8%). Standard inguinal orchiopexy was performed and no sign of testicular atrophy was recorded after 6 months of follow up. Regarding complications,

open surgery seems to have higher possibility of major complications despite total complication possibility seems similar (24). Complications such as iatrogenic undescended testis, testicular atrophy and bladder rupture have been reported (19,24,25).

There was one case in the study which required conversion to open surgery. This was a two-month-old boy and he was presented with incarcerated hernia. Incarcerated segment was reducted under laparoscopic vision but the intestines seemed ischemic and laparotomy was performed to evaluate the intestines. Affected segment was evaluated to be necrotic and resected. In an 18-day-old boy with incarcerated hernia, appendix was found in the hernia sac with significant adhesions to the right inguinal canal. After laparoscopic reduction and excision of appendix, IH repair was decided not to be performed because of the inflammated area. After one week, laparoscopic PIRS was performed without incidence.

Another clear advantage of laparoscopic IH repair is the availability to evaluate both inguinal canals properly. It allows contralateral repair of IH or PPV simultaneously. Although transinguinal laparoscopic exploration of the contralateral inguinal canal is an option in open surgery, it may not always be possible in infants whose hernia sac may be fragile and very thin. Due to technical difficulties and/or thin/ fragile hernia sac, it may be difficult to perform even in older children (26). As Endo et al. have stated, even if transinguinal exploration is performed successfully, cPPV rates may be different in transinguinal exploration and laparoscopic exploration due to the technical difficulties (23). They have presented a 21.6% contralateral PPV incidence in transinguinal exploration and 47% in laparoscopic surgery while Gollu et al. have stated a similar 28.3% positivity in transinguinal exploration (23,26). In our series, the rate was 47% (31/66); exactly the same as in the series of Endo et al. Considering the more common bilaterality in infants and newborns and challenges of performing transinguinal contralateral exploration, the advantages of laparoscopy may become more prominent. In our institution, neither contralateral transinguinal exploration nor open exploration of the other side is a standard approach. So, asymptomatic contralateral hernias or PPVs of children who undergo open surgery remain undetected until they become symptomatic. This situation may lead to the burden of another surgery; to the family, hospital and the child, and the results of laparoscopic PIRS group shows that 47% of children with preoperative diagnosis of unilateral hernia have undergone bilateral hernia repair. Other studies on laparoscopic IH repair in small infants have also shown nearly similar rates (20-61%) (1,6,16). Studies with no age limitation shows rates between 17-43% (27). By the laparoscopic approach, it seems possible to reduce the possibility of MCIH and reoperation of the children, which comes along with extra anesthesia exposure of the child, additional anxiety of the parents and increased risks of possible morbidities (27). Amano et al. have stated that regarding their 40% cPPV rate, the open group may be expected to develop contralateral hernia in same rate but only 12% of these open group developed MCIH (20). The repair of cPPV remains controversial regarding this data. However, the authors think that since PIRS is a minimally invasive method with very low testicular atrophy and major complication risks, it may be suggested to perform a prophylactic cPPV repair. Another debate on laparoscopic methods is about the costs. Laparoscopy may seem more expensive than open approach but it is not considering the possibility of a reoperation due to development of a clinically significant inguinal hernia. In addition, usage of reusable materials as we do may help to decrease costs.

Recurrence is a major problem of IH repair in young infants. Using non absorbable sutures and giving extra caution to medial aspect of inguinal ring may help to prevent recurrences, especially in male infants (4,6,18). In the laparoscopic group, there were two recurrences, and reoperation revealed that the peritoneum at the medial side of the inguinal canal was ripped and it led to loosen the entire suture. Although recurrent hernias of the open group were observed to have occured in the medial side too, lateral side of these defects were closed and smaller gaps were observed. The repair of these recurrent hernias technically were not more difficult than a primary operation as it would be expected the opposite in open repair. Thus, laparoscopic surgery of recurrent inguinal hernias also seems easier than the open approach.

Waiting the child to grow is another controversy in neonatal IH repair (28). Complication and recurrence risks are higher in young infants as well as the incarceration rates (3,28). Thus, many surgeons do not follow children with inguinal hernia more than 2 weeks or until the children reach acceptable weight as long as they do not have major comorbidities (2,29). Laparoscopic repair with 3 ports has been found to be safe and feasible in these children (2-4,6). However, considering the small body size, elasticity of the abdominal wall and small intra-abdominal space, intracorporeal suturing in these children is also technically demanding. PIRS method seems to be a technically easier method with comparable outcomes (15,16). Another advantage of PIRS is relatively less violation of the abdominal wall integrity since only one trochar is introduced.

In the present study, mean operative durations were found significantly shorter in laparoscopic PIRS group than the open group for both unilateral and bilateral hernias (24 vs. 42 and 33 vs. 65 mins respectively, $p< 0.0001$). In previous studies, laparoscopic IH repair has been reported to last generally longer or equal with open surgery (19,20). Intraperitoneal techniques requiring intracorporeal suturing, 3 port procedures and some newly introduced techniques might be responsible for these longer durations (30-33). The present study may indicate that

laparoscopic PIRS method may be superior to open approach in terms of operative times. The authors believe that this may be a result of the simplicity of the technique and extraperitoneal closure of inguinal canal without additional instrumentation other than a needle and increased bilaterality in the smaller infants. Because it is possible to repair bilateral hernias in the same setting in laparoscopic surgery while open surgery requires two different incisions and two seperate operations from beginning to the end. Reduced anaesthetical times are especially important for younger infants. Also, we did not observe any anaesthetical challenge which might be a result of an experienced team and short operative times.

Another concern which is very difficult to clarify in laparoscopic surgery is whether the position of the cord is changed or not. Kinking, distortion, angulation or some other malposition of the cord may be catastrophic for the patient, and it may not be easily recognized intraoperatively. Li et al. have evaluated the position of the cord and testicular blood flow in their study and found that neither the position of the cord nor the testicular blood flow was seemed to be affected in percutaneous IH repair (34).

There are some limitations of the study. First, the study is retrospective and selection bias can not be ignored. But all operations were performed by four surgeons and two of them performed laparoscopic surgery to all of their patients and the other two performed open surgery regardless of age and sex. This natural division may bring a relative randomization to the study even though it is not a randomized controlled study. Relatively small number of patients with short follow up time are other limitations. Since all recurrences and morbidities due to the operations tend to present within the postoperative first year, we think that the data may be reliable in terms of recurrences and postoperative complications. Absence of data on prematurity and birth weight and the missing data on development of MCIH after open surgery are the major limitations of the present study.

CONCLUSION

Laparoscopic PIRS method seems favourable in terms of operative time and detecting cPPVor asymptomatic contralateral IH in children under 3 months of age. Recurrence rates are comparable with open surgery without any major complications. Concerning MCIH in children, prospective randomized controlled studies with long follow up, especially for young infants and newborns, are necessary. Another missing data on laparoscopic IH repair by any method is its effects on the reproductive system. Even though it seems safer, it is a well known fact that open inguinal surgery is one of the most common reasons of male infertility (23). Thus, from now on, we should emphasise on the effects of laparoscopic IH repair on male reproductive system by designing long term prospective studies.

Ethics Committee Approval: The ethical approval for this study was obtained from SUAM Committee of Medical Residency Training (Decision No: 2020/01-2, Date: 22.01.2020).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - All of authors; Design - E.E., B.Y., Y.A.K.; Supervision - E.E., B.Y., Y.A.K., İ.K., A.N.A.; Data Collection and/or Processing - All of authors; Analysis and/or Interpratation - Y.A.K.; A.N.A., Ö.B.; S.E.; A.K. Literature Review - E.E., B.Y., Y.A.K., A.N.A., S.E., Ö.B.; Writing Manuscript - Ö.B., S.E., İF.Ö., A.K., İ.K.; Critical Reviews - All of authors.

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

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2021; 37 (3): 215-221

3 aydan küçük bebeklerde laparoskopik perkütan iç halka dikişi yöntemiyle açık inguinal herni onarımının karşılaştırılması

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ÖZET

Giriş ve Amaç: Küçük bebeklerde laparoskopik inguinal herni onarımı dünya çapında tam olarak kabul görmemiştir. Bu çalışmanın amacı, 3 aydan küçük çocuklarda laparoskopik perkütan iç halka süturu yönteminin güvenilirliğini ve uygulanabilirliğini değerlendirmek ve halen altın standart prosedür olarak kabul edilen açık onarım ile rekürrens ve komplikasyon oranlarını karşılaştırmaktır.

Gereç ve Yöntem: Klinikte 2016-2019 yılları arasında toplam 387 çocuğa inguinal herni onarımı yapıldı. Bunların 140'ı 3 aylıktan küçüktü ve bu hastalar iki gruba ayrıldı; laparoskopik perkütan iç halka süturu (Grup 1) ve açık cerrahi (Grup 2) yapıldı. Cerrahi yöntemin seçimi, cerrahın rutinde kullanmakta olduğu yöntem dışındaki ağırlık, cinsiyet veya herhangi bir hasta özelliğinden bağımsız olarak yapıldı. Operasyon süreleri, komplikasyonlar ve rekürrensler iki grup arasında karşılaştırıldı.

Bulgular: Toplam 140 hasta, kasık fıtığı nedeniyle ameliyat edildi. Grup 1'de 85 ve Grup 2'de 55 çocuğu bulunmaktaydı. Her grupta iki rekürrens saptandı ($p > 0,05$). Grup 1'de tek taraflı ve çift taraflı onarımların her ikisi için de ameliyat süreleri daha kısaydı ($p < 0,0001$). İki grupta da intraoperatif komplikasyon görülmedi. Grup 2'de bir majör postoperatif komplikasyon görüldü; iyatrojenik inmemiş testis, Grup 1'de postoperatif majör komplikasyon görülmedi. Laparoskopik grupta tek taraflı fıtık tanısı alan çocukların % 47'sinde bilateral kasık fıtığı (n= 31) olduğu saptandı.

Sonuç: Laparoskopik perkütan internal ring sütur yöntemi ameliyat süresi açısından uygun bir yöntem olarak görünmektedir. Ayrıca kontralateral patent prosessus vaginalis veya asemptomatik kontralateral inguinal herninin eş zamanlı tespit edilmesi avantajını taşımaktadır.

Anahtar Kelimeler: Bebekler, inguinal herni, laparoskopi

DOİ: 10.47717/turkjsurg.2021.5157

ORIGINAL ARTICLE
Turk J Surg 2021; 37 (3): 222-231

Changes and disruptions in diagnosis, treatment and follow-up of breast cancer during two periods of the COVID-19 pandemic in Turkey

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ABSTRACT

Objective: COVID-19 disease, which rapidly became a pandemic, led to significant changes in the provision of health services. This included radical changes to the supply and delivery of routine services to release resources for emergency care. During this process, a range of restrictions were imposed including the recommended rules to be followed before, during and after surgery. Health services provided for breast cancer diagnosis, treatment and follow-up have also undergone enforced changes meaning the diagnosis, treatment, and follow-up of patients with priority has come to the fore. In this study, the effect of the COVID-19 pandemic in Turkey, between March 11, 2020 and May 31, 2020 was assessed in comparison to pre-pandemic practice in terms of divided into two periods, and breast cancer diagnosis, treatment, and follow-up.

Material and Methods: Surgeons dealing with breast cancer treatment and registered to SENATURK (Turkish Senology Academy) were contacted online. The period was divided into two, between March 11th and April 30th and May 1st to May 31st, 2020. Surgeons were requested to complete two electronic evaluation forms, one for each period, investigating change in practice. Only complete responses for both periods were included in the analysis.

Results: There were 93 respondents. Except for less multidisciplinary breast councils, there was no delay in radiological and pathological diagnoses. The number of breast cancer surgeries increased in Period 2, and more COVID-19 positive breast cancer patients were operated in Period 2. Benign breast patients were delayed less frequently in Period 2. In the statistical analysis performed between the two groups, it was found that only a significant difference was in the number of outpatients with benign breasts.

Conclusion: With sufficient awareness of the risks of COVID-19 and with individual protection, breast cancer treatment was not affected during the assessed period of active pandemic in Turkey.

Keywords: Breast cancer, COVID-19, breast care, breast surgery, disruption

INTRODUCTION

Infection with a novel virion was first seen in the Wuhan region of China in December 2019 and spread rapidly to become a pandemic. The infection appeared to be extremely virulent and infectious and had a high mortality rate, particularly in the elderly and those with comorbid disease. The virus belonged to the Coronavirus family which includes viruses that caused the SARS (2002) and MERS (2012) epidemics, and the new disease was called COVID-19. The virus became known as New Coronavirus 2019 (2019-nCoV) and later as SARS-CoV-2 (1). The pandemic immediately imposed extra demands on global health resources. Radical changes to practice were made to protect both healthcare professionals and patients (2, 3). In Turkey, the first case was registered on March 10, 2020, and the first COVID-19 deaths were reported on March 15, 2020.

Since then, there have been major changes in society and in national health services to limit infectious spread and the morbidity and mortality associated with COVID-19. Health service changes have included significant disruption of routine health provision, including surgical services. Recommended rules to be followed before, during and after surgery have been published, both nationally and internationally (4,5). Health services provided for breast cancer diagnosis, treatment and follow-up have also been forced into adapting to the new conditions. There

Cite this article as: Güler SA, Özkan Güler Ö, Şimşek T, Cantürk NZ. Changes and disruptions in diagnosis, treatment and follow-up of breast cancer during two periods of the COVID-19 pandemic in Turkey. Turk J Surg 2021; 37 (3): 222-231.

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Received: 07.10.2020
Accepted: 12.08.2021
Available Online Date: 28.09.2021

DOI: 10.47717/turkjsurg.2021.5069

has been a greater emphasis on diagnosis, treatment, and follow-up of patients with priority (3,6). For this purpose, some decisions were taken, and recommendations were published (6,7). In Turkey, the fight against COVID-19 was most active until June 1, 2020, which was considered the beginning of a normalization process. The initial period, between the first cases appearing and the end of April is considered the "shock" period, while from 1st of May until the beginning of June is considered the period of relative adaptation in terms of the health professionals' and patients' behaviors.

Our aim was to evaluate the changes and disruption to the diagnosis, treatment, and follow-up of breast cancer, divided into the two periods defined, in response to the decisions taken in national health services in response to the COVID-19 pandemic.

MATERIAL and METHODS

This study was a cross-sectional design over two periods during the COVID-19 pandemic. The study was performed online as a national survey of surgical members of SENATURK (Turkish Senology Academy) treating breast cancer. The first period started from the introduction of restrictions following the detection of the first case on the 11th of March and extended until April 30th. This period may be thought of as the "shock" period (Period 1). The second period extended from the 1st of May until the 31st of May and can be thought of as the period of relative adaption (Period 2). An online questionnaire was designed for each period and sent to all members of SENATURK. During these two periods, demographic information of the surgeons dealing with breast cancer, information concerning their institutions and local approach to COVID-19, the status of breast cancer surgery during the period, the changes in surgical approach, and outpatient and diagnostic effects in this period were interrogated. All respondents were asked to answer the questionnaires in comparison to pre-COVID practice. The surveys for both periods, answered by the same surgeons were included to the study. Surgeons who did not complete the surveys and those answering only for one period were excluded.

In accordance with the decisions taken by the Republic of Turkey Ministry of Health for the pandemic period, an application was made to the Scientific Health Board via an online system and approval for the study was obtained. In addition, Kocaeli University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee granted ethical approval for the study with the date and number of 2020/36.

Statistical Package for the Social Sciences (SPSS), version 20 was used for statistical analysis (IBM Inc., Armonk, NY, USA). Results were prepared as frequency and percentages. Comparisons of categorical variables between groups were made using Pearson, Fisher's Full Chi-square test, Yates's Chi-square test and Monte Carlo Chi-square test. The ratios of categorical variables of the data between both periods were compared with Pearson, Fisher, Yates and Monte Carlo Chi Square tests.

RESULTS

A total of 93 respondents completed both parts of the survey. Demographic characteristics of the respondents are shown in Table 1. The academic level of most surgeons was Professor (48.4%) and 85% of respondents had more than 10 years' experience undertaking breast surgery. Prior to the pandemic, two thirds of the respondents carried out between one and five operations per week, with the remainder performing more. In addition, more than half saw more than twenty patients per week as outpatients.

Workplace characteristics and the estimated effect of COVID-19 on service provision at each institution are shown in Table 2. More than three quarters of the respondents worked in university teaching hospitals with a further tenth working in private hospitals. The remainder were mostly divided between state hospitals and private practice. Most respondents were in the Marmara region, which includes Istanbul, by far the most populous city in Turkey, while very few were from the East and Southeast of the country. The variation in estimated effect of the COVID-19 pandemic was striking. Nearly 10% stated that there were no cases whilst 30% indicated that all available resources were directed to caring for the SARS-CoV-2 cases. A further 38% reported that

Table 1. Demographic information of the respondents

Demographics	n (%)
Academic level	
Surgeon	21 (22.5)
Assistant Professor	6 (6.5)
Associated Professor	21 (22.6)
Professor	45 (48.4)
Specialization time	
0-10 years	14 (15.1)
10-20 years	29 (31.2)
20-30 years	37 (39.8)
Over 30 years	13 (14.0)
Number of breast cancer surgeries before pandemic (weekly)	
1-5	63 (67.7)
6-10	24 (25.8)
More than 10	5 (5.4)
None	1 (1.1)
Number of patients seen in outpatient breast cancer clinics before pandemic (weekly)	
1-10	20 (21.5)
11-20	21 (22.6)
More than 20	52 (55.9)
None	0 (0)

Table 2. Workplace characteristics of the respondents with estimated effect on service provision

Information of Institutions	n (%)
Types of institutions	
State hospital	5 (5.4)
University (Training) hospital	73 (78.6)
Private practice	5 (5.3)
Private hospital	9 (9.6)
Other	1 (1.1)
Area where the institution is located	
Marmara	44 (47.3)
Aegean	11 (11.8)
Black Sea	5 (5.4)
Mediterranean	7 (7.5)
Central Anatolia	19 (20.4)
Eastern Anatolia	3 (3.2)
Southeast Anatolia	4 (4.3)
Impact of COVID-19 of the institution you are working with	
Unaffected: No COVID-19 patients	7 (7.5)
Slightly affected: Few COVID-19 patients are presenting, resources (Ventilator, Personal protective equipment) and intensive care beds available	35 (37.6)
Moderately affected: Many COVID-19 patients presenting, resources (Ventilator, personal protective equipment) and intensive care beds limited	25 (26.9)
Very affected: Crisis situation in which all resources and intensive care beds are directed to COVID-19 patients	26 (28.0)
Having a separate operating room for COVID-19 suspicious or positive patients	
No	32 (34.4)
Yes	61 (65.6)

cases were being seen but that there were available resources and bed space while 27% stated that intensive care beds were limited. Two thirds had access to a designated COVID-19 operating theatre.

Respondents' feelings about relative risk and the precautions they undertook are shown in Table 3, divided by period. In the earlier period, more than forty percent had no contact while only fifteen percent had contact with a known COVID-19 patient. In the later period, the no known contact proportion dropped slightly whilst the known contact proportion increased to more than a quarter. Only a fifth had a personal COVID-19 diagnostic test (serology or imaging) in the first period, which increased to a third in Period 2. At the same time, less than a fifth took prophylaxis in period 1 which only increased marginally to 24% in Period 2 and the proportion reporting taking precautions in theatre did not change between the two periods, being 28% and 30% in Periods 1 and 2, respectively. The biggest concern in both periods was transmitting the virus to family members, reported by sixty percent in both periods, followed by becoming personally infected. In addition, respondents felt patients requiring that general anesthesia posed more risk and, among breast surgery methods, oncoplastic surgery was thought to be riskier in terms of contagion to the surgeon.

Changes in surgical policy are shown in Table 4 for the two periods studied. In both periods, elective (benign) cases were largely stopped during the pandemic, with only cancer and emergency cases being operated. Daily practice was not stopped completely, and breast cancer surgeries were performed. Around half of respondents carried out 1-5 breast conserving and 1-5 mastectomies per week in both periods. This proportion dropped to around 45% of respondents performing between 1-5 oncoplastic operations, while nearly a quarter opted to perform no oncoplastic surgery in either period. Around 60% reported no change in surgical technique in either period but this may have been because in Period 1 and 2, 71% and 75% reported that patients suspected of COVID-19 were not undergoing surgery, Pre-operative COVID-19 testing was not widely performed, with only 3% in Period 1 having either a PCR/serological test, CT thorax or even asked about the presence of symptoms while some centers assumed that all operated patients were positive and acted accordingly. This level of testing only rose to 10% in Period 2. In Period 1 and 2 just over 40% reported no postponements with a further 37% reporting between 1-5 postponed operations per week in Period 1 which reduced to 31% in Period 2. The most common reason in both periods for postponement was patient anxiety.

Finally, respondents were asked about aspects of outpatient clinics, non-surgical therapy and diagnostic testing in the two periods (Table 5). In both periods, breast cancer outpatient services were available in 83% of respondent's centers although the referral rate to OPD decreased by more than 90% in both periods, indeed, benign breast disease outpatient appointments were postponed, if possible, in Period 1 with only 5% reporting continuing as before while a small number sought to refer patients to another center. In Period 2, this pattern had changed significantly ($p= 0.005$) with a fifth now reporting continuing as before while somewhat fewer (77%) were postponing if possible and a similar number sought referral. Most outpatient appointments continued face-to-face while around a quarter used online or telephone communication. Two thirds of outpatient appointments were not taken if patients were suspected of COVID-19, although a small proportion of patients with possible COVID-19 continued to be seen in both periods. For existing patients receiving chemotherapy/radiotherapy/hormonotherapy, there was no disruption, with only 1-2% reporting any disruption for these services in both periods. For adjuvant therapies, there was more disruption, although more than 60% of these services continued as before

Table 3. Respondents' attitudes to perceived risk of COVID-19 and precautions taken during the two pandemic periods

	Period 1 n (%)	Period 2 n (%)	p
Contact with suspicious or positive COVID-19 patient			
No	38 (40.9)	34 (36.6)	0.337
Contact with suspicious patient	21 (22.6)	17 (18.3)	
Contact with COVID-19 positive patient	14 (15.1)	24 (25.8)	
Unknown	20 (21.5)	18 (19.4)	
Had personal COVID-19 testing or imaging			
No	73 (78.5)	62 (66.7)	0.071
Yes	20 (21.5)	31 (33.3)	
Had prophylactic or therapeutic treatment for COVID-19			
No	78 (83.9)	71 (76.3)	0.270
Yes	15 (16.1)	22 (23.7)	
Additional precautions while using surgical cautery or sealing agents during pandemic			
No	67 (72.0)	65 (69.9)	0.747
Yes	26 (28.0)	28 (30.1)	
Surgeons' personal feelings			
I'm worried about being infected with COVID-19			
I am concerned about passing COVID-19 infection to my relatives	22 (23.7)	18 (19.4)	0.711
I am not concerned about becoming infected with COVID-19 or transmission to anyone else with the measures I have taken	56 (60.2)	57 (61.3)	
	15 (16.1)	18 (19.4)	
The risk to the surgeon depending on the type of anesthesia technique in patients with COVID-19			
Local or regional anesthesia	34 (36.6)	30 (32.3)	0.537
General anesthesia	59 (63.4)	63 (67.7)	
Personal evaluation of risk of COVID-19 transmission during breast surgery by method			
Breast conserving surgery	3 (3.2)	3 (3.2)	0.924
Mastectomy	36 (38.7)	33 (35.5)	
Oncoplastic surgery	54 (58.1)	57 (61.3)	

the epidemic. Just under half of the patients newly diagnosed with breast cancer were offered postponement of treatment, and if accepted, the delay was more than three weeks in around 70%. Multidisciplinary breast clinics only continued as normal in 5% of the centers in both periods while there was a shift to video-conferencing for these clinics in around a fifth of centers. Radiological imaging was performed in more than 85% of the centers with reports being available in one week in most. Similarly, biopsies were performed as normal in more than 80% of the centers and most reports were available within two weeks, with less than 10% taking longer than two weeks to report in both periods.

DISCUSSION

The COVID-19 pandemic has swept the globe. The first registered case of COVID-19 was recorded relatively late in Turkey on March 10th, 2020, and the period of rapid change and response from this date until the end of April 2020 is the first Period in this study. From the 1st of May until the end of May, with the reduction in the number of cases and transition to the normalization process, may be considered the period of more rational adjustment and we have designated this Period 2 in the current study. Due to the high rate of infectiousness and positivity and especially because of the high rates of mortality in the co-morbidly ill and the elderly, the Turkish Ministry of Health called for extraordinary caution. All hospitals were required to change their normal practice with some degree of suspension of routine services, including cancer services, occurring. Priority was to be given to emergency cases, including in cancer services. Much disruption occurred to outpatient and surgery provision to protect the patients and those caring for them (6). Certain rules have been introduced for services providing emergency surgery to protect against COVID-19 (4). Due to this situation, there have been disruptions in some branches and slowdowns

Table 4. Changes in breast cancer surgery practice during the two pandemic periods

	Period 1 n (%)	Period 2 n (%)	p
Change in daily surgery practice during pandemic			
Daily practice unchanged compared to before pandemic	5 (5.4)	6 (6.5)	0.219
Elective (benign) cases were stopped, only cancer and emergency cases were operated	62 (66.7)	71 (76.3)	
Elective (benign) and cancer cases were stopped, only emergency cases were operated	13 (14.0)	11 (11.8)	
Daily practice completely stopped	13 (14.0)	5 (5.4)	
If the daily practice was stopped, what was the reason			
Daily practice not stopped	40 (43.0)	45 (48.4)	0.916
Surgeon on administrative leave due to age or comorbidity	1 (1.1)	1 (1.1)	
Surgeon on administrative leave due to flexible work schedule	16 (17.3)	15 (16.1)	
Personal protective equipment unavailable	0 (0)	0 (0)	
Surgeon not performing surgery due to concerns about COVID-19	14 (15.0)	9 (9.7)	
Working at COVID-19 outpatient/service/intensive care surgery	8 (8.6)	9 (9.7)	
Other	14 (15.1)	14 (15.1)	
Breast cancer surgery performed			
No	23 (24.7)	13 (14.0)	0.095
Yes	70 (75.3)	80 (86.0)	
Number of breast conserving surgeries performed			
None	6 (6.5)	5 (5.4)	0.815
1-5	45 (48.4)	49 (52.7)	
6-10	11 (11.8)	17 (18.3)	
More than 10	8 (8.6)	9 (9.7)	
Number of mastectomies performed			
None	12 (12.9)	14 (15.1)	0.850
1-5	47 (50.5)	49 (52.7)	
6-10	8 (8.6)	13 (14.0)	
More than 10	3 (3.2)	4 (4.3)	
Number of oncoplastic surgeries performed			
None	22 (23.7)	23 (24.7)	0.507
1-5	41 (44.1)	42 (45.2)	
6-10	5 (5.4)	10 (10.8)	
More than 10	2 (2.2)	5 (5.4)	
Surgical technical change due to pandemic			
No	53 (57.0)	58 (62.4)	0.794
Yes	17 (18.3)	22 (23.7)	
COVID-19 suspected patients undergoing breast cancer surgery			
No	66 (71.0)	70 (75.3)	0.253
Yes	4 (4.3)	10 (10.8)	
Number of COVID-19 suspected patients undergoing breast cancer surgery			
1-5	4 (4.3)	9 (9.7)	1.000
6-10	0 (0)	1 (1.1)	
More than 10	0 (0)	0 (0)	

Table 4. Changes in breast cancer surgery practice during the two pandemic periods (continue)

	Period 1 n (%)	Period 2 n (%)	p
Preoperative patient evaluation for COVID-19			
All routinely tested (PCR/Fast antibody); result available prior to operation	0 (0)	3 (3.2)	0.853
All had thoracic tomography; result available prior to operation	1 (1.1)	3 (3.2)	
Patients were asked about presence of symptoms (fever, cough, dyspnea) only	1 (1.1)	2 (2.2)	
Additional evaluation was not subject to the only symptomatic in the process was intervened	0 (0)	0 (0)	
All patients assumed positive and appropriate precautions taken	2 (2.2)	2 (2.2)	
Was a separate COVID-19 patient consent obtained prior to surgery?			
No	1 (1.1)	2 (2.2)	1.000
Yes	3 (3.2)	8 (8.6)	
If no breast cancer surgery performed, what was the number of breast cancer patients postponed?			0.857
None	41 (44.1)	43 (46.2)	
1-5	34 (36.6)	29 (31.2)	
6-10	12 (12.9)	13 (14.0)	
More than 10	6 (6.5)	8 (8.6)	
Causes of deferral for breast cancer surgeries if forced to postpone			
Patient's anxiety or displacement	39 (42.1)	43 (46.5)	0.954
Physician's anxiety or displacement	5 (5.4)	4 (4.3)	
The institution does not allow	16 (17.3)	16 (17.3)	
Physician's decision according to breast cancer subtypes	20 (21.5)	18 (19.4)	
Lack of information on what safe surgery will be like in COVID-19 Pandemic	9 (9.7)	10 (10.8)	
Lack of adequate equipment for hospital anesthesia or postoperative care	4 (4.3)	2 (2.2)	

in health services. Although measures are taken and certain recommendations are made to prevent patients from being victims, it is thought that the biggest suffering is in cancer cases (5).

The disruption caused by the COVID-19 pandemic has also affected breast cancer patients and the services treating them (6). The aim of this survey was to assess the situation affecting breast cancer surgery and ancillary services in Turkey. Members of the Turkish Senology Academy (SENATURK) were approached for the disruption they had experienced and their opinions on the effects on services. Ninety-three breast surgeons from across the country responded to the online questionnaire. The responses were not homogeneous, and most respondents were working in university hospitals in the Marmara region of Northwest Turkey, with relatively low rates of population infection with COVID-19.

In this group with high surgical experience, it has been observed that there is generally no contact with COVID-19 positive patients, surgeons do not need COVID-19 tests or imaging, and they do not use COVID-19 treatment for prophylactic or therapeutic purposes. When these two periods are evaluated, these data do not change. It has been revealed that surgical masks are used in the forefront in practice outside the operating room, while protective glasses, barrier, surgical mask and N95 masks are preferred more frequently in practice in the operating room. It has been observed that these measures taken are in line with those recommended in the literature (5). Again, in this group, additional measures were not taken for cautery or sealing devices. There was no difference between the two periods. It has been revealed that most of these surgeons work with anxiety to bring the COVID-19 infection to their relatives. This concern did not change in Period 2, when more information about COVID-19 was acquired, prevention measures increased, and the number of diseases decreased. The idea that surgeries performed under general anesthesia are riskier in terms of COVID-19 than local or regional anesthesia, and especially among breast surgery types, surgeries with oncoplastic breast

Table 5. The availability of breast cancer outpatient and diagnostic services

	Period 1 n (%)	Period 2 n (%)	p
Has the rate of referral to breast cancer outpatients been deliberately decreased			
No	6 (6.5)	8 (8.6)	0.782
Yes	87 (93.5)	85 (91.4)	
Breast cancer outpatient clinic service available?			
No	16 (17.2)	16 (17.2)	1.000
Yes	77 (82.8)	77 (82.8)	
Approach to benign breast diseases during pandemic			
No change from pre-pandemic period	5 (5.4)	19 (20.4)	0.005
Patients have been postponed, if possible	85 (91.4)	72 (77.4)	
Routed to different center	3 (3.2)	2 (2.2)	
Number of outpatients for breast cancer seen per week			
None	1 (1.1)	0 (0)	0.123
1-5	31 (33.3)	22 (23.7)	
6-10	24 (25.8)	22 (23.7)	
More than 10	21 (22.6)	33 (35.5)	
Breast cancer outpatient clinic contact type			
Face-to-face	54 (58.1)	52 (55.9)	0.824
Online	14 (15.1)	17 (18.4)	
Telephone	9 (9.7)	8 (8,6)	
Have you examined COVID-19 suspected patients in outpatient clinic			
No	66 (71.0)	62 (66.7)	0.495
Yes	11 (11.8)	15 (16.1)	
Number of suspected patients with COVID-19 examined per week			
1-5	9 (9.7)	15 (16.1)	0.169
6-10	2 (2.2)	0 (0)	
More than 10	0 (0)	0 (0)	
Number of breast cancer patients sent for non-surgical treatment during this period			
None	28 (30.1)	22 (23.7)	0.677
1-5	39 (41.9)	42 (45.2)	
6-10	21 (22.6)	21 (22.6)	
More than 10	5 (5.4)	8 (8.6)	
Examination request from patients operated before pandemic			
None	2 (2.2)	3 (3.3)	0.877
Yes	79 (85.0)	77 (82.8)	
The patient came, but they weren't accepted	2 (2.2)	1 (1.1)	
Internet or phone interview	10 (10.8)	12 (12.9)	
Chemotherapy/radiotherapy/hormonotherapy adjustment status for patients undergoing pre-pandemic surgery			
Not performed	1 (1.1)	2 (2.2)	1.000
Performed	92 (98.9)	91 (97.8)	

Table 5. The availability of breast cancer outpatient and diagnostic services (continue)

	Period 1 n (%)	Period 2 n (%)	p
Number of patients whose adjuvant treatment was disrupted			
None	56 (60.2)	58 (62.4)	0.316
1-5	29 (31.2)	22 (23.7)	
6-10	5 (5.4)	11 (11.8)	
More than 10	3 (3.2)	2 (2.2)	
Patient diagnosed with breast cancer but offered postponement			
No	48 (51.6)	51 (54.8)	0.769
Yes	45 (48.4)	42 (45.2)	
Postponement delay of patients diagnosed with breast cancer			
1-2 weeks	25 (26.9)	31 (33.3)	0.600
3-4 weeks	37 (39.8)	32 (34.4)	
More than 4 weeks	31 (33.3)	30 (32.3)	
Multidisciplinary breast council meetings held?			
No	65 (69.9)	61 (65.6)	0.530
Yes	28 (30.1)	32 (34.4)	
If the multidisciplinary breast council held, how did it meet?			
Scheduled but canceled	2 (2.2)	1 (1.1)	0.863
As usual	5 (5.4)	5 (5.4)	
Reducing the number of participants	3 (3.2)	5 (5.4)	
Video-conferencing or online	18 (19.4)	21 (22.6)	
Radiological imaging during pandemic period			
Not performed	14 (15.1)	10 (10.8)	0.530
Performed	79 (84.9)	82 (89.2)	
Time to final report of radiological images			
1-7 days	67 (72.0)	64 (68.8)	0.264
8-15 days	8 (8.6)	16 (17.2)	
More than 15 days	4 (4.3)	3 (3.2)	
Biopsy during pandemic period			
Not performed	17 (18.3)	12 (12.9)	0.419
Performed	76 (81.7)	81 (87.1)	
Reporting time of biopsy results			
1-7 days	37 (39.8)	39 (41.9)	0.904
8-15 days	31 (33.3)	35 (37.6)	
More than 15 days	8 (8.6)	7 (7.5)	

surgery techniques may have a higher risk in terms of COVID-19 transmission. Results were followed in parallel in both periods. Again, this information was found to be consistent in the light of the literature (3).

In line with the data obtained, the changes in breast cancer surgery preferences during this period were evaluated. In both periods, elective (benign) cases were stopped, only cancer and emergency cases were taken into surgery, and daily practice was not stopped. Contrary to what is thought, this shows that in the COVID-19 pandemic, it does not cause disruption in the surgical treatment of cancer patients. This situation was the same in terms of breast cancer surgeries, and breast cancer surgeries were not interrupted, especially in health institutions, the majority of which were university hospitals. It is seen from the data that such a disruption did not occur even in the 1st Period when COVID-19 was most active.

As breast cancer surgery, breast conserving surgery, mastectomy and oncoplastic surgery preferences were at the same level on average in both periods, they did not have superiority to each other in preference, and surgical techniques were not changed due to pandemic. It wasobserved that especially in patients whose neoadjuvant treatment was completed, the op-

erations that were the continuation of the treatment were performed primarily and there was no setback. Although the majority of patients who were operated on for breast cancer were COVID-19 negative, a small number of patients with COVID-19 positive breast cancer was operated and received special consent from these patients. An increase in the rate of COVID-19 positive patients was observed, especially in Period 2. In this Period 2, the increase in the measures taken against the disease and the decrease of fear shows the result that the priority of the treatment of cancer patients is important. Again, although the number of COVID-19 positive breast cancer surgeries is low, it is understood from the data that all patients were taken into surgery by taking precautions as if they were COVID-19 positive. Patients who needed breast cancer surgery were mostly not postponed, and a small number of patients were postponed due to the anxiety of the patient. This is similar in both periods.

In addition to evaluating the surgical status of breast cancer patients, the outpatient clinic and diagnostic situations during this period were also evaluated. Although there was a significant decrease in the rates of breast cancer referrals to outpatient clinics, there was no disruption in outpatient clinic services, but patients who applied for benign breast diseases were delayed as much as possible. When both periods were examined, this situation did not change, but benign breast patients were delayed less in Period 2. While in the 1st Period, an average of 5 breast cancer patients per week were given outpatient services per surgeon, this number increased, and the average exceeded 10 patients in Period 2. The majority of this was in the form of face-to-face examination and there was no difference in both periods. Most breast cancer outpatients have been found to be COVID-19 negative. At the end of the examination, no disruption was observed in both periods in terms of sending to surgical treatment.

Another important issue is the situation in neoadjuvant or adjuvant treatments of breast cancer patients during this period. In this regard, guidelines have been determined for the COVID-19 period and the continuity of treatment has been attempted (8, 9). It has been essential that patients with priority should receive their treatment in isolated environments. In our evaluation in our country, there was a significant demand by patients for the control examinations of patients who had pre-pandemic surgery, that the follow-up treatments such as chemotherapy/radiotherapy/hormonotherapy could be adjusted without any problems, and adjuvant treatments were mostly not interrupted in both periods.

The rate of delaying the treatment of breast cancer in both periods was equal, the patients who were delayed were postponed for an average of 4 weeks, and the patients accepted this delay by expressing their concerns.

