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

# Turkish Journal of Surgery

VOLUME 37  
ISSUE 2  
JUNE 2021

[www.turkjsurg.com](http://www.turkjsurg.com)

Hon Editor: Cemalettin TOPUZLU

VOLUME 37  
ISSUE 2  
JUNE 2021



Published by Turkish Surgical Society.

**Owner/Editorial Manager**

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(Owner on behalf of the Turkish Surgical Society)

**Print ISSN 2564-6850**

**Elektronik ISSN 2564-7032**

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06810 Çayyolu-Çankaya, Ankara, Turkey

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**Publishing House**

**bilimsel tıp**  
yayınevi  
www.bilimseltipyayinevi.com

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**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 June 2021

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

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

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

### Animal Research

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

**Table 1.** Limitations for each manuscript type

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

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

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

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

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

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

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

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

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

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### Publisher: Bilimsel Tıp Yayınevi

**Address:** Bükreş Sokak No: 3/20 Kavaklıdere, Ankara, Turkey

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**FROM THE EDITOR'S DESK**

Turk J Surg 2021; 37 (2): VIII  
10.47717/turkjsurg.2021.9903



Dear Authors of the Turkish Journal of Surgery,

It is my great pleasure to address you in this June 2021 issue of Turkish Journal of Surgery. I will take this opportunity to share my opinions about an important tool of the surgery.

Ambroise Paré, the great French surgeon of the 16th century, defined the tasks of the surgeons as follows: to eliminate that which is superfluous, restore that which has been dislocated, separate that which has been united, join that which has been divided and repair the defects of nature (1). Since then, these well-known missions of the surgeons have not changed and even today, we follow the main principles of Paré. Though the basic principles remain the same, major developments in some disciplines have exceptionally helped surgeons in order to enhance the quality of the surgery.

The first one is the great improvements in anesthesia and postoperative care. As surgeons, we should confess that without the support of modern anesthesia we would never be able to perform the current sophisticated operations.

The second important point in the surgeons' life is the development of new surgical tools and instruments. Surgery is more or less a technical work and our daily practice is surrounded by materials or devices, etc. From basic surgical instruments to the most sophisticated electronical devices, we have to use "devices". Our work depends on them. In this issue, you will be able to read a very interesting review article by Karaca et al. about the inseparable relationship between endoscopy and surgery (2). The authors are presenting the past, present and the future of the endoscopy. They are thoroughly discussing the important role of the surgeon "not only in performing but also improving" Endoscopy. I would warmly suggest you to read this article.

I hope that you will enjoy this June 2021 issue. As I always repeat: please submit your best work to the Turkish Journal of Surgery!

Kindest regards,

**Kaya SARIBEYOĞLU**

**Editor,  
Turkish Journal of Surgery**

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# Endoscopy in surgery

Ahmet Serdar Karaca , M. Mahir Özmen , Ahmet Çınar Yastı , Seher Demirer

On Behalf of the Initiative of the Board on Directors of the Turkish Surgical Society

## ABSTRACT

In the last 20 years, there have been important developments in endoscopy. Initially, endoscopy was developed and used as a diagnostic tool. As new technology developed, these devices also became the basis for therapeutic maneuvers. In recent years, flexible endoscopes have been used to perform procedures replacing traditional surgical approaches. Examples of this field are transanal minimally invasive surgery, natural orifice transluminal endoscopic surgery, endoscopic metabolic surgery and third space endoscopies. Throughout history, surgeons have played a vital role in the design and development of endoscopic techniques, procedures, and equipment. Surgeons continue to lead the advancement of endoscopy, make important contributions, and serve as role models for innovation.

**Keywords:** Endoscopy, percutaneous endoscopic gastrostomy (PEG), endoscopic retrograde cholangiopancreatography (ERCP), endoscopic ultrasound (EUS), Lumen-attaching metal stents (LAMS)

## INTRODUCTION

The desire to examine the organs of the human body through natural holes is not new (1). The history of endoscopy goes back to the time when Hippocrates (460-375 BC) described the use of a rectal speculum similar to those currently used. Similar instruments had been described in Roman medicine, including a three-bladed vaginal speculum found in the ruins of Pompeii. Albulassim (912) reflected light with a mirror to see body cavities. Venezuelan Guilio Cesare Aranzi used the camera obscura [1587] to focus a beam of light to allow viewing the nasal cavity. Bozzini [1806] used the Lichtleiter, or light conductor, at the Medical Faculty in Vienna. Using principles illustrated in Bozzini's Lichtleiter, Segalas [1826] developed the speculum urethro-cyst, which uses two small candles and a conical mirror to focus light on the bladder, allowing visual inspection. In 1853 Antonin J. Desormeaux adapted a kerosene lamp that burns alcohol and turpentine held in a chamber at the base of the handle to create a narrower beam of light, which is thought to provide a brighter illumination of the area to be visualized. Desormeaux was the first physician to use Lichtleiter in a patient and the first physician to use the term Endoscopy, as well as endoscopic instruments for diagnosis and treatment (2). Kussmual performed the first successful gastroscopy in 1886. Leiter developed an esophagoscope with a mignon lamp in 1881, and Chevalier Jackson, an otolaryngologist, first used the bronchoesophagoscope to remove foreign bodies from humans in 1907. In 1937, Rudolf Schindler developed the semi-flexible endoscope, and in 1968 McCune, Shorb and Moscovitz described the first successful endoscopic cannulation of the pancreas and bile ducts, creating the initiative for endoscopic retrograde cholangiopancreatography (ERCP). Wolf and Shinya performed the first colon polypectomy using a flexible endoscope in 1974. Ponsky and Gauderer revolutionized the nutritional care of patients by describing percutaneous endoscopic gastrostomy (PEG) in 1980, and Steigmann and Goff described endoscopic varicose band ligation in 1988 (Table 1).

In addition to the founding role played by many leading surgeons in establishing endoscopy as a diagnostic and therapeutic approach to patient care, surgical

**Cite this article as:** Karaca AS, Özmen MM, Yastı AÇ, Demirer S. Endoscopy in surgery. Turk J Surg 2021; 37 (2): 83-86.

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Available Online Date: 30.06.2021

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DOI: 10.47717/turkjsurg.2021.9988



**Table 1.** Endoscopy is part of our historical surgical heritage. Endoscopic procedures developed by surgeons

Procedure	Surgeon
Colonoscopy	Turell
Control of hemorrhage	Gaisford, Sugawa
Polypectomy	Shinya, Wolf
ERCP	McCune, Shorb
Variceal banding	Steigman
PEG	Ponsky, Gauderer
Biliary stenting	Sohendra
ERCP: Endoscopic retrograde cholangiopancreatography, PEG: Percutaneous endoscopic gastrostomy.	

endoscopists are an important element of the healthcare workforce (3). The burden of screening procedures alone has already far exceeded the labor supply in most areas, and without the contribution of surgeons skilled in performing screening, therapeutic, curative and palliative endoscopic procedures, patient access to appropriate care will be severely limited. Surgeons must perform endoscopy to benefit their patients and advance their expertise.

A study comparing the practice patterns of rural and urban surgeons showed that both groups performed endoscopy as a routine part of their practice, but rural surgeons performed significantly more endoscopy (4). A prospective analysis of 3,525 endoscopic procedures performed by surgeons, published in *Surgical Endoscopy*, showed that surgeons performed these examinations with excellent results. No complications were reported in 3,447 patients (97.8%) (5). A prospective analysis of 13,580 colonoscopies performed by surgeons showed excellent results, with a 0.2% complication rate and a 0.007% perforation rate (6). Lee et al. have demonstrated equivalent adenoma detection rates among surgeons and gastroenterologists, and contributed to the literature demonstrating that surgeon endoscopists are mindful specialists with excellent results serving the needs of their patients (7).

### Endoscopy Training

Endoscopy is one of the main tools of the practicing surgeon. General surgeons in Europe have established scientific associations and published scientific journals in order to standardize and advance the education and practices related to endoscopy, to disseminate them among their professional mothers and to share their results (Ex: European Association for Endoscopic Surgery: EAES). Likewise, similar associations have been established in the USA (Ex: Society of American Gastrointestinal and Endoscopic Surgeons: SAGES). EAES and SAGES have jointly published the journal "*Surgical Endoscopy*" as the official scientific journal since 1986. The American Board of Surgery recognized the increasing role of endoscopy in surgical practice and

in 1985 recommended that at least 29 endoscopic cases be performed by graduate surgical residents. This was based on the goal of ensuring that all surgeons are exposed to endoscopic techniques. This requirement was later changed in response to the argument that this experience set the threshold too low for a graduate assistant to be proficient in endoscopy. Effective for residents graduating in June 2009 (8), the requirement has been changed to include 35 flexible endoscopy and 50 colonoscopy as new minimum thresholds.

The American Society of Gastrointestinal and Endoscopic Surgeons (SAGES), a professional community based on the principles of performing endoscopy by the surgeon, has developed the Fundamentals of Endoscopic Surgery program as a competency-based platform for endoscopy education. This curriculum is a solid collection of didactic materials and is available to anyone who wishes to learn the practice of endoscopy, regardless of specialty, and is included in the general surgery residency curriculum.

The Turkish Ministry of Health Medical Specialization Committee established curriculum preparation commissions for all major and minor branches in 2010 and organized a workshop on 15-17 January 2010 with the participation of 94 specialization commissions. Afterwards, the commissions that continued their studies entered the curriculum they developed into the Expert Board in Medicine Curriculum Formation and Standard Determination System Database. Endoscopy education was widely included in the curriculum developed by the General Surgery Commission and agreed upon unanimously. The endoscopy training curriculum recommended by this commission and the surgical endoscopy section in the General Surgery Specialization Training Core Training Program published by the Turkish Society of Surgery in 2006 almost completely overlap. European Union of Medical Specialists (UEMS) rearranged all the curriculum, definitions, justifications of the program, compulsory knowledge and skills related to general surgery with the guidelines it published on 29 October 2010. The necessary knowledge and skills related to endoscopy during surgical training have been put in the form that has been included in this program for many years. In the section of these guidelines where the responsibility areas of general surgery are defined, "therapeutic and diagnostic endoscopy of the digestive tract" is especially emphasized among the primary areas of responsibility. A special section is reserved for endoscopy in the European Surgical Qualification Board's (UEMS, Surgery Section, Board of General Surgery) directive on "mandatory skills during surgical training".

The issue of how endoscopy training should be given during the training of surgical assistants has been researched with different aspects for many years. In all studies, it has been emphasized that endoscopy is absolutely necessary for the surgeon, but that this education should be given in accordance with technologi-



cal developments. In the last decade, with the development of techniques in which endoscopy is used as a tool (NOTES: natural orifice transluminal endoscopic surgery, robotic surgery, etc.), it has been suggested that endoscopy education should be given in this direction in many studies, especially in America and Europe. That is, the surgical assistant will not only have basic endoscopy training, but will have to learn enough to use endoscopy as a tool to be able to perform advanced surgical operations. The issue should also be carefully evaluated in terms of public health. Digestive system cancers are increasing day by day all over the world. Early diagnosis is life-saving in these diseases, and therefore, the number of people who will perform screening endoscopy should be increased. Countries such as England, America and Australia saw that the number of available physicians would not be sufficient to solve this problem and started to have trained nurses perform endoscopic procedures. Considering the results of preliminary research on the work of nurses in the practice of endoscopy, this practice has begun to become widespread. In the light of these scientific data, the British government encouraged and authorized nurses to perform endoscopy. Studies conducted after the issue had become a national policy revealed that nurses performed endoscopy as successfully and safely as doctors. Today, around 350 nurses, in addition to general surgeons and internal medicine specialists, serve the public by performing endoscopy every day in England. On the other hand, the USA and Japan have begun to authorize trained general practitioners for screening gastroscopy/colonoscopy in order to find a solution to the problem. It has been determined by scientific research that the endoscopies performed by general practitioners are as safe and successful as necessary.

Surgeons frequently use endoscopy in the preoperative, intraoperative and postoperative care of their patients. In the preoperative period, endoscopy is mainly used to diagnose conditions and localize lesions, plan surgery and provide nutritional support (9). Intraoperative endoscopy is used to localize lesions, evaluate the anatomical outcome of surgery, and test anastomotic integrity during foregut and colorectal reconstructive procedures. For instance, the image provided during fundoplication, esophageal myotomy and bariatric surgery helps the rest of the operation. Postoperative endoscopy fulfills an important clinical role in the follow-up of patients with premalignant and malignant conditions such as Barrett's esophagus, colon polyps, and post-resection follow-up needs for three examples, esophagus, stomach and colon cancer. Flexible endoscopy also plays an important role in the management of operative complications, including marginal ulcers, anastomotic leaks, fistulas, and retained biliary stones.

### The Future of Surgery and Endoscopy

Thirty years ago, the advent of operative laparoscopy marked the beginning of a new era in general surgery. Surgical procedures have changed altogether and new procedures have been

developed by taking advantage of the strengths of the laparoscopic platform. Hospital dynamics deteriorated as patients who stayed in the hospital for a week now receive outpatient treatment. Robotics has furthered these advances in some areas.

The future of surgery will be affected by the future of surgeon-performed endoscopy. The limits of third-chamber endoscopy or intramural endoscopy will continue to advance. Device developments such as lumen-attached metal stents (LAMS) will further reduce their invasiveness by shifting procedures from combined laparoscopic-endoscopic approaches to purely endoscopic techniques. An example is the treatment of choledocholithiasis following gastric bypass surgery. This clinical condition that once required laparotomy and open common bile duct exploration has been routinely treated in recent years using laparoscopic access to the remaining stomach with transabdominal ERCP. It is now becoming more common to use LAMS to provide a pathway through the remaining stomach from the digestive tract so that more conventional ERCP can be offered to the patient without the need for surgery (12,13). LAMS is also used as an effective and more durable alternative to cholecystostomy placement in cases of acute cholecystitis in those who are too weak to undergo cholecystectomy (14,15). As we continue to seek increasingly less invasive approaches to patient care, surgery will evolve and flexible endoscopy is the central platform for the next phase of our evolution as surgeons.

Endoscopic ultrasound (EUS) is an advanced endoscopic imaging technique opening new avenues of patient care that will become important in the future in surgeon-performed endoscopy and general surgery. EUS is currently a valuable imaging modality with a wide variety of diagnostic and therapeutic applications. New applications of EUS as an aid for the diagnosis and staging of GIS malignancies are constantly evolving (16). Contrast-enhanced EUS (CE-EUS) is proving useful in a variety of GIS conditions, and elastography will expand the diagnostic utility of EUS for solid lesions. EUS serves as a robust platform for therapeutic measures and will continue to increase in value for surgeons who adopt the endoscopic platform as the foundation for their future.

### CONCLUSION

The surgeon's role is to keep up with innovations. The field of endoscopy largely represents surgical innovation, and we must continue to expand the utility of the flexible endoscopy platform as it lays the foundation for the future of general and gastrointestinal surgery. Surgeon-performed endoscopy is an important component of surgical practice and a set of skills that will be critical in our quest to treat patients using increasingly less invasive approaches. We are not surgical endoscopists; we are surgeons performing endoscopy and endoscopic surgery for diagnostic and therapeutic purposes. After all, the endoscope is one of our many diagnostic and therapeutic tools that are as essential as any.

**Peer-review:** Externally peer-reviewed.

**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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## DERLEME-ÖZET

Türk J Surg 2021; 37 (2): 83-86

## Cerrahide endoskopi

Ahmet Serdar Karaca, M. Mahir Özmen, Ahmet Çınar Yastı, Seher Demirer

Türk Cerrahi Derneği Yönetim Kurulu İnişiyatifi Adına

## ÖZET

Son 20 yılda endoskopide önemli gelişmeler yaşanmıştır. Başlangıçta endoskopi bir tanı aracı olarak geliştirildi ve kullanıldı. Yeni teknoloji geliştikçe, bu cihazlar terapötik manevralar için de temel teşkil etti. Son yıllarda geleneksel cerrahi yaklaşımların yerini alan prosedürleri gerçekleştirmek için fleksibl endoskoplar kullanıldı. Bu alana örnek olarak transanal minimal invaziv cerrahi, doğal orifis transluminal endoskopik cerrahi, endoskopik metabolik cerrahi ve üçüncü boşluk endoskopileri gösterilebilir. Tarih boyunca cerrahlar endoskopik tekniklerin, prosedürlerin ve ekipmanın tasarımında ve geliştirilmesinde hayati bir rol oynamıştır. Cerrahlar, endoskopinin ilerlemesine öncülük etmeye, önemli katkılar sağlamaya ve inovasyon için rol modelleri olarak hizmet etmeye devam etmektedirler.

**Anahtar Kelimeler:** Endoskopi, perkütan endoskopik gastrotomi (PEG), endoskopik retrograd kolanjiyopankreatografi (ERCP), endoskopik ultra-son (EUS), lümen takan metal stentler (LAMS), submukozal tünelleme endoskopik rezeksiyon (STER)

**DOI:** 10.47717/turkjsurg.2021.????



# Is carpal tunnel release safe in electrical burn decompressive therapy: Six-years experience

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## ABSTRACT

**Objective:** Upper extremity electrical burn can create severe sequela and debilitation if not treated properly. Immediate decompression with fasciotomy and carpal tunnel release seem to be the most promising choice of treatment. Neurologic functional loss can be avoided if median nerve is liberated.

**Material and Methods:** During 6-year time interval, 50 out of 1158 burn patients underwent upper extremity decompressive fasciotomy with carpal tunnel release. Their hand motor function based on nerve innervation and daily usage questionnaire were followed in 12-month intervals.

**Results:** Average score rose markedly after 18<sup>th</sup> month and reached nearly normal at the end of 66<sup>th</sup> month. Median, ulnar and radial nerve function tests were all positive, and no irreversible nerve function loss observed.

**Conclusion:** All compartments of the forearm should be explored and carpal tunnel release should be added into upper extremity decompressive fasciotomy after electrical burns.

**Keywords:** Carpal tunnel, electric burn, burn

## INTRODUCTION

After the first record of death in 1879, electrical injury has been one of the worst causative burn factors (1). It is reported that an average of 3000 admissions with a death rate of one over three are seen in the United States (2). Workplace is the most encountered area, being the fourth work-related death reason (3). Victims are generally in the productive age group, and upper extremity and/or hands are involved in more than 50% of cases (3,4). Even both hands constitute not much than 3% total burned surface area (TBSA), it is accepted to be a major injury resulting dramatic disability.

Compartment syndrome after upper extremity burn can cause an additional damage to the extremities up to 72-hours (5). It was first described by Matsen as "critical increase of pressure in a limited space which restricts perfusion and viability of tissues in that space".

Even fasciotomy is performed in nearly all full thickness extremity burns, carpal tunnel release (CTR) seems to be less performed in clinical practice. Beside of the lack of sufficient number of prospective clinical trials investigating the pros and cons of adding CTR in decompressive fasciotomy, some studies have reported 37% insufficient decompression rates (6).

The reason to avoid carpal tunnel release can be the fear of damaging the median nerve. We tried to evaluate the effect of CTR on post-burn hand function assessment.

## MATERIAL and METHODS

During the time interval between May 2011 and 2016, there were 1158 moderate or severe burn patients hospitalized in İzmir Bozyaka Education and Research Hospital Burn Treatment Center. Three forearm compartments and CTR are routine surgical procedures in our center after upper extremity full thickness electrical burns.

**Cite this article as:** Cartı EB, Uçar AD, Yıldırım M. Is carpal tunnel release safe in electrical burn decompressive therapy: Six-years experience. Turk J Surg 2021; 37 (2): 87-95.

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Received: 25.11.2018

Accepted: 05.04.2020

Available Online Date: 30.06.2021

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DOI: 10.47717/turkjsurg.2021.4379

Decompressive surgery decision is always made by clinical findings of five "P's" and/or surgeons feeling without instrument using. These five "P's" of pain, pallor, paresthesia, paresis, and pulselessness are classical findings associated with elevated compartment pressure. We do not use instrumental methods such as intra-compartmental pressure monitoring, peripheral perfusion index et cetera.

Surgical anatomy and technique: Muscle component of different compartments is the primary target of the pathological process; where the nerves are the secondary targets. Following sustained vascular compromise, the muscle undergoes necrosis, fibrosis, and contracture. Associated nerve injury causes further muscle dysfunction, sensory deficits, or chronic pain. The result is a dysfunctional muscle compartment with local and distant manifestations.

The three forearm compartments are the flexor compartment which includes the finger, thumb, and wrist flexors, the lateral compartment containing the mobile wad of Henry which is represented by brachioradialis, extensor carpi radialis longus and brevis, and the extensor compartment containing finger, thumb extensors, and extensor carpi ulnaris.

The carpal tunnel is not a true compartment but may act as a closed space, and the median nerve may be subjected to the negative effects of increased pressure in case of which transverse carpal ligament should be released with exploration of the nerve in proximal forearm.

An S shaped incision starting from the antecubital region is finished in the palm center. Incision line should be kept in the burned skin area as much as possible (Figure 1). Incision crossing the joint region should not be straight. During upper limb fasciotomy, cutaneous nerve damage should be avoided while performing direct decompression of major nerves and/or ves-

sels (Figure 2). Monopolar cautery should not be used since electrical current tends to follow unfavorably in new, burned conditions, and cautery may give extra damage. Using scalpel for incisions and bipolar cautery for hemostasis is safer.