Another disruption in diagnostic services is that multidisciplinary breast councils are mostly not held in both periods. Video conference or online communication methods were preferred in the group. In both periods, the radiological imaging of breast cancer patients was mostly performed, there was no decrease in terms of imaging technique, and the results were obtained within an average of 7 days. Apart from the pandemic, there is no setback in this respect, considering that the report is issued in an average of 7 days in institutions. Again, it was seen that breast cancer patients could be biopsied for pathological diagnosis and reported within an average of 7 days, and since there was no difference in comparison with normal time, the COVID-19 pandemic did not cause disruption in the pathological diagnostic biopsies of breast cancer patients. These results were parallel for both periods.

As a result, as in the whole world except Turkey, it has also experienced serious interruptions of taking serious measures to fight pandemics tried COVID-19 due to urgent and priority health care services in cancer patients. According to our study, breast cancer patients did not experience interruptions in terms of outpatient clinic service, surgery service, postoperative adjuvant treatment and control services due to these pauses and disruptions. Except for less multidisciplinary breast councils, there was no delay in radiological and pathological diagnoses. Especially when considered as Period 1 between March 11, 2020, and April 30, 2020 and Period 2 between May 1, 2020 and May 31, 2020, the number of breast cancer surgeries increased in Period 2, and more COVID-19 positive breast cancer patients had been operated in the Period 2. Benign breast patients were delayed less frequently in the Period 2. In the statistical analysis performed between the two groups, it was found that only a significant difference was in the number of outpatients with benign breasts.

With sufficient awareness about the pandemic and with the measures of institutions, it is concluded breast cancer during the period of active pandemic in the terms of service to patients between March 11, 2020, through May 31, 2020 passed without a hitch in Turkey.

Acknowledgments

We thank to Jeremy Jones for revising the English language of the paper and thank to Canan Baydemir for her help with statistical analyses.

Ethics Committee Approval: This study was obtained from Kocaeli University Non-Invasive Clinical Research Ethics Committee (Date: 03.08.2020, No: 2020/236.

Peer-review: Externally peer-reviewed.

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

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

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2021; 37 (3): 222-231

Türkiye'de COVID-19 pandemisinin yaşandığı iki aktif dönemde, meme kanserinin tanı, tedavi ve takibinde yaşanan değişimler ve aksamalar

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ÖZET

Giriş ve Amaç: Tüm dünyada hızla yayılarak kısa sürede pandemi haline gelen COVID-19 hastalığı sebebiyle her alanda olduğu gibi, özellikle sağlık alanında da rutinler bozularak, verilen sağlık hizmetlerinde önemli değişiklikler yapılamasına karar verilmiştir. Bu süreçte özellikle mevcut sağlık kurumlarında verilen rutin sağlık hizmetlerinde COVID-19 ile savaş sebebiyle belirli kısıtlamalara gidilmiştir. Yapılacak cerrahilerin öncesi, esnası ve sonrası için uyulması önerilen kurallar ortaya koyulmuştur. Meme kanseri tanı, tedavi ve takibi için verilen sağlık hizmetleri de bu sebeple belli değişimlere uğramıştır. Önceliği olan hastaların tanı, tedavi ve takibi gündeme gelmiştir. Bu çalışmada Türkiye'de COVID-19'un aktif olarak yaşandığı 11 Mart 2020 ile 31 Mayıs 2020 arasındaki süreç, 2 döneme ayrılarak, meme kanseri tanı, tedavi ve takibi, hizmet veren cerrahların ve kurumların etkilenme süreci ile birlikte değerlendirilmiştir.

Gereç ve Yöntem: SENATURK (Türkiye Senoloji Akademisi)'ne kayıtlı, Türkiye'de meme kanseri tedavisi ile uğraşan cerrahlara çevrimiçi yollarla ulaşılarak elektronik olarak hazırlanan değerlendirme formu iletilmiş ve alınan cevaplar değerlendirilmiştir.

Bulgular: 93 katılımcının verileri değerlendirilmiştir. Multidisipliner meme konseylerinin daha az yapılması dışında, radyolojik ve patolojik tanılarda gecikme olmamıştır. 2. dönemde meme kanseri ameliyatı sayısı artmıştır ve ameliyat edilen COVID-19 pozitif meme kanseri hasta sayısı artmıştır. 2. dönemde benign meme hastalıkları açısından daha az gecikme kaydedilmiştir. Her iki grupta ayakta tedavi gören benign meme hastalarının sayısında sadece anlamlı farkın olduğu bulunmuştur.

Sonuç: Cerrahların COVID-19 pandemisi hakkında yeterli bilinçte olması hem kurumsal hem de kişisel önlemler alınmasıyla meme kanseri hastalarına hizmet açısından COVID-19 pandemisinin 11 Mart 2020 ile 31 Mayıs 2020 arasındaki aktif pandemi döneminde Türkiye'de genel olarak aksama olmadan hizmet verilmeye çalışıldığı sonucuna varılmıştır.

Anahtar Kelimeler: Meme kanseri, COVID-19, meme sağlığı, meme cerrahisi, aksama

DOİ: 10.47717/turkjsurg.2021.5069

ORIGINAL ARTICLE
Turk J Surg 2021; 37 (3): 232-241

The comparison of analgesic efficacy between ultrasound-guided continuous thoracic paravertebral block and continuous thoracic epidural block using bupivacaine - fentanyl in patients undergoing lung surgery: A prospective, randomized, controlled trial

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ABSTRACT

Objective: This study aimed to compare the efficacy and the safety of ultrasound-guided continuous thoracic paravertebral block (CTPB) to the continuous thoracic epidural block (CTEB) for pain relief in patients undergoing lung surgery.

Material and Methods: Our study included 102 patients after lung surgery at the 74 Central Hospital from 9/2013 to 12/2017. Patients were divided into 2 groups: CTPB group (n= 51) and CTEB group (n= 51). The primary outcomes were the Visual Analogue Scale (VAS) scores when patients were at rest (V_R) and movement (V_M), the total used dosage of bupivacaine - fentanyl after surgery, plasma glucose, and cortisol levels, additional doses of morphine. Adverse reactions were recorded during the study. The study was approved by the Ethics Committee of the 74 Central Hospital. All participants provided their informed consent.

Results: There were no significant differences between CTPB and CTEB groups in terms of the V_R and the V_M, total used doses of bupivacaine - fentanyl after 72-hours of surgery (p> 0.05), the increased plasma glucose, and plasma cortisol (p> 0.05), and the additional doses of morphine. The percent of patients in the CTPB group undergoing adverse reactions in the circular system and the respiratory system was lower than in the CTEB group. Adverse reactions included vascular puncture, urinary retention, and itch.

Conclusion: Ultrasound-guided CTPB is an effective intervention of pain relief after lung surgery. Its analgesic efficacy is comparable to CTEB. Also, this method had fewer adverse reactions in circulation and respiration compared to the CTEB.

Keywords: Paravertebral block, analgesia, lung surgery, epidural block, postoperative pain

INTRODUCTION

Lung surgery includes the removal of a lung, lobes of a lung, bronchopulmonary segments, or any part of the lung, or lung decortication. Lung surgery affects the circular and respiratory systems that are essential organs in the body, leading to dangerous complications. Pain causes shallow breathing and limited cough resulting in the impairments of respiratory functions, the stagnation of secretions, collapsed lung, hypoxemia, hypercapnia, and respiratory failure. They increase the risk of the reintubation of the endotracheal tube and seriously affect the patients' mental health. Taken them together, pain relief for patients after lung surgery is essential for their recovery of regular movements and their satisfaction (1,2).

There is a variety of studied treatments to reduce pain after general surgery or lung surgery including pain prophylaxis before surgery, additional treatments of morphine analogues or non-steroids anti-inflammatory drugs (NSAIDs), or nerve block. Currently, there are two latest pain management technologies, including patient-controlled analgesia (PCA) and continuous catheter-infused anesthetic into the epidural space, operative locations, and the plexus. Amongst them, thoracic epidural block (TEP) is possibly the most optimal technique for pain management after cardiothoracic surgeries. Nevertheless, this technique is contraindicated for patients having coagulopathy. It also leads to some adverse reactions, namely hypotension and injured nerves (1,3,4).

Cite this article as: Trung TT, Khoa DV, Dong TV. The comparison of analgesic efficacy between ultrasound-guided continuous thoracic paravertebral block and continuous thoracic epidural block using bupivacaine - fentanyl in patients undergoing lung surgery: A prospective, randomized, controlled trial. Turk J Surg 2021; 37 (3): 232-241.

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Received: 19.10.2020
Accepted: 04.04.2021
Available Online Date: 28.09.2021

DOI: 10.47717/turkjsurg.2021.5053

Recently, thoracic paravertebral block (TPB) is likely to be accepted for the replacement of TEB which is commonly a "golden standard" for pain management after cardiothoracic surgeries. Some advantages of TPB are the similar efficacy to relieve pain compared to TEB, a low rate of complications and a success higher rate supported by ultrasound. These features make TPB more appealing to clinical practitioners, and they need more evidence to reinforce the potential of the alternative method in various surgeries.

A disadvantage of preliminary TPB is the difficulty in the determination of loss-of-resistance and the "pop" feeling, and the detection of anatomical points. In recent decades, people have used ultrasound when applying TPB. The results have indicated that the technique helps practitioners realize the anatomical points, the directions of the needle, and the spread of the anesthetic (5, 6). Therefore, ultrasound-guided TPB is attracting anesthesiologists and is increasingly applied. However, each technique has its benefits and disadvantages (7-9).

Over the world, there is an increase in studies relating to TPB. However, these studies have reported inconsistent method, and various results are still debated (10). In Vietnam, there are only several studies relating to the TPB. Also, there is no study of the continuous thoracic paravertebral block (CTPB) as well as the application of ultrasound in pain management after lung surgeries. Thus, we conducted this study with the aim of comparing the analgesic efficacy after lung surgery between the ultrasound-guided CTPB and the continuous thoracic epidural block (CTEB) using 0.125% bupivacaine - fentanyl 2 µg/mL and evaluating the undesirable effects caused by these treatments.

MATERIAL and METHODS

Study Design

This is a prospective, parallel randomized (1:1), controlled clinical trial. The study report followed CONSORT guideline (Table S1).

The sample size of each group was calculated by the following formula previously reported (11), for the continuous variables and two controlled equivalent groups as follows:

$$n = \frac{2C}{(ES)^2}, \text{ where:}$$

C: determined from α and β (the probability that a test statistic giving $p < 0.05$)

For the null hypothesis, we chose $\alpha = 0.05$. For the alternative hypothesis, we chose $\beta = 0.1$. The constant C corresponding to the α and β values retrieved from a standard table was = 10.5. We chose the significant difference of Visual Analogue Scale (VAS) at rest between two groups by 0.59 ($p = 0.104$) with standard deviation = 0.91, followed the report of Sagiroglu et al. (12). Therefore, we had ES = 0.648. The sample size of each group was estimated at 50.1. Finally, we recruited 51 patients in each group.

The participants who met the selection criteria were randomly divided into two groups, by the simple random sampling method using function RAND in excel. The random allocation sequence was conducted by an author who did not participate in the surgical procedure. Patients were divided into two groups, receiving postoperative analgesic regimen of bupivacaine 0.125% - fentanyl 2 µg/mL via either ultrasound-guided CTPB (n= 51) or CTEB (n= 51).

The science and ethics committee of biomedical studies of 74 Central Hospital approved this study (No. 458/GCN-BV74TW). All patients provided their written informed consent before being included in this study. The study was concordant with the Declaration of Helsinki.

Patients Selection

The study was performed at the 74 Central Hospital, from 09/2013 to 12/2017, for patients who received postoperative analgesic regimen after lung surgery or lung decortication.

The inclusion criteria were patients who underwent elective lung surgery opening one-side, age ≥ 16, agreed to cooperate with the physicians for the postoperative analgesic regimen, and American Society of Anesthesiologist (ASA) class I, II (13). We excluded patients who disagreed to join the study, historically had an allergy to anesthetic drugs, currently had psychological problems, or had a local infection at the operation site. Data of the patients were excluded from our analysis if patients had postoperative complications, were on a ventilator after surgery > 4 hours, needed the reoperation, or wanted to discontinue the study.

Procedures

Patients were examined and explained the protocol before the anesthesia as the standard. All patients in this study were anesthetized with endotracheal intubation following a standard guideline using midazolam 0.04 mg/kg, fentanyl 3 µg/kg, followed by propofol 2 mg/kg and rocuronium 0.8 mg/kg, intubated with the suitable endobronchial tube, maintained with a closed circuit and low flow systems using isoflurane. Doses of analgesic medicines and isoflurane were adjusted by the scores of systolic blood pressure (P), heart rate (R), sweating (S), tear (T) which were previously reported (13). When PRST ≥ 3, an additional intravenous injection of fentanyl 50 µg was required. The relaxant medicine 0.2 mg/kg rocuronium repeatedly injected if train-of-four (TOF) ≥ 2 (appeared the second response chain of adductor pollicis muscle) to ensure complete muscle relaxation.

After dermatomal block distribution, the ultrasound-guided CTPB or CTEB procedure was performed. We used the transduc-

Table S1. Consort checklist of the study's report

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract	1a	Identification as a randomized trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions	1
Introduction			
Background and objectives	2a	Scientific background and explanation of rational	2-3
	2b	Specific objectives or hypotheses	3
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	3
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	Not applied
Participants	4a	Eligibility criteria for participants	4
	4b	Settings and locations where the data were collected	4
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	5
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	6
	6b	Any changes to trial outcomes after the trial commenced, with reasons	Not applied
Sample size	7a	How sample size was determined	3-4
	7b	When applicable, explanation of any interim analyses and stopping guidelines	Not applied
Randomization			
Sequence generation	8a	Method used to generate the random allocation sequence	4
	8b	Type of randomization; details of any restriction (such as blocking and block size)	Not applied
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	4
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions.	4
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	Not applied
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	6-7
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	Not applied
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome	7
	13b	For each group, losses and exclusions after randomization, together with reasons	Not applied
Recruitment	14a	Dates defining the periods of recruitment and follow-up	7
	14b	Why the trial ended or was stopped	Not applied
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	7

Table S1. Consort checklist of the study's report (continued)

Section/Topic	Item No	Checklist item	Reported on page No
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	7-9
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	Not applied
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Not applied
Harms	19	All important harms or unintended effects in each group	9
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	13-14
Generalizability	21	Generalizability (external validity, applicability) of the trial findings	Not applied
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	Not applied
Other information			
Registration	23	Registration number and name of trial registry	Not applied
Protocol	24	Where the full trial protocol can be accessed, if available	Not applied
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	14

er of a high-frequency ultrasound transducer linear array (frequencies of 8-15 MHz) to detect thoracic paravertebral space. A needle (Tuohy 18G) was inserted into this space. In the CTPB group, we put a catheter into the thoracic paravertebral space 2 - 6 cm of depth towards the top of patients. Meanwhile, a catheter thoracic epidural was put for the CTEB group using the loss-of-resistance technique. The locations where the transducer was put (T4-5, T5-6, or T7-8) were accordant to the locations of the incision.

Pain management after surgery was conducted if the patients were conscious, removed the endotracheal tube, had a heart rate of 60-90 beats/minute, maximal systolic blood pressure 90-140 mmHg, $SpO_2 \geq 92\%$, and VAS score ≥ 4. Patients were given a mixture of 0.125% bupivacaine and fentanyl 2 µg/mL, prepared by 0.5% bupivacaine hydrochloride (Laboratoire Aguettant, France) and 5% fentanyl (Rotex, Germany), through a catheter. A load-dose of the mixture was given, then a continuous infusion started with the concentration of 0.1 mL/kg/hour for the first 24-hours, 0.09 mL/kg/hour for the second 24-hours, and 0.08 mL/kg/h during 48-72-hours after the surgery.

If pain relief was poor or ineffective, an additional PCA intravenous morphine was given, set as following : bolus 1 mg/mL, lockout time : 15 minutes, maintain dose: not applicable, 4-hours dose limit: 10 mg. The catheter was removed when we recorded data 72 hours after the analgesic regimen. If the patients had persistent pain after the catheter removal, PCA intravenous morphine was continued as presented above.

Study Outcomes and Measurements

Our primary outcomes included the VAS score at the rest (V_R) and VAS score at the movement (VM), at 0-, 15-, 30-minutes, and 1-, 2-, 4-, 6-, 12-, 24-, 48-, 72-hours after the analgesic regimen; the additional consumption of morphine in the case patients ordered it to reduce their pain; the consumption of 0.125% bupivacaine - fentanyl 2 µg/mL; the levels of blood glucose and cortisol before the surgery, before the pain regimen, at day-1, day-2, day-3 after the surgery; the forced vital capacity (FVC), the forced expiratory volume in one second (FEV_1) and the peak expiratory flow (PEF) before the surgery, at the day-1, day-2, day-3 after the surgery. VAS score at rest was defined as the VAS score measured when patients relaxed. VAS score at the movement was defined as the VAS score measured when the patients coughed. The second outcome was the undesirable effects relating to the anesthetic technique, anesthetic medicines, and morphine analogues.

VAS score was assessed to measure the pain degrees of patients. Patients chose the best suitable images for their pain which were concordant with numeric pain degrees, where 0 = no pain, 1 - 3 = mild pain, 4 - 6 = moderate pain, 7 - 8 = severe pain, 9 - 10 = worst pain.

Statistical Analysis

The collected data was analyzed using SPSS software (version 16, SPSS Inc., USA). The quantitative variables are expressed as mean ± SD. The categorical variables were expressed as percent

(%). The differences of categorical variables by groups were assessed by $\chi 2$. The means of quantitative variables between before and after the intervention across each group were compared by paired student's t-test. The differences in means between the two groups were analyzed by independent student's t-test. The differences were statistical significance if $p< 0.05$.

RESULTS

The study was performed from 09/2013 to 12/2017. The patients in this study were enrolled as shown in Figure 1. No patients dropped out of our study. Data of all patients were included in the analysis. The characteristics relating to gender, average ages, height, weight, body mass index (BMI), and ASA score were insignificantly different ($p> 0.05$) (Table 1).

In our study, we saw insignificant differences of surgical procedure ($p= 0.687$), incision ($p= 0.084$), length of surgical skin incision ($p= 0.851$), total dose of bupivacaine ($p= 0.356$) and fentanyl between the two groups ($p= 0.356$) (Table 2). Over half of patients in each group underwent lung decortication (56.9% and 60.8% in the CTEB group and CTPB group, respectively). Lateral thoracotomy was more popular, with 98% in the CTEB group and 88.2% in the CTPB group.

After surgery, patients in both groups mainly suffered from moderate pain with the V_R at the 0-hour by 6.9 ± 1.4 and 6.5 ± 1.2, in the CTPB group and CTEB group, respectively. When they had any movement, the pain level was severe with the V_M at this time point in the CTPB group and CTEB group by 8.0 ± 1.2 and 7.8 ± 1.1, respectively. After 15 minutes of the pain relief regime, V_R strongly decreased from 6.9 ± 1.4 to 3.5 ± 1.0 in the CTPB group, and from 6.5 ± 1.2 to 3.5 ± 0.9 in the CTEB group. Similarly, patients only suffered from moderate pain instead of severe pain after 15 minutes of the regime when they had movements (V_R were 4.8 ± 0.9 and 4.4 ± 0.9). The pain levels steadily reduced across time points in both groups when they were at rest or movement. Patients only had mild pain at 72-hours after the regime in both groups. VAS scores between the two groups were not statistically different at each time point (Table 3).

The percent of patients who additionally needed PCA intravenous morphine after their surgery was 19.6% and 13.7% in the CTPB group and CTEB group, respectively, which were also not statistically different ($p> 0.05$). The total dose of morphine consumed by patients during 72 hours after surgery was 10.1 ± 6.6 mg (CTPB group) and 8.7 ± 5.2 mg (CTEB group). There was a similarity of the times patients asked for PCA (13.9 ± 8.0 vs 14.4 ± 5.1) and the times of no pain relief control between two groups (3.8 ± 2.6 vs 5.7 ± 3.6).

Before the surgery, blood glucose level was not different between the two groups ($p= 0.410$). These levels hit a peak in both groups, by 8.5 ± 2.2 mmol/l and 8.5 ± 3.0 mmol/l before the analgesic regime, then gradually decreased afterward. However, blood glucose level of patients in the CTEB group returned to

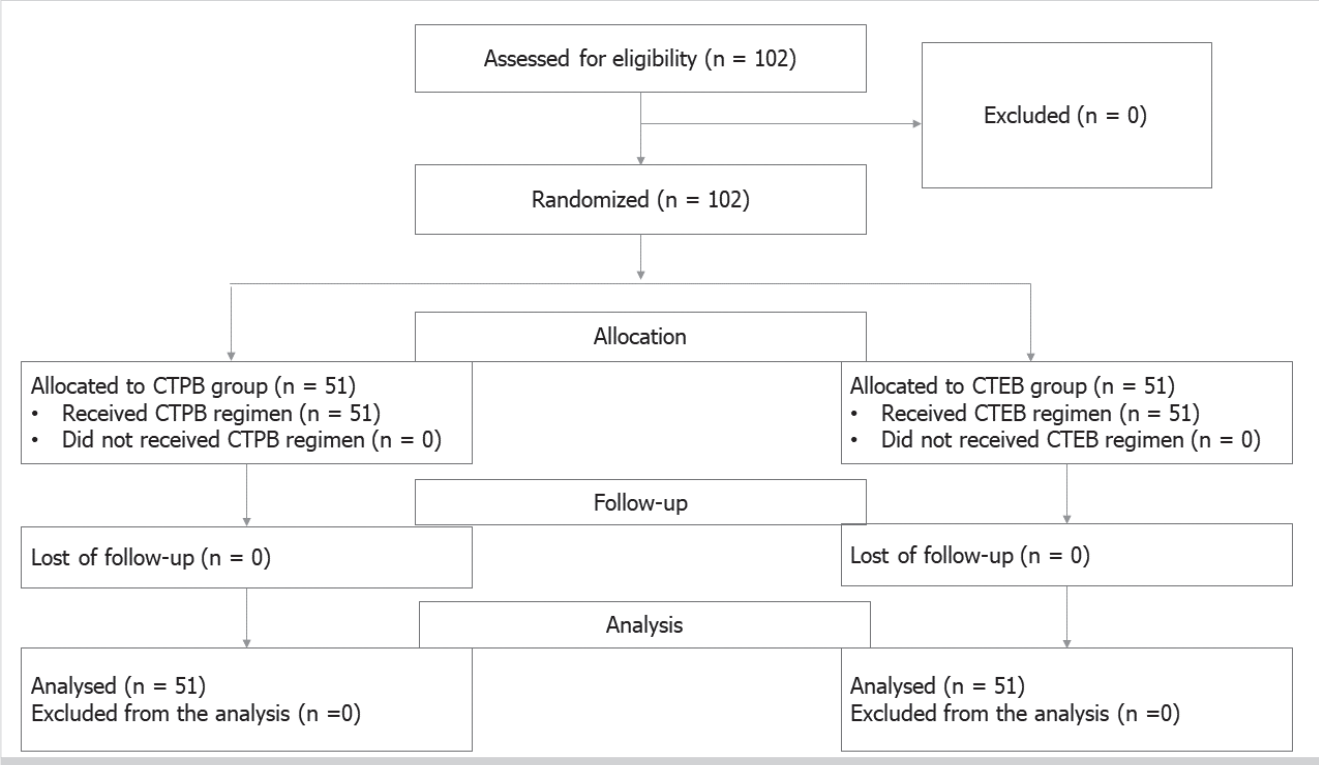

Figure 1. Patients enrollments followed CONSORT flow diagram.

Table 1. The demographic and surgical characteristics of enrolled patients in two groups

	CTPB (n= 51)	CTEB (n= 51)	p
Age (years)	48.8 ± 16.2	45.0 ± 13.5	0.205
Height (cm)	161.8 ±7.1	163.8 ± 6.3	0.135
Weight (kg)	51.0 ± 8.8	52.68 ± 8.8	0.354
BMI (kg/m^2)	19.4 ± 2.8	19.6 ± 2.7	0.833
Male (n, %)	44 (86.3%)	46 (90.2%)	0.539
Female (n, %)	7 (13.7%)	5 (9.8%)	
ASA score			
I (n, %)	7 (13.7%)	14 (27.5%)	0.087
II (n, %)	44 (86.3%)	37 (72.5%)	
Surgical procedure			
Lung removal (n, %)	22 (43.1%)	20 (39.2%)	0.687
Lung decortication (n, %)	29 (56.9%)	31 (60.8%)	
Incision			
Lateral thoracotomy (n, %)	47 (92.2%)	45 (82.2%)	0.084
Posterolateral thoracotomy (n, %)	4 (7.8%)	6 (11.8%)	0.851
Length of surgical skin incision (cm)	24.9 ± 4.2	25.1 ± 4.2	0.353

ASA: American Society of Anesthesiologist, BMI: Body mass index. The data were expressed as mean ± SD.

the normal range at the second postoperative date, which was earlier than patients in the CTPB group (at the third postoperative date). However, blood glucose levels were not significantly different between the two groups (Table 2). A similar trend was seen for blood cortisol levels. Except for a clear difference of blood cortisol level at the first postoperative date between the two groups (p= 0.021), this figure before the surgery and at other time points saw insignificant differences (p > 0.05). Nevertheless, at the third postoperative day, these levels in both groups were still remarkably higher than that before the surgery.

Before the surgery, ventilatory lung functions were similar between the two groups (Table 2). Nevertheless, patients in the CTPB group showed earlier recovery compared to the CTEB group, as shown by the visibly higher values of FVC, FEV_1, and PEF of patients receiving CTPB regime compared to patients receiving CTEP regime.

Regarding undesirable effects relating to the anesthetic technique, the percentages of vascular puncture and pain at the injection site were lower in the CTPB group compared to the CTEB group, although they were not significantly different. Our study did not record any case of pneumothorax, catheter occlusions, or infection at the injection site in both groups.

The percentage of hypotensive cases in the CTPB group were significantly less than in the CTEB group (3.9% vs 17.6%, p= 0.026). Slow breathing and motor block in both legs accounted for 9.8% and 11.8% in the CTEB group, while no case was reported in the CTPB group.

The percentage of side effects relating to morphine analogues such as vomit, nausea, urinary retention, and itch was not statistically different between both groups, although there were lower frequencies in the CTPB group compared to the CTEB group.

DISCUSSION

Our findings showed that patients in the CTEB and the CTPB group had a significant reduction of pain level after 15 minutes of treating with pain regime, which meant both procedures were effective to relieve pain. The pain levels of patients in both groups were comparable in all time-points indicating that these procedures had comparable efficacy in the reduction of pain. Interestingly, patients in the CTPB group had fewer complications compared to patients in the CTEB group.

Although there was a randomized prospective trial in 2011 showing that TPB appeared to control pain well at rest and cough than TEB, other findings showed that the differences were not remarkably different (14). A systematic review and meta-analysis previously showed that the analgesic efficacy 48 hours after thoracotomy was comparable between TPB and TEB (15). Messina et al. (2009) have also reported that the pain relief was still not much different at 72 hours after surgery, as shown by the VAS scores at rest between the two groups. Moreover, the VAS scores after coughing were similar in the 24-hour period after surgery as the report of Sagiroglu et al. (2013). Our study increased the power of the comparable efficacy between two techniques, as we found out that the VAS scores at rest or at movement at all time-points during 72 hours after surgery were not statistically different. On the other hand, our results

Table 2. Response to stress and ventilatory functions of the patients in two groups

	Before the surgery	The first postoperative date	The second postoperative date	The third postoperative date
Blood glucose (mmol/l)				
CTPB group (n= 51)	5.7 ± 1.0	7.7 ± 2.4*	6.7 ± 1.4*	6.3 ± 2.4
CTEB group (n= 51)	6.1 ± 2.7	7.4± 3.1*	6.3± 1.3	5.9 ± 1.3
p	0.410	0.525	0.102	0.325
Blood cortisol (µg/dl)				
CTPB group (n= 51)	11.3 ± 6.4	19.6 ± 6.6*	17.1 ± 5.4*	15.6 ± 4.8*
CTEB group (n= 51)	12.0 ± 5.7	22.6 ± 6.1*	17.5 ± 5.3*	14.9 ± 5.1*
p	0.521	0.021	0.732	0.503
FVC (l)				
CTPB group (n= 51)	2.78 ± 0.94	1.33 ± 0.31*	1.83 ± 0.56*	2.46 ± 0.67**
CTEB group (n= 51)	2.88 ± 0.73	1.00 ± 0.39*	1.50 ± 0.44*	2.18 ± 0.6*
p	0.574	0.000	0.001	0.032
FEV_1 (l)				
CTPB group (n= 51)	2.27 ± 0.71	0.68 ± 0.22*	1.2 ± 0.34*	1.86 ± 0.60*
CTEB group (n= 51)	2.42 ± 0.61	0.62 ± 0.20*	0.94 ± 0.33*	1.71 ± 0.55*
p	0.244	0.117	0.000	0.193
Gaensler (%)				
CTPB group (n= 51)	82.5 ± 12.54	52.7 ±17.42*	67.9 ± 19.56*	76.5 ± 17.35**
CTEB group (n= 51)	85.2 ± 9.44	65.7± 19.54*	63.4 ± 20.08*	79.6 ±19.32**
p	0.217	0.001	0.262	0.390
PEF (l)				
CTPB group (n= 51)	5.42 ± 1.75	1.18 ± 0.25*	2.40 ± 0.25*	4.27 ± 0.82*
CTEB group (n= 51)	5.82 ± 1.6	1.05 ± 0.28*	1.83 ± 0.19*	3.52 ± 0.69*
p	0.238	0.011	0.000	0.000

The data were shown as mean ± SD.
* < 0.01 compared to before the surgery.
** < 0.05 compared to before the surgery.

even showed that pain relief was significantly reduced after 15 minutes of the analgesic regime while the previous reports recorded at 2, 4, or 6 hours after treatment (4,12,15). On the other hand, other studies used 0.25% bupivacaine, the mixture of 0.25% levobupivacaine and fentanyl 1.6 µg/mL, or 0.45% ropivacaine for the analgesia (4,12,16). Our analgesic regimen using the mixture of 0.125% bupivacaine and fentanyl 2 µg/mL showed the similar efficacy that the pain levels reduced to mild in patients of both groups.

Postoperation often sees the elevation of cortisol and glucose levels, as they are signals of surgical trauma and stress. These levels could be regulated by the analgesic regimens, therefore, they were often used to assess the efficacy of pain relief after the surgery (17,18). Differing from the results of Gulbahar et al. (2010) who saw that only glucose blood levels notably increased after the thoracotomy, our results showed that both the blood glucose and blood cortisol levels after the surgery strongly increased compared to normal conditions, and were much higher than that before the surgery. These results indicated that patients in our study suffered stress response after lung removal or lung decortication, as these procedures could cause extremely severe pain. Nevertheless, our results were in line with this study in which postoperative levels of blood glucose and blood cortisol were not different between the two groups on the first date after regimens.

Interestingly, our results found that a significant difference happened on the second postoperative day between the two groups when the blood glucose level in the CTEB group was not remarkably different from the day before surgery. Till the third operative day, the blood glucose concentration of patients in CTPB was indifferent from the date before the surgery. Moreover, although blood cortisol levels were insignificantly different be-

Table 3. VAS score at rest (V_R) and at movement (V_M) between the two groups

Time	V_R			V_M		
	CTPB group (n= 51)	CTEB group (n= 51)	p	CTPB group (n= 51)	CTEB group (n= 51)	p
0-min	6.9 ± 1.4	6.5 ± 1.2	0.178	8.0 ± 1.2	7.8 ± 1.1	0.276
15-min	3.5 ± 1.0*	3.5 ± 0.9*	1.000	4.8 ± 0.9*	4.4 ± 0.9*	0.056
30-min	2.9 ± 0.8*	3.1 ± 0.7*	0.237	3.9 ± 0.9*	3.7 ± 0.7*	0.201
1-hour	2.7 ± 0.6*	2.7 ± 0.5*	0.724	3.6 ± 0.8*	3.6 ± 0.7*	1.000
2-hours	2.6 ± 0.6*	2.7 ± 0.8*	0.483	3.4 ± 0.6*	3.4 ± 1.0*	0.731
4-hours	2.6 ± 0.6*	2.5 ± 0.6*	0.746	3.1 ± 0.6*	3.2 ± 0.9*	0.315
6-hous	2.5 ± 0.9*	2.4 ± 0.6*	0.286	3.1 ± 1.1*	3.0 ± 0.7*	0.467
12-hours	2.1 ± 0.6*	2.2 ± 0.6*	0.532	2.6 ± 0.8*	2.6 ± 0.8*	0.715
24-hours	1.9 ± 0.5*	2.0 ± 0.7*	0.197	2.4 ± 0.5*	2.5 ± 0.6*	0.404
48-hours	1.6 ± 0.6*	1.7 ± 0.7*	0.550	2.1 ± 0.6*	2.3 ± 0.6*	0.216
72-hours	1.4 ± 0.8*	1.5 ± 0.8*	0.607	2.0 ± 0.6*	2.0 ± 0.5*	0.553

The data was shown as mean ± SD. VAS: Visual Analog Scale
* < 0.01 compared to 0-min.

tween the two groups on all studied days, these values were still much higher than before the surgery in both groups indicating that the stress response had not been very well controlled.

Two of the criteria used to evaluate the analgesic efficacy are the percentage of patients needing additional analgesic intervention, and the total dose of morphine. Although Sagiroglu et al. (2013) have revealed that the total additional dose of morphine after 24 hours in the PB group was higher than in the EP group, no significant differences were determined (p= 0.056). Gulbahar et al. (2010) have shown that the times that patients ordered additional morphine sulfate between the two groups at the first, the second, and the third postoperative date were not significantly different. Our results were concordant with these previous reports which supported the similar efficacy between the two groups.

The worst pain after thoracic surgery is an important cause of poor ventilation efficiency and restricted cough, which affects long and deep breathing. Effective pain management would reduce the failure of lung functions, or sometimes would reverse them and prevent postoperative complications. Our results showed that after surgery, lung functions were impaired remarkably compared to that before the surgery (p< 0.01). The recovery of these ventilatory functions after surgery in the CTPB group was better than the CTEB group, as shown by the significantly higher values of FVC and PEF at all studied days. FEV_1 values of CTPB groups were also higher than in CTEB groups, although they were not significantly different. These results were in line with another report indicating the decreased lung volume 4 hours after the surgery observed in both PB and EB groups (19). The patients in this study who received the analgesic regimen with PB showed better improvement than patients in the EP group as well. The results might be attributed to the sole affection on the operated lung of the PB that did not cause any impairment of another lung's functions.

Regarding undesirable effects, PB only blocks the sympathetic on one side resulting in lower percentages of hypotensive patients receiving PB regimen when compared to the EP. Many studies have indicated similar results that patients in the PB group had a smaller percentage of complications of hypotension than patients in the EP group (20-22). Only Huyen (2017) has reported that the difference was not statistically different between the two procedures (p= 0.48). Our study revealed that the hypotension was not very serious amongst the patients. The patient with the lowest blood pressure by 86 mmHg only needed a faster speed of the infusion, but no requirement of ephedrine.

We recorded that motor block in both legs was only observed in patients in the CTEB group. This proved that the anesthetic medicines covered all nerve roots inside the pleural space and spread across the underneath levels which resulted from the diffusion of the anesthetic medicines to the pleural space after the injection. On the other hand, because of the continuous injection of anesthetic medicines into the epidural space, the medicines could partly diffuse to the cerebrospinal fluid via the epidural space. In our study, no case had anesthesia in the complete spinal cord, anesthesia in epidural when conducting the PB intervention, or the toxicity relating to anesthesia.

The frequency and the serious degrees of the undesirable effects relating to the anesthesia, for example, vascular puncture and pain at the injection site, were also lower in the PB group than the EP group, although they were not significant. This advantage might be due to the ultrasound-guided technique that benefited the surgeons to determined anatomical points. This result was also similar to the report of Naja and Longqvist (23).

The most popular side effects in our study were vomitting and nausea caused by morphine analogues. Despite they were not dangerous, they caused discomfort in patients after the surgery. For urinary retention, a lower frequency was observed in the CTPB group than the CTEB group because PB blocks the motor nerve which affects one side of the body, resulting in the available bladder sensation.

In our study, we used ultrasound to support the CTPB because it increased the accuracy of surgical manipulation and the safety of the surgery. Ultrasound helps surgeons determine the vertebra, the pulmonary pleura, the thoracic paravertebral space, the distance between skin and the vertebra, the distance between skin and the pulmonary pleura, the distance between skin and thoracic paravertebral space. Also, it is possible to detect the movement of the needle, confirm the presence of the needle or catheter in the thoracic paravertebral space. All those gains of ultrasound-guided CTPB improved the efficacy and safety of the procedure (24-27). Bakshi et al (2017) have also supposed that this procedure was valuable to manage postoperative pain, especially after one-side surgeries (27). Some complications including pleural perforation, pneumothorax could be avoided in the ultrasound-guided CTPB. Besides, ultrasound-guided CTPB also reduces the number of needle pokes and helped place catheter properly (28). These suggestions were also observed in our study.

Taken all together, we realized that PB had a good effect on pain management after the surgery. Its efficacy was comparable to EP (a gold standard for postoperative analgesia after thoracic surgery). On top of that, CTPB under ultrasound-guidance using bupivacaine - fentanyl also had a smaller percentage of side effects. Patients receiving this regimen had fewer pulmonary complications and recovered the ventilatory functions better. Our results are expected to reinforce the current findings and provide clinicians with more evidence to apply this technique.

Our limitation includes a small eligible patients delivering to our hospital that made the study prolonged. The sample was collected at only one hospital that could not represent to Vietnamese population and population in other countries as a whole. In addition, the assessment of VAS scores might be subjective and have affected the precision of the results. We recommend a study of multiple centers being conducted to confirm the effects.