Functional outcome measurement after upper extremity decompressive surgery (UEDS) was performed with physical examination and questionnaire. We do not perform electromyography since it is an invasive method and can create medicolegal and ethical consequences. Physical exam of the hands was performed with the motor function tests of the muscle groups and corresponding nerve (Table 1). The questionnaire had 10 points giving chance to the patient comparing their hand function in daily and/or professional workup before and after the injury (and UEDS). The questions asked were nonspecific such as;

- How well did your hand(s) work from the last interview until now?
- How was the sensation (feeling) in your hand(s) from the last interview until now?
- How difficult was it for you to hold a hot object like a water filled glass during the last week?
- How difficult was it for you to dress up from the last interview until now?
- Describe the pain in your hand(s)/wrist(s) during the last six months?
- Are you satisfied with the appearance of your hand(s) and forearm(s)?
- Do you experience additional difficulty with the motion of your fingers and wrist?

Some specific conditions related to the patients' job or habits are additionally considered. Habitual fishing, frequent keyboard



**Figure 1.** Secondly healing of right forearm fasciotomy and carpal tunnel release operation. Note that fasciotomy line has been kept in burned area and tissue gap will probably be closed secondarily without grafting.





**Figure 2.** Isolation and liberation of median nerve shown at the tip of the clamp.

**Table 1.** Median and ulnar nerve motor function test chart

Instruction to the patient	Checked muscle(s)	Innervated (checked) nerve
Bend the tip of your thumb	Flexor Pollicis Longus	Median nerve
Bend the tip of your finger while stabilizing their PIP joint	Flexor Digitorum Profundus	Median nerve (radial half), Ulnar nerve (ulnar half)
Bend your finger at the middle joint while stabilizing their other fingers	Flexor Digitorum Superficialis	Median nerve
Touch the thumb to the small finger	Thenar Muscles (radial group)	Recurrent branch of median nerve
Spread your fingers apart	Interosseous Muscles	Deep branch of ulnar nerve
Grasp a piece of paper forcefully between the thumb and radial side of the index proximal phalanx (Froment's sign)	Adductor Pollicis	Deep branch of the ulnar nerve
Bring your little finger away from the others	Hypothenar Muscles	Deep branch of ulnar nerve
Bring your thumb out to the side	Abductor Pollicis Longus Extensor Pollicis Brevis	Posterior interosseous branch of the radial nerve
Lay your hand flat on a table and to "Lift only your thumb off the table"	Extensor Pollicis Longus	Posterior interosseous branch of the radial nerve
Straighten your fingers	Extensor Digitorum Communis	Posterior interosseous branch of radial nerve
Point with your index finger with the rest of your hand in a fist	Extensor Indicis Proprius Extensor Digiti Minimi	Posterior interosseous branch of radial nerve
Make a fist and strongly bring your wrist back" and palpate over the tendons	Extensor Carpi Radialis Longus	Radial nerve
	Extensor Carpi Radialis Brevis	Deep branch of radial nerve
Pull your hand up and out to the side	Extensor Carpi Ulnaris	Posterior interosseous branch of the radial nerve

user, tailor, construction worker, farmer etc. are some examples for case specific additional question generation. After a 10 to 15 minutes of conversation, patients were asked to give a number between one (the worst) to 10 (the best-same before injury) for any limitation using their hands for daily living activities or professional works including fine works. If both hand UEDS was performed, worse hand function was accepted as reference arm. The points were recorded in six-month intervals. Every six-month interval groups were compared with themselves assuming that their preinjury scores were 10.

We did not obtain an ethical committee approval since this study is a retrospective observational study based on routine laboratory, imaging and physical examination findings which are mandatory during diagnosis, treatment and follow-up periods of the patients. Patients' (or his/her relatives when patient was unconscious) informed consents were obtained. This study was constricted under the considerations of Helsinki Declaration.

Statistical analysis was carried out by using Statistical Package for the Social Sciences version 22.0 (SPSS Inc., Chicago, IL, USA). Differences between groups or within groups were assessed by using Student t test for parametric data. p values less than 0.05 were accepted to be statistically significant.

## RESULTS

During the six-year time interval between May 2011 and 2016, there were 1158 upper extremity burns. High voltage electric, as a causative factor, was found in 133 (11.4%) patients. We recruited 78 patients that underwent UEDS procedure. Upper extremity contact point was detected, and decompressive surgery was performed in 67 (85.8%) patients. Of them, there were 31 (46.2%) patients having contact point at both hands. Contact

point other than upper extremity were identified in 33 (24.8%) patients. There were varying degrees of electric arc flame burns ranging between 2-44% (TBSA) at different sites of the body, mainly the anterior trunk and extremities. Patients with mental problems, having previous upper extremity motor or sensation deficits, Mangled Extremity Severity Score more than eight, not willing to participate, coexisting severe trauma other than thermal or electrical burn, required death musculoskeletal tissue excision were exclusion criteria. Additional follow up resulted in 50 patients leaving the study subject pool. Mean age was 43.2 (14-67) years and female/male ratio was 5/45.

Time between injury to surgery was 14.6 (1-22) hours. Bilateral decompressive surgery was performed in 15 (30%) patients. CTR and median nerve visualization and liberation are sine qua non for UEDS. We do not routinely open Guyon's channel. Loose retention sutures are put by using no:1 polypropylene sutures and further tightened after extremity swelling and tonus are reduced for primary closure preparation. By using this technique, 30 (60%) needed no grafting procedure, and thus primary closure could be achieved. There was no reoperation for postoperative complication and/or additional decompression requirement. Extremity elevation, low molecular weight heparin prophylaxis, intravenous hydration based on urinary output were routine follow up protocol. Length of hospital stay in decompressive surgery patients was 32.4 (18-56) days. Median operation duration was 46 (22-255) minutes for only UEDS and additional procedure (fascial excision, grafting, amputations etc.). The only UEDS performed patient number was 17 (34%).

Every patients' hand function status point (HFSP) was recorded by using a questionnaire we created (Table 2). We assumed

**Table 2.** Hand function survey chart

Hand function status point	Months											
	6	12	18	24	30	36	42	48	54	60	66	72
1												
2												
3	2											
4	5											
5	5	8										
6	12	2										
7	10	11	2									
8	11	10	7	9	6	3	2	1	1			
9	5	8	12	9	10	10	9	8	5	4	2	1
10		8	22	22	20	18	14	12	10	9	7	5
Total patient number	50	47	43	40	36	31	25	21	16	13	9	6
% not full recovery	100	83	49	45	44	42	44	43	38	30	20	17
1: I absolutely cannot use my hand for any time as if I lost my hand(s). 10: I can use my hand(s) as what before injury or UEDS as if they weren't happened.												

**Table 3.** Average scores of the questionnaires

Groups	Average score before injury and UEDS (assumed to be)	Average score after injury and UEDS	p
72. month	10	9.83	NS
66. month	10	9.77	NS
60. month	10	9.69	NS
54. month	10	9.56	NS
48. month	10	9.52	NS
42. month	10	9.48	NS
36. month	10	9.22	NS
30. month	10	9.38	NS
24. month	10	9.32	NS
18. month	10	9.25	NS
12. month	10	7.68	0.04
6. month	10	6.52	0.03

NS: Not significant.  
UEDS: Upper extremity decompressive surgery.

that HFSP was 10 before injury and UEDS and every 6-month interval, average rescoring points were compared (Table 3). The average HFSP from the beginning of the UEDS was 6.52 and rise to 7.68 at the end of 12. month. After 18 months, HFSP reached to 9.25 and followed a plateau until 72. month (Figure 3). We found that HFSP before and after injury and UEDS was statistically significant at sixth and 12. months ( $p=0.03$  and  $p=0.04$ ), respectively. The percentage of patients' interpretation for not full recovery (points other than 10) were 100% at the first sixth month but decreased to half after 18. month. After drawing a plateau until the 48. month, second drop was detected down to 17% (Table 2).

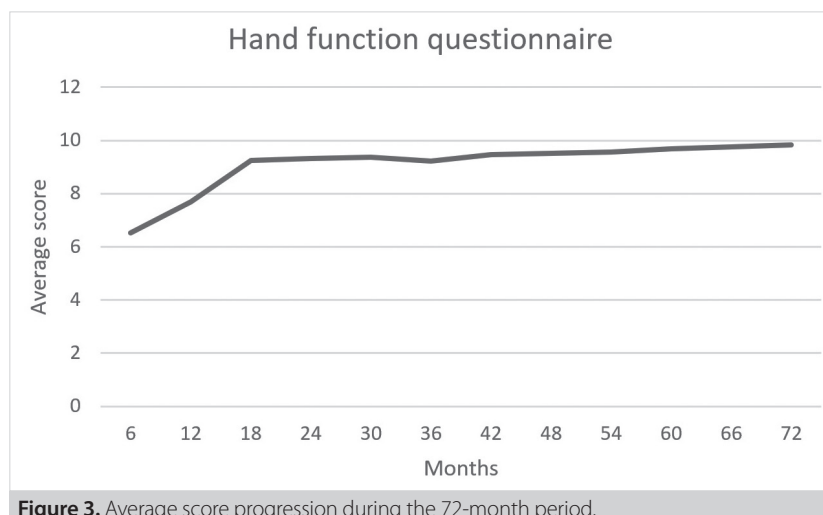
Motor function assessment of the median and ulnar nerve based on the muscle group movement instructions (Table 2)

were detected in all patients. Secondary healing, graft healing, hand stiffness due to interosseous connective tissue damage may reduce the strength and range of motion of the muscle groups but movements in definitive extend could be visualized. This showed us that nerve innervation to every expected muscle of the hand was preserved after UEDS.

## DISCUSSION

Upper extremities are prone to involve injury in more than 80% of burn cases (7). Although both hands burn constitutes less than 3% TBSA, their burn related sequela results very dramatic disabilities if not treated promptly (8).

Upper extremity nerve compression occurs in approximately 2% of the patients with severe burns (9). Patients with thermal burns greater than 20% TBSA are also candidates for peripheral

**Figure 3.** Average score progression during the 72-month period.

nerve compression in acute or long term follow up period (10). Sheridan et al. have demonstrated that 81% of the patients operated could have reached normal hand function when treated properly (11).

There is no clear data about the incidence of Carpal Tunnel Syndrome (CTS), and scarcity of the literature raises the question whether this is an uncommon problem or overlooked. Fortunately, some well documented large series exist and the incidence is 2-41% after electrodiagnostic work up (9,10,12,13). Unfortunately, we did not perform any diagnostic tests to detect CTS so we cannot figure out the exact rate in our series.

Electrical and nonelectrical burns are quite different entities. Demographically, electrical burns mostly occur in the male population according to the literature, and low voltage (<1000 V) groups include more females and children whereas high voltage (>1000 V) group includes more male patients, which is relevant with our results. Upper extremity flame or scald burns effect the tissues from outside to inside in descending severity, whereas electrical burn excluding its arc burn, the most affected part is the core of the extremity. One can easily fall in a mistake by looking at the living, bleeding skin of the extremity while deep muscle and compartment ingredients have been heavily burned in fact (Figure 4). Hand wrists have disadvantageous anatomy where low resistant tissues are spared by high

resistant tissues such as bone and tendons. Generation of high temperature from inside out fashion makes wrist region more than other body parts electric pass through. Skin is the main resistant organ to the electrical current. Wet, thin skin has low resistance and, in this case, internal tissues are much more effected than on the body with dry and thick skin coverage area. Five mechanisms of electrical burn damage are as follows: 1. Cell membrane resting potential alteration causing tetany of the muscles and tissue damage, 2. Conversion of electrical energy to thermal energy results coagulation necrosis, 3. Mechanical trauma due to contractions and/or falls (muscle rupture, bone fractures, internal organ damages), 4. The arc flame which has a temperature of 2500-10000°C, 5. Blood flow obstruction resulting ischemic necrosis (14-16).

Normal intramuscular pressure ranges from 0 to 10 mmHg, and capillary perfusion threatens after pressure exceeds 30 mmHg. Some authors suggest decompression for compartment pressures greater than 30 mmHg (17-20) while some accepts 45 mmHg as a critical threshold pressure, below which compartment syndromes were not observed (8). Since most of the heavily burned patients are hypotensive in acute period, a lower threshold of 30 mmHg should be anticipated. Of course, there are several factors other than pressure elevation such as direct trauma, synovitis, wrist hyperextension, tight dress-



**Figure 4.** Burned deep muscle components shown at the tip of right angle clamp while skin and superficial muscles are intact.



ing and fibrosis, vessel obstruction but duration of pressure elevation may be as important as the magnitude of pressure elevation (21-23). Muscle necrosis in a normotensive patient can occur after eight hours of exposure to pressures of only 30 mmHg (21) and pressure between 40 and 50 mmHg presents a critical threshold beyond which nerve function is altered (24). The main symptoms are progressive onset of numbness in the median nerve distribution and pain in the fingers on passive extension in this case (25). Late onset nerve compression syndromes can be caused by the formation of scar tissue or heterotopic bone (26).

Phillips et al. have demonstrated that the earliest and most reliable indicator of increased compartment pressure is alteration in vibratory sensory testing using a 256-cps tuning fork in cooperative patients (27). There are several methods for compartment pressure prediction such as direct intramuscular monitoring, Xenon 133 scans, and et cetera, but these tests are not applicable neither for continuous monitoring nor multiple simultaneous screening.

After UEDS, a question rising how to evaluate hand function during follow up. Assessment methods such as Michigan Hand Outcomes Questionnaire (MHQ) and the Test d'Evaluation des Membres Supérieurs des Personnes Âgées (TEMPA) are not specifically designed for burned patients in which all the soft tissues and bony components are damaged in certain extend but instead, cover variety of patients including neuromuscular or rheumatologic disorders. They mainly deal with the range of motion and grip strength, but it is important to assess an individual's ability to use their hands in ordinary day life and profession for long follow up period. Patient generated scoring system seems to be more useful for burned patients since all the tissues in the hand and wrist regions are damaged at different levels. Functional categorization of the patients based on a performance is a good idea and challenged before (10). We, therefore, created a grading system of a 10-level scale for the patients for interpretation with the help of MHQ, TEMPA and Sheridan et al. (11,28-30). While checking motor functions of the median and ulnar nerves, we did not wait to see the precise and full power movements, instead motion or motor movements of corresponding muscle groups that were visible, sensible and sufficient to do patients' needs were accepted. Factors such as secondary healing, graft healing, hand stiffness due to the interosseous connective tissue damage may be the reason for poor or imprecise motor functions. What they should give importance during the tests and exact understanding of the questions were well understood by the patients since in hospital stay time was long enough for this.

We had no pre-burn values of the parameters, and test we studied in this trial and this will never be. Evaluation of success rate for the management of this kind of unexpected trauma will only

have post-injury values. Patients may change their job, life style, habits and find some new ways to continue their daily life. This makes patients get accustomed to living in a new condition and forget their previous hand skills. Also, they may pretend to be normal, healthy, well skilled people as other unburned people and subconsciously give high points to the questionnaire. We always tried to make patients to remember their pre-burn life, skills and jobs while doing the survey.

Patient mental status after trauma and/or changing the interpretation criteria during late times are not studied in this study since we have no pre-burn mental examination, but most of the literature working on this showed no differences in mean score on mental functions between patients with burns and scores were found to be the similar with the healthy population (31).

If we accept that the points between 1-9 reflect the problems with daily life, marked improvement trends were observed during 12. to 18. months and after 60. months. This, however, differs with the study carried out by Xiao et al, in which they have observed 12-14% of patients mean TBSA (4%) 15 weeks after discharge and in 3% of patients (mean TBSA 69%) at least two years after discharge (32). Their interpretation explains the relation between TBSA and daily life activity recovery rate in time.

The consensus of UEDS after electrical burn has been undisputable for a long time (33,34). Beside escharotomy, electrical burns require other decompressive therapies such as fasciotomies or nerve releases with the recommendation level of B (35). Neurological complication was the most common sequela (24). Peripheral neuropathy rates vary widely, from 2% to 84% (36-38). Since most of the electrical burns are work related and/or has medicolegal consequences, malpractice considerations create a hesitation of including CTR to UEDS. Additional damage to the median nerve will never be differentiated from burn related functional loss, and this puts the burn surgeon under the spotlight of compensation procedures. Our study does not contain a control group, i.e., no carpal tunnel opened group. If there was, there might be no difference found. This speculation is supported with the ulnar nerve functional preservation in our series even we did not open the Guyon's canal routinely. However, it has been speculated that the release of the carpal tunnel will also reduce the Guyon's canal pressure, and release of Guyon's canal should not necessarily be done even ulnar nerve palsy is present (39). Likewise, decompression of the arm and forearm generally improves the digital perfusion, and digital escharotomy is not required in most of the cases (11).

## CONCLUSION

Median and/or ulnar nerve palsy after electrical injury is uncommon but devastating. Whether or not the carpal tunnel and Guyon's canal be released during UEDS is not answered

clearly in the literature (33,40). In clinical practice, these injuries are mostly work related and be a subject for medicolegal and compensation circumstances. Although the beneficial effect of such decompression has not been proven up to now, most surgeons would continue to decompress the carpal tunnel. Otherwise, median or ulnar nerve palsies will be considered a sequela of incomplete, insufficient surgery i.e. leaving the nerves under compression and irreversible functional loss of the hand. On the other hand, liberation of the median nerve may cause inadvertent surgical damage. It will never be differentiated that nerve malfunction is whether from the injury or a malpractice at all. Since patient homogenization is difficult due to the diverse varieties of the patients and ethical issues of having informed consent from the patient at poor cooperation in early time of injury, a randomized study will probably not be possible (41). Our study has shown that performing CTR in UEDS is safe and leads no neurological palsies in expert hands providing that there is no acute and marked tissue (bone, muscle, tendon etc.) loss at the forearm, wrist and hand.

**Ethics Committee Approval:** The approval for this study was obtained from İzmir Bozyaka Education and Research Hospital Clinical Research Ethics Committee (Decision No: 4, Date: 18.08.2015).

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - E.B.Ç., A.D.U., M.Y.; Design - E.B.Ç., A.D.U., M.Y.; Supervision - E.B.Ç., A.D.U., M.Y.; Materials - E.B.Ç., A.D.U., M.Y.; Data Collection and/or Processing - E.B.Ç., A.D.U., M.Y.; Analysis and/or Interpretation - E.B.Ç., A.D.U., M.Y.; Literature Review - E.B.Ç., A.D.U., M.Y.; Writing Manuscript - E.B.Ç., A.D.U., M.Y.; Critical Reviews - E.B.Ç., A.D.U., M.Y.

**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 (2): 87-95

### Elektrik yanıkları sonrası karpal t nel a ılması g venli midir? Altı yıllık deneyim

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####  ZET

**Giri  ve Ama :**  st ekstremit  elektrik yanıkları, uygun  ekilde tedavi edilmezse  iddetli sekel ve fonksiyon kaybı yaratabilir. Fasiyotomi ve karpal t nel a ılması ile derhal dekompresyon, en umut verici tedavi se ene i olarak g r nmektedir. Median sinir serbestle tirilir ise, n rolojik fonksiyon kayıptan ka ınılabilir.

**Gere  ve Y ntem:** Altı yıl arayla toplam 1158 yanık hastasının 50'sinde  st ekstremit  dekompresif fasiyotomi ve karpal t nel serbestle tirilmesi yapıldı. Sinir innervasyonuna dayanan el motor fonksiyonu ve g nl k el kullanım anketi 12 aylık aralıklarla takip edildi.

**Bulgular:** Ortalama skor 18. aydan sonra belirgin bir  ekilde y kseldi ve 66. ayın sonunda normal seviyeye ula tı. Median, ulnar ve radial sinir fonksiyon testi pozitif ve geri d n   olmayan sinir fonksiyon kaybı g zlenmedi.

**Sonuc:**  n kolun t m b l mleri ara tırılmalı ve elektrik yanıklarından sonra  st ekstremit  dekompresif fasiyotomiye karpal t nel serbestle tirilmesi eklenmelidir.

**Anahtar Kelimeler:** Karpal t nel, elektrik yanı ı, yanık

**DOI:** 10.47717/turkjsurg.2021.4379



# Factors predicting prolonged hospitalization after abdominal wall hernia repair - a prospective observational study

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## ABSTRACT

**Objective:** The aim of this study was to identify the factors predicting prolonged hospitalization following abdominal wall hernia repair.

**Material and Methods:** This was a prospective observational study which included patients operated for elective and emergency abdominal wall hernias. Details of the patients including demographic profile, hernia characteristics, and perioperative factors were collected. Patients were followed up till discharge from the hospital to record the postoperative local and systemic complications. Patients who stayed for more than three days were considered as longer hospital stay. Analysis was performed to identify factors associated with the longer hospital stay.