CONCLUSION

Ultrasound-guided CTPB has a good effect on pain relief after lung surgery. Its efficacy was comparable to the EP, and the undesirable effects on the circular system, respiratory system were less than EP. The percent of side effects in patients using bupivacaine - fentanyl was low. It also did not lead to any dangerous complications. Ultrasound-guided CTPB could replace the EP for postoperative anesthesia, especially when EP is contraindicated or failed.

Ethics Committee Approval: The study was obtained from 74 Central Hospital Bromedical Studies Ethics Committee (No: 458/GCN-BV74TW).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept -T.T.T., T.V.D.; Design - T.T.T.; Supervision -T.V.D.; Materials - All of authors; Data Collection and/or Processing - T.T.T.; D.V.K.; Analysis and/or Interpretation - T.T.T.; D.V.K.; Literature Search- T.T.T.; D.V.K.; Writing Manuscript -T.T.T.; D.V.K.; Critical Reviews - T.T.T.

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

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2021; 37 (3): 232-241

Akciğer cerrahisi geçiren hastalarda ultrason eşliğinde sürekli torasik paravertebral blok ile bupivakain-fentanil kullanan sürekli torasik epidural blok arasındaki analjezik etkinliğin karşılaştırılması: Prospektif, randomize, kontrollü bir çalışma

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ÖZET

Giriş ve Amaç: Bu çalışmanın amacı, akciğer cerrahisi yapılan hastalarda ağrı yönetimi için kullanılan ultrason rehberliğinde sürekli toraksik paravertebral blok (CTPB) ile sürekli toraksik epidural blok (CTEB) yöntemlerinin etkinliği ve güvenirliliğini karşılaştırmaktı.

Gereç ve Yöntem: Çalışmaya, Eylül 2013 ve Aralık 2017 tarihleri arasında 74 Central Hastanesi'nde akciğer cerrahisi uygulanan 102 hasta dâhil edildi. Hastalar iki gruba ayrıldı: CTPB grubu (n= 51) ve CTEB grubu (n= 51). Birincil sonuçlar, hastalar dinlenme (V_R) ve hareket (V_M) halindeyken ölçülen Vizüel Analog Skala (VAS) skorları ile operasyon sonrası kullanılan toplam bupivakain-fentanil dozu, plazma glikoz ve kortizol seviyeleri ve ek morfin dozlarıydı. Çalışma süresince advers reaksiyonlar kaydedildi. Çalışma, 74 Central Hastanesi Etik Kurulu tarafından onaylandı. Tüm hastalardan bilgilendirilmiş onam alındı.

Bulgular: CTPB ve CTEB grupları arasında V_R ve V_M, cerrahi sonrası 72. saatte kullanılan toplam bupivakain - fentanil dozu (p> 0,05), artmış plazma glikoz, plazma kortizol (p> 0,05) ve ek morfin dozları açısından anlamlı bir fark yoktu. CTPB grubundaki hastaların dolaşım ve solunum sisteminde advers reaksiyonlar görülme oranı CTEB grubundakilere kıyasla daha düşüktü. Advers reaksiyonlar, vasküler ponksiyonu, idrar tutma ve kaşınma isteği idi.

Sonuç: Ultrason rehberliğinde CTPB, akciğer cerrahisi sonrası ağrı yönetiminde etkin bir müdahale şeklidir. Analjezik etkinliği CTEB'ninkine benzemektedir. Ayrıca, CTEB'ye kıyasla bu yöntem dolaşım ve solunum sisteminde daha az advers reaksiyona sebep oldu.

Anahtar Kelimeler: Paravertebral blok, analjezi, akciğer cerrahisi, epidural blok, postoperatif ağrı

DOİ: 10.47717/turkjsurg.2021.5053

ORIGINAL ARTICLE
Turk J Surg 2021; 37 (3): 242-246

The management of xanthogranulomatous cholecystitis

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ABSTRACT

Objective: Xanthogranulomatous cholecystitis (XGC) is a rare variant of chronic cholecystitis. This rare pathology is characterized by severe and progressive fibrosis of the gallbladder wall as well as infiltration of fat-laden macrophages.

Material and Methods: The final pathology report of 8213 cholecystectomies performed between 2011 and 2019 was evaluated retrospectively, and patients whose pathology result was reported as XGC were included in the study. Patients' demographic characteristics, pathology results, and surgical methods were evaluated. Logistic regression analysis was performed for risk factors on conversion to open cholecystectomy.

Results: The rate of XGC among cholecystectomies was 0.91%. Mean age of the patients was 57.32 years. Laparoscopic cholecystectomy was applied to 92% (n: 69) of the patients. None of the patients had cancer suspicion in the preoperative period, but cancer suspicion was found in 10.6% of the patients during the operation. With the frozen test, unnecessary surgeries were prevented in these patients. Conversion rate to open cholecystectomy was found to be 26.09%. The most common reason for conversion to open cholecystectomy (66.7%) was intense fibrosis. Increased gallbladder wall thickness and acute cholecystitis were found to be statistically significant risk factors in ultrasonography ($p< 0.05$). Total complication rate in XGC cases was 3.9%.

Conclusion: XGC is an extremely rare disease and is difficult to diagnose before cholecystectomy. Especially in preoperative USG, in cases with no suspicion of malignancy, but with suspected malignancy during the operation, histopathological examination with frozen method before extensive surgery may prevent unnecessary dissection and related morbidities.

Keywords: Cholecystitis, xanthogranulomatous, laparoscopic cholecystectomy

INTRODUCTION

Xanthogranulomatous cholecystitis (XGC) is a rare variant of chronic cholecystitis (1). This rare inflammatory disease of the gallbladder is characterized by severe proliferation of the fibrotic tissue accompanied by the accumulation of lipid-laden macrophages and acute and chronic inflammatory cells (2,3). XGC is a benign condition, but it often extends into neighboring organs, and its macroscopic appearance may be confused with gallbladder cancer (4,5). Therefore, unnecessary major surgical procedures can be performed on patients with XCG (6).

XCG can present clinically with acute or chronic cholecystitis. Differential diagnosis between XGC and gallbladder cancer is often difficult, especially in patients with severe fibrosis (4,5). Laparoscopic cholecystectomy (LC) is the gold standard in the treatment of benign gallbladder diseases. XGC has a high conversion rate from LC to open cholecystectomy (OC) (7,8).

The aim of the present study was to reveal the general demographic and clinical characteristics of patients with XCG. Additionally, it was aimed to evaluate risk factors affecting conversion to OC and perioperative complications in patients with XCG.

MATERIAL and METHODS

In our study, we adhered to the World Medical Association's Helsinki Declaration regarding human material and data. In this study, the final pathology reports of cholecystectomies performed in our clinic between 2011 and 2019 were evaluated retrospectively. Our study was approved by the Research Ethics Committee of Health Sciences University, Hamidiye Scientific (Decision No: 2020-24/7).

Cite this article as: Şimşek G, Şahin A, Metin ŞH, Ulutaş ME, Arslan K. The management of xanthogranulomatous cholecystitis. Turk J Surg 2021; 37 (3): 242-246.

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Received: 27.11.2020
Accepted: 19.04.2021
Available Online Date: 28.09.2021

DOI: 10.47717/turkjsurg.2021.5020

Patients and Study Design

Patients whose final pathology result was reported as XGC were included in the study. The parameters evaluated in the patients included in the study were as follows:

- Demographic characteristics
- Preoperative ultrasonography (USG) findings (gallstone and gallbladder wall thickness)
- Aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT) values.
- Anamnesis of acute pancreatitis or acute cholecystitis attack
- Indications for cholecystectomy and surgery type (OC or LC)
- The number of patients converting from LC to OC
- Reasons for conversion to OC.
- Perioperative complications and treatments.
- The management of patients with suspected malignancy in the preoperative period or during surgery.
- Presence of accompanying other malignancy.

Patient files, electronic hospital records, surgical book records, and polyclinic follow-up records of the patients were examined. Patients with missing data in their records were not included in the study. For conversion to OC; male sex; acute cholecystitis attack; biliary pancreatitis attack; increase in gallbladder wall thickness on USG; and AST, ALT, ALP, and GGT values higher than normal limits were evaluated as risk factors. These risk factors were evaluated using logistic regression analysis.

Statistical Analysis

SPSS for Windows, version 22 (IBM Corp, Armonk, NY) was used for statistical analysis, and $p < 0.05$ was accepted as the statistical significance limit. Shapiro-Wilk normality test was applied before choosing the statistical method. If normality assumption could not be achieved in any of the groups, nonparametric test methods were preferred. Mann-Whitney U test was applied to compare the variables obtained by the measurement. In terms of categorical variables, Chi-square and Fisher's exact test were used for differences and relationships between the groups.

Logistic regression analysis was performed to determine the risk factors considered to affect the transition to open cholecystectomy. The relevant odds, 95% confidence interval, and p values were presented. Comparative results were presented with median and average in quantitative variables and proportions in qualitative variables.

RESULTS

Of the 8213 cholecystectomy specimens evaluated in our study, 75 were detected to have XGC. The incidence of XGC was 0.91% among all cholecystectomies. Mean age of the patients was 57.32 years, and 48% were females (Table 1).

Table 1. Demographic characteristics, preoperative USG findings and operation types of XGC patients

Age	
Average	57.32 ± 5.2
Sex	
Male	52% (n= 39)
Female	48% (n= 36)
Preoperative USG gallstone	73.3% (n= 55)
Preoperative USG gallsludge	26.7% (n= 20)
Preoperative USG gallbladder wall thickness increase	32% (n= 24)
Lap. cholecystectomy	92% (n= 69)
Open cholecystectomy	8% (n= 6)
Conversion rate to open cholecystectomy	26.09% (n= 18)

Table 2. Indications for cholecystectomy in Xanthogranulomatous cholecystitis patients

Chronic calculus cholecystitis	50.7% (n= 38)
Acute calculus cholecystitis (same hospitalization)	20% (n= 15)
Acute calculus cholecystitis attack	14.7% (n= 11)
Acute pancreatitis attack	10.7% (n= 8)
Common bile duct stone operation	2.7% (n= 2)
Incidental operation	1.3% (n= 1)

On preoperative USG, stones were reported in 73.3% of the patients and sludge in 26.7% of the patients. Only 32% of the patients had increased gallbladder wall thickness (Table 1).

Laparoscopic surgery was started in 92% of the patients, but 26% (n= 18) of these patients were converted to OC. Eight patients had an OC; two had common bile duct stones [Endoscopic retrograde cholangiopancreatography (ERCP) was performed but not successfully], and six patients had previous surgery. The most common indication for cholecystectomy in the patients was chronic stony cholecystitis (50.7%) (Table 2).

The most common reason for conversion to OC was found to be severe fibrosis (66.7%). Difficulty in dissecting Callot's triangle (5.5%) and previous surgeries (27.8%) were other reasons for conversion to OC.

Logistic regression analysis of the risk factors for conversion to OC revealed that increase in wall thickness increase and acute cholecystitis attack on USG were statistically significant risk factors ($p< 0.05$) (Table 3).

There was no suspicion of gallbladder cancer in USG performed in the preoperative period in any patient in the study. However, gallbladder cancer was suspected in eight patients (all of whom were patients who were converted to OC) during surgery. Biopsy

Table 3. Logistic regression analysis results of risk factors associated with conversion to open cholecystectomy

	OR [95% C.I]	p
Increase in gallbladder wall thickness on USG	3.654 [1.184-11.231]	**0.02**
Male sex	0.889 [0.303-2.605]	0.830
Acute cholecystitis attack	4.800 [1.519-15.164]	**0.005**
Biliary pancreatitis attack	0.941 [0.092-9.671]	0.959
Elevated AST level	1.441 [0.123-16.920]	0.770
Elevated ALT level	1.500 [0.33-6.75]	0.595
Elevated ALP level	2.688 [0.78-9.25]	0.109
Elevated GGT level	1.750 [0.581-5.267]	0.317

AST: Aspartate aminotransferase, ALT: Alanine transaminase, ALP: Alkaline phosphatase, GGT: Gamma-glutamyl transferase.

Table 4. Postoperative complication in XCG patients

Postopoperative complication	3.9% (n= 3)
Major bile duct injury	1.3% (n= 1)
Bilioma	1.3% (n= 1)
Surgical site infection	1.3% (n= 1)
Re-operation	1.3% (n= 1)

was taken from all eight patients, and frozen sections were performed. Extensive surgery was not performed because the biopsy results were reported as benign. The final pathologic examination results of these eight patients' cholecystectomy materials were also reported as XCG. Concurrent gallbladder cancer was not detected in any patients included in our study.

Postoperative complications were found in three patients in our study. Surgical site infection was seen in the patient who was converted from laparoscopy to OC. Biliary injury and biloma were seen among patients who underwent LC. The biliary injury was Bismuth type 2 and was treated with Roux-en-Y hepaticojejunostomy. The patient with biloma was treated with wig drainage and an ERCP-stent (Table 4).

In our study, the rate of accompanying malignancy (n= 2) was found as 2.6%. One patient had colon cancer and the other had stomach cancer.

DISCUSSION

The incidence of XGC has been reported as 0.9% in 4773 cholecystectomies in St James's University Hospital, England. However, it has been reported in the literature that this rate is around 8%, especially in studies from India (1). The rate of 0.91% detected in 8213 cholecystectomies in our study reflects that the frequency of XGC in our country is similar to Europe. The difference in the incidence of XGC between the sexes is quite low, and mean age of onset is 53.1 years (1). In our study, there was no significant difference in the sex distribution of the patients, and mean age was found as 57.32 years.

The most common preoperative symptom in patients with XGC is abdominal pain, and the most common examination finding is Murphy's sign (9-11). When the indications for cholecystectomy in patients with XCG were examined, the most common was chronic calculus cholecystitis (50.7%). The frequency of acute calculus cholecystitis attack among patients with XGC was found as 34.6% (n= 26). The frequency of acute pancreatitis attack was found as 10.7% (n= 8). Some 10-15% of the adult population in Western societies has gallstones. The rate of acute cholecystitis in patients with gallstones is around 20% (12). In view of these data, the rate of acute cholecystitis attack seems to be high in patients with XGC in our study. However, no study has demonstrated the relationship between XGC and acute cholecystitis. Although there is a very strong relationship between XGC and gallstones, not all patients with XGC will have stones. The relationship between XGC and gallstones has been reported as between 92% and 100% (1,10,13). In our study, the rate of stones on USG was found as 73.3% (n= 55). However, bile sludge was detected using USG in all patients without gallstones.

In our study, no cancer suspicion was reported on preoperative USG in any patients. The incidence of gallbladder cancer associated with XGC has been determined as 3.3% in Europe. In addition, approximately 10% of the patients with XGC had gallbladder cancer mixed with XGC, and patients received over or under treatment (1). None of the patients with XCG in our study had associated gallbladder cancer. However, in eight (10.6%) patients, it was determined that there was a suspicion of cancer during surgery. A perioperative biopsy was performed in these patients. Biopsies were evaluated using frozen sections. Biopsy results were reported as benign in all cases. Only cholecystectomy was performed on these patients, and extensive surgery was avoided. Gallbladder cancer was not detected in the definitive pathology results in any of these patients. In cases with no suspicion of gallbladder cancer on preoperative USG imaging, the frozen section may prevent extensive surgical resections in

the presence of perioperative cancer suspicion. There are no data on such an approach in the literature.

Laparoscopic cholecystectomy is the gold standard treatment for cholelithiasis worldwide. The conversion rate to OC is between 1% and 15% (13). In our study, the rate of deficit conversion in patients with XGC was found as 26.09% (n= 18). This rate is quite high compared with the literature. Reasons for conversion to OC include intense fibrosis and inflammation, inability to dissect Callot's triangle, ambiguous anatomy, life-threatening bleeding, and major bile duct injuries (14). In our study, the most common reason for conversion to OC in patients with XCG was severe fibrosis in 66.7% (n= 12). Other reasons were difficulty in dissecting Callot's triangle 5.5% (n= 1) and previous surgery 27.8% (n= 5).

Many risk factors for conversion to OC have been evaluated in the literature (15). Obesity, increased gallbladder wall thickness, age over 65 years, presence of common bile duct stones, impacted stones in the neck of the gallbladder, previous upper abdominal surgery, male sex, high ALP levels, elevated total bilirubin levels, emergency surgery, high white blood cell (WBC) levels, and high ASA scores have been defined as risk factors for conversion to OC in the literature. However, it has been emphasized that scoring systems that include these factors rather than a single factor are more useful (9-11). In our study, we evaluated the risk factors for conversion to OC in patients XGC using logistic regression analysis. We did not find a risk analysis for conversion to OC in XGC patients in the literature. Increased gallbladder wall thickness and acute cholecystitis attack in patients with XGC were statistically significant risk factors for conversion to OC (Table 3).

The frequency of major bile duct injury in LC is 0.2% (16). We found that the rate of major biliary injury due to LC was 1.3% in patients with XGC. This rate is high compared with major bile duct injury due to LC. However, there is no specified rate for major bile duct injury in patients with XCG in the literature.

CONCLUSION

XGC is a very rare disease, and it is difficult to diagnose before performing cholecystectomy. There is a strong relationship between XGC and gallstones. XGC increases the conversion rate from LC to OC. Risk factors affecting conversion from LC to OC in patients with XGC are increased gallbladder wall thickness and acute cholecystitis attack. In patients with no suspicion of gallbladder cancer on preoperative USG but with suspected perioperative gallbladder cancer, performing biopsy with frozen section may prevent overtreatment.

Ethics Committee Approval: Study approval obtained from SBU Hamidiye Scientific Research Ethics Committee (Date: 20.11.2020, Number: 20/445).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - G.Ş.; Design - G.Ş.; Materials - Ş.H.M., A.Ş.; Data Collection and/or Processing - M.E.U.; Analysis and/or Interpratation - A.Ş.; Literature Review - G.Ş.; Writing Manuscript - G.Ş.; Critical Reviews - K.A.

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

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2021; 37 (3): 242-246

Nadir bir kolesistit nedeni: ksantogranulamatöz kolesistit

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ÖZET

Giriş ve Amaç: Ksantogranülomatöz kolesistit (KSGK) kronik kolesistitin nadir görülen bir varyantıdır. Bu nadir patoloji safra kesesi duvarında ciddi ve ilerleyici fibrozis yanında yağ yüklü makrofajların infiltrasyonu ile karakterizedir.

Gereç ve Yöntem: 2011-2019 yılları arasında yapılan 8213 kolesistektominin nihai patoloji raporu retrospektif olarak değerlendirildi ve patoloji sonucu KSGK olarak rapor edilen hastalar çalışmaya dahil edildi. Hastaların demografik özellikleri, patoloji sonuçları, ameliyat şekilleri değerlendirildi. Açık kolesistektomiye dönüşte risk faktörleri için lojistik regresyon analizi yapıldı.

Bulgular: Kolesistektomiler içinde KSGK oranı %0,91'di. Hastaların ortalama yaşı 57,32'ydi. Hastaların %92 (n: 69)'sine laparoskopik kolesistektomi uygulanmıştı.Hiçbir hastada preoperatif dönemde kanser şüphesi yoktu ancak operasyonda kanser şüphesi hastaların %10,6'sında bulundu. Frozen tetkiki ile bu hastalarda gereksiz cerrahilerin önüne geçildi. Açık kolesistektomiye dönme oranı %26,09 olarak bulundu. Açık kolesistektomiye en sık dönme nedeni (%66,7) yoğun fibrozisti. Açık kolesistektomiye dönme için irdelenen risk faktörlerinden ultrasonografide safra kesesi duvar kalınlığı artışı ve akut kolesistit geçirmek istatiksel olarak anlamlı risk faktörü olarak bulundu ($p< 0,05$). KSGK vakalarında toplam komplikasyon oranı %3,9'du.

Sonuç: KSGK oldukça nadir bir hastalık olup kolesistektomi öncesi tanı koymak güçtür. Özellikle preoperatif yapılan ultrasonografide malignite şüphesi olmayan ancak operasyonda malignite kuşkulu vakalarda ekstansif cerrahi öncesi frozen yöntemi ile histopatolojik inceleme yapmak gereksiz diseksiyonu ve buna bağlı morbiditeleri engelleyebilir.

Anahtar Kelimeler: Kolesistit, ksantogranülomatöz, laparoskopik koleistektomi

DOİ: 10.47717/turkjsurg.2021.5020

ORIGINAL ARTICLE
Turk J Surg 2021; 37 (3): 247-252

Quality of life assessment after parathyroidectomy in symptomatic primary hyperparathyroidism using the SF-36 questionnaire

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ABSTRACT

Objective: Primary hyperparathyroidism (PHPT) is a systemic disease which, along with bone and stone disease, also causes several subjective symptoms which impairs the quality of life (QoL). However, NIH guidelines do not include non-specific physical and neuropsychological symptoms as an indication of parathyroidectomy. SF-36 is one of the most commonly used tools for assessing QoL; it measures both physical health (PH) and mental health (MH).

Material and Methods: This is a prospective observational study including 50 patients of symptomatic PHPT. Patients were categorized into normocalcemia (8.5-10.4 mg/dL), mild hypercalcemia (10.5-11.9 mg/dL), moderate hypercalcemia (12-13.9 mg/dL), and severe hypercalcemia (>14 mg/dL). QoL was assessed by using SF36 survey both pre-operative and three months after parathyroidectomy.

Results: There was an overall improvement in QoL of individual groups both in PH and MH components ($p< 0.001$). The improvement was more substantial for bodily pain, role physical, vitality and mental health. Although QoL was affected in patients with mild hypercalcemia, it was more affected in patients with severe hypercalcemia. The improvement in MH scores was dependent on the level of pre-operative calcium; however, the improvement in PH scores was independent of pre-operative calcium ($p= 0.698$).

Conclusion: This study showed improvement in all aspects of PH and MH of SF-36 after parathyroidectomy, even in normocalcemics. Despite the fact that current guidelines for the management of PHPT do not include QoL as an indication for parathyroidectomy, we propose that parathyroidectomy should be considered, if patient is fit for surgery.

Keywords: Primary hyperparathyroidism, quality of life, parathyroidectomy, SF-36

INTRODUCTION

Primary hyperparathyroidism (PHPT) is the third most common endocrine disorder and is caused by a single adenoma in 80%-90% of patients (1). PHPT is a systemic disease as overproduction of PTH and hypercalcemia causes an alteration in bone metabolism (53%), nephrocalcinosis (40%), nephrolithiasis (70%), cardiovascular involvement (61%) along with neuropsychiatric symptoms (37% to 62%) (2-5). The majority (80%) of PHPT patients in the Western population are asymptomatic and are diagnosed on a routine biochemical investigation. However, in India, the majority of patients who are diagnosed with PHPT either have prolonged neglected bone disease or recurrent stone disease. Symptomatic patients with severe osteoporosis suffer from multiple fractures and non-healing of fracture. Additionally, patients with undiagnosed PHPT with renal stones undergo multiple endoscopic or open procedures for renal stone disease. PHPT patients also have several subjective symptoms associated with hypercalcemia like easy fatigability, back pain, weakness, memory loss, mood swings, depression, dyspepsia and constipation.

Reduced quality of life (QoL) in PHPT is not only due to cardiovascular involvement, severe osteopenia, and stone disease but also due to countless other associated subjective symptoms. Surgery offers a cure in the majority and is measured as the definitive. Treatment is according to the consensus statement of international guidelines. However, NIH guidelines do not include non-specific physical and

Cite this article as: Mohan B, Abuji K, Dahiya D, Tandup C, Bhadada S, Behera A. Quality of life assessment after parathyroidectomy in symptomatic primary hyperparathyroidism using the SF-36 questionnaire. Turk J Surg 2021; 37 (3): 247-252.

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Received: 10.12.2020
Accepted: 19.04.2021
Available Online Date: 28.09.2021

DOI: 10.47717/turkjsurg.2021.5156

neuropsychological symptoms as an indication of parathyroidectomy in PHPT patients. Surgery brings improvement in bone health; however, improvement of psychological dysfunction is still a matter of debate. There are studies from the Western world where QoL was assessed and found to have significant improvement by using various tools like Pasieka's parathyroid symptoms score, Short-Form health survey (SF-36), primary hyperparathyroidism quality of life questionnaire (PHPQOLQ) and a disease-specific Quality-of-Life questionnaire.

Objective data addressing QoL of these patients from India are limited. SF-36 is one of the most commonly used tools. It is an excellent psychometric, well organized and validated health-related questionnaire which measures both physical health (PH) and mental health (MH), and it is also easy to administer in a short period of time where the contact time with the patient is short. Therefore, the present study aimed to evaluate QoL using the SF-36 questionnaire in patients with PHPT before and after three months of curative parathyroidectomy.

MATERIAL and METHODS

This was a prospective observational study which included 50 symptomatic PHPT patients from a tertiary care center in North India. PHPT was diagnosed by laboratory values of serum parathormone levels (PTH), serum calcium levels, and localized by Tc 99m sestamibi parathyroid scintigraphy. Patients with secondary or tertiary hyperparathyroidism, age <18 years or patients with multiple endocrine neoplasia were excluded. All patients underwent open focused parathyroidectomy. Approval from the institutional ethical committee was obtained.

Demographic profile, biochemical, radiological, operative and histological details were recorded. Study population was categorized as normocalcemia (8.5-10.4 mg/dL), mild hypercalcemia (10.5-11.9 mg/dL), moderate hypercalcemia (12-13.9 mg/dL), and severe hypercalcemia (>14 mg/dL). SF-36 questionnaire was used to assess QoL. Patients were asked to fill in the questionnaire within one week before surgery and three months after parathyroidectomy.

Curative parathyroidectomy was defined as the patient having persistent normal serum calcium and PTH levels three months after parathyroidectomy. Should patients in the normocalcemic group achieve normal PTH levels and serum calcium below pre-operative levels during follow up, they labelled themselves as having curative parathyroidectomy.

SF-36 Questionnaire

Short-form health survey has 36-items patient-related validated survey of QoL, which was developed by RAND Corporation, California, USA. SF-36 questionnaire consists of thirty-six questions measuring PH components (physical function, role physic, bodily pain, general health and MH components (vitality, social functioning, role emotion, general mental health). The response for each item was scored from 0-100, and the mean score of each domain was calculated. Lower score implied poor QoL, whereas higher score indicated the excellent QoL.

Statistical Analysis

All data were analyzed by SPSS 26 (Statistical Package for the Social Sciences, IBM). Kolmogorov Smirnov tests of normality checked normality of data. Descriptive statistics were presented as mean ± standard deviation for normally distributed variables and median [interquartile range (IQR)] for non-normally distributed variables. Descriptive statistics using parametric comparisons (t-test) were calculated. Subgroup analysis was presented as one-way ANOVA; all tests were two-sided with a 95% confidence interval.

RESULTS

Mean age of the study group was 40.8 ± 13.9 years; the majority were females (60%, n= 30). Demographic profile and presenting symptoms are shown in Table 1. The majority had single gland involvement (96%, n= 48), and only two patients had double gland disease (4%, n= 2). Parathyroid adenoma was confirmed on histopathology in all patients.

Biochemical Profile

Pre-operative mean PTH was 401 pg/dL (SD= 633.67) and serum calcium was 12.25 mg/dL (SD= 1.65) which normalized in all patients after surgery (Table 2). Serum PTH levels did not correlate with the severity of hypercalcemia (p= 0.521).

Table 1. Demographic characteristics of patients with PHPT (n= 50)

Age (years)	40.8 ± 13.9
Symptoms	
Bone pain	44 (88%)
Fatigue	39 (78%)
Muscle pain	38 (76%)
Renal disease	35 (70%)
Depression	22 (44%)
Difficulty in concentration	18 (36%)
Memory loss	17 (34%)
Anxiety	15 (30%)
Irritation	15 (30%)
Sleep deprivation	13 (26%)
Polyuria	12 (24%)
Nocturia	07 (14%)
Biochemical Parameters	
Serum PTH (mean)	401 pg/ml
Serum Calcium (mean)	12.25 mg/dL
Normocalcemia (8.5-10.4 mg/dL)	05 (10%)
Mild hypercalcemia (10.5-11.9 mg/dL)	18 (36%)
Moderate hypercalcemia (12-13.9 mg/dL)	20 (40%)
Severe hypercalcemia (>14 mg/dL)	07 (14%)

Table 2. Biochemical parameters before the operation and three months after parathyroidectomy		
	Pre-operative	**Post-operative at three months**
Serum calcium (mg%) (mean ± SD)	12.25 ± 1.65	9.3 ± 0.85
Serum PTH (pg/ml) (mean ± SD)	401 ± 633.67	44 ± 37.73
SD: Standard deviation.		

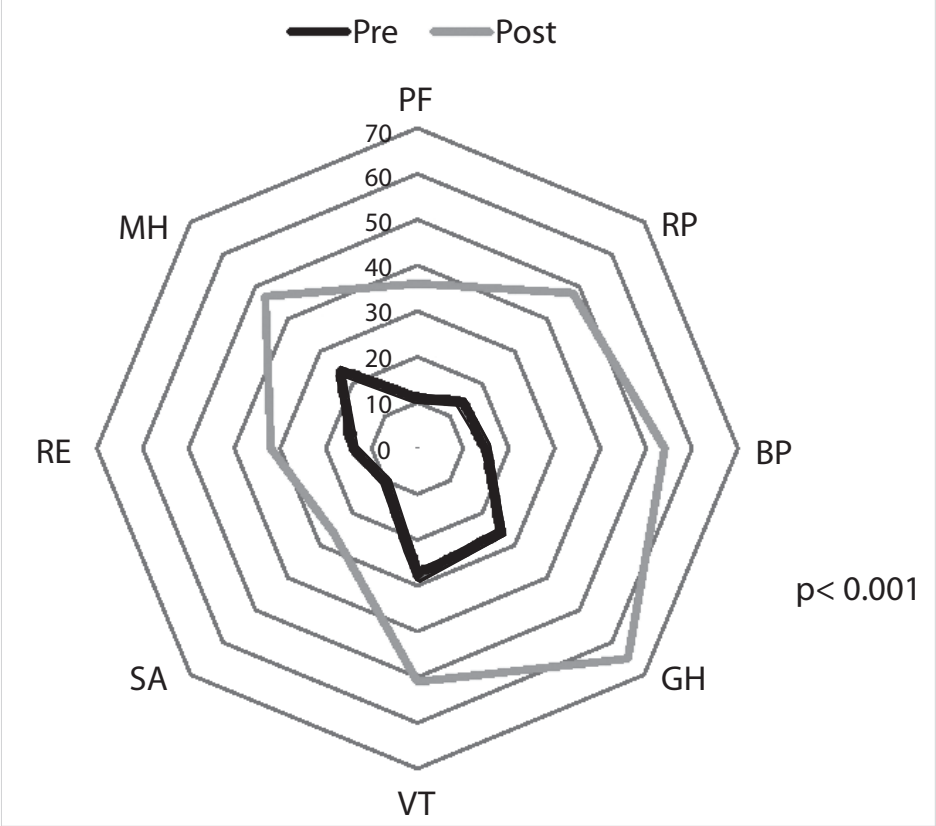

Figure 1. Comparison of mean pre-operative scores and post-operative scores in different aspects of physical health-physical function (PF), role physic (RP), bodily pain (BP), general health (GH), and mental health-vitality (VT), social activity (SA), role emotion (RE), general mental health (MH).

Quality of Life Assessment

Preoperatively, PHPT patients had significantly lower PH (49 ± 13) and MH (61 ± 17), and it improved significantly after three months of curative parathyroidectomy (PH 82 ± 6, MH 81 ± 9, p< 0.001). There was an overall improvement in QoL of individual groups both in PH and MH components (Figure 1). The improvement was more substantial for bodily pain, role physical, vitality and general mental health.

Subgroup Analysis

Improvement in all aspects of PH and MH scores was observed in patients who underwent parathyroidectomy (p< 0.01). Although QoL was affected in patients with mild hypercalcemia, it was more affected in patients with severe hypercalcemia with improvement in both PH and MH score after parathyroidectomy (Table 3). The improvement in mean MH scores was found to be dependent on the level of pre-operative calcium levels. However, the improvement in mean PH scores was independent of pre-operative calcium levels (p= 0.698). Mean MH scores were compared between groups using one-way ANOVA and were found to be statistically significant (p= 0.032).

DISCUSSION

Patients with PHPT experience various systemic and neuropsychological symptoms which attribute to reduce QoL. In this study, the impact of parathyroidectomy on QoL in PHPT patients was assessed using the SF-36 questionnaire, and it was found that there was a significant improvement in QoL after parathyroidectomy even in patients who were normocalcemic. We found considerable improvement in bodily pain, role physical, vitality and mental health.

Table 3. Comparison of QoL pre and post-operative parathyroidectomy based on serum calcium levels

Grades of hypercalcemia	QoL	Pre-operative	Post-operative (after three months)	p
Normocalcemia	PH	65 ± 8	89 ± 9	0.002
	MH	80 ± 13	91 ± 7	0.018
Mild hypercalcemia	PH	50 ± 11	80 ± 6	0.005
	MH	60 ± 18	81 ± 7	0.028
Moderate hypercalcemia	PH	49 ± 16	84 ± 7	0.007
	MH	66 ± 12	82 ± 10	0.001
Severe hypercalcemia	PH	33 ± 13	75 ± 8	0.001
	MH	38 ± 10	69 ± 9	0.009

PH: Physical health, MH: Mental health, p value calculated with paired t test.

In a prospective multicenter study by Weber et al. where 194 patients of PHPT with elevated depression scores and suicidal ideation were included, QoL was evaluated using the SF-36 questionnaire. Pre-operative SF-36 score was significantly lower in PHPT patients as compared to 186 patients who underwent thyroidectomy. However, there was an increase in QoL after parathyroidectomy over one year (6).

In a meta-analysis, the extent of improvement of QoL in PHPT patients after parathyroidectomy was assessed by both SF-36 and Pasieka scales. They included six studies where QoL was evaluated; 238 patients were assessed by SF-36 score, and Pasieka score was used in 203 patients, and it was found that parathyroidectomy significantly improves short- and medium-term health-related QoL after parathyroidectomy (7). In a prospective cohort analysis by David et al. which included 74 patients who underwent parathyroidectomy for PHPT and QoL was assessed using SF-36 survey before surgery and one year after parathyroidectomy. Of 74 patients, 43 were asymptomatic and 29 were symptomatic. There was significant impairment in 5 of 8 domains preoperatively with significant improvement in 7 of 8 domains postoperatively in all patients. However, the improvement was significantly more apparent in symptomatic patients, but asymptomatic patients with impaired mental health and energy level preoperatively showed improvement after parathyroidectomy (8).

Roman et al., in 28 patients with PHPT, have used the Beck Depression Inventory and Spielberger State-Trait Anxiety Inventory for assessing depression and anxiety and the Rey Auditory Verbal Learning Test and Groton Maze Learning Test for evaluating the cognitive function. They observed that PHPT patients were associated with higher depression score and more significant problem in spatial learning; with improvement in these parameters after parathyroidectomy. However, they did not assess QoL. However, in the present study, additional information regarding improvement in QoL was shown after parathyroidectomy, although cognitive functions were not measured by SF 36 surgery (9).

In this study, improvement in MH scores was found to be dependent on the level of pre-operative calcium levels, whereas PH scores were independent. Also, normocalcemic patients had a decreased QoL, which improved significantly after parathyroidectomy. It explains that PTH had a direct effect on QoL. In a prospective multicenter study by Bannani et al. where SF-36 questionnaire was used to assess QoL, it has been found that QoL was affected similarly among normocalcemic or hypercalcemic PHPT patients in both physical and mental aspects. There was an improvement in both physical QoL and non-specific symptoms (such as fatigue, anxiety, bone pain, muscular weakness and abdominal distension) after parathyroidectomy, but the improvement was more pronounced in the hypercalcemic PHPT patients (10). Beysal et al. have shown that normocalcemic and hypercalcemic PHPT patients had a similar risk of cardiovascular risk factors, kidney stones, metabolic syndrome and low glucose tolerance, and parathyroidectomy improved these risk factors among both groups. Recent studies have also reported that about 20 per cent of normocalcemic PHPT progresses into hypercalcemic PHPT, the majority within 2-4 years of diagnosis (11).

Limitations

SF-36 does not give information about cognitive function. The sample size for this study was small.

CONCLUSION

This study showed improvement in all aspects of PH and MH of SF-36 after parathyroidectomy, even in patients with normocalcemia. Preoperatively, QoL was significantly lower concerning role physical, general health and the physical component, and improvement was more considerable for bodily pain, role physical, vitality and mental health. Even though current guidelines for the management of PHPT do not include QoL as an indi-

cation for parathyroidectomy, we propose that parathyroidectomy should be considered for patients with PHPT even when they do not meet the current NIH criteria but they are fit for surgery.

Ethics Committee Approval: This study was obtained from Postgraduate Instute of Medical Education and Research, Chandigard (Date: 21.12.2018, Decision no: 002145).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - D.D.; Design - K.A.; Supervision - D.D.; Data Collection and/or Processing - B.M.; Analysis and/or Interpratation - K.A.; Literature Review - K.A.; Writing Manuscript - K.A.; Critical Reviews - C.T., A.B.

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

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2021; 37 (3): 247-252

SF-36 anketi kullanılarak semptomatik primer hiperparatiroidide paratiroidektomi sonrası yaşam kalitesinin değerlendirmesi

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ÖZET

Giriş ve Amaç: Primer hiperparatiroidizm (PHPT), kemiklerde veya taş oluşumlarıyla gelişen hastalıklarla yaşam kalitesini (QoL) bozan ve çeşitli öznel semptomlara neden olan sistemik bir hastalıktır. Bununla birlikte, NIH kılavuzları, paratiroidektominin bir göstergesi olarak spesifik olmayan fiziksel ve nöropsikolojik semptomları içermemektedir. SF-36 ise, yaşam kalitesini değerlendirmek için en yaygın kullanılan araçlardan biridir ve hem fiziksel sağlığı (PH) hem de zihinsel sağlığı (MH) ölçer.

Gereç ve Yöntem: 50 semptomatik PHPT hastasını içeren prospektif bir gözlemsel çalışma yapıldı. Hastalar normokalsemi (8,5-10,4 mg/dL), hafif hiperkalsemi (10,5-11,9 mg/dL), orta derecede hiperkalsemi (12-13,9 mg/dL) ve şiddetli hiperkalsemi (> 14 mg/dL) olarak kategorize edildi. QoL, SF36 anketi kullanılarak hem ameliyat öncesi hem de paratiroidektomiden üç ay sonra değerlendirildi.

Bulgular: Hem PH hem de MH bileşenlerinde bireysel grupların QoL'sinde genel bir iyileşme görüldü (p< 0,001). İyileşme bedensel ağrı, fiziksel rol, canlılık ve zihinsel sağlık için daha önemliydi. Hafif hiperkalsemili hastalarda yaşam kalitesi etkilenmiş olmasına rağmen, bu durum şiddetli hiperkalsemili hastalarda daha fazla saptandı. MH skorlarındaki iyileşme, ameliyat öncesi kalsiyum düzeyine bağlıyken, PH skorlarındaki düzelme ameliyat öncesi kalsiyumdan bağımsızdı (p= 0,698).

Sonuç: Bu çalışmanın sonuçları, normokalsemiklerde bile paratiroidektomiden sonra SF-36'nın PH ve MH'sinin tüm yönlerindeki iyileşmeyi göstermektedir. PHPT'nin tedavisinde mevcut kılavuzlar paratiroidektomi için bir endikasyon olarak QoL'yi içermese de, hastalar cerrahiye uygunsa paratiroidektominin düşünülmesini önermekteyiz.

Anahtar Kelimeler: Birincil hiperparatiroidizm, yaşam kalitesi, paratiroidektomi, SF-36

DOİ: 10.47717/turkjsurg.2021.5156

ORIGINAL ARTICLE
Turk J Surg 2021; 37 (3): 253-259

Role of intra-abdominal pressure in the outcomes of perforation peritonitis: A prospective observational study

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ABSTRACT

Objective: Intra-abdominal pressure (IAP) has been investigated for its role in causing morbidity and mortality, with various studies showing different degrees of correlation. There remains paucity of literature on this subject, applied to patients of perforation peritonitis, especially in the Indian subcontinent.

Material and Methods: It is a prospective observational study involving 40 patients of perforation peritonitis undergoing exploratory laparotomy. IAP was measured as per WSACS (World Society of Abdominal Compartment Syndrome) guidelines. APACHE II (Acute Physiology And Chronic Health Evaluation- II) and SOFA (Sequential Organ Failure Assessment) were calculated. Data was collected regarding occurrence of prolonged ileus, burst abdomen, duration of hospital stay, 30 day mortality, and was statistically analyzed to correlate with IAP.

Results: At admission, mean IAP was 13.37 mmHg, and the incidence of IAH was 65%. IAH was seen in 17.9% and 7.6% at 24 h and 48 h post-operatively. Incidence of prolonged ileus and burst abdomen were 7.7% and 22.5% respectively. Mortality rate was 17.5%. Mean duration of hospital stay was 13.45 days. Post-operative IAP correlated with mortality (p: 0.014) and post-operative SOFA score ($p< 0.05$). Statistically significant correlation was also seen with the occurrence of prolonged ileus (p: 0.006). IAP did not significantly correlate with APACHE II score, occurrence of burst abdomen, and duration of hospital stay.

Conclusion: Rise in IAP correlates with deterioration of SOFA score, and also with the occurrence of prolonged ileus. IAP is also a predictor of mortality. IAP measured post-operatively (24 and 48 hours) had a better correlation with these outcomes than the value measured at admission. No statistically significant correlation of IAP with the occurrence of burst abdomen and duration of hospital stay could be found, which warrants further studies with a larger population.

Keywords: Perforation peritonitis, intra-abdominal pressure, intra-abdominal hypertension, abdominal compartment syndrome

INTRODUCTION

Perforation peritonitis is a common surgical emergency associated with morbidity as well as mortality, most of which is attributed to sepsis and multi-organ dysfunction syndrome. An important, yet often unrecognized factor contributing to the exacerbation of adverse outcomes in these patients is the increase in intra-abdominal pressure (IAP) which may be due to spillage of bowel contents, peritoneal inflammation causing third-space fluid accumulation, bowel edema, adynamic ileus and abdominal wall spasm. The resultant intra-abdominal hypertension may be seen in as many as 66% of patients of perforation peritonitis (1).

Increased IAP adversely impacts the functioning of various organ systems- respiratory, cardiac, renal, gastro-intestinal, which inevitably leads to increase morbidity and mortality (2).The presence of IAH in critically ill patients has been recognized as an independent predictor of mortality (3).

Much of western literature on IAP/IAH/ACS has focused on the critically ill, comprising patients of trauma, burns, medical as well as surgical illnesses admitted in the intensive care units (ICU). Although the number of published studies in patients of acute surgical illnesses is steadily increasing, there is still a paucity of literature on IAP in patients of perforation peritonitis, especially in the Indian subcontinent (4). We conducted a study to evaluate the role of IAP and correlate it with organ dys-

Cite this article as: Kumar NP, Bains L, Lal P, Mishra A, Beg MY, Maranna H. Role of intra-abdominal pressure in the outcomes of perforation peritonitis: A prospective observational study. Turk J Surg 2021; 37 (3): 253-259.

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Received: 06.10.2020
Accepted: 19.04.2021
Available Online Date: 28.09.2021

DOI: 10.47717/turkjsurg.2021.4945

function, prolonged ileus, burst abdomen, duration of hospital stay and 30-day all-cause mortality.

MATERIAL and METHODS

This was a prospective observational study conducted in a single unit in the Department of Surgery at a tertiary care hospital in New Delhi, India, over a period of one year. The study was approved by the institutional ethics committee. Study population consisted of patients of perforation peritonitis. Inclusion criteria were age ≥18 years, and patients undergoing exploratory laparotomy. Abdominal drain placement prior to laparotomy, pregnancy, previous abdomino-pelvic surgery and failure of urethral catheterization were exclusion criteria. Using the general formula for sample size calculation by z-statistics, a sample size of 246 was estimated. However, a sample size of 40 was taken for convenience (Figure 1). Written informed consent was taken from the patients or their legal representatives. Primary end point of the study was to determine the value of IAP in patients of perforation peritonitis. Secondary end points were organ dysfunction (SOFA score), occurrence of prolonged ileus, burst abdomen, duration of hospital stay and 30 day all-cause mortality.

Relevant data were retrieved from the clinical notes that included patient particulars, clinical examination findings (including vitals), and reports of lab investigations. APACHE II and SOFA scores were calculated at the time of admission (5,6). Intra-abdominal pressure was indirectly determined by measuring urinary bladder pressure with a Foley's catheter according to the World Society of Abdominal Compartment Syndrome (WSACS) guidelines using saline manometry (7). A conversion factor of 1.36 was used to convert IAP values in cm H_2O to mmHg.

Pre-operatively, IAP measurements were taken at the time of admission, just before induction of general anesthesia (GA), and soon after induction of GA, but before laparotomy. Post-operatively IAP was measured and SOFA score was calculated at 24 and 48 hours. Occurrence of burst abdomen, occurrence of prolonged ileus, and duration of hospital stay were noted. Patients were followed-up until 30 days postoperatively for mortality data.

Intra-abdominal hypertension (IAH) was defined by a sustained IAP of 12 mmHg or higher. Prolonged ileus was defined as the absence of bowel sounds and a 24 hour-gastric output (via Ryle's tube) of more than 500 ml even after 3 days of laparotomy. Burst abdomen was defined as post-operative separation of abdominal musculo-aponeurotic layers. Duration of hospital stay was measured from the day of admission until the day of discharge from the hospital. Mortality included deaths occurring within 30 days of laparotomy irrespective of the cause.

Statistical Analysis

The collected data was entered in MS-Excel and analyzed by SPSS version 25.0. For continuous variables, mean (with standard deviation) was reported. For categorical variables, proportions and percentages were reported. For quantitative data, Student t-test was used. Pearson's correlation co-efficient was used to correlate intra-abdominal pressure with the outcomes. P-values <0.05 was taken for statistical significance.

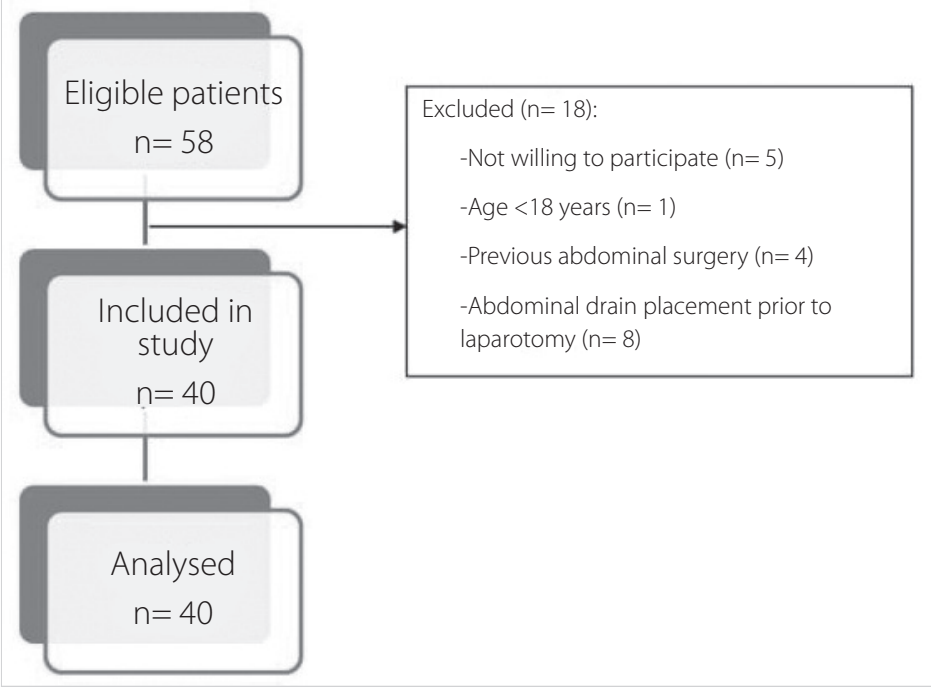

Figure 1. Patient recruitment in the study.

Table 1. Master table (*Values expressed as mean ± SD (Range)	
n= 40	
1. Mean age(years)	37.375 (18-70)
2. Sex (M:F)	24:16
3. Etiology of perforation peritonitis	Acid peptic disease (47.5%) Tuberculosis (22.5%) Enteric fever (10%) Blunt trauma abdomen (7.5%) Acute mesenteric ischemia (5%) Acute appendicitis (2.5%) Crohn's disease (2.5%) Penetrating trauma (2.5%)
4. Mean IAP in mmHg	At admission: 13.73 ± 4.30 Pre-induction: 13.44 ± 4.90 Post-induction: 13.31 ± 4.28 24 h post-op: 9.37 ± 2.97 48 h post-op: 8.16 ± 2.93
5. Mean APACHE II score	7.55 ± 4.96 (0-21)
6. Mean SOFA score	At admission: 2.25 ± 1.65 (0-6) 24 h post-op: 2.82 ± 2.98 (0-13) 48 h post-op: 2.82 ± 3.20 (0-13)
7. Occurrence of prolonged ileus	7.7% (n= 3)
8. Occurrence of burst abdomen	22.5% (n= 9)
9. Mortality	17.5% (n =7)
10. Duration of hospital stay (n= 33)	13.45 ± 10.28 days (Median 9 days)

RESULTS

Mean intra-abdominal pressure at admission was 13.73 mmHg while mean post-operative IAP was 8.77 mmHg. Incidence of IAH at admission was 65% (grade I IAH 37.5%, grade II IAH 22.5%, grade III and IV IAH 2.5% each). One patient died within 24 hours of surgery, due to which post-operative IAP values at 24 and 48 hours were obtained for 39 patients only. Post-laparotomy, normal IAP was seen in 82% and 92% after 24 and 48 hours of surgery, respectively. Grade I IAH was present in 15.4% patients after 24 hours of surgery, and 5.1% after 48 hours. Grade II IAH was seen in 2.5% patients after 24 as well as 48 hours. None of the patients had grade III or IV IAH post-operatively. Other relevant values have been shown in Table 1.

Pearson correlation co-efficient was calculated to determine the correlation between IAP measured at various time periods with the prognostic scores calculated at specified time intervals (Table 2). At Pearson co-efficient level of 0.05, the IAP measured after 24 hours of surgery correlated with SOFA score measured after 48 hours, which was statistically significant (p value 0.021). At the level of 0.01, statistically significant correlation was found between IAP measured after 24 hours, as well as after 48 hours of surgery (Table 3). Linear regression analysis using scatter plots between IAP and corresponding SOFA score revealed a small positive correlation between the two variables, which progressively increased from pre-operative to post-operative period (Figure 2).

Table 2. Distribution of IAP in patients of perforation peritonitis at specified time intervals					
IAP in mmHg (IAH Grade)	**<12 (no IAH)**	**12-15 (Grade I)**	**16-20 (Grade II)**	**21-25 (Grade III)**	**>25 (Grade IV)**
At admission (n= 40)	35%	37.5%	22.5%	2.5%	2.5%
Before induction of GA (n= 40)	35%	37.5%	22.5%	2.5%	2.5%
After induction of GA (n= 40)	37.5%	30%	30%	2.5%	0
24 h post-surgery (n= 39)	82.05%	15.4%	2.5%	0	0
48 h post-surgery (n= 39)	92.3%	5.1%	2.5%	0	0

Table 3. Correlation between intra-abdominal pressure (IAP) and prognostic scores								
	APACHE II at presentation		**SOFA score at presentation**		**SOFA score after 24 hours of surgery**		**SOFA score after 48 hours of surgery**	
	r	p	r	p	r	p	r	p
IAP at presentation	0.250	0.120	0.258	0.108	0.193	0.240	0.151	0.359
IAP before induction of GA	0.252	0.117	0.230	0.154	0.158	0.336	0.115	0.486
IAP after induction of GA	0.141	0.384	0.182	0.260	0.025	0.880	0.005	0.978
IAP after 24 hours of surgery	0.152	0.355	0.133	0.420	0.310	0.055	**0.368***	**0.021**
IAP after 48 hours of surgery	0.190	0.246	0.198	0.227	**0.482****	**0.002**	**0.565****	**<0.001**

*Correlation is significant at 0.05 level (2-tailed).
**Correlation is significant at 0.01 level (2-tailed).

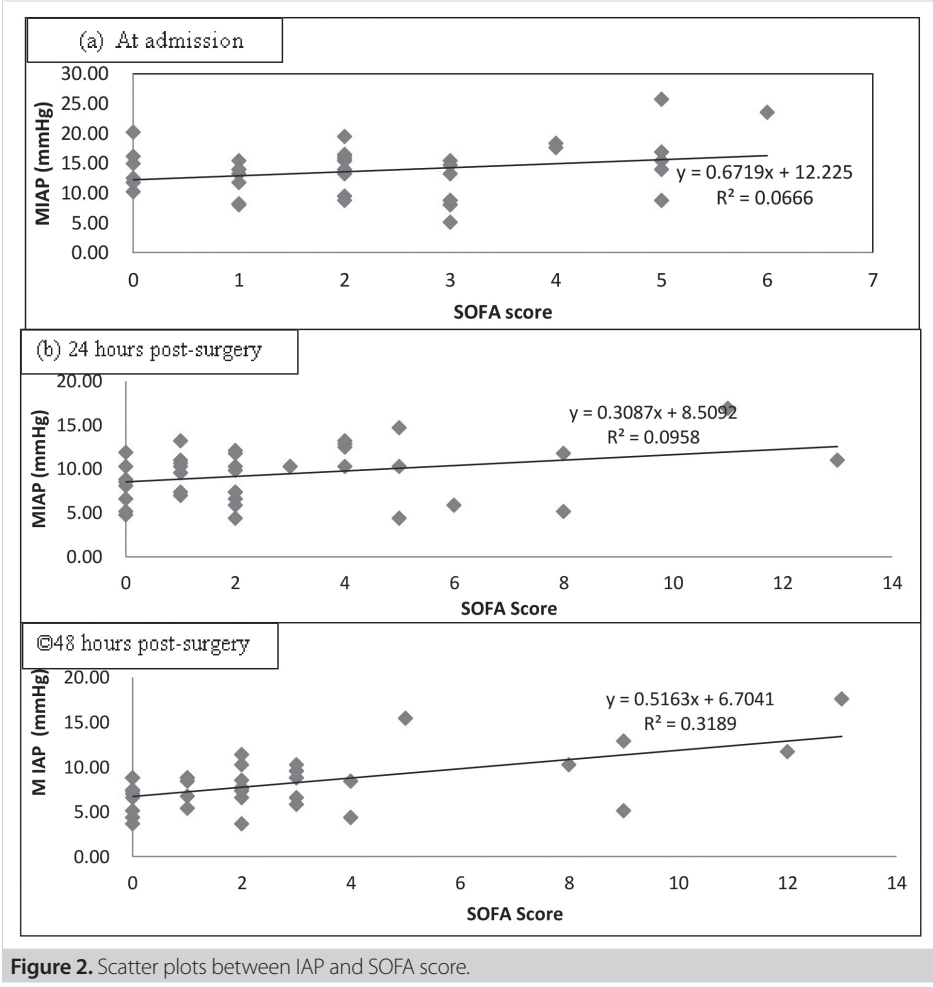

Figure 2. Scatter plots between IAP and SOFA score.

Table 4. Correlation between intra-abdominal pressure (IAP) and outcomes

Outcome	Value	Correlation with IAP (t-value)*	p
Mortality rate	17.5% (n= 7)	2.587	**0.014**
Incidence of prolonged ileus	7.7% (n= 3)	2.948	**0.006**
Incidence of burst abdomen	22.5% (n= 9)	1.087	0.284
Duration of hospital stay (in survivors)	13.45 days (n= 33)	-0.198	0.226

*t-value depicting the highest correlation with the mean IAP (amongst the mean IAP at 5 specified time periods) and the corresponding p-value has been shown.

Mortality rate was 17.5%, with majority of deaths occurring in the age group of 31-40 years (42.5%). IAP measured at 48 hours post-operatively correlated with mortality (p value 0.014). There was a positive correlation with IAP measured at 24 hours, but it was not statistically significant. Prolonged ileus was seen in 7.7% of the patients, and in them, the IAP measured at all five time periods correlated significantly (highest correlation seen with IAP just before induction of GA). Burst abdomen was seen in 22.5% of the cases, but its occurrence did not correlate significantly with IAP. Mean duration of hospital stay among the survivors was 13.45 days, and was not associated with the IAP.

DISCUSSION

Intra-abdominal hypertension (IAH) is defined as the sustained or repeated pathologic elevation of IAP >12 mmHg. Abdominal compartment syndrome is defined as a sustained increase in IAP > 20 mmHg that is associated with new organ dysfunction (8). Rise of IAP in perforation peritonitis is contributed by a number of factors. Site of perforation facilitates the escape of bowel gases and luminal contents. The spillage of these contents incites an inflammatory process that may involve the entire peritoneal cavity. A number of chemical mediators act on the large available surface area of the peritoneum and result in

third-space accumulation of fluid which can be as high as 4 to 6 liters (9). Edema of the abdominal contents increases their volume. In addition, adynamic ileus ensues that further distends the gut with fluid and swallowed air. Fluid secretion into the gut is markedly enhanced, whilst absorption of the fluid from the gut is markedly impaired. There is therefore, sequestration of a large volume of fluid within the lumen of the gut. Marked peritoneal inflammation is often associated with guarding. This spasm of the abdominal musculature impedes abdominal wall expansion, thereby contributing to the increase in IAP.

In our study, mean IAP in patients of perforation peritonitis, measured at admission was 13.73 ± 4.30 mmHg. Following this measurement, Ryle's tube insertion was done and patients were resuscitated to be taken up for surgery. The patients were then shifted inside the operating room where IAP was measured just prior to induction of GA. Mean value was 13.44 ± 4.90 mmHg, which was slightly less than the IAP at admission. This can be explained by gastric decompression following Ryle's tube insertion. Post-induction, but prior to laparotomy, the mean value was 13.31 ± 4.28 mmHg. This further fall can be explained by relaxation of the abdominal muscles caused by muscle relaxants that are used as a part of general anesthesia. In fact, neuromuscular blockade is one of the proposed non-operative methods of management of IAH/ACS in non-surgical patients (10). It can be seen in Table 2 that there is a slight increase in the incidence of grade II IAH after induction of general anesthesia. This paradox can be attributed to the effect of positive airway pressure during which the diaphragm is pushed down, thereby marginally increasing the IAP. The next measurements of IAP were taken at 24 and 48 hours post-operatively. Mean values were 9.63 ± 2.96 and 8.44 ± 2.9 mmHg, respectively, both falling in the range of normal IAP. Overall, mean post-operative IAP was 8.77 ± 3.01. Incidence of IAH at admission in our study was 65%. Post-operatively, IAH was seen in only 17.9% and 7.6% respectively at 24 and 48 hours respectively.

Mean IAP in the cases studied by Sugrue et al. (11) before and after decompression is 16.6 ± 9.4 mm Hg and 10.3 ± 3.1 mm Hg, respectively, while Meldrum et al. (12) have reported IAP values of 27 ± 2.3 and 14 ± 4.6 mmHg, respectively. Daga and coworkers (13) have reported an overall 65% incidence of IAH at admission, which is similar to our study. The incidence of IAH fell to just 8% after 24 hours of surgery, which was lower than in our study. Kidwai et al. (1) in their study have reported an overall IAH incidence of 32%, while that in the sub-group of patients with perforation peritonitis was 66.32%. In the IROI study, IAH was present in 34.0% of the critically ill patients on the day of ICU admission (14). The severity of intra-abdominal hypertension was as follows: grade I, 47.5%; grade II, 36.6%; grade III, 11.7%; and grade IV, 4.2%.

A large number of studies have demonstrated that raised IAP adversely affects various organ systems (15-17). This dysfunction is often reflected in the deterioration of prognostic scores such as APACHE II and SOFA score, which are widely used world over.

Mean APACHE II score at admission in our study was 7.55 ± 4.96 (range 0-21), and there was no correlation with the values of IAP. Mean SOFA score at admission, and post-operatively at 24 and 48 hours respectively were 2.25 ± 1.65, 2.82 ± 2.98 and 2.82 ± 3.20. In our study, 24 hours post-operative SOFA score correlated with IAP measured after 48 hours of surgery and was significant (p value 0.021). Also, 48 hours post-operative SOFA score correlated significantly with both the IAP values measured post-operatively (24 and 48 hours, p value 0.002, <0.001 respectively) (Table 3).

Median baseline APACHE II score reported by De-Waele and coworkers was 25.5 (20.0-31.8). The higher score was because the study included patients with established ACS who were to undergo decompressive laparotomy (DL). Median SOFA score before DL was 10 (7-12) which initially increased to 11 (8-13) at 24 h (p= 0.02), then reduced to 9 (5-13) on day 3 (p= 0.871) and 6 (4-11) on day 7 (p= 0.098) after DL. Their study confirmed the beneficial effect of timely DL on organ dysfunction (18).

In a study by Kulkarni et al., mean APACHE II score was 11.38 (range of 1-23). They concluded that APACHE-II score between 11 and 20 was a better predictor of risk of mortality in patients with perforation peritonitis (19). In the study by Pereira and colleagues, mean SOFA score on admission was 6.54 ± 2.71, while it was higher in patients with the diagnosis of ACS (8.42 ± 1.27) (20). The authors have concluded that SOFA score at admission higher than 7 correlated with IAH, with an accuracy of 68.8% (p< 0.03). Dorigatti et al. have concluded in their study that elevated IAP correlated with higher central venous pressure (CVP) (p= 0.0421); positive end-expiratory pressure (PEEP) (p= 0.0056); elevated airway pressure (p= 0.0015); accumulated fluid balance (p= 0.0273), and elevated SOFA (p= 0.0393) in septic patients (21).

Mortality rate in our study was 17.5%. A similar mortality rate (16.7%) has been reported in another study (22). The mortality rate reported by Meena et al. was 14.7% while Jhobta et al. (23) has reported mortality rate of 10%.

In our study, among the various IAP values, statistically significant correlation with mortality was seen only with post-operative IAP measurement taken at 48 hours (p value 0.014). Kidwai and colleagues have reported that elevated IAP pre-operatively and post-operatively at 6 hours was found to independently predict the occurrence of death (p< 0.05) but not at 0, 12 and 24 hours post-operatively (p> 0.05) (1). In the IROI study, the authors have concluded that the severity of intra-abdominal hypertension during the first 2 weeks of the ICU stay was identified as an independent predictor of 28- and 90-day mortality, whereas the presence of intra-abdominal hypertension on the day of ICU admission did not predict mortality (14).

Prolonged ileus was seen in only 7.7% (n= 3) patients. In these patients, its occurrence correlated significantly with all five IAP values, highest with IAP just before induction of GA (p value 0.006). Agrawal and colleagues have reported occurrence of prolonged ileus in 8% of patients but found no statistically significant correlation with IAP (24).

It has been postulated that poor healing and possible dehiscence of abdominal surgical wounds may result from reduced blood flow to the abdominal wall caused by increased IAP (25). Burst abdomen occurred in 22.5% (n= 9) cases and there was no correlation with IAP. A similar incidence (20%) has been reported in one Indian study (26). No significant association has been found between IAP at any point of time and occurrence of burst abdomen in the study by Khan et al. (27).

Among the 33 survivors, mean duration of hospital stay was 13.45 ± 10.28 days (median 9 days). There was no correlation with IAP measurements. Mean post-operative duration of hospital stay was 7.6 ± 4.2 days in the study by Gupta et al. Another study reported a prolonged hospital stay in 47% of the cases (13). Al-Bahrani et al. found have that a high admission IAP is associated with prolonged intensive care stay (28).

Intra-abdominal pressure undoubtedly influences patient outcome, contributing to both mortality as well as morbidity, although to a varying extent. While some outcomes may be significantly affected, others tend to be less conducive to the changes in IAP.

The study has a few limitations. First, the sample size was relatively small as the study was conducted in only one surgery unit of the institute. Second, the duration of symptoms was not taken into consideration. Also, some patients were operated within a few hours of admission, while some others needed longer time for optimization prior to be taken up for surgery. This difference in time lag could not be accounted for in the study. Third, there is a possibility of human observational bias as the IAP was read on a saline manometer instead of a digital pressure transducer. Fourth, the first post-operative measurement of IAP was taken only after 24 hours of surgery even though some studies have shown that post-operative IAP measured at much earlier times (4-6 hours) predicts outcomes. Lastly, occurrence of burst abdomen is multi-factorial and IAP is only one of the putative factors. The confounding effect of other factors could not be eliminated.

CONCLUSION

Rise in IAP correlates with deterioration of SOFA score and also with the occurrence of prolonged ileus. It is also a predictor of mortality. IAP measured post-operatively (24 and 48 hours) had a better correlation with these outcomes than the value measured at admission. No statistically significant correlation could be found with the occurrence of burst abdomen, as well as duration of hospital stay. Further understanding of these relationships warrants studies with a larger sample size. Thus, IAP measurement is a simple inexpensive bedside tool which can be regularly used in clinical practice to understand its role in the outcomes of these patients, and for their better management.

Ethics Committee Approval: This was obtained from Maulana Azad Medical College and Associated Hospital Instutional Ethics Commitee. (Date: 21.10.2018, Decision no: 17/IEC/MAMC/2018/15)

Peer-review: Externally peer-reviewed.

Author Contributions: Concept –L.B., P.L., P.K.N.; Design – L.B., P.K.N., A.M.; Supervision –P.L., A.M., P.K.N., L.B.; Data Collection and/or Processing - L.B., P.K.N., M.Y.B.; Analysis and/or Interpretation – L.B. P.K.N., P.L., A.M.; Literature Search – L.B. P.K.N., P.L., A.M.; Writing Manuscript – P.K.N., L.B., H.M., Critical Reviews – All of authors.

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

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2021; 37 (3): 253-259

Perforasyon peritonitinin sonuçlarında karın içi basıncın rolü: İleriye dönük bir gözlemsel çalışma

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ÖZET

Giriş ve Amaç: Karın içi basıncın (IAP), morbidite ve mortaliteye etkisindeki rolünü araştıran çeşitli çalışmalarda farklı korelasyon dereceleri göstermiştir. Bu konuda perforasyon peritoniti hastalarında, özellikle Hint yarımadasındaki çalışmalara dayanan literatür eksikliği vardır.

Gereç ve Yöntem: Bu araştırma, laparotomi yapılan perforasyon peritonitli 40 hastayı içeren prospektif bir gözlemsel çalışmadır. IAP, WSACS (World Society of Abdominal Compartment Syndrome) yönergelerine göre ölçülmüştür. Bu itibarla hastalarda APACHE II (Acute Physiology and Chronic Health Evaluation- II) ve SOFA skorları (Sequential Organ Failure Assessment) hesaplandı. Uzamış ileus, evantrasyon, hastanede kalış süresi, 30 günlük mortalite ile ilgili veriler toplandı ve IAP ile korelasyon gösterecek şekilde istatistiksel olarak analiz edildi.

Bulgular: Başvuru sırasında ortalama IAP 13,37 mmHg ve IAH insidansı %65 idi. Ameliyat sonrası 24. saat ve 48. saatte IAH %17,9 ve %7,6'da görüldü. Uzamış ileus ve evantrasyon insidansı sırasıyla %7,7 ve %22,5 idi. Ölüm oranı %17,5 idi. Ortalama hastanede kalış süresi 13,45 gündü. Ameliyat sonrası IAP mortalite (p: 0,014) ve ameliyat sonrası SOFA skoru (p< 0,05) ile korele idi. Uzamış ileus oluşumu ile de istatistiksel olarak anlamlı korelasyon görüldü (p: 0,006). IAP, APACHE II skoru, patlama karnının oluşumu ve hastanede kalış süresi ile anlamlı bir korelasyon göstermedi.

Sonuç: IAP'deki artış, SOFA skorunun bozulması ve ayrıca uzamış ileus oluşumu ile ilişkilidir. IAP ayrıca mortalitenin bir öngörücüsüdür. Postoperatif olarak ölçülen IAP (24 ve 48 saat), bu sonuçlarla, başvuru sırasında ölçülen değerden daha iyi bir korelasyona sahipti. IAP'nin evantrasyon oluşumu ve hastanede kalış süresi ile istatistiksel olarak anlamlı bir korelasyonu bulunamamıştır. Bu daha geniş bir popülasyonla yapılacak daha ileri çalışmaları desteklemektedir.

Anahtar Kelimeler: Perforasyon peritoniti, karın içi basınç, karın içi hipertansiyon

DOİ: 10.47717/turkjsurg.2021.4945

ORIGINAL ARTICLE
Turk J Surg 2021; 37 (3): 260-265

Management of sacrococcygeal pilonidal sinus disease in children: A survey study in Turkey

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ABSTRACT

Objective: Sacrococcygeal pilonidal sinus disease is common in children. The disease reduces the quality of life of patients with symptoms such as pain and chronic discharge. Variable surgical techniques have been described for the treatment of pilonidal sinus disease. This study aims to evaluate clinical approach of Turkish pediatric surgeons to children with pilonidal sinus disease.

Material and Methods: Survey questions were prepared through a literature review for controversial issues. The participants were asked pre-selected and checkbox questions. The survey was sent to 450 pediatric surgeons, members of the Association of Turkey Pediatric Surgery via a link to Google Forms.

Results: Nineteen percent (88) of the members responded. Seventy five (85.2%) of the pediatric surgeons stated that they did not perform additional preoperative imaging. Surgical excision methods were preferred more than minimally invasive procedures (102 to 46). Sixty (68.2%) of the participants preferred preoperative prophylactic single dose intravenous antibiotics and postoperative oral antibiotics. Regarding the participants' practices, poor local hygiene, overweight, wide or deep sinus pit were stated as the most common causes of recurrence. Vast majority of the pediatric surgeons recommended laser epilation (%85.2) and slimming (59.1%) to patients.

Conclusion: Various studies have been published from Turkey for pilonidal sinus disease. As seen in the current study, Turkish pediatric surgeons do not have a common opinion in pilonidal sinus disease and prefer surgical excision methods more frequently. Prospective randomized studies with bigger number of patients are required to establish common guidelines in disease management.

Keywords: Pilonidal sinus, child, surveys and questionnaires

INTRODUCTION

Although it is not as common as it is in adult population, sacrococcygeal pilonidal sinus disease (PSD) is not very rare in children (1). The disease reduces the quality of life of patients with symptoms such as pain and chronic discharge (2). There are many different approaches to PSD management (3). Variable surgical techniques have been described for the treatment of PSD, and optimal choice remains controversial (4). The ideal treatment for PSD should lead to a cure with rapid recovery period and associated morbidity as low as possible especially in adolescents concerning the effects of longer time with disease at school and social life (4,5). However, there is no ideal approach, and the treatment of the disease varies between centers (6). PSD is common in Turkish adolescents (7). The study aims to evaluate the clinical approach of Turkish pediatric surgeons to children with PSD.

MATERIAL and METHODS

The survey questions were prepared through a literature review for controversial issues in PSD treatment. The participants were asked pre-selected and checkbox questions about their demographic features, preoperative preparation, surgical techniques, approach to patients with different symptoms, postoperative advice and follow-up. The questionnaire was tested online among the authors before it was sent to the participants. The study was approved by the local ethical committee. The approval for the study was obtained from the clinical practices local ethics committee of the university in 13.07.2020 (No: I6-367-20). The survey was sent without excluding any members via a link to Google Forms. The survey was sent to the participants only once via e-mail and it was expected to be answered within a month.

Cite this article as: Gurbanov A, Ergün E, Göllü G, Ateş U. Management of sacrococcygeal pilonidal sinus disease in children: A survey study in Turkey. Turk J Surg 2021; 37 (3): 260-265.

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Received: 17.11.2020
Accepted: 19.04.2021
Available Online Date: 28.09.2021

DOI: 10.47717/turkjsurg.2021.5100

RESULTS

Eighty-eight members responded. The response rate of the participants was 19.5%. Thirty-four (38.6%) of them had more than 16 years of experience in pediatric surgery. Half of the participants (47.7%) were working in university hospitals. The majority of the participants (72.8%) stated that they treat an average of 0 to 20 pilonidal sinus patients annually. Only seven (8%) surgeons stated that they treated 40 or more PSD patients annually. Demographic features of the participants are given in Table 1. Seventy five (85.2%) of the pediatric surgeons stated that they did not perform additional preoperative imaging. The most (12.5%) preferred imaging method was ultrasonography (USG). Eighty-one of the participants (92.1%) preferred surgical intervention when there could be no drainage. When the pediatric surgeons were asked about their preferred treatment methods, it was seen that surgical excision methods were preferred more than minimally invasive procedures (102 to 46). The most preferred surgical technique was "Excision and primary closure" (62.5%). The most commonly applied of minimally invasive methods was "phenol injection" (34.1%). It was seen that most of the participants did not routinely apply phenol repeatedly but only when the patient's complaints lasted. Detailed preoperative approaches are given in Table 2. In the approach to complicated patients (abscess developed and/or has a large defect and/or recurrent), surgical excision techniques (62.5%) were preferred as the primary approach more than minimally invasive techniques. Thirty-four (38.6%) of the participants suggested clinical follow-up for asymptomatic patients. In pediatric patients, it was seen that there was no surgical procedure without anesthesia for PSD and the most preferred method was general anesthesia (55.7%). Sixty (68.2%) of the participants preferred preoperative prophylactic single dose intravenous antibiotic and postoperative oral antibiotic in patients with PNS disease. Five participants (%5.7) stated that they did not use antibiotics before or after the operation. Detailed intraoperative approaches are given in Table 3. Regarding the participants' practices, poor local hygiene, overweight, wide or deep sinus pit were stated as the most common causes of recurrence. The vast majority of pediatric surgeons recommended laser epilation (%85.2) and slimming (59.1%) to patients. Forty-two (47.7%) of the participants stated that children needed 2-7 days for wound care after surgery, and 29 (33%) participants stated that their patients returned to school or work within 8-14 days after intervention. Detailed postoperative approaches are given in Table 4.

DISCUSSION

The present study showed that there are many different approaches in PSD among the Turkish pediatric surgeons.

Majority of the participants in this study did not use preoperative imaging. Usually, complementary investigations are seldom needed because the diagnosis of pilonidal sinus disease is clinically easy (6). Nonetheless, x-ray imaging, sonography or magnetic resonance imaging are sometimes useful to eliminate anorectal fistula, or posterior anorectal tumor or sacral osteomyelitis (8-10). However, imaging methods such as ultrasonography and MRI play an important role in the planning and treatment of pilonidal sinus disease and helps to determine the prognosis of the disease (11,12).

In this study, the participants preferred surgical excision methods more frequently than minimally invasive methods in the treatment of PSD. The most preferred surgical excision method was excision with primary midline closure followed by excision with secondary healing and 'excision with flap closure techniques, respectively.

In the literature, although there was no significant difference between primary closure and secondary healing techniques after excision in terms of length of hospitalization, duration of postoperative pain and recurrence rate, the recovery time of patients in the first group was significantly shorter (5,13,14).

There is a limited number of child studies for " Excision with flap closure ", and it is recommended to be used in complicated cases (15). However, it is emphasized that this method has a lower rate of recurrence compared to other excision methods (16,17).