**Results:** A total of 200 consecutive patients of abdominal wall hernia were included over a period of two years. Female sex ( $p < 0.05$ ), obesity ( $p = 0.022$ ), and smoking and alcohol consumption ( $0.002$ ) led to a prolonged hospital stay. Patients with incisional hernias ( $p < 0.05$ ), American Society of Anesthesiologists (ASA) class of two or more ( $p = 0.002$ ), complicated hernia ( $p = 0.007$ ), emergency surgeries ( $p = 0.002$ ), general anesthesia ( $p = 0.001$ ), longer duration of surgery ( $>60$  minutes,  $p < 0.05$ ), usage of drain ( $p < 0.05$ ), and surgical site infection (SSI,  $p = 0.001$ ) were significantly associated with increased length of hospital stay. Whereas, age distribution, socio-economic status, co-morbidities, recurrent surgery, type of hernia repair and the level of surgeon did not affect the length of hospital stay.

**Conclusion:** The risk factors associated with prolonged hospital stay in patients undergoing abdominal wall hernia repair were female sex, obesity, smoking and alcoholism, incisional hernia, complicated hernias, higher ASA class, and prolonged duration of surgeries.

**Keywords:** Ventral hernia, hospital stay, stay length, hospitalization, hernia, ventral

## INTRODUCTION

Abdominal hernia surgery is the most common elective general surgical procedure carried out which includes groin (inguinal, femoral), primary ventral (epigastric, umbilical), incisional and recurrent hernias (1,2). There are several predictors for longer hospital stay in all types of hernia which raises healthcare costs. In general, inguinal, epigastric, and umbilical hernias have got a better outcome, lesser operative time, lesser postoperative complications, and shorter duration of hospital stay. Akinci et al. have reported that longer duration of surgery, strangulation, high American Society of Anesthesiologists (ASA) class, systemic and local postoperative complications are associated with longer hospital stay in patients with incisional hernia (3). In a similar study, coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), low serum albumin and use of steroids have been found to be risk factors for delayed wound healing and prolonged hospital stay especially in elderly patients (4). On the contrary, it has been reported that COPD, use of steroids, obesity, and previous infected wounds were not associated with risk of infection and duration of hospital stay in patients undergoing hernia repair surgery (5). Sartelli et al. have quoted that the many of the abdominal wall hernias are operated on emergency basis and this carries more incidence of postoperative complications, morbidity and hence prolonged hospital stay (6).

Longer hospital stay does not only increase the cost of health care system but also the loss of man days which has both personal and social impact. The knowledge

**Cite this article as:** Shankar H, Sureshkumar S, Gurushankari B, Sreenath GS, Kate V. Factors predicting prolonged hospitalization after abdominal wall hernia repair - a prospective observational study. Turk J Surg 2021; 37 (2): 96-102.

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Received: 13.08.2020

Accepted: 10.02.2021

Available Online Date: 30.06.2021

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DOI: 10.47717/turkjsurg.2021.4961

about the factors which determine the duration of hospital stay will help in effective channeling and better management of healthcare resources (7). Individual studies on inguinal, ventral and incisional hernias have already been published (1-3). Hence, this assessment was carried out for abdominal wall hernias as a whole. There are limited studies in the literature determining the predictors of hospital stay following abdominal wall hernia repairs. Hence, this study was undertaken to determine the variables affecting prolonged hospitalization after abdominal wall hernia repairs.

## MATERIAL and METHODS

### Study Design and Setting

This was a prospective cohort study to determine the factors affecting prolonged hospitalization in patients undergoing abdominal wall hernia repair. The study was conducted in the department of Surgery, in a tertiary care hospital over a period of two years. Institute ethics committee approval was obtained. All provisions of the Declaration of Helsinki were followed in this study.

### Patient Enrollment and Follow-Up

All consecutive adult patients posted for emergency and elective abdominal wall hernia repair with the preoperative diagnosis of inguinal hernia, primary ventral hernia (epigastric, umbilical and paraumbilical) and incisional hernias were included in the study. Patients with any additional surgical procedures carried out were excluded from the study. Informed written consent was taken from all patients included in the study. Patient demographic profile including age, sex, height, weight, body mass index (BMI) and socioeconomic status (8) were collected. Detailed history including significant past medical history, co-morbidities and habits of smoking and consuming alcohol were noted and a detailed clinical examination was carried out for all patients.

American Society of Anesthesiologists (ASA) class, type of anesthesia, operative procedure carried out, details of the operating procedures including duration of the procedure, type of surgery and the grade of surgeon were noted. Postoperatively patients were followed up till discharge from the hospital to record the post-operative local and systemic complications. The patients were discharged from the hospital when clinically fit as per department protocol. Patients who stayed for more than three days were considered as longer hospital stay (9). Analysis was performed to identify factors associated with the longer hospital stay. Analysis was done for preoperative, perioperative and postoperative factors predicting the length hospital stay in each group.

### Sample Size

The sample size was calculated using OPENEPi® software. Considering length of hospital stay as the primary variable (6), the standard deviation of 0.90 and the power of the study as 90%, the sample size was calculated to be 200.

## Statistical Analysis

The data obtained from the study was analyzed using SPSS 20.0 (IBM Corporation, New York, U.S.A) software. Various demographic, preoperative, perioperative and postoperative parameters recorded were summarized using mean/ median (continuous data) and proportions (binary data).

Chi square test or Fisher test was used for analyzing categorical variables. A multivariate logistic regression analysis with the final outcome (length of hospital stays) as the dependent factor was performed in order to identify independent predictors for the length of hospital stay after abdominal wall hernia repair. A p value of less than 0.05 was considered statistically significant.

## RESULTS

A total of 200 consecutive patients with abdominal wall hernia as per inclusion criteria operated on elective and emergency basis were enrolled in the study. Age distribution of abdominal wall hernia patients ranged from 19 to 76 years with a mean age of  $47.43 \pm 14.57$  years. Majority of the patients were males, with a male female ratio 2.7:1 (146 vs 54). Majority (67%) of the patients were within the normal BMI category. The BMI ranged from 16.80-37.53 kg/m<sup>2</sup> with a mean BMI:  $22.19 \pm 3.20$ . Out of 149 patients, 74.5% belonged to socioeconomic class 4. 64% of the patients had habit of either smoking or alcohol consumption or both. Length of stay was significantly longer in the female sex ( $p < 0.05$ ), higher BMI ( $p = 0.022$ ) and patients who had the habit of consuming alcohol and smoking (0.002). Whereas, age ( $p = 0.789$ ) and socio-economic status ( $p = 0.699$ ) did not affect the length of hospital stay (Table 1).

Groin hernias were the most common type (72.0%) of abdominal wall hernia in the study population. Among the inguinal hernia right side being the common type with 39.5% whereas left inguinal hernia was 22.5% and bilateral inguinal hernia was 9.5%. About 5% of the patients had epigastric hernia, another 5% of patients had umbilical or paraumbilical hernia and 0.5% had femoral hernia. No rare type of hernia was encountered during the study period. About 13.5% of abdominal hernia patients presented with complications (irreducible, obstructed and strangulated). Recurrent hernia accounted for 0.5% of all abdominal wall hernias. About 39% of the patients had pre-existing systemic illness. Majority of them had more than one co morbid illness including hypertension, diabetes, coronary artery disease etc. Majority of the patients belonged to ASA class 1 or class 2. Among all types of hernia, incisional hernia patients had significantly longer hospital stay ( $p < 0.0001$ ). Also, patients with complications ( $p = 0.007$ ), and patients with ASA class 2 or more ( $p = 0.002$ ) had significantly longer hospital stay (Table 2). Length of stay did not significantly differ between primary and recurrent hernia repair (0.083), and presence of co-morbidity ( $p = 0.118$ ) did not contribute to the significantly longer hospital stay.



**Table 1.** Demographic profile versus prolonged hospitalization

	No of cases N (%)	Short stay <3 days	Long stay >3 days	p
Sex				
Male	146 (73.0)	72 (49.3)	74 (50.7)	0.0001*
Female	54 (27.0)	11 (20.4)	43 (79.6)	
Age				
18-40	68 (34.0)	29 (42.6)	39 (57.4)	0.789 <sup>#</sup>
41-60	67 (33.5)	26 (38.8)	41 (61.2)	
>60	65 (32.5)	28 (43.1)	37 (56.9)	
BMI				
Under weight (<18.55)	24 (12.5)	16 (66.7)	08 (33.3)	0.022
Normal (18.55-24.99)	134 (67.0)	53 (39.6)	81 (60.4)	
Over weight (25.00-29.99)	38 (19.0)	14 (36.8)	24 (63.2)	
Obese (≥30.00)	04 (02.0)	00 (00.0)	04 (100.0)	
Socio-economic strata				
Class 1	00 (00.00)	00 (00.0)	00 (00.0)	0.699
Class 2	00 (00.00)	00 (00.0)	00 (00.0)	
Class 3	31 (15.50)	15 (48.4)	16 (51.6)	
Class 4	149 (74.50)	60 (40.3)	89 (59.7)	
Class 5	20 (10.00)	08 (40.0)	12 (60.0)	
Personal habits				
No habits	72 (36.00)	20 (27.8)	52 (72.2)	0.002
Smoking	24 (12.00)	13 (54.2)	11 (45.8)	
Alcohol consumption	21 (10.50)	15 (71.4)	06 (28.6)	
Both smoking and alcohol consumption	83 (41.50)	35 (42.2)	48 (57.8)	

\* Fisher's exact test. # Unpaired-t test.

\* As per Modified Kuppasamy's classification of socio-economic scale.

Most of the hernia repairs were elective surgeries (88%). Spinal anesthesia (67%) and meshplasty for the repair were predominantly carried out in both elective and emergency set up. Trainees performed most of the procedures (89%) and the duration of the surgery ranged from 30-180 minutes ( $75.38 \pm 29.22$  minutes). the primary ventral hernia surgeries have taken less than 60 minutes and 66.7% incisional hernia surgeries have taken a range of 60-120 minutes. Drain was used for 44 (22%) patients and all incisional hernia required drain placement which in turn led to prolonged duration of surgery. About 33 (16.5%) patients developed SSI, among which incisional hernia had a higher tendency which was statistically insignificant and the level of surgeon did not affect the occurrence of SSI. General anesthesia ( $p=0.001$ ), emergency surgeries ( $p=0.002$ ), surgeries performed more than 60 minutes ( $p<0.05$ ), usage of drain ( $p<0.05$ ) and surgical site infection ( $p=0.001$ ) has significantly delayed the discharge of the patients after hernia repair. The type of repair ( $p=0.314$ ) and the level of surgeon ( $p=1.000$ ) did not significantly alter the length of stay (Table 3).