Table 1. Demographic features of the participants

How many years have you been a pediatric surgeon?			
0-5 years	14 (15.9%)	6-10 years	19 (21.6%)
11-15 years	21 (23.9%)	16 and more years	34 (38.6%)
Which institution do you work in?			
Public hospital	9 (10.2%)	Education - research hospital	26 (29.5%)
University hospital	42 (47.7%)	Private hospital	11 (12.5%)
On average, how many pilonidal sinus patients do you treat per year?			
0-10	32 (36.4%)	10-20	32 (36.4%)
20-30	6 (6.8%)	30-40	11 (12.5%)
40 and more	7 (8%)		

Table 2. Preoperative approaches			
Preoperative imaging			
No	75 (85.2%)	Sacral x-ray	2 (2.3%)
Ultrasonography	11 (12.5%)	Computed tomography	2 (2.3%)
Magnetic resonance tomography	5 (5.7%)		
Treatment options			
Excision with primary midline closure	55 (62.5%)	Endoscopic treatment	6 (6.8%)
Excision with secondary healing	34 (38.6%)	Conservative treatment	4 (4.5%)
Excision with flap closure	13 (14.8%)	Aethoxysklerol treatment	2 (2.3%)
Phenol treatment	30 (%34,1)	Microsinusectomy	4 (4.5%)
Surgical method preferred reason			
Surgical experience	57 (64.8%)	Minimally invasive	30 (34.1%)
Low recurrence rate	47 (53.4%)	Other methods do not benefit	13 (14.8%)
Short processing time	20 (22.7%)	Be reliable	29 (33%)
How many times do you apply phenol in routine practice? (Total answers: 34)			
For once	9 (26.5%)	Three times	8 (23.5%)
Twice	3 (8.8%)	As the complaints repeat	14 (41.2%)
If you apply phenol repeatedly, how often do you apply it? (Total answers: 30)			
Weekly	2 (6.7%)	Monthly	2 (6.7%)
Biweekly	2 (6.7%)	If recurrence develops	20 (66.7%)
Every three weeks	4 (13.3%)		

Although surgical excision techniques are used more frequently in the treatment of pilonidal sinus, invasive surgical techniques contain the risk of wound infection and require a long postoperative wound healing period (18).

In the last years, as in many areas of pediatric surgery, there is a tendency to turn towards minimally invasive methods in the treatment of pilonidal sinus disease (19,20). It is thought that as the studies on the field of minimally invasive treatments increase, those who turn to this field will increase (21). In the current study, about one third of the participants stated that they used minimally invasive methods.

Among the minimally invasive methods, the most preferred one was phenol injection. Phenol injection is gaining popularity as a minimally invasive method in the treatment of PSD (22,23). The method has started to be widely applied today because it can be performed daily, it is re-applicable, and applicable under local anesthesia and sedation. It also has the advantages of low surgical costs, low risk of postoperative infection and low need for postoperative wound care (18,24-26).

Two-thirds of the pediatric surgeons stated that they perform phenol injection only once and repeat the application only when recurrence occurs. Only ten participants routinely administered phenol injections; twice or more.

Even though it is not proven by randomized controlled studies, it has been stated that two or more phenol applications in PSD treatment have higher success rate than one-time phenol application (27,28).

Forty percent of the participants who made more than one phenol injection in their routine practice stated that they repeated the application every three weeks. Dogru O. recommends applying phenol injection three times with two-week intervals (29).

Minimally invasive methods are also useful in recurrent cases (28,30). In recurrent cases, participants preferred surgical excision techniques more frequently.

In the current study, clinical follow-up and conservative treatment were the most preferred in the approach to asymptomatic cases. Doll D. et al. argue that prophylactic surgery will not benefit in asymptomatic cases, and follow-up will be sufficient (31).

CONCLUSION

Various studies have been published from Turkey for PSD. The vast majority of these studies are case series and introduction or comparing of the treatment methods, and there are limited studies such as review on disease management. As seen in the current study, Turkish pediatric surgeons do not have a common opinion in pilonidal sinus disease and prefer surgical excision methods more frequently. Prospective randomized studies with bigger number of patients are required to establish common guidelines in disease management.

Table 3. Intraoperative approaches. IV – intravenous; AB - antibiotic			
Approach to complicated patients			
Excision with primary midline closure	26 (29.5%)	Excision with flap closure	19 (21.6%)
Excision with secondary intention healing	10 (11.4%)	Minimally invasive methods	7 (8%)
Minimally invasive methods first, surgical excision if unsuccessful			26 (29.5%)
Approach to asymptomatic patients			
Conservative treatment	21 (23.9%)	Surgical excision	20 (22.7%)
Minimally invasive methods	13 (14.8%)	Clinical follow-up	34 (38.6%)
Approach in patients with multiple pilonidal sinus pits or large sinus cavities			
Surgical excision	60 (68.2%)	Minimally invasive methods	28 (31.8%)
Anesthesia method			
Without anesthesia	0	Regional - spinal anesthesia	47 (53.4%)
Local anesthesia	18 (20.5%)	Intravenous sedation	20 (22.7%)
General anesthesia			49 (55.7%)
Antibiotic therapy during surgery			
Preoperative IV prophylaxis	5 (5.7%)	Postoperative oral antibiotic	6 (6.8%)
IV prophylaxis and postoperative oral AB	60 (68.2%)	IV AB before and after surgery	12 (13.6%)
I don't use antibiotics			5 (5.7%)

Table 4. Postoperative approaches									
Postoperative recommendations									
Laser hair removal	78 (88.5%)				Peroral antibiotic therapy		34 (38.6%)		
Do not lie back	40 (45.3%)				Slimming		53 (60.2%)		
Local treatment with antibiotics	19 (21.6%)				Negative pressure wound therapy		1 1.1%)		
Wound care period after surgery									
1 day	13 (14.8%)	2-7 days	42 (47.7%)	8-14 days	22 (25%)	15-21 days	5 (5.7%)	22 and more	6 (6.8%)
Postoperative control									
First day after surgery	4 (4.5%)				Weekly		34 (38.6%)		
Monthly	12 (13.6%)				If recurrence		5 (5.7%)		
Daily or weekly until the wound care need is over	33 (37.5%)								
Time back to school or work after surgery									
1 -2 days	14 (15.9%)	3-7 days	24 (27.3%)	8-14 days	29 (33%)	15-21 days	12 (13.6%)	22 and more	9 (10.2%)
The most common cause of recurrence									
Poor local hygiene	68 (77.3%)		Overweight		58 (65.9%)	Surgery technique		47 (53.4%)	
Large sinus cavities	43 (48.9%)		Prolonged sitting		42 (47.7%)	Preoperative abscess		27 (30.7%)	
Male sex	25 (28.4%)		Delayed treatment		21 (23.9%)	No AB postoperatively		18 (20.5%)	
Smoking	9 (10.2%)		High patient age		8 (9.1%)				

Ethics Committee Approval: The study was obtained from Ankara University Human Researches Ethical Committee (Decision No: İ6-367-20, Date: 13.07.2020).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.Q., E.E., U.A.; Design - A.Q., E.E.; Supervision - U.A., G.G.; Data Collection and/or Processing - A.Q., E.E.; Analysis and/or Interpratation - G.G., U.A.; Literature Review - A.Q., E.E.; Writing Manuscript - U.A.; Critical Reviews - E.E., G.G., U.A.

Conflict of Interest: The authors declare that they have no conflict of interest.

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2021; 37 (3): 260-265

Çocuklarda sakrokoksigeal pilonidal sinüs hastalığının yönetimi: Türkiye'de bir anket çalışması

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ÖZET

Giriş ve Amaç: Sakrokoksigeal pilonidal sinüs hastalığı çocuklarda yaygındır. Bu hastalık ağrı ve kronik akıntı gibi semptomları ile hastaların yaşam kalitesini düşürür. Pilonidal sinüs hastalığının tedavisi için çeşitli cerrahi teknikler tarif edilmiştir. Bu çalışma Türk çocuk cerrahların pilonidal sinüs hastalığı olan çocuklara klinik yaklaşımlarını değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntem: Anket soruları, tartışmalı konular için bir literatür taraması yoluyla hazırlandı. Katılımcılara önceden seçmeli ve onay kutulu sorlar soruldu. Anket, Türkiye Çocuk Cerrahisi Derneği üyesi 450 çocuk cerrahına Google Formlar bağlantısı üzerinden gönderildi.

Bulgular: Üyelerin %19'u (88) ankete yanıt verdi. Çocuk cerrahlarının 75'i (%85,2) ameliyat öncesi ek görüntüleme yapmadıklarını belirtti. Minimal invaziv işlemlere göre cerrahi eksizyon yöntemleri daha çok tercih edildi (102-46). Katılımcıların 60'ı (%68,2) preoperatif profilaktik tek doz intravenöz antibiyotik ve postoperatif oral antibiyotiği tercih etti. Katılımcılar kötü lokal hijyen, fazla kilo, geniş veya derin sinüs çukuru nüksün en yaygın nedenleri olarak belirtilmektedir. Çocuk cerrahlarının büyük çoğunluğu hastalara lazer epilasyon (%85,2) ve zayıflama (%59,1) önermişlerdir.

Sonuç: Pilonidal sinüs hastalığı için Türkiye'den çeşitli çalışmalar yayınlanmıştır. Bu çalışmada da görüldüğü gibi Türk pediatrik cerrahların pilonidal sinüs hastalığı konusunda ortak bir görüşü yoktur ve daha sık cerrahi eksizyon yöntemlerini tercih etmektedir. Hastalık yönetiminde ortak kılavuzlar oluşturmak için daha fazla sayıda hasta içeren prospektif randomize çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Pilonidal sinus, çocuk, anket

DOİ: 10.47717/turkjsurg.2021.5100

ORIGINAL ARTICLE
Turk J Surg 2021; 37 (3): 266-276

Turkish primary care physicians' attitudes and knowledge of obesity and bariatric surgery: a survey study

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ABSTRACT

Objective: This survey study attempted to determine Turkish primary care physicians' (PCP) knowledge, attitudes, and perceptions of obesity treatment and bariatric surgery. Moreover, the relationship between the duration of practice as a physician, and especially the indications for bariatric surgery and referral to surgery were investigated.

Material and Methods: A survey of 27 questions was administered via social media and the internet using the SurveyMonkey platform. The physicians who responded to the survey were grouped based on the duration of working life. Among these groups, the responses to the questions about bariatric surgery were compared using univariate analysis.

Results: A total of 1044 physicians responded to the survey. The number of physicians who strongly agreed that a PCP should play role in the treatment of obesity was 743 (71.1%). The most important reason for not undertaking this treatment was reported as the requirement for a multidisciplinary approach to obesity treatment (51.5%, n= 537). The percentage of those who thought that patients with a body mass index (BMI) above 40 kg/m^2 should be referred to surgery was 72.3%,while the percentage of those referring patients with a BMI of 35-40 kg/m^2 and comorbidities to surgery was 53.3%, and the percentage of those referring patients with a BMI of 35-40 kg/m^2 and uncontrolled diabetes to surgery was 35.9%. Physicians who were new to the profession were found to evaluate surgical indications more positively ($p< 0.05$).

Conclusion: This study found that PCPs in Turkey had a basic knowledge of obesity treatment and were willing to treat and follow up these patients. However, it was observed that they could not adequately focus on this issue due to the requirement for a multidisciplinary approach to the disease and the workload. It was found that the young physicians› level of knowledge of bariatric surgery was higher, but their attitudes towards patient referral were similar.

Keywords: Primary care physicians, obesity treatment, obesity surgery, survey study

INTRODUCTION

Obesity is a serious public health problem with an increasing prevalence worldwide. According to the data of the Ministry of Health, 41% of women and 20.5% of men in Turkey are obese (1). These rates indicate that Turkey is among the countries with the highest prevalence of obesity. Despite all the measures taken and warnings, the prevalence of obesity does not decrease (2). Obesity treatment is complex and requires a multidisciplinary approach. Depending on its severity, the treatment approach may be diet, exercise, lifestyle modifications and medication, endoscopic interventions, and surgery for patients with an indication (3).

Primary care physicians (PCPs) are usually the first to encounter these patients, treat, follow up, and refer them, and participate in their postoperative long-term follow-ups. Therefore, their knowledge of treatment, approaches, and facilities is of great importance. It has been determined that only 29% of obese individuals in the USA are recorded when they visit a physician, and the physicians are reluctant to offer treatment, refer, and motivate these patients due to various factors (4,5).

Among all modalities, bariatric surgery has been the most effective treatment approach so far. It provides both more and long-term postoperative weight loss. The improvement rate of metabolic problems secondary to obesity is much higher. A meta-analysis of thirty-eight randomized controlled studies has found mortality rate following bariatric surgery as 0.18% (6). Despite all documented advantages of surgery, a significant bias remains about the surgery. Therefore, surgical approaches are not offered as an option to many patients who may benefit from it. Primary care

Cite this article as: Özgüç H, Narmanlı M, Çırnaz H. Turkish primary care physicians' attitudes and knowledge of obesity and bariatric surgery: a survey study. Turk J Surg 2021; 37 (3): 266-276.

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Received: 23.11.2020
Accepted: 19.05.2021
Available Online Date: 28.09.2021

DOI: 10.47717/turkjsurg.2021.5149

physicians are at the forefront of obesity treatment, follow-up, and referral to surgery. Referral of obese patients to surgery by their PCPs is important and increases the rate of accepting surgery. A study from Canada has shown that primary care physicians directed only.

42% of obese patients for treatment due to various factors. These factors have generally been reported as a negative attitude towards the disease and treatment, workload, lack of knowledge, insufficient infrastructure, and lack of motivation (7-9).

Identifying problems and deficiencies in this field is particularly important in terms of developing training programs. Results from different countries and regional studies will provide valuable insight into measures to be taken and what to do. There is no published Turkish study on the subject. The primary aim of the present study was to evaluate Turkish PCPs' basic level of knowledge, attitudes, and perceptions of obesity treatment and bariatric surgery with a survey study, and on what subjects they demand information and support. The secondary aim of this study was to investigate the relationship between the duration of practice as a physician, knowledge of the indications for bariatric surgery, and referral to surgery.

MATERIAL and METHODS

Survey Design

The target population of the study was determined as PCPs working as family physicians in Turkey. The survey was prepared by a surgeon experienced in bariatric surgery by reviewing similar studies in the literature, including standard guidelines. The members of the Board of Directors of the Turkish Society for Metabolic and Bariatric Surgery then assessed the survey and contributed to it. The prepared survey was administered to a pilot sample of 10 PCPs as a pre-test survey, and it was finalized as a survey of 27 questions to be completed approximately within 6 minutes following their responses and comments. The survey included questions about consent (1 question), demographic data and workload (6 questions), basic knowledge of obesity evaluation, treatment, attitude (11 questions), basic knowledge of surgery, indications, follow-up, referral to surgery, and training (9 questions). The questions about demographic data,

attitude towards obesity, and demands in practice were multiple-choice and open-ended, while the other questions were prepared as a five-point Likert scale (strongly disagree, disagree, neutral (no idea), agree, strongly agree). The survey questions are presented in Appendix 1. The approval for the study was obtained from the Ethics Committee of Uludag University ethics committee approval number: 2019-10/4). An information letter was prepared for the survey and consent was obtained from all participants for the scientific use of the study results.

Data collection and Statistical Analysis

There were 25 thousand PCPs working as family physicians in Turkey in 2019, according to the data of the Ministry of Health of Turkey (1). It was planned to reach 1023 physicians with a margin of error of 3% at a 95% confidence interval. The survey was introduced via the SurveyMonkey website. The link of the survey was distributed via social media and sent to association websites as well as randomly selected physicians. A total of 1044 PCPs responded to the survey. The physicians who responded to the survey were grouped based on the duration of practice as follows: 0-5 years of experience, 6-10 years of experience, 11-20 years of experience, 21-30 years of experience, and over 30 years of experience. Among these groups, the responses to the questions about bariatric surgery were compared using univariate analysis. Chi-square test or Fisher's exact test was used for comparison. The level of significance was set at $p<0.05$. Statistical analysis results were acquired using the SurveyMonkey software.

RESULTS

Demographic Results

A total of 1044 physicians responded to the survey. Of the respondents, 906 (79.1%) were working in the most populous 4 major cities of Turkey with a total number of family physicians of 8178. While none of the physicians working in 29 provinces responded to the survey, 1 to 33 physicians from the other forty-eight provinces participated in the survey. Analysis of age distribution of the physicians who participated in the survey revealed that the majority of the participants were in the age range of 31-40 (378, 36.2%) years and 41-50 (315, 30.1%) years. Considering the distribution of duration of practice, those with 11-20 years of experience (321, 30.75%) ranked first, while those with 21-30 years of experience (267, 25.57%) ranked second. While the number of patients examined by 355 (34.1%) physicians per week was between 201 and 300, 277 (26.61%) physicians reported that they examined 301-400 patients per week. Of the physicians, 224 (21.58%) stated that 11-15% of their patients were obese, and 222 (21.39%) stated that 16-20% of their patients were obese. The demographic distribution of the physicians who responded to the survey, their workload, and the number of patients who had undergone bariatric surgery and followed up by them are presented in Table 1.

Level of Knowledge and Attitude towards Obesity Treatment

The percentage of physicians who strongly agreed with the question "obesity is a chronic disease defined as an excessive accumulation of body fat to an extent to impair health" was 38.1% (n:398), while the percentage of those who agreed with that was 53.9% (563). The percentage of physicians who strongly agreed that the reason for the increase in obesity prevalence was a sed-

Table 1. Demographic data and workloads of physicians participated in the survey

Province of work (81)	
4 major cities	906 (79.1%)
Other provinces (48)	138 (20.9%)
Age distribution	
24-30 years	203 (19.4%)
31-40 years	378 (36.2%)
41-50 years	315 (30.2%)
51-60 years	136 (13%)
Over 60 years	12 (1.2%)
Duration of practice	
0-5 years	198 (19.9%)
6-10 years	205 (19.7%)
11-20 years	321 (30.7%)
21-30 years	267 (25.6%)
Over 30 years	53 (5.1%)
Weekly number of patients	
0-100	115 (11%)
101-200	190 (18.2%)
201-300	356 (34.1%)
301-400	278 (26.6%)
401-500	75 (7.2%)
Above 500	30 (2.9%)
Rate of obese patients	
0-5%	85 (8.2%)
6-10%	212 (20.3%)
11-15%	226 (21.6%)
16-20%	225 (21.5%)
21-25%	164 (15.8%)
26-30%	80 (7.7%)
31-40%	39 (3.7%)
Above 40%	13 (1.2%)
Number of patients who had undergone bariatric surgery	
Yes	344 (32.9%)
No	700 (67.1%)

entary lifestyle and easy access to food was 40.8% (n:426), and the percentage of physicians who agreed with that was 47.8% (n:499). While a significant proportion of physicians agreed with the knowledge that the prevalence of obesity in Turkey is around 30%, 204 physicians (19.6%) strongly agreed, 544 physicians (52.2%) agreed, and 221 physicians (21.2%) were neutral in this regard. The most commonly used diagnostic method for obesity was the Body Mass Index (BMI) with 98.9% (n= 1032), followed by waist circumference measurement (52.5%, n= 548). A significant proportion of physicians did not use a single parameter. However, only 37 (3.5%) of the physicians stated that they always recorded their patients' height and weight, while 294 (28.2%) physicians stated that they often recorded the height and weight of their patients. The number of physicians who strongly agreed that a PCP should play a role in the treatment of obesity was 155 (14.8%), while the number of physicians who agreed with that was 588 (56.3%). The most important reason for not taking responsibility for obesity treatment was reported to be a requirement for a multidisciplinary approach (51.5%, n= 537). The percentage of physicians who defined patients with a BMI of 30 kg/m^2 and above as obese was 82.8% (n:864). The percentage of physicians who agreed with the proposition that the target should be a weight loss of 5-10% of body weight to have a significant change in health parameters and quality of life was 55.2% (n= 576), while the percentage of physicians who strongly agreed with that proposition was 10.2% (n= 107). The percentage of physicians who stated that they were neutral in this regard was 25.8% (n= 269), while the percentage of physicians who stated that they disagreed with that was 8.2% (n= 86). The percentage of physicians who refer their patients who fail to lose weight with a comprehensive diet and exercise program to surgery was 37.6% (n=393), while the percentage of those who stated that they would use medical treatment was 24% (n= 251), the percentage of those stated that they would recommend alternative treatment methods (such as acupuncture, hypnosis, ozone therapy, etc.) was 17.1% (n= 179), the percentage of those who stated that they would recommend a stricter diet was 15.8% (n= 165), and the rate of physicians who stated that they would refer the patient to a higher-level center (endocrinology, psychiatry) was 5.4% (n= 56). The responses of the primary care physicians to the questions measuring obesity evaluation and perception are shown in Table 2.

Knowledge, Indications, and Attitudes Towards Bariatric Surgery

Of the participants, 32.5% (n= 339) acquired their knowledge of obesity and metabolic surgery from conferences and congresses, 28.4% (n= 297) during their medical education, and 24.07% (n= 251) from internet-social media and press (Figure 1). In the responses given regarding the three indications for bariatric and metabolic surgery today, the percentage of those who thought that patients with a BMI above 40 kg/m^2 should be referred to surgery was 72.37% (agree: 56.3% (n= 588), strongly agree: 16.1% (n= 168)), the percentage of those who referred patients with a BMI of 35-40 kg/m^2 and comorbidities to surgery was 53.3% (agree: 42.3% (n= 440), strongly agree: 11% (n= 115), the percentage of those who referred patients with a BMI of 35-40 kg/m2 and uncontrolled diabetes was 35.9% (agree: 30.1% (n= 315), strongly agree: 5.7% (n= 60)). The majority of physicians accepted that obesity and metabolic surgery was the most effective method for the treatment of morbidly obese patients, but they had no information on mortality rates. The percentage of physi-

Table 2. The results of the questions prepared as a Likert scale to measure the physicians' evaluation and perception of obesity with multiple-choice/open-ended answers (the full sentences of the questions are presented in Annex 1). Values are given in percentages

Questions	Strongly disagree	Disagree	Neutral	Agree	Strongly agree	β
Q2 (Obesity definition)	0.9% (n= 9)	1.4% (n= 15)	5.7% (n= 59)	53.9% (n= 563)	38.1% (n= 398)	4.27 ± 0.71
Q3 (Reason)	1% (n= 10)	2.1% (n= 22)	8.3% (n= 87)	47.8% (499)	40.8% (426)	4.25 ± 0.77
Q4 (Prevalence)	0.7% (n= 7)	6.3% (n= 66)	21.3% (n= 222)	52.2% (n= 545)	19.5% (n= 204)	3.84 ± 0.83
Q5 (Acceptance)	1% (n= 10)	8% (n= 84)	19% (n= 207)	56.3% (n= 588)	14.9% (n= 155)	3.76 ± 0.84
Q6 (Treatment target)	0.6% (n= 6)	8.3% (n= 86)	25.8% (n= 270)	55.2% (n= 576)	10.1% (n= 106)	3.66 ± 0.79
Q7 (Treatment success)	8.5% (n= 89)	27.5% (n= 287)	24.5% (n= 256)	36.1% (n= 377)	3.4% (n= 35)	2.98 ± 1.05
Q8 (Diagnostic methods)	Body Weight 34.9% (n= 364)	BMI 98.9% (n= 1033)	Waist Circumference 52.5% (n= 548)	Waist-to-hip Ratio 3 2.7% (n= 341)	Skinfold Thickness 8.1% (n= 85)	
Q9 (Records)	Never 2.2% (n= 23)	Rarely 19% (n= 198)	Sometimes 47.1% (n= 492)	Frequently 28.2% (n= 294)	Always 3.5% (n= 37)	
Q10 (Diagnostic criteria for obesity)	BMI> 25≤29. 93.5% (n= 37)	BMI ≥30 82.8% (n= 864)	BMI ≥35 11.1% (n= 116)	BMI ≥40 2.2% (n= 23)	No knowledge 0.4% (n= 4)	
Q11 (Reason for not undertaking)	Intense clinic hours 12.2% (n= 127)	Lack of knowledge6.2% (n= 65)	Inadequate physical facilities 9.5% (n= 99)	Reluctance of patients 7.7% (n= 80)	Multidisciplinary approach 51.4% (n= 537)	Other[α]13 (n= 136)
Q12 (Advice to unsuccessful patients)	Strict diet %15.8 (n= 165)	Medical treatment %24 (n= 251)	Alternative treatment %17.2 (n= 179)	Surgery %37.6 (n= 393)	Other[μ] %5.4 (n= 56)	

[β]: Average of responses to the questions on the Likert scale (Arithmetic mean ± standard deviation).
[α]: The most common responses to this option are should absolutely undertake, the lack of dietician support, and reluctance of physician.
[μ]: The most common responses to this option are referral to a higher-level center, dietician, and psychology-psychiatry.

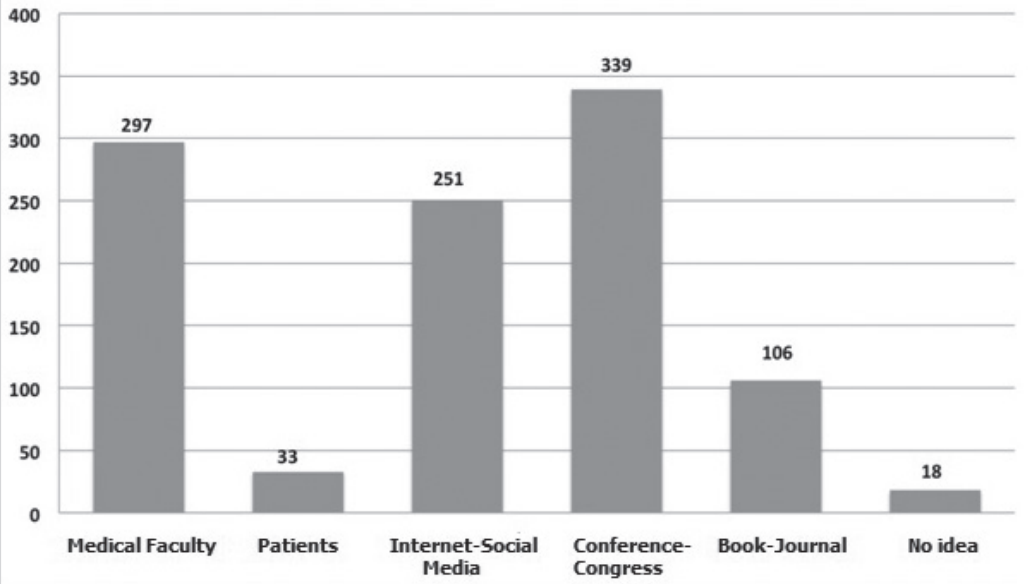

Figure 1. The responses given by the physicians participated in the survey to the question about how they acquired their knowledge of bariatric surgery (Q13). The physicians stated that they obtained this knowledge mostly during conferences-congresses.

cians who stated that they would refer their first-degree relatives to surgery when they have an indication was 48% (n= 502), and the percentage of those who strongly agreed with that was 9.6% (n=100). The percentage of physicians who stated that they were neutral in this regard was 32.1% (n= 335). The reasons for not referring patients to surgery were reported as cost (56.7%), high risk (56.4%), and patient refusal (41.2%). The physicians stated that they would like to be informed about indications for surgery (89.5%), complications (74.7%), efficacy (69.1%), and long-term follow-up protocols (65%). Of the physicians who participated in the survey, 67.1% had patients who had undergone bariatric surgery and who were followed up by them. The responses about bariatric surgery are shown in Table 2.

Table 3. The results of the questions containing multiple-choice and open-ended answers to measure the knowledge and attitudes of the physicians participated in the survey regarding bariatric surgery (the full sentences of the questions are presented in Annex 1)

Questions	Strongly disagree	Disagree	Neutral	Agree	Strongly agree	β
Q14 (BMI≥40)	0.3% (n= 3)	6.3% (n= 66)	21% (n= 219)	56.3% (588)	16.1% (168)	3.82 ± 0.78
Q15 (35≤ BMI <40)	1% (n= 10)	10.8% (n= 113)	35% (n= 365)	42.2% (n= 441)	11% (n= 115)	3.52 ± 0.86
Q16 (30≤ BMI <35)	1.8% (n= 19)	18.1% (n= 190)	44.2% (n= 462)	30.1% (n= 315)	5.7% (n= 60)	3.20 ± 0.86
Q17 (Surgery success)	0.5% (n= 5)	4.9% (n= 51)	21.8% (n= 227)	54.9% (n= 574)	17.9% (n= 187)	3.85 ± 0.78
Q18 (Bariatric surgery mortality)	0.2% (n= 2)	2.6% (n= 27)	65.3% (n= 682)	28.1% (n= 294)	3.7% (n= 39)	3.33 ± 0.60
Q19 (Recommending surgery)	1.2% (n= 13)	9% (n= 94)	32.1% (n= 335)	48% (n= 502)	9.7% (n= 100)	3.56 ± 0.83
Q20[δ] (Reason for not recommending surgery)	Lack of knowledge 15.6% (n= 160)	Not effective 5.7% (n= 59)	Patient refusal 41.1% (n= 423)	High cost 56.7% (n= 583)	High risk 56.4% (n= 580)	Other[α] 10.8% (n= 111)
Q21 (Need for knowledge of bariatric surgery)	Indications 89.5% (n= 935)	Complications 74.7% (n= 781)	Efficacy 69.1% (n= 722)	Follow-up protocols 65.1% (n= 680)	None 1.8% (n= 19)	

[β]: Average of responses to the questions on the Likert scale (Arithmetic mean ± standard deviation)
[α]: The most common responses to this option are that they find it effective and would refer their patients, weight regain is high, and they disapprove of changes in physiology and anatomy.
[δ]: More than one option could be selected.

Table 4. The responses of the physicians participating in the survey to the question about three classical indications for bariatric and metabolic surgery. It was found that the physicians who have just started working as professionals were more knowledgeable about indications for surgery. Values are given in percentages (numbers)

	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
Q14 (BMI≥40)					
0-5 years	0.5 (1)	3.6 (7)	14.8 (29)[δ]	59.7 (117)	21.4 (42)[α]
6-10 years	0.5 (1)	5.4 (11)	18 (37)	61 (125)	15.1 (31)
11-20 years	0 (0)	6.5 (21)	24.9 (80)	54.5 (175)	14 (45)
21-30 years	0 (0)	9.4 (25)	21.7 (58)	53.6 (143)	15.4 (41)
Over 30 years	1.9 (1)	3.9 (2)	27.5 (14)	49 (25)	17.5 (9)
Q15 (BMI ≥35<40)					
0-5 years	0.5 (1)	7.6 (15)	27 (53)[β]	50.8 (100)[Φ]	14.2 (28)[Ω]
6-10 years	0.5 (1)	13.7 (28)	41.5 (85)	38.5 (79)	5.8 (12)[ω]
11-20 years	1.2 (4)	10 (32)	37.8 (121)	42.2 (135)	8.7 (28)
21-30 years	1.5 (4)	12 (32)	30.8 (82)	41 (109)	14.7 (39)
Over 30 years	0 (0)	8 (4)	44 (22)	32 (16)	16 (8)
Q16 (BMI ≥30<35)					
0-5 years	2 (4)	19.2 (38)	32.8 (65)[Ψ]	40.4 (80)[φ]	5.6 (11)[π]
6-10 years	1.5 (3)	18 (37)	51.7 (106)	25.8 (53)	2.9 (6)
11-20 years	1.88 (6)	14 (45)	49.2 (158)	29.3 (94)	5.6 (18)
21-30 years	2.2 (6)	23.6 (63)	38.6 (103)	28.8 (77)	6.7 (18)
Over 30 years	0 (0)	11.8 (6)	54.9 (28)	19.6 (10)	13.7 (7)

Q14: [δ]: vs. 11-20 years, >30 years [α]: vs. 11-20 years, Q15: [β]: vs. 6-10 years, 11-20 years, >30 years, [Φ]: vs. 6-10 years, 21-30 years, >30 years, [Ω]: vs. 6-10 years, [ω]: vs. 0-5 years, 21-30 years, >30 years, Q16: [Ψ]: vs. 6-10 years, 11-20 years, >30 years, [φ]: vs. years 6-10 years, 11-20 years, 21-30 years, >30 years. [π]: vs. >30 years.

Table 5. The responses of the physicians participating in the survey to the questions about efficacy of bariatric surgery, mortality rate, and recommendation. Unlike the responses given to the questions about indications, it was found that physicians who have just started working as professionals had less knowledge of the efficacy of surgery and mortality rates. There was no difference between the durations of practice in terms of recommending surgery. Values are given in percentages (numbers)

	Strongly disagree	Disagree	Neutral	Agree	Strongly agree
Q17 (efficacy of surgery)					
0-5 years	1 (2)	7.1 (14)	21.2 (42)	49.5 (98)$^{\varphi}$	21.2 (42)
6-10 years	0 (0)	3.4 (7)	22.9 (47)	56.1 (115)	17.6 (36)
11-20 years	0.9 (3)	3.4 (11)	19.9 (64)	59.5 (191)	16.2 (52)
21-30 years	0 (0)	6.7 (18)	23.2 (62)	52.8 (141)	17.2 (46)
Over 30 years	0 (0)	2 (1)	25.5 (13)	52.9 (27)	19.6 (10)
Q18 (mortality rate)					
0-5 years	0 (0)	1.5 (3)	76.8 (152)$^{\delta}$	18.7 (37)$^{\beta}$	3 (6)
6-10 years	0 (0)	2.9 (6)	60 (123)	34.6 (71)	2.4 (5)
11-20 years	0.6 (2)	2.2 (7)	60 (192)	33.1 (106)	4 (13)
21-30 years	0 (0)	4.1 (11)	67 (179)	24.3 (65)	4.5 (12)
Over 30 years	0 (0)	0 (0)	66.7 (34)	27.4 (14)	5.9 (3)
Q19 (recommending surgery)					
0-5 years	2 (4)	8.6 (17)	27.3 (54)	50.5 (100)	50.5 (100)
6-10 years	2 (4)	5.8 (12)	32.7 (67)	53.2 (109)	53.2 (109)
11-20 years	0.3 (1)	10.3 (33)	34.9 (112)	46.1 (148)	46.1 (148)
21-30 years	1.5 (4)	10.1 (27)	31.8 (85)	45.7 (122)	45.7 (122)
Over 30 years	0 (0)	5.9 (3)	35.3 (18)	43.1 (22)	43.1 (22)

Q17: $^{\varphi}$: vs. 11-20 years.
Q18: $^{\delta}$: vs. other groups, $^{\beta}$: vs. 6-10 years, 11-20 years.

Duration of Practice and Indications for Surgery

The analysis of the duration of practice and the knowledge of three classical indications accepted today revealed that physicians who were new to the profession evaluated the indications more accurately ($p< 0.05$). However, there was no significant difference in terms of referring first-degree relatives when indicated and risk perception ($p> 0.05$) (Tables 3 and 4). The responses of the physicians regarding the efficacy of bariatric surgery, mortality rate and recommendation are presented in the Table 5.

DISCUSSION

This survey study conducted with the participation of 1044 PCPs in Turkey evaluated PCPs' knowledge and attitudes towards obesity and bariatric surgery. PCPs' basic levels of knowledge of identifying obesity, its etiology, and targets are sufficient and their attitudes were positive. It was determined that they could not focus on this issue due to the requirement for a multidisciplinary treatment approach and the workload although they were willing to follow up, treat and guide patients for obesity and surgical treatment. Young physicians were found to make more accurate evaluations in terms of the indications for surgery, but there was no difference between the physicians in terms of professional experiences due to reasons such as cost and risk perception of referring patients to surgery.

Studies conducted in our country have shown an obesity prevalence of around 30% (1). Of the physicians who participated in the survey, 72% agreed with this rate (agree 52.2%, strongly agree 19.5%), while approximately one of the five physicians (22%) had no idea about this. This rate is important since it may indicate a lack of knowledge of the significance of the problem. Studies have shown varying rates of PCPs evaluating their patients with BMI. It appears that especially waist circumference, which is used for obesity assessment, is measured less frequently (9-11). In our study, almost all physicians used BMI to assess obesity and most of them were not satisfied with a single parameter. It was found that physicians did not have any problems in evaluating patients, but there was a problem with recording parameters. About half of the physicians were occasionally recording these values.

The fact that the first and most important steps in obesity treatment are diet, exercise, and behavior modification is an accepted approach in all guidelines (12). However, a considerable proportion of patients cannot achieve success with these approaches. This is much more pronounced in patient groups with an indication for surgery (13,14). Of the physicians, 36% thought that this treatment approach would be successful, while 27.5% stated that it would fail, and 24.5% did not have a definite idea about it. This rate has been found around 16% in the study of Fogelman et

al. (15). These studies have shown that there may be differences among countries. These differences may be related to the number of physicians who participated in the survey, country, and question technique. Again, in another USA survey study, 88% of the PCPs participating in the survey have stated that diet and exercise are successful in the treatment of obesity, but about 30% of them have stated that they do not have enough time to discuss this issue and motivate their patients (16).

Another problem is patient adherence to these recommendations and advice. Another study has found that only 22% of patients followed these recommendations and again the weight loss of only 23% of patients was due to the doctor's advice (17). Although PCPs have key roles in both treatment and prevention, they have important limitations, especially in using some interventions and approaches. A significant proportion of the physicians who participated in the survey had a substantial workload. One of the factors determining success in this patient group is close attention and motivation, which reduces the time that physicians taking care of many patients can allocate to these patients. Problems in the long-term follow-up of the patients remain a barrier for physicians who play a key role in the fight against obesity in our country. The high number of patients examined on a daily basis shows that physicians cannot adequately focus on this patient group in routine practice. However, in our study, the physicians stated that the most important reason for not paying enough attention to this patient group was the requirement of a multidisciplinary approach. This is a significant finding since it shows that physicians are willing to deal with this issue despite a considerable workload if an adequate organization could be made. The results of the study show that a better guideline, a better organization, and coordination between relevant departments are required for primary care physicians. The healthcare centers recently opened in our country and the perfection studies on bariatric surgery can bring PCPs to an important position in terms of guiding and following this issue.

Another result obtained in our study was that the percentage of physicians who stated that they would refer patients who failed to lose weight to surgery with these treatment approaches was 37.6%. The physicians stated that they would recommend alternative treatments (such as acupuncture, ozone, hypnosis) that are not included in the guidelines to 17% of these patients. These results show that there is lack of knowledge of treatment algorithms. The vast majority of the physicians who participated in the survey seemed to agree that there is a need for more training on obesity and bariatric surgery. Although the reported mortality rates for bariatric surgery are 0.2-0.1%, 65.3% of the physicians who participated in the survey stated that they did not have any information on this issue. The rate of positive responses about effective surgical techniques in obesity treatment was high. However, the rate of reluctance to refer their relatives to surgery was high due to the perception of cost and risk. A survey study by Conaty et al. on 150physicians has found that 21% of physicians were reluctant to refer patients due to complications and risk perception. Despite the considerable contribution of bariatric surgery to the health status of morbidly obese patients, it has been observed that risk perception has a deterrent effect. Many studies on this subject have shown that PCPs do not give priority and importance to obesity treatment, with a negative perception of bariatric surgery risks. Interestingly, similar results have been obtained among surgeons who do not perform bariatric surgery (8,18-20). In particular, physicians' lack of knowledge of the indications for surgery, risks and types of surgery, and long-term follow-ups cause them not to feel comfortable in guiding patients.

In this study, physicians' attitudes towards the indications for surgery were determined by presenting three cases. Two questions described cases of an indication for surgery in accordance with the National Health Institute (NIH) consensus criteria. Recent studies have shown that gastric bypass surgery has positive effects on type 2 diabetes, regardless of weight loss (14). As a result of these studies, the concept of metabolic surgery has emerged and a new indication has been included in the guidelines. Today, surgical treatment is recommended as an alternative approach if type 2 diabetic patients with a BMI between 30-35 kg/m^2 cannot achieve success with medical treatment (21). The third question regarding the indication for surgery was in the form of a metabolic surgery case with this indication. In the first two relevant questions, the percentage of physicians who referred patients to surgery was higher than the case of an indication for metabolic surgery (strongly agree/agree ratio 72.4% vs. 43.3% vs. 35.9%). The rate of referring patients with this relatively new indication to surgery was lower compared to other indications. This rate is only 14.5% in the study of Sarwer et al. (22). In our study, this rate was 36% (agree 30.1%, strongly agree 5.74%). The probable reason for such a result may due to the fact that the study of Sarwer is older dated. This reveals the importance of including this new indication and the concept of metabolic surgery in all education programs.

Another important result revealed by the comparison based on duration of practice was that the young physician group had a higher willingness to refer patients to surgery. This difference becomes evident, especially in indications for metabolic surgery. There are not many studies on this subject in the literature. A pilot study conducted on a small number of PCPs in England obtained a contrary result. However, this study included a total of 35 physicians, and there were only eight junior physicians (23). Higher willingness of young physicians is the possible result regarding the increasing interest in the subject in recent years, establishment of more training programs in academic

hospitals, and increased use of bariatric surgery. Another possible reason is the inadequacy of postgraduate training programs for PCPs. Again, the pessimistic attitude caused by intense clinic hours over the years may be another reason. It has been found that physicians who have received special training on obesity and its treatment during their medical education refer a higher number of patients to surgery (24). Another interesting result that emerged in our study was that the group of physicians who were new to the profession had less knowledge of surgical success and risk perception compared to other physicians. Training programs to be created will enable physicians to refer more patients to bariatric surgery and increase the positive perception of surgery in patients. Modifications to be made especially in the medical education process are of extreme importance.

Our study has some limitations. Despite the high number of respondents, most of the physicians were from four major cities. Therefore, even though the study numerically reached a power level, it may not homogeneously reflect the generalphysician population throughout Turkey. However, it is believed that receiving responses from 1044 physicians can still provide an insight into the countrywide physician population. Another limitation was that the study measured the general perception and knowledge level rather than specific conditions. The reason for this was to create a general profile. Another criticism that can be made about the survey methodology may be not knowing the exact number of physicians reached via the survey, therefore not be able to provide an exact response rate. This was attempted to be overcome with repeated calls when necessary by reaching all social media platforms used by PCPs and managers. Participation in the survey was completely voluntary and no award was given for participation.

In conclusion, this study demonstrated that despite their basic knowledge of obesity treatment and willingness to take part in the treatment and follow-up of these patients, the physicians in our country could not adequately focus on this issue due to the requirement for a multidisciplinary approach to the disease and the workload. Young physicians' level of knowledge of bariatric surgery was higher, but their attitudes were similar in terms of patient referral, especially due to risk perception and cost. The demand for training on almost all subjects was high. Organizing postgraduate training programs, establishing curricula on bariatric surgery in medical faculty education programs will positively contribute to the knowledge and perception of this issue. Training on possible complications, risk-benefit perception, and especially long-term follow-up will increase the self-confidence of PCPs.

Ethics Committee Approval: The approval for the study was obtained from the Ethics Committee of Uludag University ethics committee approval number: 2019-10/4).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept -H.Ö., M.N.; Design - H.Ö., M.N.; Supervision - H.Ö.; Materials - M.N., H.Ç.; Data Collection and/or Processing - H.Ç.; Literature Review - H.Ö., M.N.; Writing Manuscript - H.Ö.; Critical Reviews - H.Ö.

Conflict of Interest: The authors declare that they have no conflict of interest.

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2021; 37 (3): 266-276

Türkiye birinci basmak hekimlerinin obezite ve bariatrik cerrahi hakkında bilgi ve tutumları: Anket çalışması

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ÖZET

Giriş ve Amaç: Bu anket çalışması Türkiye birinci basamak hekimlerinin (BBH) obezite ve bariatrik cerrahi hakkındaki bilgi, tutum ve algılarını ölçmek amacıyla yapılmıştır. Ayrıca hekimlerin çalışma süreleri ve özellikle bariatrik cerrahi ve cerrahiye hasta yönlendirmeleri arasındaki ilişki araştırılmıştır.

Gereç ve Yöntem: Yirmi yedi soruluk bir anket Survey monkey üzerinde yürürlüğe konarak sosyal medya ve internet aracılığıyla hekimlere ulaştırıldı. Hekimler çalışma sürelerine göre gruplandırıldı. Bu gruplar bariatrik cerrahiye verdikleri cevap açısından univaryans analiz kullanılarak karşılaştırıldı.

Bulgular: Toplam 1044 hekim ankete katıldı. Obezite tedavisinde BBH'lerinin önemli bir rol oynayabileceğine kesinilkle katılan/katılan hekim sayısı 743 (%71,1) olmuştur. Bu hastaların tedavilerini üstlenmemelerinin en önemli nedeni olarak tedavinin multidispliner olması belirtilmiştir (%51,5, n= 537). Beden kitle indeksi (BMİ) 40 kg/m^2 üzeri olan hastaları cerrahiye yönlendireceğini söyleyen hekim oranı %72,3, BMİ 35-40 kg/m^2 olan ve beraberinde yandaş hastalığı olan hastaları cerrahiye yönlendirme oranı %53,3 ve BMİ 30-35 kg/m^2 ve kontrolsüz diyabeti olan hastaları yönlendirme oranı %35,9. Çalışma süresi daha yeni olan hekimlerin cerrahi endikasyonları daha olumlu değerlendikleri bulunmuştur (p< 005).

Sonuç: Bu çalışmada Türkiye BBH'lerinin obezite tedavisi konusunda temel bilgi düzeyine sahip oldukları ve tedaviye katılma konusunda istekli oldukları görülmüştür. Bununla beraber multidisipliner yaklaşım gerekmesi ve iş yükü nedeniyle bu hastalarla ilgilenemediklerini belirtmişlerdir. Çalışma süresi açısından daha yeni olan hekimlerin hastaları cerrahiye yönlendirme açısından daha yüksek bilgi oranına sahip oldukları ancak hastaları sevketme oranının benzer olduğu görülmüştür.

Anahtar Kelimeler: Birinci basamak hekimler, obezite tedavisi, obezite cerrahisi, anket çalışması

DOİ: 10.47717/turkjsurg.2021.5149

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2021; 37 (3): 266-276

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DOİ: 10.47717/turkjsurg.2021.5149

Appex 1: Survey Questions

1. I consent to participate in the study and my answers to be used for research purposes.

I approve

2. Obesity is a chronic disease defined as "an excessive accumulation of body fat to an extent to impair health".

O Strongly disagree

O Disagree

O Neutral

O Agree

O Strongly agree

3. The most important reason for the increase in obesity prevalence all over the world is easy access to high-energy foods and a sedentary lifestyle.

O Strongly disagree

O Disagree

O Neutral

O Agree

O Strongly agree

4. Studies have shown that the prevalence of obesity in the adult population in our country is around 30%.

O Strongly disagree

O Disagree

O Neutral

O Agree

O Strongly agree

5. A primary care physician should undertake the treatment and provide the necessary recommendations when an obese patient visits for weight loss.

O Strongly disagree

O Disagree

O Neutral

O Agree

O Strongly agree

6. A weight loss of 5-10% of body weight should be targeted for a significant change in health parameters and quality of life of an obese patient.

O Strongly disagree

O Disagree

O Neutral

O Agree

O Strongly agree

7. Patients who are included in the diet-exercise-behavioral therapy program for besity are generally successful in achieving their weight loss goals.

O Strongly disagree

O Disagree

O Neutral

O Agree

O Strongly agree

8. What is the most common method you use for diagnosing obesity? (You can choose more than one option)

O Body weight

O Body Mass Index

O Waist circumference

O Waist-to-hip ratio

O Skinfold thickness

9. How often do you record the height and weight of the patients you examine?

O Never

O Rarely

O Sometimes

O Frequently

O Always

10. In what case is a patient defined as obese according to the criteria currently used in routine practice?

O A body mass index of 25-29.9 kg/m^2

O A body mass index > 30 kg/m^2

O A body mass index >35 kg/m^2

O A body mass index >40 kg/m^2

O Do not know

11. What is the most important reason for a primary care physician not to undertake obesity treatment in your opinion?

O Intense clinic hours

O Lack of knowledge

O Inadequate physical and medical facilities

O Reluctance of patients

O Requirement for a multidisciplinary approach

O Other (please specify)

12. What would you recommend to an obese patient who is unsuccessful in losing weight with a comprehensive diet and exercise program

O A stricter diet-exercise program

O Medical treatment

O Alternative methods (Acupuncture, ozone, hypnosis, etc.)

O Refer to surgery

O Other (please specify)

13. How did you acquire your knowledge of obesity and metabolic surgery

O During medical education

O From patients

O Internet-social media, press

O Conferences/congresses

O Books/journals

O I have no knowledge on this subject

14. A patient with a body mass index of 41 kg/m^2 who cannot lose weight with diet-exercise-lifestyle modifications should be referred to bariatric and metabolic surgery.

O Strongly disagree

O Disagree

O Neutral

O Agree

O Strongly agree

15. Patients with a body mass index of 36 kg/m2 and obesity-related concomitant diseases (such as type 2 diabetes, hypertension, dyslipidemia, sleep apnea) who cannot lose weight with diet-exercise-lifestyle modifications should be referred to bariatric and metabolic surgery.

O Strongly disagree

O Disagree

O Neutral

O Agree

O Strongly agree

16. Bariatric and metabolic surgery should be considered an alternative for a patient with type 2 diabetes and a body mass index of 33 kg/m^2 if hyperglycemia is inadequately controlled despite the use of optimal medical treatment (druginsulin).

O Strongly disagree

O Disagree

O Neutral

O Agree

O Strongly agree

17. Bariatric and metabolic surgery is the method providing the longest and largest amount of weight loss in morbidly obese patients among the methods known and used.

O Strongly disagree

O Disagree

O Neutral

O Agree

O Strongly agree

18. According to the literature data, the 30-day mortality rates for bariatric and metabolic surgery procedures are less than 0.5% today.

O Strongly disagree

O Disagree

O No idea

O Agree

O Strongly agree

19. I would refer a first-degree relative of mine to bariatric and metabolic surgery when indicated.

O Strongly disagree

O Disagree

O Neutral

O Agree

O Strongly agree

20. If you do not refer a patient with an indication for bariatric and metabolic surgery for this purpose, what could be the reason? (You can choose more than one option)

O I have no knowledge

O I do not find it effective

O Patient refusal

O High cost

O High risk

O Other (please specify)

21. In your opinion, what should the primary care physician know about bariatric and metabolic surgery? (you can choose more than one option)

O Indications

O Complications

O Efficacy

O Postoperative long-term follow-up protocols

O None

22. Do you have a patient who had undergone bariatric or metabolic surgery and whose long-term follow-up is carried out by you?

O No

O Yes

23. Your age

O 24-30 years

O 31-40 years

O 41-50 years

O 51-60 years

O Over 60 years

24. How many years have you been a physician?

O 0-5 years

O 6-10 years

O 11-20 years

O 21-30 years

O 31-40 years

O Over 40 years

25. The province you work in

26. How many patients do you examine per week?

O 0-50

O 51-100

O 101-200

O 201-300

O 301-400

O 401-500

O Above 500

27. What is the approximate rate of obese patients among the patients you examine?

O 0-5%

O 6-10%

O 11-15%

O 16-20%

O 21-25%

O 26-30%

O 31-40%

O Above 40%

ORIGINAL ARTICLE
Turk J Surg 2021; 37 (3): 277-285

Lessons learned from blunt trauma abdomen: Surgical experience in level I trauma centre

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ABSTRACT

Objective: The number of accident cases is increasing day by day, so as the challenges. With an emphasis on trauma care, the government started a 120 bedded level I trauma centre in northern India catering to a population of 2.8 million in June 2018. Through this article, we aimed to share our experience of blunt abdominal trauma management from a new level I trauma centre.

Material and Methods: In this retrospective observational study, historical analysis of all available records from July 2018 to March 2020 was done. Inclusion criteria included blunt trauma abdomen with or without associated injuries. Data regarding age, sex, mechanism of injury, time taken to reach the hospital, the pattern of solid organs and hollow viscus injuries, associated extra abdominal injuries, mode of treatment, complications, length of ICU and hospital stay, and mortality were reviewed.

Results: Overall, 154 cases sustained abdominal injuries during the study period. Seventy-five percent were male. The most common cause of blunt trauma abdomen was road traffic crashes. Operative management was required in 57 (37.01%) cases while 97(62.98%) were managed non-operatively (NOM). Mean ICU stay was 05.73 days, while the average hospital stay was 12 days (range 10-60 days). Procedures performed included splenectomy, liver repair, primary closure of bowel injury, and stoma formation. Complications occured in 16.88% cases and the overall mortality rate was 11.68%.

Conclusion: The study revealed that among 154 cases of fatal blunt abdominal trauma, road traffic crash was the most common cause of blunt abdominal trauma, predominantly affecting males. The visceral and peritoneal injury frequently perceived was liver in 40 cases (25.9%), spleen 66 (43%), intestine 21(13.6%) and kidney 13 cases (09%). Abdominal injury was associated with other injuries like head, chest and extremity injuries in 52.5% cases. Duration of injury, presence of associated injury and preoperative ventilation requirement were independent predictors of mortality apart from contributary factors such as clinical presentation, organ involved and presence of complications.

Keywords: Motor vehicle accidents, trauma, abdominal injuries, outcome, prehospital care

INTRODUCTION

In developing countries where modernization and industrialization are still going on, trauma emerges as a major cause of preventable death. In fact, at the present, trauma is the sixth leading cause of morbidity and mortality worldwide (1).The abdomen is the most frequently injured region after head injury and long bone fractures, and 25% of all abdominal trauma requires abdominal exploration (2,3). In cases of pre-existing underlying pathology, even trivial trauma to the abdomen can lead to significant haemorrhage and mortality if remains undiagnosed. Traditionally, abdominal trauma is classified either as blunt or penetrating (4). Penetrating injuries include stab wounds and gunshot wounds while blunt abdominal injuries include motor vehicle crashes, fall from height, and physical assault (5). Blunt trauma abdomen is usually missed during the initial primary survey unless repeatedly looked for. In due course of time, this delay in diagnosis and inadequate management can prove fatal. It is imperative that we must supplement clinical examination with radiological imaging such as focused assessment with sonography in trauma (FAST) to diagnose free fluid in the peritoneal or pericardial cavity and contrast-enhanced computed tomography (CECT) torso to detect visceral abdominal and chest injuries. Blunt trauma to the abdomen can cause injuries to both solid and enteric viscera. Solid visceral injuries involve injuries to the spleen, liver, kidney, and present with signs of shock, whereas enteric injuries present with peritonitis and sepsis (6-9).

Cite this article as: Singh A, Prasad G, Mishra P, Vishkarma K, Shamim R. Lessons learned from blunt trauma abdomen: Surgical experience in level I trauma centre. Turk J Surg 2021; 37 (3): 277-285.

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Received: 07.08.2020
Accepted: 16.07.2021
Available Online Date: 28.09.2021

DOI: 10.47717/turkjsurg.2021.4886

Data regarding the etiology and outcome of abdominal injuries from our region is lacking. Hence, the primary objective of our study was to assess the etiology, causes, pattern of injury, and clinical outcome of blunt abdominal trauma cases while the secondary objective was to assess the predictors of mortality.

MATERIAL and METHODS

Retrospective analysis of data from the emergency room services of a 120-bed level I trauma centre was used to discuss the impact and outcome of only blunt abdominal injury cases. Historical analysis of case records of all patients admitted in the emergency from July 2018 to March 2020 was done after obtaining ethical clearance from the institutional ethical committee vide letter PGI/BE/447/2020 dated 10 July 2020. Informed written consent was taken routinely while admitting the cases. We included all cases of blunt trauma abdomen with or without associated injuries in the study. The present analysis excluded the cases of penetrating abdominal injuries, and those who died during the resuscitation without undergoing any imaging. Since the post-mortem facility in our institute was not available, records of post-mortem reports were neither traced nor analysed. All cases were initially managed according to the advanced trauma life support (ATLS) guidelines. All cases underwent FAST during the primary survey, and we subjected those who were FAST positive or suspected to have abdominal injuries to CT Torso. Our management protocol of blunt trauma abdomen was based primarily on hemodynamic stability. Unstable cases with FAST positive were directly shifted to the operation theatre, whereas we managed stable cases according to the CT Findings. Repeat radiological investigations (FAST/CECT) were done whenever required. We did initial management of all postoperative cases in the surgical intensive care unit. The patient was shifted to the surgical ward once he/she was off mechanical ventilation and was hemodynamically stable. By day 2/3, we tried to start enteral feeding in all patients. Cases were discharged with proper discharge summary and advice. First follow up was in the surgical outpatient department (SOPD) after the first week. A proper record of all follow-up visits was maintained. We sent cases requiring rehabilitation to physical medicine and rehabilitation department for physiotherapy.

Data regarding age, sex, time taken to reach the hospital, the pattern of solid organs and hollow viscus injuries, associated extra-abdominal injuries, mode of treatment, complications, length of ICU and hospital stay, and mortality were reviewed. Length of ICU stay was defined as the period from admission to the ICU until transfer out from ICU. Hospital stay was defined as the period from admission until discharge or until in hospital death. Ventilator hours were defined as the number of hours the case was on mechanical ventilation. Mortality was defined as death during hospital stay either because of trauma or due to complications arising out of trauma. Continuous variable was presented as mean± standard deviation/median (Q1, Q3 i.e interquartile range) whereas categorical variables as frequency (%). Independent samples t test and Mann Whitney U test were used to compare the means/medians respectively between patient´s outcomes (non-survivor and survivor). Time taken to reach the hospital was compared among three groups, using Kruskal Wallis H test. Chi-square test or Fisher's exact test was used to compare the proportions between the groups. In order to assess the predictors of the non-survivors, binary logistic regression analysis was used. Variables significantly associated with patients' outcomes were further used to estimate odds ratio in univariate analysis and adjusted odds ratio for multivariate analysis. P value <0.05 was considered as statistically significant. Statistical package for social sciences version-23 (SPSS-23, IBM, Chicago, USA) was used for data analysis.

RESULTS

Abdominal trauma was present in 179 of 1456 cases (12.29%) presenting in the emergency department. Out of these 179 cases, 16 (8.9%) were penetrating abdominal injury, hence excluded from the study. A total of 9 cases (5.02%) died during resuscitation without undergoing any imaging, so we also excluded them. Out of 154 cases included in the study, an overwhelming majority was male (117, 75.97%) while 37 (24.02%) were females, with a male to female ratio of 3.1:1 (Table 1). It is clear from Table 1 that the majority of cases in the present study were in 31-50 years age group (106, 68.8%), followed by >51 years age group (24, 15.5%). In the majority of cases (103, 67%), the immediate cause of abdominal trauma was road traffic crashes, followed by assault in 28 (18.18%) and fall from height in 23 (14.93%) cases. Sixty-seven (65%) cases were four-wheeler occupants, while 36 (34.9%) were two-wheeler occupants. 7 occupants of four-wheeler and 10 occupants of two-wheeler cases died as a result of injuries (Table 2). A total of 116 (75.3%) cases used government ambulance to reach the hospital while 38 (24.6%) cases used personal vehicles to reach the hospital. Out of these 116 cases, 14 did not survive while 4 cases died among those who used personal vehicles. However, there was no significant correlation (p value 0.745) found between the two modes of transport and mortality (Table 2). Overall, associated injuries were seen in 81(52.59%) cases, with chest injuries being most common (39, 25.32%) followed by extremities injuries in 25 (16.23%) and head injury in 17 (11.03%) cases (Table 1). The majority of cases presented with abdominal distension (57, 37.01%), which was followed by pain in the abdomen in 49 (31.8%), pain with guarding and rigidity in 29 (18.8%), and shock in 19 (12.33%) cases (Table 2). Sixty-one (39.61%) cases reached our institute within 1-10 hours (Table 3). Twenty-four (15.5%) cases reached after a delay of 11-20 hours. On comparing the time to reach in hospital with mode of injury, significant difference (p< 0.05) was seen between the various modes of injury although there was no significant difference (p>

Table 1. Demographic profile, age, associated injury, and clinical presentation at time of admission

Variables	No of cases (n= 154, %)
Age in years	
<18	10 (6.4%)
18-30	14 (9.0%)
31-40	61 (39.6%)
41-50	45 (29.2%)
>51	24 (15.5%)
Sex	
Male	117 (75.9%)
Female	37 (24%)
Associated injury	81 (52.5%)
Chest	39 25.3%)
Head	25 (16.2%)
Extremity	17 (11.0%)
Clinical presentation at time of admission	
Abdominal Distension	57 (37.0%)
Pain only	49 (31.8%)
Pain with Guarding/Rigidity	29 (18.8%)
Shock	19 (12.3%)
Presented in Frequency (%)	

0.05) observed in the median duration of time to reaching hospital among three types of accidents (Table 3). The majority of cases (97, 62.98%) were managed non-operatively, while 57 (37.02%) underwent emergency laparotomy. That means the ratio of NOM to operative method was 1:1.7. Details regarding organ of injury, mode of treatment and various surgical procedures performed are shown in Table 4. Out of these 57 cases, 48 (84.12%) were taken for laparotomy either because of hemodynamic instability or due to feature of peritonitis. Failure of NOM occurred in 9 (9.2%) cases. Out of these 9 cases, 5 cases were of pancreatic injury, who were given a trial of nonoperative management, but these cases ultimately underwent laparotomy because of severe abdominal distension in 3 and hemodynamic instability in the remaining 2 cases. Four cases of mesenteric injuries were also given a trial of NOM, but because of the development of signs of peritonitis, we considered laparotomy after 48 hours of observation. Intraoperatively, the bowel was found to be in the pre gangrenous stage, requiring resection and anastomosis in all 4 cases (Figure 1a). Out of those 48 cases undergoing exploratory laparotomy, 8 (16.6%) were shifted to OT without any radiological imaging except FAST because of hemodynamic instability. Damage control surgery was done in 7 (12.2%) cases. Four of them were of liver injuries, in which only liver packing was done during the initial procedure and repeat exploration after 48 hours (Figure 1b). Two cases of splenic injuries required re-exploration within 24 hours of splenectomy because of increased drain output. On re-exploration, no bleeder was found and packing of splenic fossa was done. We removed the pack after 48 hours. In 1 case of urinary bladder injury who presented with associated pelvic injury and gross hemoperitoneum, damage control surgery with the packing of retro vesical space, application of external fixator, and intraperitoneal repair of urinary bladder was done. In 3 of our cases, who underwent laparotomy, no obvious solid or visceral injuries were found apart from hemoperitoneum caused either by mesenteric injury or retroperitoneum hematoma. We did emergency intubation in the receiving area in 27 (17.5%) cases. During the postoperative period, we shifted all cases in the surgical ICU as per our departmental protocol. The patient was shifted to the surgical ward once he/ she was off mechanical ventilation and was hemodynamically stable. Mean ICU stay was 5.73 days, (range 3-18 days) while the average hospital stay was 12 days ranging from 4 to 60 days. Overall complication rate was 16.88% (26) cases. Postoperative complications observed in our study included septicemia in 9 (5.8%), anastomotic leak in 3 (1.9%), and pancreatic fistula in 2 (1.29%) cases. Twelve (7.7%) of our cases required dialysis for acute renal failure, out of whom 3 (1.94%) died during the treatment. Overall mortality rate was11.68% (18 cases). Out of these 18 cases, 7(4.54%) died while on conservative management because of associated grievous head injuries while 11 (7.14%) died in the postoperative period. Further analysis of data showed that the mean age of non survivors in the present study was 32.21 ± 11.38 years, while for survivors it was 29.16 ± 14.80 years. The male: female ratio in the non-survivor group was 5:1. That means for every 5 men, 1 female died due to injury. There was no significant statistical difference between the two age groups or sex (p 0.389, 0.160, 0.002 respectively). However, significant statistical difference was found for duration of injury, ICU stay, and ventilation hours (p value 0.023, 0.002, <0.001) (Table 2). In order to assess the predictors of the non-survivor, binary logistic regression analysis was used. Out of various analysed variables, only 7 variables came out to be significantly associated with patients' outcomes which were further used to estimate odds ratio in univariate analysis and adjusted odds ratio for multivariate analysis (Table 5). In univariate analysis, duration of injury, clinical symptoms, any complications, pre-op ventilation, and organs involved in the injury were found to be possible factors for mortality. In multivariate analysis, out of the above variables, only two variables i.e. duration of injury (adjusted Odds ratio: 1.03 (95% CI: 1.01-1.04, p< 0.05) and associated injury (adjusted Odds ratio: 4.85, 95% CI: 1.42-16.52, p< 0.05) showed significant and independent risk factor for patient mortality (Table 5).

DISCUSSION

Blunt trauma abdomen can be called a silent killer because if not managed properly, the results can be catastrophic. Despite the recent advances in imaging techniques, the evaluation and diagnosis of intra-abdominal injuries still remain a challenge for

Table 2. Distribution of demographic and clinical variables between the Non-Survivor and Survivor Groups

Variables	Non-Survivor (n= 18)	Survivor n= 136)	P
Age	32.21 ± 11.38	29.16 ± 14.80	0.389 $
Sex (Female)	3 (15.7%)	34 (25.1%)	0.160
Sex (Male)	15 (83.3%)	102 (75%)	0.002
Duration of Injury	48 (7,96)	12 (6, 48)	0.023#
Hospital stay	6 (4,18)	10 (9, 13)	0.926#
ICU stay	7 (5,18)	4 (3, 5)	0.002#
Ventilator hours	96 (72,96)	48 (24, 72)	<0.001#
Four-wheeler	7 (38.8%)	60 (44.1%)	0.457
Two-wheeler	10 (55.5%)	26 (19.1%)	0.541
Mode of Injury			0.881
RTA	12 (66.6%)	91 (67.4%)	0.986
Fall from Height	4 (22.2%)	19 (14%)	0.604
Assault	2 (16.6%)	26 (18.3%)	0.614
Mode of transport to hospital			0.999
Ambulance	14 (77.7%)	102 (75.6%)	0.745
Personal vehicle	4 (21.1%)	34 (25%)	0.746
Clinical symptoms			<0.001
Tenderness	5 (5.3%)	24 (17.6%)	0.005
Pain	1 (5.5%)	48 (35.2%)	0.141
Shock	3 (10.5%)	16 (11.7%)	<0.001
Distension	9 (50%)	48 (35.2%)	0.038
Treatment mode			0.094
Non-operative	7 (38.8%)	91 (66.9%)	0.094
Operative	11 (61.1%)	46 (33.8%)	0.058
Complications	7 (36.8%)	8 (5.9%)	<0.001
Preop ventilation	16 (84.2)	11 (8.1%)	<0.001
Type of injury			0.042
No injury	4 (21.1%)	72 (52.6%)	0.01
Head Injury	10 (52.6%)	7 (5.1%)	0.001
Other Injury	4 (2.2%)	60 (44.1%)	0.116

RTA: Road traffic accident.
$ Mean±Standard deviation compared by Independent samples t test
# Median (Q1, Q3 i.e. Interquartile range) compared by Mann Whitney U test.
Frequency (%) compared by Chi square test used or Fisher exact test. p< 0.05 significant.

the treating doctors (10). In addition, delay or missed diagnosis leads to increased morbidity and mortality (11). The reported incidence of intra-abdominal injury is approximately 13% with bowel and mesenteric injuries occurring in 1-5% of cases (12,13). In this study, mean age of the males was 29 +/-13years, and the female mean age was 28+/-16 years. The majority of our cases were of the young productive age group, a finding which aligns with previous studies (14). Our study showed male predominance of the victims (75.9%). Fleming S et al. have found that in a group of 100 cases, 62% were men (15). In a study by Farahmand N et al., 60% were male cases, which was comparable to our observations (16). In our study, the incidence of the mode of injuries was similar as reported in the literature (17-19). Among the road traffic crashes, the majority of cases were four-wheeler occupants (67, 65%) followed by two-wheeler occupants (36, 34.9%). Forty-four percent of the four-wheeler occupants survived as compared to 19% of two-wheeler occupants. The average duration to reach our institution was 14.56

Table 3. Association between time to reach to hospital and the organ involved with mode of injury

Time to reach to hospital in hours	Patients with mode of Injury (154)				
	RTI A (n= 103, 66.8%)	Fall from height B (n= 23, 14.9%)	Assault C (n= 28, 18.3%)	p	Multiple comparisons between pairs (p< 0.05)
0-10	37 (36.0)	13 (56.5)	11 (39.28)	**<0.001**	AB, AC
11-20	18 (17.5)	4 (17.3)	2 (7.1)	**<0.001**	AB, AC
21-30	12 (11.6)	-	2 (7.1)	**0.014**	AC
31-40	3 (2.9)	1 (4.3)	2 (7.1)	**0.027**	AB
41-50	9(8.7)	1 (4.3)	2 (7.1)	**<0.001**	AB, AC, BC
51-60	3(2.9)	2 (8.6)	1 (3.5)		-
61-70	4(3.9)	-	2 (7.1)		-
71-80	8(7.8)	-	2 (7.1)	**0.039**	AC
81-90	3(2.9)	1 (4.3)	-	0.826	-
91-100	4(3.9)	-	3 (10.7)	0.568	-
101-110	2(1.9)	1 (4.3)	1 (3.5)	0.999	-
Median (Q1, Q3)	12 (6, 48)	12(7, 48)	12(4, 72)	0.962#	-
Organ Involved					
Liver	27 (26.2)	4 (17.5)	9 (32.2)	**<0.001**	AB, AC, BC
Spleen	39 (37.8)	17 (73.9)	10 (35.6)	**<0.001**	AB, AC, BC
Gall Bladder	4 (3.9)	-	-	**-**	-
Pancreas	4 (3.9)	-	1 (3.5)	**0.034**	AC
Small	11 (10.7)	-	2 (7.1)	**0.47**	AC
Large bowel	5 (4.8)	1 (4.3)	2 (7.1)	**0.024**	AB, AC
kidney	8 (7.8)	1 (4.3)	4 (14.5)	**<0.001**	AB, AC, BC
Urinary Bladder	3 (2.9)	-	-	-	
Urethra	2 (1.9)	-	-	-	

Presented in Frequency (%) compared by Chi square test / Fisher exact test followed by multiple comparisons.
#Median (Interquartile range) compared by Kruskal Wallis H test. P<0.05 significant.

hours. Thirty-nine percent of the cases reached in our institution within 1-10 hours of sustaining the injury, followed by 15.5% in the next 11-20 hours. We tried to correlate the time taken to reach the hospital with the mode of injury and found that cases involved in motor vehicle crashes reached hospital early as compared to cases of fall from height or assault. An explanation for this significant difference could be the obvious visible injuries during the crashes. Co-passenger or the people around the site of crashes also help in early referral to nearby health-care centres either by dialling 108 or 100. Whereas, individual injuries occurring during an assault or fall from height remain unnoticed until grievous in nature. We found the spleen to be the most commonly injured organ as against the liver which was reported in other series (20-22). Injury to the intestine was seen in 13.6%, majority of which due to road traffic crashes. Jagannatha et al. have found this incidence to be 25%, which is in concurrence with our study (23). The incidence of renal injury was 9% in agreement with Khichi et al. (16.3%), Meng MV et al. (10 %) and Sah D et al. (11.4%) (24-26). Gall bladder injury was seen in 2.5% cases, comparable to the findings of Singh et al. (7.07%) (27). We also tried to correlate the organ involved with the mode of injury and concluded that the spleen, liver, and small bowel were the commonly injured organs both in road traffic crashes and assault (Table 3). As can be seen from Table 3, road traffic crashes are responsible not only for the majority of solid organ injury but also for hollow viscus injury as well. In our series, all 3 cases of bladder injuries and 2 cases of urethral injury were because of motor vehicle crashes. All of these 5 cases were associated with pelvic fractures. For pelvic fractures, we did pelvic stabilization with an external fixator in the same setting. We found intraperitoneal rupture of the bladder in 3 cases, which was repaired primarily during laparotomy. Railroad technique along with suprapubic cystostomy was used in two cases who presented with urethral injury. One of these 2 cases required an

Table 4. Organ of injury and various surgical procedures performed

Sl no	Injured organ	Total no of case (%) (n= 154)	No of non-operated cases (%)	No of operated cases (%)	Surgical procedure performed
1.	Liver	40 (25.9%)	27 (67.5%)	13 (32.5%)	Hepatic resection/repair
2.	Gall bladder	04 (2.5%)	-	04 (2.5%)	Cholecystectomy
3.	Spleen	66 (43%) *	57 (86.3%)	09 (13.6%)	Splenectomy
4.	Pancreas	05 (3.2%)	-	05 (100%)	Spleenopancreatectomy
5.	Kidney	13 (09%)	10(76.9%)	03 (23.0%)	Nephrectomy
6.	Intestines (Small/ large/mesentery)	21 (13.6%) *	06(28.5%)	15 (71.4%)	Primary bowel repair /Mesenteric tear repair/Resection anastomosis/ stoma formation
7.	Urinary Bladder	03 (1.9%)	-	03 (100%)	Intraperitoneal Bladder repair
8.	Urethra	02 (1.2%)	-	02 (100%)	Urethral repair

*Includes cases of hepatic injury.

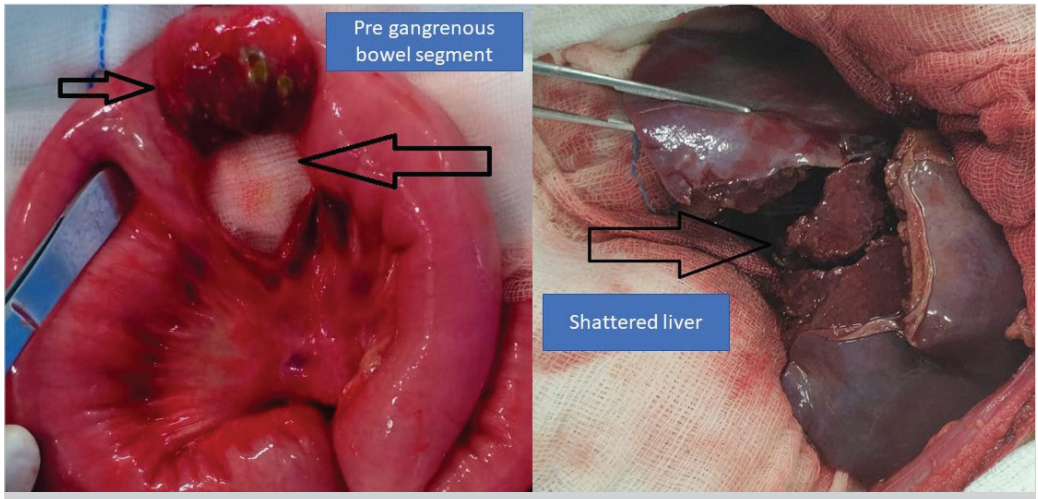

Figure 1. A. Pregangrenous segment of bowel, **B.** Hepatic Injury where packing was done as damage control surgery.

Table 5. Predictors of mortality (n= 154)

	Univariate analysis #		Multivariate analysis $	
Variables	OR (95 CI)	p	AOR (95 CI)	p
Duration of Injury	1.02 (1.01-1.04)	<0.001	1.03 (1.01-1.04)	**<0.001**
Clinical Symptoms (Yes)		<0.001	--	--
Tenderness (Yes)	0.46 (0.04-5.25)	0.532	--	--
Pain (Yes)	1.31 (0.18-9.80)	0.790	--	--
Shock (Yes)	80.5 (13.3-486.8)	<0.001	--	--
Distension (Yes)	Ref		--	--
Any Complications (Yes)	9.26 (2.86-29.97)	<0.001	--	--
Pre-op Ventilation (Yes)	60.1 (15.2-238.7)	<0.001	--	--
Any Associated Injuries (Organs involved in Injury)	4.16 (1.31-13.19)	0.015	4.85 (1.42-16.52)	**0.012**

Outcome variable: Death/Alive. #Univariate /$Multivariate Binary Logistic Regression Analysis used, OR: Odds ratio, AOR: Adjusted Odds ratio, p< 0.05 significant

end to end urethral anastomosis, which was done by the urology department of our institute. Analysis of our data showed that the most common presenting symptom was abdominal distension as against abdominal pain reported in other series (28). Delayed presentation leading to gross hemoperitoneum or perforation peritonitis was the reason, as can be seen that 12.33% of our cases presented with shock. In our study, we observed associated injuries in 81 (52.59%) cases while there was no association in 73 (47.40%) cases. Nikhil Mehta et al., in their retrospective study of 71 cases, have found 14% head injury and 40% chest injuries which included hemothorax (14%), pneumothorax (6%) and rib fractures 20% (2). In our study group, 39 (25.32%) chest injuries were present, most of them treated conservatively with intercostal tube drainage either for hemothorax or pneumothorax while 8 (20.15%) required posterolateral thoracotomy for retained hemothorax.