Multivariate logistic analysis was carried out for statistically significant parameters on univariate analysis such as gender (Females,  $p=0.031$ ), BMI (Obese,  $p=0.002$ ), personal habits (Both alcohol consumption & smoking,  $p=0.008$ ), type of hernia (Incisional hernia,  $p=0.0001$ ), type of presentation (Irreducible, obstructed & stran-

gulated;  $p=0.023$ ), ASA (class 2,  $p=0.001$ ), type of surgery (emergency,  $p=0.002$ ), type of anesthesia (general anesthesia,  $p=0.001$ ), drain usage (drain used,  $p<0.05$ ), surgical site infection (present,  $p=0.001$ ) and the duration of surgery (60-120 minutes & >120 minutes;  $p=0.005$ ) (Table 4). On multivariate logistic analysis gender (Females,  $p=0.031$ ), BMI (Obese,  $p=0.002$ ), personal habits (Both alcohol consumption & smoking,  $p=0.008$ ), type of hernia (Incisional hernia,  $p=0.0001$ ), type of presentation (Irreducible, obstructed & strangulated;  $p=0.023$ ), ASA (class 2,  $p=0.001$ ) and the duration of surgery (60-120 minutes & >120 minutes;  $p=0.005$ ) were independently associated with prolonged hospital stay.

## DISCUSSION

In the present study, parameters such as female sex, obesity, alcohol consumption & smoking, incisional hernia, irreducible, obstructed and strangulated hernia, higher ASA class, longer duration of surgery were independently associated with prolonged hospital stay. Abdominal wall hernia repair is the most commonly performed general surgical procedure accounting for 15-18% of all surgical procedures done with an incidence of 100 to 300 per 100000 per annum in various countries (1,10,11). It has a major impact on the economy of the health care system as well as the patients. Analysis and the knowledge of various risk factors contributing to prolonged hospital stay in abdominal wall hernia repair not only reduces the financial burden on the

**Table 2.** Comparison physiological status and type of hernia with prolonged hospitalization

	No of cases N (%)	Short stay < 3 days	Long stay > 3 days	p
Co-morbidity				
Nil	143 (71.50)	69 (48.3)	74 (51.7)	0.118
Hypertension (HTN)	24 (12.00)	06 (25.0)	18 (75.0)	
Diabetes mellitus (DM)	06 (03.00)	01 (16.7)	05 (83.3)	
Ischaemic heart disease (IHD)	05 (02.5)	01 (20.0)	04 (80.0)	
More than one comorbidity	22	6	16	
ASA Class				
Class 1	145 (72.50)	70(48.3)	75 (51.7)	0.002
Class 2	55 (27.50)	13(23.6)	42 (76.4)	
Class 3	00 (00.00)	00(00.0)	00 (00.0)	
Class 4	00 (00.00)	00(00.0)	00 (00.0)	
Type of hernia				
Groin hernias	144 (72.00)	74 (51.4)	70 (48.6)	0.0001
Primary ventral hernia	20 (10.00)	09 (45.0)	11 (55.0)	
Incisional hernia	36 (18.00)	00 (00.0)	36 (100.0)	
Presentation				
Reducible	173 (86.50)	80 (46.2)	93 (53.8)	0.007
Irreducible	24 (12.00)	03 (12.5)	21 (87.5)	
Obstructed	02 (01.00)	00 (00.0)	02 (100.0)	
Strangulated	01(00.50)	00 (00.0)	01 (100.0)	
Previous surgery				
Recurrent	09 (04.50)	01 (11.1)	08 (88.9)	0.083
Primary	191 (95.50)	82 (42.9)	109 (57.1)	

\* Fisher's exact test. # Unpaired-t test.

\* As per Modified Kuppusamy's classification of socio-economic scale.

health care system but would also contribute to better post-operative outcomes in patients. This study brought out the major independent risk factors for prolonged hospital stay in patients undergoing hernia surgery.

Inguinal hernia is the most common type of all abdominal wall hernias and ventral hernias are the second most common type (11,12). Similarly, in the present the study, inguinal hernia accounted for 72% of all the cases and incisional hernia was the second common type (18%). Studies on abdominal wall hernias have found that age of the patients did not affect the hospital stay similar to the present study (11,12). In the present study, it was found that majority of the patients were men (73% v/s 27%). This trend may be due to males being more involved in strenuous physical work than females and hence there is greater incidence of abdominal hernias in males. It was also found that the duration of hospital stays with respect to the sex group, female sex being a strong predictor for prolonged hospital stay. The probable reason for this trend in the present study is the type of hernia, where most of the incisional hernia patients were women. Incisional hernia patients had significantly increased length of hospital stay. Obesity is a significant risk factor for prolonged hospital stay, development of surgical site infection and the recurrence of hernia (13-15). The present study also supported a similar view and found that higher BMI was asso-

ciated with a prolonged hospital stay. This tendency towards a prolonged hospital stay in obese patients can be elucidated in view of associated comorbidities, greater likelihood of prolonged surgery and a higher incidence of surgical site infection.

Malnutrition, obesity, immunosuppression and diabetes mellitus have been significantly reported to prolong the length of hospital stay (16). In the present study, the distribution of abdominal wall hernia patients according to their socioeconomic class showed that all patients belonged to class 3 or above and the length of stay did not show any significant difference among the different socioeconomic strata (8). The reason could be that none of the study patients belonged to socioeconomic class 1 & 2 and hence the comparison was between the lower three strata among the socioeconomic class. It was found that the incidence of abdominal wall hernia is greater in lower socioeconomic classes, like other reports documented (17). This could be attributable to the fact that malnutrition and undernourishment are more prevalent in lower socioeconomic classes and they are exposed to more strenuous physical work compared to the higher socioeconomic class. Studies have shown that smoking interferes with collagen metabolism and weakens the abdominal wall soft tissue layers and hence is implicated as a causative factor for the development of hernia (18). Smoking and alcohol intake also lead to a prolonged hospital stay after

**Table 3.** Comparison of anesthesia and surgical characteristics on prolonged hospitalization

	No of cases N (%)	Short stay <3 days	Long stay >3 days	p
Type of surgery				
Elective	176 (88.0)	80 (45.5)	96 (54.5)	0.002
Emergency	24 (12.0)	03 (12.5)	21 (87.5)	
Type of anesthesia				
Spinal anesthesia	134 (67.00)	70 (52.2)	64 (47.8)	0.001
General anesthesia	66 (33.00)	13 (19.7)	53 (80.3)	
Type of repair				
Anatomical repair	31 (15.50)	11 (35.5)	20 (64.5)	0.314
Meshplasty	165 (82.50)	69 (41.8)	96 (58.2)	
Others*	04 (02.0)	03 (75.0)	01 (25.0)	
Level of surgeon				
Trainee	178 (89.00)	74 (41.6)	104 (58.4)	1.000
Consultant	22 (11.00)	09 (40.1)	13 (59.9)	
Duration of surgery				
<60 minutes	92 (46.00)	55 (59.8)	37 (40.2)	0.0001
60-120 minutes	94 (47.00)	28 (29.8)	66 (70.2)	
>120 minutes	14 (07.00)	00 (00.0)	14 (100.0)	
Drain usage				
Drain used	44 (22.00)	00 (00.00)	44 (100.0)	<0.05
Drain not used	156 (78.00)	83 (53.2)	73 (46.8)	
Surgical site infection (SSI)				
Surgical site infection	33 (16.5)	00(00.00)	33 (100.0)	0.001
No complications	167 (83.5)	83(49.7)	84 (50.3)	

\*Others include TEP (Totally Extra-Peritoneal repair) - 04.

**Table 4.** Multivariate logistic regression analysis for independent factors for prolonged hospitalization

Variables	Odds ratio	Confidence interval	p
Sex (Female)	0.276	0.086-0.888	0.031
Body mass index (BMI $\geq 30.00$ )	1.18	1.066-1.347	0.002
Smoking and alcohol consumption	0.236	0.081-0.689	0.008
Type of hernia (incisional hernia)	5.659	2.300-13.923	0.0001
Type of presentation (Irreducible, obstructed & strangulated)	3.101	1.171-8.211	0.023
ASA* (> class 3)	3.755	1.668-8.451	0.001
Duration of surgery (60-120 minutes & >120minutes)	2.616	1.334-5.132	0.005

hernia repair (19). Similarly, in the present study, smoking and alcohol intake were significantly associated with a prolonged hospital stay.

Incisional hernia has been reported to be associated with a prolonged the length of hospital stay after hernia repair (3). Similarly, in the present study, incisional hernia was associated with prolonged hospital stay. This could be of the fact that incisional hernia in itself lengthens the duration of repair, and there are more complications associated with its repair. Irreducibility, obstruction and strangulation have been associated with prolonged duration of hospital stay after hernia repair (3). Similar findings were observed in the present study. This could be due

to the fact that these surgeries may require bowel resection and anastomosis and general anesthesia leading to increase operative duration and post-operative complications leading to prolonged hospital stay. Elderly patients are associated with coexisting systemic diseases which leads to prolonged hospital stay (20). However, in the present study, co-morbidities were not associated with prolonged hospital stay as majority of the patients had groin hernias and most of the patients were less than 55 years of age.

Higher ASA and general or regional anesthesia have been reported to prolong the length of hospital stay similar to that of the present study (3,20). Patients who underwent laparoscopic



repair had significant shorter hospital stay (9,21,22). In the present study, very few patients underwent laparoscopic hernia repair. Although, hernia surgery is more often carried out as an elective procedure, emergency hernia repair is associated with prolonged hospital stay (3,23,24). Similar findings were noted in the present study. This is probably due to the presence of complicated hernia, hemodynamic instability as most of them belonged to a higher ASA class. As noted in the present study, other reports have also shown that longer duration of surgery was associated with a prolonged hospital stay (3). Increased duration of surgery predisposes for the increased incidence of complications related to surgery, tissue injury, and anesthesia. Use of drains in incisional hernia and ventral hernia repair prolongs the hospital stay (4,25). In the present study, drain placement prolonged hospital stay. Drain usage directly increases the duration of surgery, predisposes to development of wound infection and hence prolongs the hospital stay. The higher the rate of infection, the longer the hospital stay after abdominal wall hernia repairs (5,26,27). In the present study, development of SSI was associated with longer hospital stay and incisional hernia had a higher tendency to develop SSI compared to other types. It was found that the greater the duration of surgery, the higher the incidences of SSI. The occurrence of SSI could be associated with malnutrition as most of the study patients belonged to a lower socioeconomic class and also due to coexisting diseases.

The strength of this study was that it included all types of abdominal wall hernia. It compared both emergency and elective procedure. Parameters like ASA and type of anesthesia were included. Like any other study this also has limitations. Majority of the hernia repair were performed by open method, there were very limited laparoscopic repairs to compare. Although we tried to include all important variables which may lead to prolonged hospital stay, due to the inherent limitations of this type of study, some could have inadvertently been left out. This was single center study with its own limitation.