Out of 81, 26 (32.09%) cases with abdominal injuries were missed during primary survey leading to delayed diagnosis and poor outcome. The reason being FAST negative at the time of presentation with masked clinical symptoms was related to abdominal injuries. This highlights the fact that cases with polytrauma need repeated examination at regular intervals by members of the trauma team, along with repeated radiological examination as and when required. CT scan remains the gold standard for the detection of solid organ injuries (29). In addition, a CT scan of the abdomen can reveal other associated injuries, notably vertebral and pelvic fractures and injuries in the thoracic cavity (30).

Our policy of initial management of all postoperative cases in the surgical ICU increased our survival rate as suggested by our low mortality rate of 11.6%, whereas the reported mortality in other series was 6.1-26% (31). We observed acute renal failure in 12 (7.7%) cases. Out of these 12 cases, 5 (41.6%) presented with shock in the emergency department while the remaining 7 (58.3%) developed renal failure in the postoperative period. Three (25%) died despite undergoing hemodialysis in the postoperative period because of multiorgan dysfunction. We observed that it is necessary to have adequate infrastructure for hemodialysis, and a nephrologist should be a core member of trauma teams. Other complication includes bowel anastomotic leak, seen in 3 (1.94%) cases, which were conservatively managed as controlled enterocutaneous fistula with total parental nutrition. Two cases of pancreatic fistula, developed on postoperative day 4 after distal spleenopancreatectomy, were given octreotide treatment during their stay in the hospital and both of them responded to the treatment. Nine (5.8%) cases who developed septicemia were treated with broad-spectrum antibiotics in the surgical ICU. In our study, the initial nonoperative treatment rate was 58.44%, with an approximate success rate of 90%, a finding which is higher as compared with other reported series (32). We accept that the complication rate of 16.88% and the surgical intervention rate of 37% in our study was higher but comparable with the other reported studies where the reported rate was 10 to 27% (33,34). The learning curve of the treating trauma team as well as the supporting paramedical staff was one of the predominant contributory factors. Others were being lack of infrastructures such as non-availability of digital subtraction angiography (DSA) and lack of experience of the supporting staff (nurses) in trauma care. Efforts are going on to rectify these obstacles and we hope in the near future that we will be able to improve our services by leaps and bounds. Limitations of our study include retrospective design, small sample size because of the low influx of cases, and short follow-up period as these are the initial data from a newly created trauma centre.

CONCLUSION

The study revealed that among 154 cases of fatal blunt abdominal trauma, road traffic crash was the most common cause of blunt abdominal trauma, predominantly affecting males. The visceral and peritoneal injury frequently perceived was liver in 40 cases (25.9%), spleen in 66 (43%), intestine in 21(13.6%) and kidney in 13 cases (9%). Abdominal injury was associated with other injuries like head, chest and extremity injuries in 52.5% cases. Duration of injury, presence of associated injury and preoperative ventilation requirement were independent predictors of mortality apart from contributary factors such as clinical presentation, organ involved and presence of complications.

Ethics Committee Approval: Ethics committee approval was granted for this study from the ethics committee of Sanjay Gandhi Institute of Medical Sciences (Ethics No. PGI/BE/437/2020). Subjects were enrolled in the study after obtaining voluntary informed consent according to the Declaration of Helsinki.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.S.; Design - A.S.; Supervision - G.P.; Data Collection and/or Processing - P.M.; Analysis and/or Interpratation - P.M.; Literature Review - K.V., R.S.; Writing Manuscript - A.S.; Critical Reviews - R.S., G.P.

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

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2021; 37 (3): 277-285

Künt batın travmasından alınan dersler: Birinci seviye travma merkezinin cerrahi deneyimi

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ÖZET

Giriş ve Amaç: Kaza sayısı gün geçtikçe artarken zorlukları da beraberinde getirmektedir. Hükümet, travma tedavisine vurgu yaparak, 2018 yılının Haziran ayında, Kuzey Hindistan'da 2,8 milyonluk bir nüfusa hizmet veren 120 yataklı 1. seviye bir travma merkezini hizmete geçirdi. Bu makale aracılığıyla, yeni bir seviye I travma merkezinden künt batın travması yönetimi deneyimlerimizi paylaşmayı hedefledik.

Gereç ve Yöntem: Bu geriye dönük gözlemsel çalışmada, Temmuz 2018'den Mart 2020'ye kadar mevcut tüm kayıtların tarihsel analizi yapıldı. Çalışmaya dahil edilme kriterleri, ilişkili yaralanmalarla birlikte veya yaralanmalar olmaksızın künt batın travmasıydı. Yaş, cinsiyet, yaralanma mekanizması, hastaneye ulaşma süresi, katı organlar ve içi boş organ yaralanmaları, ilişkili ekstra abdominal yaralanmalar, tedavi şekli, komplikasyonlar, YBÜ ve hastanede kalış süresi ve mortalite ile ilgili veriler gözden geçirildi.

Bulgular: Genel olarak, çalışma süresi boyunca 154 vaka batın yaralanmalarına maruz kaldı. Yüzde yetmiş beşi erkekti. Künt batın travmasının en yaygın nedeni karayolu trafik kazalarıydı. 57 (%37,01) vakada cerrahi yönetim gerekli olurken, 97 (%62,98) vakada nonoperatif (NOM) tedavi uygulandı. Ortalama YBÜ kalış süresi 05.73 gün, ortalama hastanede kalış süresi 12 gün (dağılım 10-60 gün) idi. Gerçekleştirilen prosedürler arasında splenektomi, karaciğer onarımı, bağırsak yaralanmasının birincil kapatılması ve stoma oluşumu yer alır. Vakaların %16,88'inde komplikasyonlar meydana geldi ve genel ölüm oranı %11,68 idi.

Sonuç: Çalışma, 154 ölümcül künt batın travması olgusu arasında, karayolu trafik kazasının, ağırlıklı olarak erkekleri etkileyen künt batın travmasının en yaygın nedeni olduğunu ortaya koydu. Sıklıkla algılanan viseral ve periton yaralanması 40 olguda (%25,9) karaciğer, 66 (%43) olguda dalak, 21 (%13,6) olguda bağırsak ve 13 olguda (%09) böbrek idi. Batın yaralanması %52,5 olguda kafa, göğüs ve ekstremite yaralanmaları gibi diğer yaralanmalarla ilişkilendirildi. Yaralanma süresi, ilişkili yaralanmanın varlığı ve ameliyat öncesi vantilasyon gereksinimi, klinik görünüm, tutulan organ ve komplikasyonların varlığı gibi katkıda bulunan faktörlerin yanı sıra, mortalitenin bağımsız belirleyicileriydi.

Anahtar Kelimeler: Motorlu taşıt kazaları, travma, batın yaralanmaları, sonuç, hastane öncesi bakım

DOİ: 10.47717/turkjsurg.2021.4886

ORIGINAL ARTICLE
Turk J Surg 2021; 37 (3): 286-293

Missed pancreatic injury in patients undergoing conservative management of blunt abdominal trauma: Causes, sequelae and management

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ABSTRACT

Objective: Pancreas is a less commonly injured organ in blunt abdominal trauma. This study aimed to analyze the management and outcomes of patients in whom the pancreatic injury was missed during the initial evaluation of blunt abdominal trauma.

Material and Methods: We retrospectively (2009-2019) analyzed the details and outcome of patients who underwent conservative management of blunt abdominal trauma, where the diagnosis of pancreatic injury was missed for at least 72 hours following trauma.

Results: A total of 31 patients with missed pancreatic injury were identified. All patients were hemodynamically stable following trauma and most (21) were initially assessed only by an ultrasound. A delayed diagnosis of pancreatic injury was made at a mean of 28 (4 to 60) days after trauma when patients developed abdominal pain (31), distension (18), fever (10) or vomiting (8). On repeat imaging, 18 (58.1%) patients had high grade pancreatic injuries including complete transection or pancreatic duct injury. Seven (22.5%) patients were managed conservatively, seventeen (54.8%) underwent percutaneous drainage of intra-abdominal collections, seven (22.5%) underwent endoscopic or surgical drainage procedure for symptomatic pseudocyst. Eleven (35.4%) patients needed readmissions to manage recurrent pancreatitis, intra-abdominal abscess and pancreatic fistula. Three patients required pancreatic duct stenting for pancreatic fistula. There was no mortality.

Conclusion: Pancreatic injury may be missed in patients who remain hemodynamically stable with minimal clinical symptoms after abdominal trauma, especially if screened only by an ultrasound. In our series, there was significant morbidity of missed pancreatic injury.

Keywords: Pancreatic injury, missed injury, blunt trauma abdomen, ultrasound abdomen

INTRODUCTION

Pancreas is a less commonly injured organ in blunt abdominal trauma. The incidence of pancreatic injury in blunt abdominal trauma is estimated to be 2 to 5% (1,2). The most common mechanisms of injury include motor vehicle accidents in adults and bicycle handle bar injuries in children (3). Solitary pancreatic injury is uncommon and 80 to 90% patients of pancreatic trauma have at least one other associated abdominal organ injury (4). During initial evaluation of abdominal injury, attention is generally absorbed on the more immediate and catastrophic injuries like the liver and spleen injuries leading to hemorrhagic shock or intestinal perforation leading to septic shock or peritonitis. Pancreatic injury by virtue of its location in retro-peritoneal space can remain asymptomatic initially or present with non-specific signs and symptoms. A number of patients who remain hemodynamically stable after trauma with minimal abdominal signs may initially be evaluated using an ultrasound, especially in rural areas or small clinics where computed tomography (CT) scan is not available. Focused assessment with sonography for trauma, while being excellent for detecting liver or splenic injuries and fluid in abdomen, has a limited role in the diagnosis of pancreatic injury (5,6). Computed tomography (CT) scan is used as the imaging modality of choice for the assessment of pancreatic and associated organ injuries and their complications (7). In as many as 20 to 40 % of the patients with pancreatic injury, the initial computed tomography (CT) scan on admission may fail to show any gross abnormality (7,8). The evolving nature of pancreatic injury often leads to delayed changes which can only be detected in sequential imaging done after a gap of 24 to 48 hours (9). Serum amylase can be

Cite this article as: Gupta V, Sodha VS, Kumar N, Gupta V, Pate R, Chandra A. Missed pancreatic injury in patients undergoing conservative management of blunt abdominal trauma: Causes, sequelae and management. Turk J Surg 2021; 37 (3): 286-293.

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Received: 28.06.2021
Accepted: 16.07.2021
Available Online Date: 28.09.2021

DOI: 10.47717/turkjsurg.2021.5425

normal in one third of patients with pancreatic injury (2). Other modalities of imaging like magnetic resonance cholangiopancreatography (MRCP) or endoscopic retrograde cholangiopancreatography (ERCP), which are used to image pancreatic duct and its disruption, have a limited role in an acute trauma setting. Hence, with subtle clinical and radiological findings, a number of pancreatic injuries may be initially missed in blunt abdominal trauma. The aim of this study was to analyze the management and outcomes of patients in whom pancreatic injury was missed during the initial evaluation of blunt abdominal trauma.

MATERIAL and METHODS

Study Design

This was a retrospective analysis of prospectively maintained database of patients admitted to a major tertiary care center and university hospital in northern India, from January 2009 to January 2019.

Inclusion Criteria

This study included all patients who had a delayed diagnosis of pancreatic injury, made more than 72 hours after an initial conservative management of blunt abdominal trauma.

Exclusion Criteria

1) Patients with documented pancreatic injury during initial evaluation (within 72 hours) of blunt abdominal trauma were excluded from the study.

2) Patients who underwent any surgical intervention for abdominal injuries in the first 72 hours following trauma were excluded from the study.

Data Collection

Variables recorded in the database included demography, time of presentation after injury, mechanism of injury, associated injuries, symptoms at presentation, serum amylase and lipase levels, grade of pancreatic injury, management, duration of hospital stay, complications and outcome.

Assessment and Management of Pancreatic Injury

Patients were resuscitated with IV fluids and treated with antibiotics and hyperalimentation as and when required. Multi detector computed tomography (MDCT) of the abdomen was used to confirm and grade the pancreatic injury in all cases. American Association of the Surgery of Trauma classification of pancreatic Trauma-Organ Injury Scale (AAST-OIS) (10) was used for the grading of pancreatic injury on the basis of contrast enhanced computed tomography (CECT) abdomen findings (Table 1). MRCP was performed selectively to evaluate patients with suspected pancreatic ductal injury and ERCP was reserved for pancreatic duct stenting. Depending on the clinical scenario patients were managed either conservatively or with percutaneous drainage (PCD) or surgery.

Ethics

This was an observational study, and no experimental interventions were carried out. The patients were treated according to the ethical guidelines of the "World Medical Association Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects" adopted by the 18th World Medical Association (WMA) General Assembly, Helsinki, Finland, June 1964, as revised in Tokyo 2004.

Statistics

Descriptive statistics were mainly used. Quantitative variables were expressed as mean +/- standard deviation and qualitative variables were expressed as percentage. Chi-square and t test were used if applicable on IBM Statistical Package for the Social Sciences (SPSS) Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.

RESULTS

A total of 31 patients met the inclusion criteria of the study. As expected, most of the patients were young (mean age 20.6 years) males (90.3%). Road traffic accident was the most common mode of injury (77.4%), followed by assault and fall. Demographic details are shown in Table 2. All patients were initially managed conservatively for blunt trauma. Most patients (n= 27) sustained injury in small villages or rural areas. Seven patients considered the injury to be trivial and did not seek medical attention immediately after trauma. Others were managed in primary (4) or mid-level health centers (3) or private clinics (17) and were discharged after a mean of 4 days (1 day to 12 days) of admission. An ultrasound report

Table 1. American Association for the Surgery of Trauma classification of pancreatic trauma-Organ Injury Scale (AAST-OIS)

Grade	Injury	Description
I	Hematoma Laceration	Minor contusion without ductal injury Superficial laceration without ductal injury
II	Hematoma Laceration	Major contusion without ductal injury or tissue loss Major laceration without ductal injury or tissue loss
III	Laceration	Distal transection or pancreatic parenchymal injury with ductal injury
IV	Laceration	Proximal transection or pancreatic parenchymal injury involving the ampulla
V	Laceration	Massive disruption of the pancreatic head

Table 2. Population characteristics of 31 patients with delayed diagnosis of pancreatic injury after initial conservative treatment in blunt trauma abdomen

Characteristic	Result
Age in years (range)	20.6 (7-38)
Sex	
Male	28 (90.3%)
Female	3 (9.6%)
Location of accident	
Rural	27 (87.1%)
Urban	4 (12.9%)
Mechanism of injury	
Road traffic accident	24 (77.4%)
Assault	5 (16.1%)
Fall	2 (6.4%)
Associated injuries	
Total	16 (51.6%)
Liver	7 (22.5%)
Spleen	4 (12.9%)
Non-abdominal injuries	5 (16.1%)
Time from Injury to diagnosis of pancreatic injury (days)	28 (4-60)
Symptoms at diagnosis of pancreatic injury	
Pain in abdomen	31 (100%)
Distension of abdomen	18 (58.1%)
Fever	10 (32.2%)
Vomiting	8 (25.8%)
Vitals at diagnosis of pancreatic injury (mean)	
Pulse	88/min
BP	108/74mm hg
Labs at diagnosis of pancreatic injury (mean / range)	
Hb	10.86 gm/dl (8-13)
TLC	12.3 x 109/L (6900-25200)
Platelet count	127 x 109/L (87-224)
Bilirubin	1.4 mg/dl (0.9-2.4)
Serum creatinine	1.35mg/dl (0.8-2.1)
Serum amylase	742.5 U/L (196-1940)

Hb: Haemoglobin, BP: Blood pressure, TLC: Total leucocyte counts.

was available in 21 patients, none of which showed any evidence of pancreatic injury.

Three patients had a computed tomography (CT) scan performed at the time of initial evaluation, none of which showed any evidence of pancreatic injury. Only one patient had a repeat computed tomography (CT) scan performed 12 days after the injury due to abdominal distension which showed peri-pancreatic collection, and the patient was referred to us. Eleven patients (35.4%) had associated liver or splenic injuries which were also managed conservatively as per our study criteria. On average, a delayed diagnosis of pancreatic injury was made at 28 (4 to 60) days after trauma when patients developed clinical manifestations of pancreatic injury. Abdominal pain was present in all patients, followed by abdominal distension (58.1%), fever (32.2%) and vomiting (25.8%). All patients were resuscitated if needed, and imaging in the form of contrast enhanced computed tomography (CECT) was obtained in all patients. 41.9% of the patients had low grade (Grade I/II) injuries and 58.1% had high grade injuries (Grade III/IV). Further details and management based on grade of injury are shown in Table 3.

Table 3. Grading of pancreatic injury and management of 31 patients with delayed diagnosis of pancreatic injury after initial conservative treatment in blunt trauma abdomen

Grade	No of patients	Conservative	Percutaneous drainage	Surgery	Complications
I	4 (12.9%)	4	0	0	None
II	9 (29%)	3	6	0	None
III	14 (45.1%)	0	9	5	Pancreatic fistula (n= 3) Pancreatic abscess (n= 2) Pancreatitis (n= 4)
IV	4 (12.9%)	0	2		Pancreatic abscess (n= 2)

Serum Amylase

Initial reports of serum amylase following trauma were not available. We measured serum amylase when patients presented to us with complications. Mean serum amylase levels were 742.5 U/L (normal range, 40 to 140 U/L). Mean serum amylase levels in Grade 1 and 2 injuries was 376.5 + 102.9 U/L and that in Grade 3 and 4 injuries was 1040.8 + 386.8 U/L. This difference was statistically significant in unpaired t test with $p< 0.0001$.

Management

Conservative

Seven out of 31 (22.5%) patients were managed conservatively. All had Grade I or II injuries.

Percutaneous Drain Placement

Overall, 17 out of 31 patients needed PCD by interventional radiology. Six out of 31 (19.3%) patients required a placement of single drain, most common site of collection being lesser sac. Eleven out of 31 (35.4%) patients required multiple PCD placement to drain all intraabdominal collections. Most common sites being lesser sac followed by left paracolic and pelvis. PCD's were removed at a mean of 23.6 days (range 11 to 60 days) days after the placement.

ERCP With Pancreatic Duct Stenting

Three patients developed high output pancreatic fistula from the percutaneously placed drain (> 500 ml/day) which continued for more than 2 weeks. MRCP was suggestive of ductal injury with communication at region of body in two and body-tail junction in one patient. All of these patients underwent pancreatic duct (PD) stenting by ERCP. In all three patients, drain output reduced subsequently and drain was removed in 38, 46 and 60 days respectively.

Surgical drainage

Seven out of 31 (22.5%) required surgical drainage for a symptomatic pseudocyst (mean size of 8.4 cm). The procedure was carried out at an average of 98.7 days after the trauma. Endoscopic cystogastrostomy was done in 4 patients, who had a pseudocyst in lesser sac and significant bulge on posterior gastric wall on endoscopy. One patient developed a pseudocyst in lesser sac without a significant gastric bulge and underwent laparoscopic cystogastrostomy. Roux-en-Y cystojejunostomy was done in two patients (one patient had two pseudocysts and same roux limb was used to drain both pseudocysts).

Hospital Stay

Mean duration of hospital stay was 12.4 days (range, 8 to 20 days).

Follow Up

In long-term follow-up after discharge (9 months to 10 years), a further morbidity rate of 35.4% (11/31) was seen, leading to readmissions. Pancreatitis developed in 4 patients and all were managed conservatively. Recurrent intraabdominal collections developed in 4 patients and were managed by insertion of percutaneous drainage and antibiotics. Persistent pancreatic fistula in 3 patients was managed by pancreatic duct (PD) stenting. All these complications were seen in patients with grade III or IV injury. No morbidity was observed in patients undergoing pseudocyst drainage. There was no mortality in any group. Also, follow-up imaging revealed smaller (<5 cm) pseudocysts in 6 more patients. These were either asymptomatic or managed conservatively for mild associated pain.

DISCUSSION

Through this paper, we bring to light a number of cases of pancreatic injury sustained during blunt abdominal trauma which were initially missed and presented later with symptoms after a gap of 4 to 60 (mean 28) days after the injury. There seems to be a number of reasons as to why the pancreatic injury was missed initially.

First, all patients in our group were hemodynamically stable patients, undergoing non-operative treatment. This implies that we have auto selected patients with less severe injuries, which are more likely to be missed. In a study by Leppäniemi AK and Haapiainen RK (11), delayed diagnosis or missed early diagnosis was more likely in patients with isolated pancreatic injuries, absent or minimal other associated abdominal injuries or in those undergoing non-operative management without any follow-up imaging. Miller et al. have studied 338 patients with liver trauma out of which 89% patients underwent non-operative management. In the non-operative group, missed injury

occurred in seven (2.3%), while there was no missed injury in operative group (12). Our series also included a significant number of grade III and IV injuries. This suggests that even higher grade pancreatic injuries may be clinically silent (pancreatic lucid interval) in the initial few days after trauma and present themselves later with growing pseudocysts or peripancreatic collections.

Second, all of our patients belonged to smaller towns and rural areas of the state. All but three patients underwent initial management of abdominal trauma at primary health centers or small private clinics where CT scan was not available. Also, since patients remained clinically and hemodynamically stable, ultrasound abdomen might have been thought to be sufficient by the treating physician. Pancreatic injuries are very likely to be missed on an ultrasound. Jeffrey et al. (5) have reviewed ultrasound findings in 4 patients with surgically proven acute pancreatic trauma. Despite technically sound sonograms, pancreatic injuries could not be detected before surgery in any of the patients.

A CT performed shortly after ultrasound was able to demonstrate changes of pancreatic trauma in each case. Ultrasound findings suggestive of pancreatic injury can be simply enlargement of the pancreas or diffuse edema simulating pancreatitis. Peripancreatic fluids may be a sign of pancreatic contusion (13). Real-time contrast-enhanced US can give additional information, but its role should not be considered as a replacement for CT (14). In spite of these shortcomings, ultrasound does have a definite role in the follow-up of complications such as pseudocysts and fluid collections.

Third, even a CT scan can miss pancreatic injury in the initial part of investigation. CT is the most commonly used diagnostic modality for suspected pancreatic trauma and its complications. CT has a reportedly variable sensitivity (65%-80%) and specificity for detecting pancreatic trauma (4,15,16). CT is not a very sensitive test for pancreatic ductal injury (17). Specific signs of pancreatic injury include laceration, transection, focal pancreatic enlargement and inhomogeneous enhancement. Fluid collections like hematoma and pseudocyst can be seen communicating with the pancreas at the site of laceration or transection. Nonspecific signs include peripancreatic fat stranding, peripancreatic fluid collections, fluid between the pancreas and splenic vein, hemorrhage, thickened left anterior pararenal fascia and associated injuries to adjacent structures (15). The pancreas may appear normal in 20% to 40% of the patients when CT is performed within 12 hours after trauma because pancreatic injuries may produce little change in the density, which may not be detectable (4,18). This is likely due to obscuration of the laceration plane, hemorrhage, and close apposition of the pancreatic fragments. On repeat scanning at 12 to 24 h, an abnormality which was initially ambiguous or subtle becomes more evident. Findings become more radiologically apparent over time with the development of post-traumatic pancreatitis, edema, leakage of pancreatic enzymes, and subsequent auto-digestion of the surrounding parenchyma (4,19). Inability to detect early pancreatic trauma with CT may not be a limitation of CT technology but reflects the evolving nature of pancreatic trauma. An initial pancreatic contusion can progress to subsequent pancreatic transection with progressive autodigestion of the pancreatic gland.

Serum Amylase

Raised serum amylase can be useful in diagnosis, but there is poor correlation between raised amylase and pancreatic trauma because amylase may be elevated in injuries of the salivary gland, in duodenal trauma, hepatic trauma, and injuries to the head and face, and in an intoxicated patient (20,21). Almost one third of patients may have a normal serum amylase at initial presentation in spite of pancreatic transection. A raised amylase level after blunt pancreatic trauma is time dependent, and a persistently elevated or a rising amylase level is a more reliable indicator of pancreatic trauma, but it does not indicate the severity of the injury (22). All our patients had elevated amylase levels, which is probably a reflection of late presentation and evolved pancreatic injury.

Management and Outcome of Missed Pancreatic Injury

Patients presented to us at an average of 4 weeks after blunt trauma. Patients were initially managed with fluid resuscitation, antibiotics and hyperalimentation as and when required. None of the patients were hemodynamically critical at presentation to us. Patients complained of abdominal pain, vomiting and fever which was attributable to either fluid collections (sterile/infected) or localized symptomatic pseudocysts. Our results indicate that most patients could be managed non-surgically by drain placement into the fluid collections. Those who presented with well-formed symptomatic pseudocysts could be managed by an endoscopic or surgical drainage procedure. Morbidity rate was 35.4 % in the non-operative group and included pancreatitis, pancreatic abscess and recurrent pancreatic fistula.

ERCP with PD stenting was needed in three patients who had persistent/recurrent pancreatic fistula non-respondent to conservative measures. A transpapillary stent can reduce the leaking of pancreatic juice by bridging the disruption, or it can reduce the pressure of the pancreatic duct by allowing preferential flow through the stent into the pancreatic sphincter. We generally give a trial of Octreotide to control a high output (> 500 ml/day) pancreatic fistula. There was no morbidity in the surgically managed patients. There was no mortality in either of the groups in this series.

Operative vs Non-Operative Management of Pancreatic Injury in Blunt Trauma Abdomen

There is a general consensus that stable patients with low grade pancreatic injuries without pancreatic ductal injury (grade I and II) can be successfully managed conservatively with low morbidity (<20%) and mortality (9, 23). Surgical treatment is mostly recommended for high grade injury with main pancreatic duct disruption (grades III, IV, V). For grade III injuries, distal pancreatectomy + splenectomy is the standard surgery of choice (8,24). If the injury occurs at the neck, then pancreaticojejunostomy may be done as an alternative. For grade IV injuries, pancreatic drainage is recommended as part of damage control surgery (23, 25). For pancreatic injury grade V, treatment options vary from drainage to single or two stage pancreaticoduodenectomy (23). Diagnostic delays and main pancreatic duct leaks are associated with increased morbidity and mortality (26-28). Early surgical management is associated with decreased morbidity and length of hospital stay particularly for injuries to body and tail of pancreas (27,28). In a study of 39 high-grade pancreatic injuries (grades III and IV), patients who received conservative treatment were observed to required longer hospitalizations, more days of total parenteral nutrition and a greater incidence of complications (29). Conservative management of high grade injuries is a topic of controversy. In recent years there have been increasing numbers of publications describing conservative management of high grade pancreatic injury with successful outcomes (30-33).

Hamidian et al. (30) have compared 39 patients with major ductal injury undergoing surgical management with 12 patients undergoing conservative management. They have concluded that both operative and non-operative management of major grade blunt pancreatic injuries are acceptable, depending on the clinical condition, with similar complication rates.

Morbidity remains high with non-operative management; however, majority of the complications can be managed non-operatively. In hemodynamically stable patients, a controlled leak walled off as a pseudocyst, absent associated organ injuries and absent pancreatic necrosis predict a higher success rate for non-operative strategy of high grade pancreatic injuries. Koganti et al. (33) have studied 34 patients with grade III/IV trauma out of which 26 were initially under a conservative management. 10 of them could be successfully managed without any operation. On multivariate logistic regression, presence of necrosis and associated organ injury predicted failure of conservative management. Development of a pseudocyst was associated with a success of non-operative treatment. They concluded that non-operative measures should be attempted in a select group of grade III and IV blunt pancreatic trauma who are hemodynamically stable with a controlled leak walled off as a pseudocyst without associated organ injuries and pancreatic necrosis.

Our study also supports the feasibility of conservative management in patients with high grade (III and IV) pancreatic injuries, who remain hemodynamically stable. In our group of auto triaged patients, late complications were managed either with radiological drainage or a surgical drainage procedure. There was significant morbidity (35.4%), but no mortality. Morbidity was significantly less in patients who developed a pseudocyst.

The interpretation of this study is limited due to its retrospective nature and the limited sample size. Our series of patients do not represent the complete spectrum of pancreatic injuries, especially more severe injuries involving hemodynamically unstable patients. Also, most of our patients were initially evaluated only by an abdominal ultrasound.

CONCLUSION

Pancreatic injury may be missed in patients who remain hemodynamically stable with minimal clinical symptoms after abdominal trauma, especially if screened only by an ultrasound. Follow up imaging by CT can prevent such missed cases. Late complications of missed injury can cause significant morbidity; however, these can be usually managed by percutaneous drain placements or pseudocyst drainage. An endoscopic transpapillary stent can be useful option for pancreatic fistula.

Ethics Committee Approval: The study was obtained from King George's Medical University Instutional Ethics Committee (Date: 05.01.2021, Number: 20).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept –V.G., A.C.; Design – V.G., A.C.; Supervision –V.G., A.C.; Materials - All of authors; Data Collection and/or Processing - V.G., A.C., V.S.S., N.K.; Analysis and/or Interpretation – V.G., A.C., V.S.S., N.K.; Literature Search- All of authors; Writing Manuscript – V.G., A.C.; Critical Reviews – All of authors.

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

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2021; 37 (3): 286-293

Künt karın travmasının konservatif tedavisi uygulanan hastalarda gözden kaçan pankreas yaralanması: Nedenleri, sekelleri ve tedavisi

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ÖZET

Giriş ve Amaç: Künt batın travmalarında pankreas en az hasar alan organdır. Bu çalışmanın amacı, künt batın travması sonrası yapılan ilk değerlendirmede pankreas yaralanması atlanan hastaların tedavilerini ve sonuçlarını analiz etmekti.

Gereç ve Yöntem: Travma sonrası pankreas yaralanması tanısının en az 72 saat süresince atlanmış olduğu künt batın travmalı hastaların konservatif tedavilerinin sonuçlarını ve detaylı bilgilerini retrospektif olarak (2009-2019) değerlendirdik.

Bulgular: Pankreas yaralanması atlanan 31 hasta saptandı. Travma sonrası tüm hastalar hemodinamik olarak stabildi ve çoğunluğu (21) sadece ultrason ile değerlendirilmişti. Hastalarda karın ağrısı (31), distansiyon (18), ateş (10) veya kusma (8) gelişince travma sonrası pankreas hasarının gecikmiş tanısı ortalama 28 günde (4-60 gün) konulmuştu. Tekrarlanan görüntülemede tam pankreas transeksiyonu ve pankreas yolu yaralanması dâhil yüksek dereceli pankreas hasarı 18 (%58,1) hastada görüldü. Yedi hasta (%22,5) konservatif olarak tedavi edilirken on yedi hastada (%54,8) intraabdominal birikimler perkutan drenaj ile tedavi edildi ve yedi hasta (%22,5) semptomatik psödokist için endoskopik ya da cerrahi drenaj işlemlerine tabi oldu. Tekrarlayan pankreatit, intraabdominal apse ve pankreas fistülü sebebiyle on bir hasta (%35,4) tekrar hastaneye kaldırıldı. Pankreas fistülü için üç hastada pankreas yolu stentlemesi gerekti. Mortalite olmadı.

Sonuç: Özellikle sadece ultrason görüntülemesi yapılan, karın travması sonrası hemodinamik olarak stabil ve minimal klinik belirtiler gösteren hastalarda pankreas yaralanması atlanabilir. Bizim serimizde önemli oranda atlanan pankreas yaralanması morbiditesi mevcuttu.

Anahtar Kelimeler: Pankreas yaralanması, gözden kaçan yaralanma, künt travma karın, karın ultrasonu

DOİ: 10.47717/turkjsurg.2021.5425

ORIGINAL ARTICLE
Turk J Surg 2021; 37 (3): 294-298

A new approach in bariatric operations: bridged mini gastric by-pass. Is rabbit model suitable for an experimental study?

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ABSTRACT

Objective: Obesity is a global health epidemic with considerable co-morbidities. The increasing demand for bariatric surgery has led to the emergence of new techniques. We modified previously described Mini Gastric By-pass(MGB) technique via leaving a bridge at the most cranial 2 cm of the fundus of the human stomach to the follow-up and treatment of the remnant stomach and duodenum. We would like to entitle this new technique as Bridged MGB and aimed to apply on rabbits as an experimental study.

Material and Methods: The study was performed in the experimental animal laboratory of university after ethical approval was taken from the local ethics committee. Described new technique was applied to 2.1 and 3.2 kg 2 New Zealand rabbits.

Results: As a result of the operations, one of the rabbits died on the day of the operation; the other rabbit was exitus postoperatively on the third day. In autopsies, although no problem was detected at the anastomoses, necrosis was detected in the large curvature of both rabbits.

Conclusion: Rabbit, one of the popular experimental animals, has been shown to be different from the human gastrointestinal system in both arterial and topographic aspects and it has been emphasized that it varies according to the species and even the diet and the climate. We believe that our study failed as a result of these differences and that animals more similar to humans should be used in gastrointestinal experimental studies.

Keywords: Experimental study, mini gastric bypass, rabbit

INTRODUCTION

Obesity and obesity-related disease (O-ORD) is a global health epidemic with considerable co-morbidities. Six hundred and fifty million adults and over 340 million children and adolescents are overweight or obese according to the World Health Organization (1). Surgical solutions have become increasingly popular following technical advances. Approximately 216.000 individuals underwent bariatric surgery in the United States according to the American Society for Metabolic and Bariatric Surgery since 2016 (2).

In the long-term, diet, exercise and conservative treatment are not effective enough to manage O-ORD as much as surgery (3-5). As bariatric and metabolic surgery, a lot of techniques have been described from a simple operation like adjustable gastric banding, to more complex procedures like biliopancreatic diversion (BPD). All by-passed techniques, such as Roux-en-Y gastric bypass (RYGB), duodenal switch (DS/BPD), single anastomosis duodeno-ileal bypass (SADI), transit bipartition/its modification and ileal interposition are based on whether the foregut or hindgut theory or the combination of both (3,6-8).

Mini-Gastric Bypass (MGB) has been an increasingly popular bariatric procedure worldwide. A lot of studies have demonstrated the advantages of MGB, and MGB recently has been the third most common bariatric operation in most countries, second common in India (5,9-11). MGB was first described by Rutledge 23 years ago (7,11,12). Although MGB is accepted as a standard technique, still there are

Cite this article as: Sümer A, Çelik S, Vartanoğlu Aktokmakyan T, Pekşen Ç, Savaş OA, Talih T, et al. A new approach in bariatric operations: bridged mini gastric by-pass. Is rabbit model suitable for an experimental study?. Turk J Surg 2021; 37 (3): 294-298.

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Received: 16.05.2020
Accepted: 16.08.2020
Available Online Date: 28.09.2021

DOI: 10.47717/turkjsurg.2021.4874

some doubts about it (4-6). MGB has not been fully recognized worldwide for various reasons such as the risk of bile reflux and unknown cancer in long-term follow-up.

For this reason, researches are ongoing to find the best and most useful technique to treat the O-ORD. Some modifications have been applied to MGB to get better results. One of them is One Anastomosis Gastric Bypass (OAGB) modified by Carbajo in which the created the gastric pouch and afferent jejunal loop are suspended by the continuous sutures both above and below the anastomosis for fixation (13). The other one is obstructive stapleless pouch one anastomosis defined by Ospanov considering a modification of MGB. However, apart from one anastomosis, there are significant differences between Ospanov's technique and MGB (10).

The most important handicap of MGB technique like the RYGB is leaving a closed remnant stomach that cannot be reached by endoscopy in case of complications and emergencies such as bleeding, remnant stomach hematoma, endoscopic retrograde cholangiopancreatography (ERCP) for choledocholithiasis and cholangitis.

In this experimental study, we aimed to modify the previously described technique by leaving a bridge at the most cranial part of the fundus to eliminate the handicap of MGB and to solve closed remnant stomach problems.

MATERIAL and METHODS

The study was approved by the University of Van Yüzüncü Yıl, Regional Committee of Ethics (31008, 03/05/2017). The Experiment was conducted at the experimental animal laboratory of the Veterinary Faculty of the University.

For pre-study, 2 rabbits were given high calorie (Protein: %17; Metabolic Energy: 2700 kcal; Crude ash: %7; Crude oil: %3.17; Crude fiber: %4.5; Sodium: 0.41 mg/kg; Vit A: 12000 mg/kg; Vit D3: 3600 mg/kg; Vit E: 24 mg/kg) feed for four weeks and weight gain was achieved. 2.1 and 3.2 kg 2 New Zealand rabbits fasted for 2 days before the operation(only free access to water as possible). 5 mg/kg XylazineHCl and 50 mg/kg Ketamine HCl were used as anesthesia for the operation.

Surgical Technique

The operation area of the rabbit was sterilized and a mid-line incision was made from the xiphoid down to the pubis. A shorter incision may be preferred. Scrape fine subcutaneous tissue to expose linea alba. Linea alba was isolated, using a scalpel blade, a blade incision was made parallel to the linea alba (14).

The stomach was explored and prepared for transection. The starting point of the stapler was determined as 2-3 cm away from the pylorus (Figure 1). The lesser sac was reached by cutting the hepatogastric ligament at the incisura angularis, the

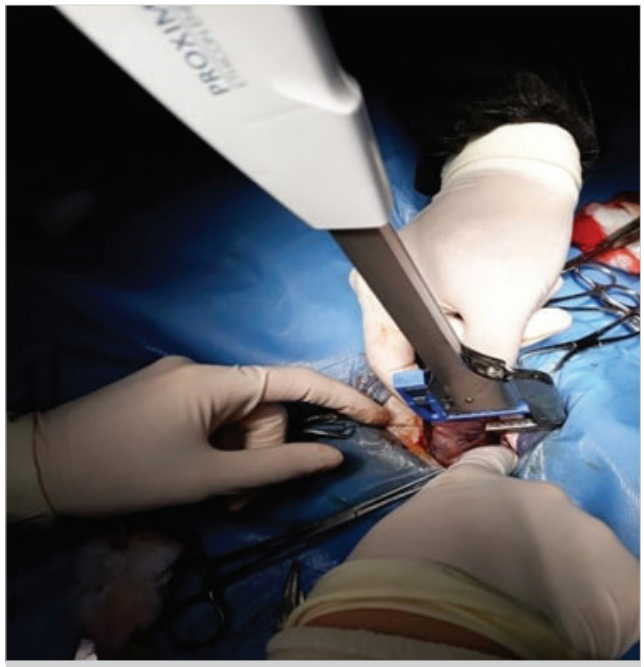

Figure 1. Placement of first stapler and transection of the gastric wall from minor curvature.

stapler (Proximate Reloadable Stapler, 30 mm (TX), 3.5 mm, Blue, Ethicon Endo-Surgery, LLC Guaynabo Puerto-Rico 00969 USA) was pushed forward to the midline 2 cm in length. After 2 cm, the stapler was directed towards the minor curvature and continued to the angle of HIS. It was terminated approximately 1 cm before the HIS angle for rabbits. In this way, 30-50% of the stomach was separated into a chamber. An anastomosis was brought to the stomach chamber by placing the jejunal segment at a distance of about 30 cm to the Trietz's ligament (could be said two-fifth of the small intestine) (Figure 2). 5/0 polyglactin suture was used for the anastomosis of gastrojejunostomy. After the completion of the anastomosis, the abdominal wall was sutured by 3/0 polyglactin. After the operations, the rabbits were fed post-operatively eighth hour with water.

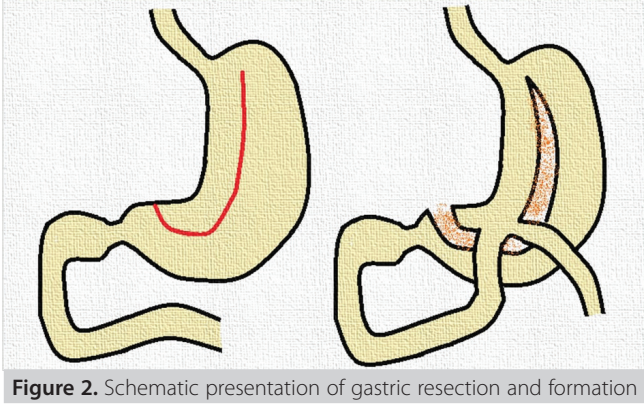

Figure 2. Schematic presentation of gastric resection and formation

RESULTS

One rabbit died on the same day of the surgery, while the other died after three days. At the end of the third day of the operations, we decided to terminate the study due to the death of both rabbits. During autopsy, any problem with the anastomosis could not be observed. However, necrosis developed at the greater curvature of rabbits.

DISCUSSION

Philosophically, innocents are not harmed in any religion, holy book, or ideology. However, we, as bariatric surgeons, punish two completely normal organs such as the stomach and small intestine, for the treatment of obesity and diabetes. In this perspective, the most important question to be answered by bariatric surgeons is: How right is it to irreversibly close the remnant stomach or remove a large piece of a completely normal organ to treat other diseases (8).

Bariatric surgery is a very dynamic surgical area. So far, several surgical techniques have evolved to find the best procedure in terms of weight loss and metabolic control that is associated with the fewest side-effects and complications. However, to tell the truth, all defined bariatric and metabolic surgical techniques are historical and go back to Billroth I or Billroth II gastrointestinal anastomosis (6,8,15,16).

MGB is widely used as a third commonly performed primary bariatric procedure after Laparoscopic sleeve gastrectomy (LSG) and RYGB. MGB has been used for about 23 years. This technique was described by Robert Rutledge (12). MGB has some advantages such as a simpler, safer, easier, and faster operation to compare other bypassed techniques. Moreover, evidence shows that MGB has a lower risk of long-term complications and metabolic effects are better than RYGB (4-6,8). On the other hand, MGB has some disadvantages. Mineral, vitamin deficiency, and bile reflux rate are higher in MGB. Recently, some modifications of the original MGB technique have been published by Carbajo as OAGB and by Ospanov as obstructive stapleless pouch one anastomosis (10,13). Nevertheless, these two modifications could not eliminate the most important handicap of the MGB.

The most important handicap of MGB technique, like RYGB, is leaving a closed remnant stomach that cannot be reached by endoscopy (6,8). To eliminate this handicap of MGB and to solve closed remnant stomach problems, we have developed a new modification technique via leaving a bridge at the most cranial part of fundus such as artificial gastro-gastric fistula(GGF). Because the outer diameter of the distal part of the duodenoscope is 13.7 mm, we leave 2 cm GGF (7,8).

Possible advantages of this new modified technique can be hypothesized as below:

1. Never touch and destroy the Angle of His
2. Not removing 75-80 % of the stomach as in Sleeve Gastrectomy and protection of organ
3. No short gastric vessel bleeding
4. Allow for endoscopic intervention to observe the remaining stomach (6).

Rabbits are widely used as popular experimental animals and their arterial supply from the left and right gastric arteries, short gastric arteries, and left and right gastroepiploic arteries like in the human stomach (17,18) However, macroscopic descriptions of the arterial pattern often differ and are incomplete in textbooks and atlases as well as in research articles (19).

Ikegami et al. have suggested that short gastric arteries supplied the gastric fundus on the parietal surface of the stomach and the greater curvature which varied in number from 2 to 6, with 4 arteries (37%) being the most frequent. (19) In contrast, Abidu-Figueiredo et al. (20) have reported that the number of short gastric arteries varied from 0 to 5, with 0 (33.4%) being the most frequent and that these arteries, when present, were distributed only to the greater curvature. These differences may be due to the possibility that Abidu-Figueiredo et al. used another breed of New Zealand rabbits, such as New Zealand Red, and/or were not able to visualize arteries distributed to the parietal surface of the stomach (21). In this current study, two rabbits died at the beginning of the experiment and formed a question in our minds that there may be anatomical variations between rabbit and human stomach. The rabbits may have different fundic arterial supply and the reason for the failure of the technique was attributed to this.

The study of Nath et al. (22) has suggested that there are important differences in the topographical and biometrical anatomy of the digestive tract of rabbits. They have also attributed the reason for these differences to the breed difference. Moreover, they have claimed that the differences in size and weight of the digestive tract of rabbits may also be due to age, food habits, and the effects of the climate. It was determined that gastric arterial supply differed even in their species and also various abnormalities of the digestive tract. The structure and physiology of the rabbit stomach are not suitable for this type of surgery because rabbits' stomach is a natural bezoar. Instead of rabbits; preferring pigs that are more similar to human beings can be considered, especially in gastric operations. (20-22). In the current experimental study, two rabbits, on which bridged mini-gastric bypass surgery was performed, were dead because of grater curvature necrosis. This may be the root of the incompleteness of the right gastro-epiploic arterial supply to the fundus. In our another experimental rabbit study, we compared Magenstrasse & Mill and sleeve gastrectomy, and we lost only two of 20 rabbits. Because of removing greater curvature

in sleeve gastrectomy, mortality rate was less in this study and was 10% (23).

CONCLUSION

As a result, this new technique may be an option for bariatric surgery in humans (at least in theory) but for an experimental model, it is not suitable for rabbits. Rabbits, whose gastric arterial supply differs according to their species, should be reconsidered in terms of gastric surgery techniques, especially in experimental trials.

Ethics Committee Approval: The study was approved by the University of Van Yüzüncü Yıl, Regional Committee of Ethics (31008, 03/05/2017).

Peer-review: Externally peer-reviewed.

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

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

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

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ORİJİNAL ÇALIŞMA-ÖZET
Turk J Surg 2021; 37 (3): 294-298

Bariatrik cerrahide yeni bir yaklaşım: *bridged mini gastrik bypass*. Tavşan modeli deneysel bir çalışma için uygun mudur?

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ÖZET

Giriş ve Amaç: Obezite, önemli morbiditelere neden olabilen küresel bir sağlık sorunudur. Bariatrik cerrahiye artan talep yeni tekniklerin ortaya çıkmasına neden olmuştur. Daha önce tarif edilen Mini Gastrik By-pass (MGB) tekniğini, insan mide fundusunda 2 cm açıklık bırakarak, kalan mide ve duodenumun takip ve tedavisinde bir köprü olarak kullanmayı amaçladık. Bu yeni tekniğe Bridged MGB adını vererek; deneysel bir çalışma olarak tavşanlara uygulamayı hedefledik.

Gereç ve Yöntem: Bu çalışma, yerel etik kuruldan etik onay alındıktan sonra üniversitenin deney hayvanı laboratuvarında gerçekleştirildi. 2,1 ve 3,2 kg olan iki Yeni Zelanda tavşanı üzerinde tarif edilen yeni teknik uygulanmıştır.

Bulgular: Operasyonlar sonucunda, tavşanlardan biri operasyon günü ex olurken; diğer tavşan postoperatif üçüncü günde ex oldu. Otopsilerde anastomozlarda herhangi bir sorun saptanmamasına rağmen; her iki tavşanın mide büyük kurvaturlarında nekroz saptandı.

Sonuç: Popüler deney hayvanlarından biri olan tavşanın hem arteriyel hem de topografik açılardan insan gastrointestinal sisteminden farklı olduğu ve türlere, hatta diyete ve iklime göre değişiklik gösterdiği vurgulanmıştır. Çalışmamızın bu farklılıklar sonucunda başarısız olduğuna inanıyoruz ve insanlara daha benzer hayvanların gastrointestinal deneysel çalışmalarda kullanılmasını öneriyoruz.

Anahtar Kelimeler: Deneysel çalışma, mini gastrik bypass, tavşan

DOİ: 10.47717/turkjsurg.2021.4874

CASE REPORT
Turk J Surg 2021; 37 (3): 299-302

Incidental giant adrenal lymphangioma presenting as a non-functional cystic mass

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ABSTRACT

Adrenal masses can be encountered with many different clinical manifestations and a diverse spectrum of etiologies in clinical practice. Recent advances in imaging and laboratory studies as well as their increasingly widespread use and easy accessibility have currently made it possible to diagnose a greater number of surrenal masses than ever. The basic approach principles vary for incidentally detected masses, benign/malignant masses, and hormonoactive masses. Lymphangiomas are benign congenital malformations of lymphatic channels that primarily affect the neck and head region. They typically affect children younger than 2 years of age, they are uncommon in adults and they rarely involve surrenal glands. In this paper, we aimed to present a woman with a hormonally inactive right giant adrenal mass showing recent rapid growth, which was diagnosed to be a lymphangioma in an atypical localization in histopathological examination. The patient was operated with right adrenalectomy and total mass excision via laparoscopic lateral transperitoneal approach.

Keywords: Adrenal masses, laparoscopic surgery, lymphangioma

INTRODUCTION

When deciding to proceed with surgery for adrenal masses, their size, hormonal activity, imaging signs suggestive of malignancy, and growth rate at serial examinations should be taken into account. There is no consensus for a size threshold beyond which surgical intervention becomes necessary. While some authors have advocated that surgical mass excision should be limited to masses larger than 6 cm based on the knowledge that masses smaller than 6 cm are associated with a negligible risk of malignancy, some others have recommended surgery for masses larger than 3 cm and some others for masses larger than 4 cm (1). Herein, it was aimed to present a woman with a nonfunctional giant right adrenal mass that turned out to be a lymphangioma, a tumor that is uncommonly considered in the differential diagnosis in this localization.

CASE REPORT

A 39-year-old female had been under follow-up at an outside center for a right adrenal mass for 8 years. She presented to our urology department after her mass had grown rapidly and caused abdominal pain over the last 6 months. Her past history was not notable for any disorder. On physical examination, she had tenderness in her right lateral and right upper quadrants. Biochemical tests and hemogram parameters were in normal range. A preoperative endocrinologial evaluation including a 24-hour urine collection for vanylmandelic acid, epinephrine, metanephrine, norepinephrine, normetanephrine, dopamine; plasma renin and angiotensin levels; and 1 gr dexamethasone suppression test were all normal. An abdominal computed tomography (CT) revealed a well-bordered mass lesion with a size of 86x70 mm and millimetric calcifications in the right adrenal gland; the mass was primarily considered to be a surrenal cyst shifting surrounding structures. Magnetic resonance imaging (MRI) examination demonstrated a cystic lesion measuring 9x7 cm in the right adrenal gland, which appeared hypointense on axial T1A and axial

Cite this article as: Kafadar MT, Özyuvalı E, Miryaguboğlu AM, Çaviş T, İnan A. Incidental giant adrenal lymphangioma presenting as a non-functional cystic mass. Turk J Surg 2021; 37 (3): 299-302.

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Received: 06.12.2016
Accepted: 12.06.2017
Available Online Date: 28.09.2021

DOI: 10.47717/turkjsurg.2021.3785

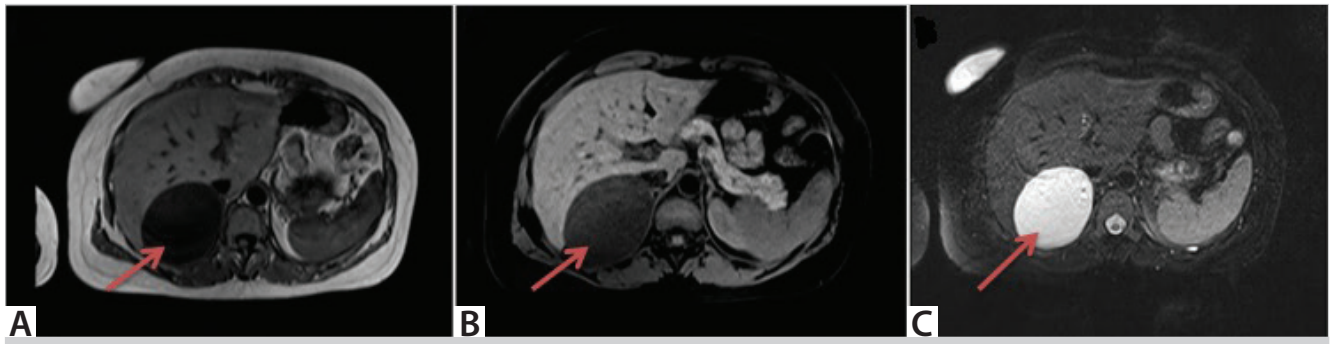

Figure 1. A cystic lesion in the adrenal gland; which appears hypointense on axial T1A (a), axial fat suppression T1A images (b) and hyperintense on fat suppression T2A images (c).

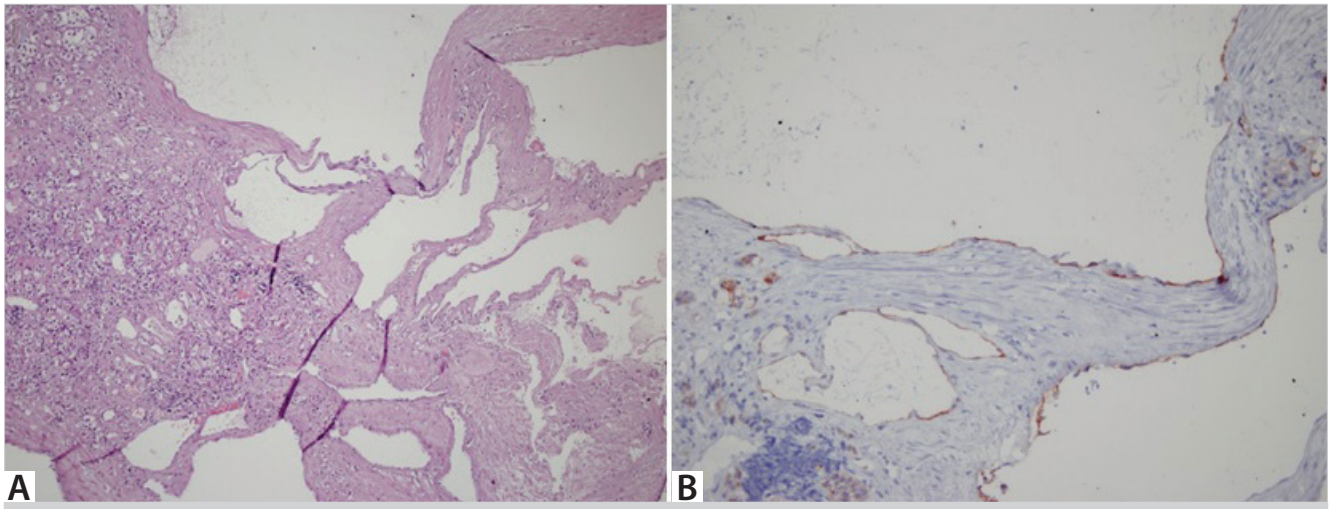

Figure 2. Histological view of the lymphangioma of the right adrenal gland; multiloculated cyst within the adrenal gland (a), cells positively stained with CD31 and D2-40 on the wall of the multilocular cystic lesion which contains areas of focal dystrophic calcification and is divided by fine septae (b). (H&E:200x).

fat suppression T1A images and hyperintense on axial fat suppression T2A images (Figure 1a,b,c). A surgical intervention was scheduled on the basis of recent rapid growth, signs of compression, and patient's desire to become pregnant. The patient underwent laparoscopic lateral transperitoneal right adrenalectomy in which the mass and the right adrenal gland were excised. The patient had no problem during the postoperative period and was discharged 2 days later. Immunohistochemical examination showed CD31-and D2-40-positive cells on the wall of the multilocular cystic mass, and the lesion was identified as a lymphangioma (Figure 2a,b). Informed consent was obtained from patient who participated in this case.

DISCUSSION

Despite the general knowledge that adrenal mass lesions are typically benign and do not release any hormones, each mass should also be evaluated and differential diagnosis should be done for hypersecretory syndromes or tumor development (2). The management of hormonally inactive adrenal masses is primarily based on lesion size. As inactive masses smaller than 3 cm are typically of benign character, their conservative follow-up is usually recommended. Inactive masses between 3-5 cm in size can be conservatively managed when they appear homogenous in radiological imaging studies. However, surgery should be considered whenever radiological studies indicate growth. Hormonally active masses should be surgically excised irrespective of their size (3).

CT and MRI are the most appropriate imaging modalities for differentiating adenoma, carcinoma, and pheochromacytoma from one another. These imaging modalities are also very beneficial for determining surgical candidacy from an anatomicopathological standpoint (4).

Following the introduction of laparoscopic surgery for adrenal adenomas, it has been rapidly incorporated into clinical practice, and studies comparing laparoscopic and open surgeries have been published. Laparoscopic surgery has the main advantages of short hospital stay, reduced postoperative pain, rapid re-

covery, and better cosmetic outlook. Since its first introduction, laparoscopic approach has been the technique of choice for the treatment of benign functional and non-functional adrenal mass lesions (5). Recently, indications of laparoscopic interventions have been extended to larger adrenal masses and adrenal metastatic lesions. Different laparoscopic techniques have been defined for the resection of adrenal masses, including lateral transabdominal, lateral retroperitoneal, anterior transabdominal, and posterior retroperitoneal approaches. Among these, lateral transperitoneal approach is widely used for adrenal mass lesions (6).

Adrenal cysts are rare, typically asymptomatic lesions that are usually detected postmortem, they are clinically important since they can be confused with malignant lesions. Symptomatic lesions manifest with the tirad of pain, palpable mass, and inferior displacement of the kidney. These lesions have 4 major groups, which are the parasitic, endothelial, epithelial and pseudocytsic types. Despite affecting every age from newborn to old age, they are most commonly observed in middle-aged women (7).

Lymphangiomas are benign congenital malformations of lymphatic channels that primarily affect the neck and head regions. Approximately 50% of these lesions are diagnosed at the time of birth and 90% during the first 2 years of life. They are quite rare in adulthood. Ninety-five percent of lymphangiomas are located in the neck and axillary region while the rest develop in mediastinum, mesentery, omentum, retroperitoneum, and bones. Their diagnosis is made by physical examination, history taking and imaging studies (8).

Cystic lymphangiomas are composed of sequestered lymphatic sacs. Although the histogenesis of lymphanigomas is still debated, some researchers assume that they are acquired lesions secondary to the obstruction of chylous vessels by inflammatory, traumatic and degenerative conditions. In contrast, cystic lymphangiomas have been reported to occur congenitally, as a result of the proliferation of embryonic lymph sac remnants. It is the general opinion that lymphangiomas are composed of sequestered lymphatic sacs that fail to establish a link with main lymphatic channels (9).

Despite having a benign character, cystic lymphangiomas may lead to compression of adjacent organs and obstruction and they may also invade surrounding structures. No spontaneous regression is expected in adulthood lymphangiomas. Total surgical excision is necessary for their treatment. Incision, drainage and repeat aspirations have been used as primary therapies, although recurrences and infections have proved ineffective (9,10). As the mass lesion of our patient had recently grown rapidly and compressed surrounding structures, surgical excision was decided despite the lack of any suspicion for a malignancy.

CONCLUSION

Albeit rare, lymphangiomas should be considered in the differential diagnosis of adrenal masses in adult patients. Definite diagnosis is made after the surgical removal by histological and immunohistochemical examinations. As they are deeply located in the retroperitoneal area, lateral transperitoneal laparoscopic surgery can be readily used for their treatment owing to its advantages such as shorter hospital stay, early return to daily life and superior cosmetic outcomes.

Peer-review: Externally peer-reviewed.

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

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

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

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OLGU SUNUMU-ÖZET
Turk J Surg 2021; 37 (3): 299-302

Non-fonksiyonel kistik kitle şeklinde presente olan insidental dev sürrenal lenfanjiom

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ÖZET

Sürrenal kitleler klinikte çok farklı etiyolojiler ve farklı klinik bulgularla karşımıza çıkabilmektedir. Görüntüleme ve laboratuar tekniklerinde sağlanan gelişmeler ve bunların giderek daha yaygın ve kolay kullanılması, daha fazla sürrenal kütlenin tanımlanabilmesini sağlamaktadır. İnsidental kütlelere, benign/malign kütlelere ve hormonoaktif kütlelere yaklaşım birbirlerinden farklıdır. Lenfanjiyomlar esasen baş ve boyun bölgesini etkileyen lenfatik kanalların benign konjenital malformasyonlarıdır. Genellikle iki yaş altı çocuklarda görülen lenfanjiomların, erişkin hastada ve özellikle sürrenalde görülmesi çok beklenmez. Bu makalede, takipte son zamanlarda hızlı büyüme tespit edilen, hormonal olarak inaktif sağ dev surrenal kütlesi olan ve histopatolojik incelemede alışılmadık lokalizasyonuyla lenfanjiom tanısı alan bir erişkin kadın olgu sunuldu. Olguya laparoskopik lateral transperitoneal yaklaşımla sağ sürrenalektomi ile birlikte total kütle eksizyonu yapıldı.

Anahtar Kelimeler: Adrenal kütle, laparoskopik cerrahi, lenfanjiom

DOİ: 10.47717/turkjsurg.2021.3785

CASE REPORT
Turk J Surg 2021; 37 (3): 303-306

Coexistence of low-grade mucinous neoplasm and carcinoid (collision tumor) within multiple appendiceal diverticula: a case report

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ABSTRACT

Neoplasms of the appendix are very rare. They usually show glandular or neuroendocrine differentiation, and when they both occur in the same area, it is called a "collision tumor." Low-grade mucinous neoplasms associated with appendiceal diverticula are also uncommon. The appendectomy specimen of a 60-year-old man contained dense and mucoid luminal content on the distal tip, and similarly a solid, yellow, lumen-obscuring tumor with a diameter of 1.5 cm at the base of the appendix was detected. Microscopically, there were three diverticula that comprised herniation of the mucosal layer through the appendiceal wall. Interestingly, all of the diverticula and the normal-appearing appendiceal wall were lined by adenomatous epithelium. The luminal portion had pools of mucin-containing, rare clusters of low-grade epithelium that gave rise to the diagnosis of a "low-grade mucinous neoplasm." The solid-appearing tumor was diagnosed as a "neuroendocrine neoplasm," and there was no transition zone between these two types of tumors. There are some cases that have been reported as low-grade mucinous neoplasms associated with appendicular diverticula and collision tumors consisting both mucinous neoplasms and carcinoid tumors in the literature; our case has a unique appearance with two different types of tumors both in the appendix wall and within multiple diverticula.

Keywords: Appendix, mucinous neoplasm, carcinoid, diverticuli

INTRODUCTION

Neoplasms of the appendix are rarely seen clinical entities, accounting for approximately 2% of all appendectomy specimens (1). They usually show glandular or neuroendocrine differentiation and sometimes may contain both cell types at once (2). The term "collision tumor" is used when both epithelial and neuroendocrine tumors are seen in the same area without juxtaposing on each other (3). Low-grade mucinous neoplasms associated with appendiceal diverticula are also uncommon (2). We report a case of a 60-year-old male with a concurrent low-grade mucinous neoplasm and carcinoid tumor both within the appendix and the appendiceal diverticula, the coexistence of which is unique.

CASE REPORT

A 60-year-old man presented with abdominal discomfort since 2 months and frequent pain in the right lower quadrant. His laboratory results were within normal limits except for mild anemia and a slight increase in the leukocyte count and carcinoembryonic antigen level. All tumor markers were negative. On physical examination, a palpable mass was identified in the right lower quadrant, and the appendix seemed cystically dilated in abdominal ultrasonography. With these findings and a suspected clinical diagnosis of mucocele, the patient underwent appendectomy. Written consent of the patient was obtained. On gross examination, the appendix measured 6.5 cm in length and 2 cm in diameter. The distal portion (tip) of the appendix contained dense and mucoid luminal content and seemed cystically dilated. The cut surface of appendiceal wall seemed irregular and had a thinned appearance with multiple outpouchings measuring 1-2 mm each (Figure 1). However, serial cuts toward the proximal portion revealed a solid, yellow, lumen-obscuring tumor with a diameter of 1.5 cm at the base of the ap-

Cite this article as: Ekinci N, Gün E, Avcı A, Er A. ACoexistence of low-grade mucinous neoplasm and carcinoid (collision tumor) within multiple appendiceal diverticula: a case report. Turk J Surg 2021; 37 (3): 303-306.

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Received: 24.04.2017
Accepted: 27.10.2017
Available Online Date: 28.09.2021

DOI: 10.47717/turkjsurg.2021.3877

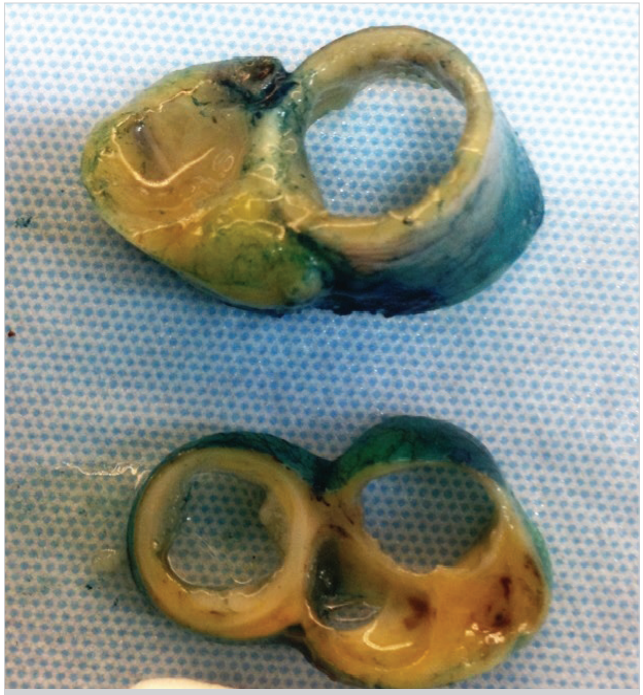

Figure 1. Appendiceal lumen with multiple diverticula.

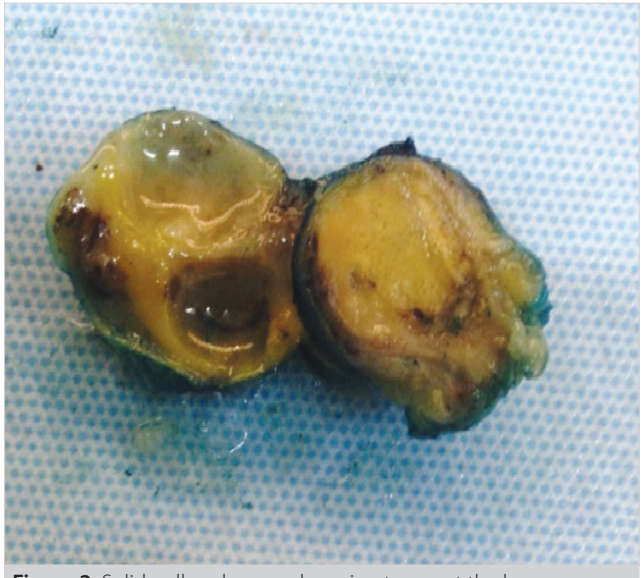

Figure 2. Solid, yellow, lumen-obscuring tumor at the base.

pendix (Figure 2). Microscopically, there were three diverticula measuring 2-3 mm that comprised herniation of the mucosal layer through the appendiceal wall. Interestingly, all of the diverticula and the normalappearing appendiceal wall were lined by adenomatous epithelium (Figure 3). This epithelium seemed pseudostratified and contained elongated, crowded columnar cells with hyperchromatic nuclei and showed acute inflammation within the stroma (Figure 4). The luminal portion had pools of mucin-containing, rare clusters of low-grade epithelium that gave rise to the diagnosis of a low-grade mucinous neoplasm.

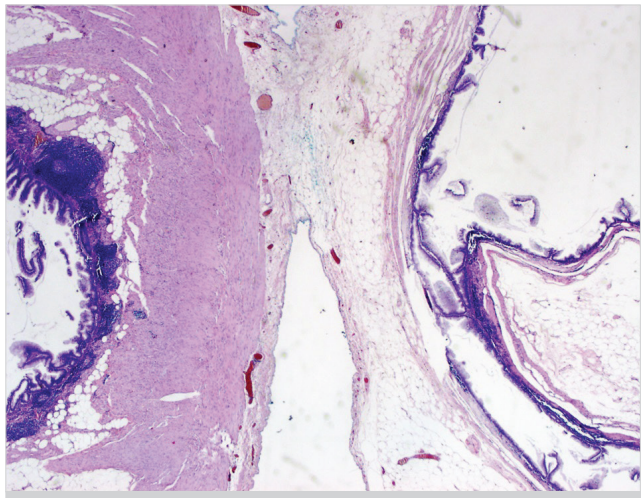

Figure 3. Appendiceal wall and diverticula lined by adenomatous epithelium.

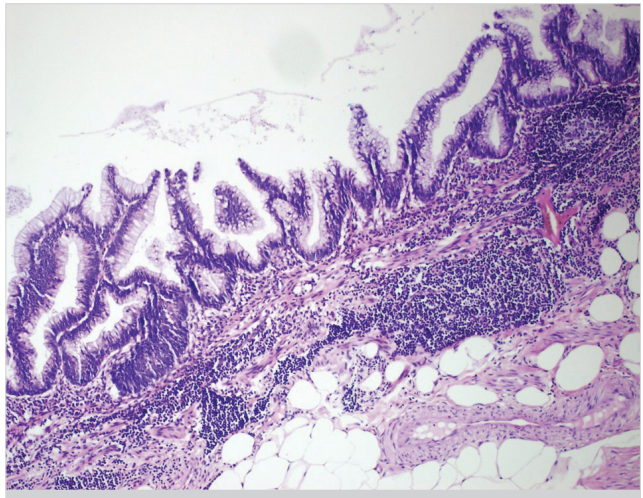

Figure 4. Pseudo-stratification and hyperchromatic nuclei in the adenomatous epithelium.

Sections toward the proximal portion of the appendix showed another type of tumor with a solid appearance infiltrating the entire thickness of the appendiceal wall and the diverticula. It consisted of uniform tumor cells with no mitosis forming acini with nested and trabecular pattern, which was diagnosed as a neuroendocrine neoplasm of WHO Grade I (Figure 5). These cells were immunohistochemically positive for chromogranin A and synapt physin. Ki-67 index was lower than 1%. There was no transition zone between these two types of tumors. The final diagnosis was a collision tumor of a low-grade mucinous neoplasm with carcinoid tumor both within the appendix and multiple appendiceal diverticula. The surgical department was informed and right hemicolectomy was suggested to the patient; however, he did not accept to have anothersurgery. On follow-up for 6 months after the operation, the patient was free of the disease.

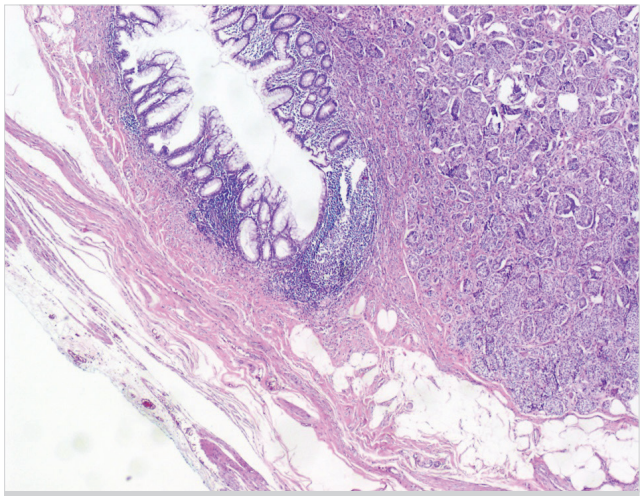

Figure 5. Neuroendocrine neoplasm WHO Grade I. Inset shows strong positivity with chromogranin A.

DISCUSSION

Low-grade mucinous neoplasms are rare in the appendix, comprising less than 1% of all appendiceal lesions; however, it is considered the most common cause of mucocele that is widely used as a clinical term to identify the lesions that produce mucin. Low-grade mucinous neoplasms are considered appendiceal counterparts of intestinal adenomatous lesions (4-6). Acquired diverticula are also uncommon and seen in 1%–2% of all appendiceal lesions. They have been widely investigated to understand the underlying mechanism of coexistence with appendiceal mucinous neoplasms (7). The coexistence of these two lesions has been reported by several authors and reported in approximately 30%–40% of cases with low-grade appendiceal neoplasms. However, it remains controversial whether they coexist by chance or there are other reasons in the pathogenesis that also give rise to ques tions about the formation of pseudomyxoma peritonei (2, 8). Carcinoid tumors are the most common appendiceal tumors, and they are usually found incidentally in appendectomies performed for acute appendicitis (1). The term collision tumor represents the condition when both the epithelial and carcinoid tumors are seen in the same area without any transitions in between. There are some controversial issues and hypothesis about the formation of these collision tumors; however, they are most likely believed to form independently from two different neoplasms as a result of biclonal malignant transformation (9). There are some cases that have been reported as low-grade mucinous neoplasms associated with appendicular diverticula and collision tumors consisting of both mucinous neoplasms and carcinoid tumors in the literature (2,6,7,10). However, in our case, the entire appendiceal wall consisted of multiple appendiceal diverticula; in addition, there were two different types of tumors without any invasive foci and transition zone in between.

The surgical approach to carcinoid tumors and low-grade mucinous neoplasms is controversial. For carcinoids, the most recent guidelines indicate that a right hemicolectomy should be performed when the tumor size is >2 cm and if there is lymph node metastasis, highgrade findings (high mitotic activity), and positive surgical margins (11). For mucinous appendiceal neoplasms (low-grade mucinous neoplasm in our case), the assessment should be made depending on the malignancy potential and the lymph node involvement of the lesion. However, because the initial operation is usually urgent, a mesenteric fat resection may not be performed in the first place, which leads to another controversial issue (12). The survival rates following right hemicolectomy compared with those following appendectomy have not been discussed clearly in the literature, and therefore more studies are needed in this context.

CONCLUSION

Collision tumors of the appendix are rare lesions. To the best of our knowledge, our case is the first with two different types of tumors both in the appendix wall itself and within multiple diverticula. Surgical approach to these tumors remains controversial and more clinical and prognostic studies are needed.

Peer-review: Externally peer-reviewed.

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

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

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

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OLGU SUNUMU-ÖZET
Turk J Surg 2021; 37 (3): 303-306

Multipl apendiks divertikülünde düşük dereceli müsinöz neoplazm ve karsinoid (kollüzyon tümör) birlikteliği: bir olgu sunumu

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ÖZET

Apendiksin neoplazileri oldukça nadirdir. Genellikle glandüler ya da nöroendokrin diferansiyasyon gösterirler ve aynı alanda bir arada oldukları-nda "kollüzyon tümör" olarak adlandırılırlar. Apendiks düvertikülüyle birlikte olan düşük dereceli müsinöz neoplazmlar de oldukça nadirdir. 60 yaşında erkek hastanın appendektomi materyalinde kistik olarak dilatasyona uğramış distal kısımda yoğun, mukoid lümen içeriği izlendi. Benzer şekilde apendiks tabanında 1,5 cm çapında lümeni tıkayan solid, sarı-beyaz bir tümör görüldü. Mikroskopik olarak her biri apendisyel duvara mukozal tabakanın herniasyonuyla karakterli 3 adet divertikül izlendi. İlginç olarak, tüm divertiküller ve normal görünen apendiks duvarı adenamatöz epitelle döşeliydi. Lümende nadir düşük dereceli epitel fragmanları taşıyan müsin gölcüklerinin varlığı ile "düşük dereceli müsinöz neoplazm" tanısı kondu. Solid görünen tümör ise nöroendokrin neoplazi olarak değerlendirildi ve bu iki tip tümör arasında geçiş zonu izlenmedi. Literatürde apendiks divertikülüyle ilişkili düşük dereceli müsinöz neoplazm ve karsinoid tümörden oluşan kollüzyon tümörler bildirilmiştir ve bizim olgumuz hem apendiks duvarında hem de multipl divertikül içinde iki ayrı tümörün varlığı ile son derece ilginç bir birliktelik göstermektedir.

Anahtar Kelimeler: Apendiks, müsinöz neoplazi, karsinoid, divertikül

DOİ: 10.47717/turkjsurg.2021.3877