## CONCLUSION

Risk factors associated with prolonged hospital stay in patients undergoing abdominal wall hernia repair were female sex, obesity, smoking and alcoholism, incisional hernia, complicated hernias, higher ASA class and prolonged duration of surgeries. The knowledge of these risk factors helps in identifying patients who may have prolonged hospital stay. This can aid in planning and reducing the burden on hospital resources as well as help the surgeons in providing better post-operative outcomes in patients undergoing abdominal wall hernia surgery.

**Ethics Committee Approval:** The approval for this study was obtained from Jawaharlal Institute of Postgraduate Medical Education and Research Ethics Committee (Decision No: IEC/ISC/2012/5228, Date: 10.12.2012).

**Peer-review:** Externally peer-reviewed.

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

**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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## ORJİNAL ÇALIŞMA-ÖZET

Türk J Surg 2021; 37 (2): 96-102

### Karın duvarı fıtığı onarımı sonrası uzamış hastanede kalmayı öngören faktörler - prospektif gözlemsel çalışma

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#### ÖZET

**Giriş ve Amaç:** Karın duvarı fıtığı onarımının ardından hastanede kalış süresinin uzamasını öngören faktörleri belirlemek.

**Gereç ve Yöntem:** Bu, elektif ve acil abdominal duvar fıtığı nedeniyle opere edilen hastaları içeren prospektif bir gözlemsel çalışmadır. Demografik profil, fıtık özellikleri ve perioperatif faktörler dahil olmak üzere hastaların detayları toplandı. Postoperatif lokal ve sistemik komplikasyonları kaydetmek için hastalar hastaneden taburcu oluncaya kadar takip edildi. Üç günden fazla kalan hastalar hastanede kalış süresi olarak kabul edildi. Daha uzun hastanede kalış ile ilişkili faktörleri belirlemek için analiz yapıldı.

**Bulgular:** İki yıllık bir süre boyunca 200 ardışık karın duvarı fıtığı hastası dahil edildi. Kadın cinsiyeti ( $p < 0,05$ ), obezite ( $p = 0,022$ ), sigara ve alkol tüketimi ( $0,002$ ) hastanede uzun süre kalmıştır. Kesi fıtığı olan hastalar ( $p < 0,05$ ), Amerikan Anesteziyologlar Derneği (ASA) sınıfı 2 veya daha fazla ( $p = 0,002$ ), karmaşık fıtık ( $p = 0,007$ ), acil ameliyatlara ( $p = 0,002$ ), genel anestezi ( $p = 0,001$ ), daha uzun cerrahi süresi ( $> 60$  dakika;  $p < 0,05$ ), dren kullanımı ( $p < 0,05$ ) ve cerrahi alan enfeksiyonu (SSI;  $p = 0,001$ ) hastanede kalış süresinin artması ile anlamlı derecede ilişkili idi. Oysa yaş dağılımı, sosyo-ekonomik durum, eşlik eden hastalıklar, tekrarlayan cerrahi, fıtık tipi ve cerrah seviyesi hastanede kalış süresini etkilemedi.

**Sonuç:** Karın duvarı fıtığı tamiri yapılan hastalarda hastanede uzun süre kalmayla ilişkili risk faktörleri kadın cinsiyet, obezite, sigara ve alkolizm, insizyon fıtığı, komplike fıtıklar, daha yüksek ASA sınıfı ve uzamış ameliyat süreleridir.

**Anahtar Kelimeler:** Ventral herni, hastanede kalma, kalma süresi, yatış, fıtık, ventral

**DOI:** 10.47717/turkjsurg.2021.4961



# Laparoscopic cholecystectomy for mild acute gallstone pancreatitis-indication itself is a good predictor of (minimal) intraoperative difficulty-a retrospective cohort study

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## ABSTRACT

**Objective:** The literature predicting difficulties during Laparoscopic Cholecystectomy (LC) for Acute Gallstone Pancreatitis (AGP) is mainly focused on the timing of operation. In our experience, LC for AGP is rarely difficult irrespective of the timing of operation. The aim of this study was to assess intra-operative difficulties in mild AGP patients to verify this observation.

**Material and Methods:** A retrospective analysis of all consecutive patients who underwent LC for mild AGP between 2014 and 2018 in a single centre was performed. Patients with known alcohol abuse, post-endoscopic retrograde cholangiopancreatography (ERCP) induced pancreatitis, and those with chronic pancreatitis were excluded. Univariate weighted analysis was performed with 11 factors, with a linear threshold boundary defined as the mean distance between the four degrees of difficulty (DoD 1-4).

**Results:** Ninety-six patients (Male= 33, median age= 56; Female= 63, median age= 52) were analysed. Majority of the patients were an ASA of two (n= 50; 52%) with a median BMI of 28 (range 18-50). Five procedures were technically difficult (DoD $\geq$  3) and only one procedure was converted to open operation. Univariate analysis showed that duration of pancreatitis >6 days (p= 0.002) and evidence of acute cholecystitis (p< 0.05) are associated with a difficult LC (DoD $\geq$  3). The rest of the factors did not influence DoD.

**Conclusion:** Based on this result, we suggest that LC for mild AGP is rarely difficult, and this finding can be used in practice for selecting these patients for training lists.

**Keywords:** Acute gallstone pancreatitis, degree of difficulty, laparoscopic cholecystectomy

## INTRODUCTION

Common indications for Laparoscopic cholecystectomy (LC) can be broadly categorised based on the organs affected by gallstones. These include the gallbladder (biliary colic or acute cholecystitis), common bile duct (obstructive jaundice or cholangitis) and pancreas (gallstone pancreatitis).

The Degree of Difficulty (DoD) during LC varies widely, and surgeons have attempted to develop scoring systems to predict intraoperative difficulties (1-3). Our group has been working on predicting these difficulties and has presented our findings in the literature. Our first paper suggested that C-Reactive Protein (CRP) is the single most useful predictor in difficult LC's (4). CRP, being a reliable marker of inflammation, predicts the difficulties secondary to inflammation of gallbladder (due to stones in gallbladder itself). Our second study suggested that the "indication" along with the degree of inflammation encountered aids in the prediction of intraoperative difficulties during LC (5). Furthermore, this finding was based on our observation that LC was rarely difficult in patients with mild acute gallstone pancreatitis.

A recent multicentre prospective randomised trial of 249 patients by da Costa DW. et al. (6) has investigated risk factors for difficult LC's for mild acute gallstone pancreatitis (AGP). The authors have established that male sex, previous endoscopic sphincterotomy and delaying cholecystectomy for more than two weeks predicted a difficult LC after mild AGP (6). They have further clarified that the probability

**Cite this article as:** Maitra I, Bennett G, Morais C, Date R. Laparoscopic cholecystectomy for mild acute gallstone pancreatitis- indication itself is a good predictor of (minimal) intraoperative difficulty- a retrospective cohort study. Turk J Surg 2021; 37 (2): 103-108.

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Received: 05.06.2020

Accepted: 07.03.2021

Available Online Date: 30.06.2021

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DOI: 10.47717/turkjsurg.2021.5084

of difficulty was increased from 18% to 55% when these factors were present.

These findings are contrary to our previous studies (that was not specific for AGP) which suggested that LC for AGP is generally not difficult irrespective of the timing of the operation (5). The number of patients with mild AGP in this study was relatively small. We have, however, subsequently observed the same trend in our current practice.

The aim of this study was to assess intraoperative difficulties in mild AGP patients to verify the findings of our previous study.

## MATERIAL and METHODS

This is a single centre retrospective case note study of all consecutive patients who underwent Laparoscopic Cholecystectomy for Acute Gallstone Pancreatitis between 2014 and 2018. Patients were identified from a prospectively kept database of operations and from the internal trust coding department at the Trust. IRB approval was not applicable.

The Atlanta classification was utilised in identifying patients with mild AGP. Mild AGP is defined as an absence of organ failure or the presence of organ failure that does not exceed 48 hours in duration) (7). Patients with known alcohol abuse and those with chronic as well as severe pancreatitis were excluded.

Key demographic, clinical and surgical data were identified from prospectively kept database as well as case notes. Clinical data included Body Mass Index (BMI), ASA, a prior history of biliary colic or cholecystitis, pancreatitis or upper abdominal surgery. Further clinical information collected included a history of previous ERCP, complications at ERCP (if any), the number of days between sphincterotomy (if any), the number of days between admission and LC (and reasons for delay >50 days), and the duration of pancreatitis (number of days between admission and discharge, excluding days in hospital eluding to a social delayed discharge). Surgical data included the degree of difficulty of LC (primary outcome measure—documented or inferred from operation notes on the Evolve™ database to allow uniformity in the data set) operating time, the reason for conversion and the histology of the specimen after operation.

The difficulty of cholecystectomy was ascertained using the Nassar scale interpreted from the operative notes and findings (grades 1–4) (8). This scale was published in 1995 and grades operative findings from the gallbladder, cystic pedicle and associated adhesions. A difficult LC was indicated by a DoD  $\geq 3$ .

Data analysis was performed within a MATLAB R2014b environment (MathWorks Inc., USA). P-values were estimated based on an ANOVA tests for univariate and multivariate comparisons. Multivariate analysis was performed with 13 factors (male sex, age, presenting complaint, BMI, ASA, prior pancreatitis, prior biliary colic, evidence of cholangitis, evidence of cholecystitis at

operation, history of upper abdominal surgery, prior ERCP, days between admission and cholecystectomy, and duration of pancreatitis) by means of multiple linear regression (MLR), with a linear threshold boundary defined as the mean distance between the two predicted clusters ( $\text{DoD} \leq / \geq 3$ ). Multivariate analysis is employed when the data have non-linearity or non-distinguishing features in unique variables (e.g., when employing univariate analysis), when the signal is complex and composed of overlapping features, or when the data changes over time or by other physical parameters (9). MLR is a well-known multivariate regression method where the weights for the input variables are calculated in at least-squares fashion. The predicted response is obtained by multiplying the regression coefficients by the original variables used for model construction. The data was auto-scaled before analysis to normalise the influence of different units into the model.

This study is reported in line with the STROCSS criteria (10).

## RESULTS

Ninety-six patients with mild AGP were included in the study.

Patient Demographics and Clinical data are summarised in Table 1 and Table 2 respectively.

Three patients had previous upper abdominal surgery. All had a midline laparotomy wound (Left Hemicolectomy; Hartmann's

**Table 1.** Demographics (n= 96)

Age (range and median)	21-85 (54.5)
Male sex (n/%)	33 (34)
ASA 1 (n/%)	24 (25)
ASA 2 (n/%)	50 (52)
ASA 3 (n/%)	21 (22)
ASA 4 (n/%)	1 (1)
BMI (range and median)	18-50 (28)

**Table 2.** Clinical data (n= 96)

Previous documented evidence of biliary colic (history) (n/%)	15 (16)
Previous documented evidence of cholecystitis (imaging) (n/%)	7 (7)
Previous documented cholangitis (history) (n/%)	1 (1)
Previous upper abdominal surgery (n/%)	3 (3)
Prior ERCP to LC (n/%)	12 (13)
Number of days between sphincterotomy (if performed) and LC (range and median)	1-147 (14)
Number of days between AGP admission and LC (range and median)	2-365 (18)
Duration of pancreatitis (range and median)	2-10 (5)

**Table 3.** Degree of difficulty (n= 96) and operating time

	n (%)	Operating time in minutes median (minimum/maximum)
DoD 1	60 (63)	36 (26, 58)
DoD 2	31 (32)	62 (60/110)
DoD 3	4 (4)	72 (62/140)
DoD 4	1 (1)	125 (121/130)

**Table 4.** p value for univariate analysis of DoD of each clinical parameter among all patients (p< 0.05 is statistically significant; p< 0.001 is statistically highly significant)

Clinical parameter	DoD ≥3 (mean ± 95% CI)
Male sex	p= 0.697
Age (21 to 85)	p= 0.897 (53 ± 3.2)
ASA (1 to 4)	p= 0.961 (2 ± 0.1)
BMI (18-49)	p= 0.837 (30 ± 1.4)
Previous documented evidence of biliary colic	p= 0.836
Previous history of cholangitis	p= 0.747
History of upper abdominal surgery	p= 0.616
Prior ERCP to LC	p= 0.101
Number of days between AGP admission and LC	p= 0.350 (60 ± 16.6)
Evidence of acute cholecystitis	p= 0.04
Duration of pancreatitis in days	p= 0.002 (6 ± 0.8)

for perforated Diverticular disease; previously perforated duodenal ulceration).

Only one patient had documented cholangitis but did not require subsequent ERCP.

Twelve patients had a prior ERCP to their LC. One patient had an unsuccessful ERCP and sphincterotomy. The documented reason for this was that the gastroenterologist was unable to cannulate the CBD safely.

It was established that 22 patients (23%) had a delay between their initial AGP diagnosis and LC of over 50 days. Only one patient in this cohort had a difficult LC (DoD= 3). It was determined that non-compliance to recommendations for early LC were a combination of patients needing further optimisation/investigations prior to LC (n= 6; 27%), patient choice to delay LC (n= 3; 14%), and pregnancy in AGP pertaining delay to LC (n= 2; 9%). The major limiting factor was hospital resources and day bed availability (n= 11; 50%).

The degree of difficulty and operating times are shown in Table 3.

Five percent of the patients (n= 5) had a DoD from 3 or 4 (difficult LC). The patient with a DoD of four was converted. The reasons for conversion outlined evidence of cholecystitis with Calot's being impossible to clarify with dense adhesions between Calot's and the duodenum.

Histologically, all 96 patients had a degree of chronic cholecystitis. The only patient, who had LC converted to open with DoD 4, had histological diagnosis of acute on chronic cholecystitis.

Uni and Multivariate analyses of predictive factors for conversion

Based on a univariate comparison using ANOVA testing, factors found to be significant in predicting a difficult LC (DoD ≥ 3) were a duration of pancreatitis >6 days and evidence of acute cholecystitis at operation, which were all statistically significant (p< 0.05). All other factors did not influence DoD ≥ 3 (Table 4).

As expected, the operation time behaved approximately linear (R= 0.975) with DoD (Figure 1), where larger operation times were associated with larger DoD values. In addition, all DoD values (1-4) were statistically highly significant from each other based on the operation time alone (p< 0.001), thus this factor alone can be used to estimate the DoD.

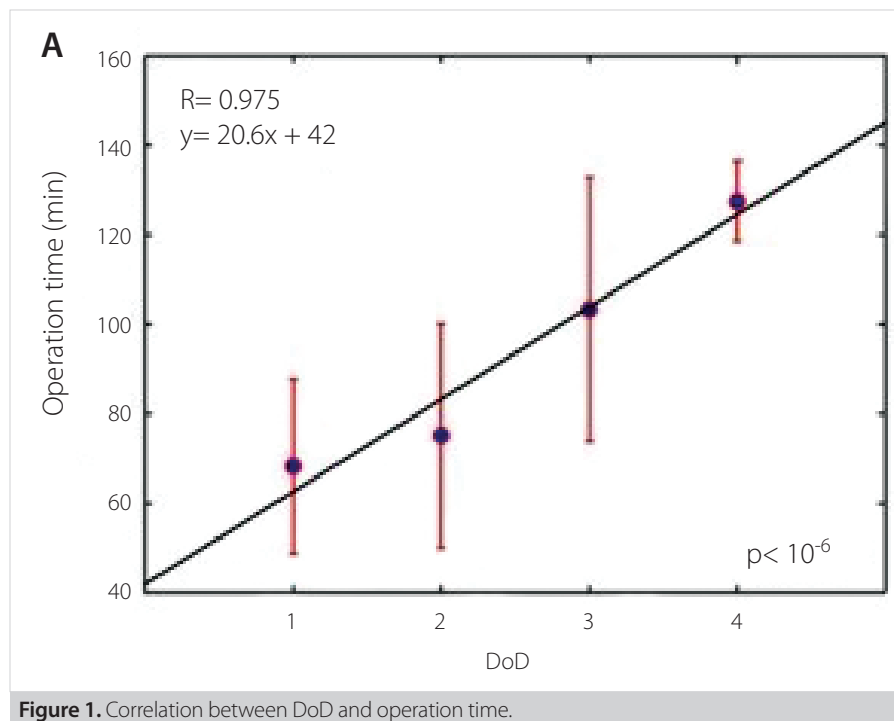
## DISCUSSION

This retrospective case note review showed that only five (5%) LC's out of 96 for mild AGP from 2014 to 2018 was 'difficult' (DoD ≥ 3) due to associated acute cholecystitis and required conversion.

Three previous studies have been directed on assessing difficulty of LC after mild AGP (11-13). Difficulty ranged from 18 to 33% in these studies. This is in contrast to our findings of only five patients (5%) which had difficult procedures regardless of timings of surgery after the primary diagnosis of mild AGP.

We propose a theory for our finding of ease of LC for mild AGP. Most patients with mild AGP have small gallstone/sludge that passes easily through a wide cystic duct resulting in transient obstruction of sphincter of Oddi and pancreatitis. A wide cystic duct is unlikely to become obstructed by stones making biliary colic or cholecystitis less likely in these patients. This may be a possible aetiological theory as to why mild AGP patients rarely have gallbladder inflammation and why these patients do not present difficulties during LCs.





**Figure 1.** Correlation between DoD and operation time.

The only patient whose LC was converted to open had acute cholecystitis that resulted in difficulty in visualisation of Calot's and subsequent conversion. This finding again suggests that AGP itself does not increase the DoD in LC but associated GB pathology does.

A recent prospective study of a U.K. database of 8820 patients advocates a six-point scoring system for prediction of operative difficulty during LC (14). The system gives a maximum of three-points for the indication for the procedure. The system scores zero if the indication is AGP. Other scoring systems also give low scores for pancreatitis as a prognostic factor for a difficult LC (15,16). This correlates well with our study findings.

Further analysis of our data showed that a duration of pancreatitis  $>6$  days ( $p = 0.002$ ) and evidence of acute cholecystitis ( $p < 0.05$ ) were associated with  $\text{DoD} \geq 3$ . Other implicated independent risk factors such as male sex or evidence of previous ERCP in the current literature were not statistically significant in the prediction of difficulty or conversion. This is contrary to previous studies and data sets (1,2).

Some studies have used operative time as a surrogate marker of difficulty. Operating time, no matter how highly dependent on surgical skill and institutional policies, precludes direct comparison amongst surgeons and in between centres (17,18).

The established Nassar operative difficulty scale was utilised in our study as this has been found to be a significant independent predictor of operative duration, conversion to open surgery, 30-day complications and 30-day reintervention (all  $p < 0.001$ ) (3).

Our group further looked at the patients with severe AGP in this timeframe. We found three patients who had severe AGP with evidence of pancreatic necrosis on CT Imaging. Two were females, one was male, and the age range of patients was between 51 and 58 (median 52). All were ASA 2 with a BMI  $< 28$ .

Only one patient with severe AGP had an intraoperative of DoD 4 and had a "laparoscopic converted to open" cholecystectomy. The operation note documented "unable to see Calot's triangle safely" as well as "acute cholecystitis". This was confirmed on histology.

AGP related LC form 5-10% of all the LC done in this institute and this simple negative predictor of difficulty helps us to select the patients for training lists.

The main limitation of this study is wide variation in timing of operation after primary diagnosis of AGP and LC (between two and 150 days) for the reasons mentioned above. Though retrospective in nature, most of the data in this study was obtained from a prospectively driven database. Findings of a correlation between AGP and operative difficulty would not have been different if the study were to be prospective.

## CONCLUSION

In conclusion, our results clearly indicate that LC for mild AGP should not be difficult unless there is evidence of concurrent acute cholecystitis. This simple negative predictor can be used for selection of patients for training lists.

**Ethics Committee Approval:** It is stated by NHS Lancashire Teaching Hospitals that this study is considered to be Service Evaluation which means designed and conducted care and does not require ethical review.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - R.D.; Design - R.D.; Supervision - R.D.; Data Collection and/or Processing - I.M., G.B.; Analysis and/or Interpretation - C.M.; Literature Review - R.D., I.M.; Writing Manuscript - I.M.; Critical Reviews - I.M., R.D.

**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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## ORJİNAL ÇALIŞMA-ÖZET

Türk J Surg 2021; 37 (2): 103-108

**Hafif akut safra taşı pankreatitinde laparoskopik kolesistektomi-endikasyonun kendisi (minimal) intraoperatif zorluğun iyi bir prediktörüdür-retrospektif bir kohort çalışması**Ishaan Maitra<sup>1</sup>, Grace Bennett<sup>1</sup>, Camilo Morais<sup>2</sup>, Ravindra Date<sup>1</sup><sup>1</sup> Lancashire Eğitim Hastaneleri, Genel Cerrahi Anabilim Dalı, Preston, Birleşik Krallık<sup>2</sup> Central Lancashire Üniversitesi, Eczacılık ve Biyomedikal Bilimler Fakültesi, Preston, Birleşik Krallık**ÖZET**

**Giriş ve Amaç:** Akut safra taşı pankreatiti (AGP) için laparoskopik kolesistektomi (LC) sırasındaki zorlukları tahmin eden literatür, esas olarak operasyonun zamanlamasına odaklanmıştır. Deneyimlerimize göre, AGP için LC, operasyonun zamanlamasına bakılmaksızın nadiren zordur. Bu çalışmanın amacı, bu gözlemi doğrulamak için hafif AGP hastalarında intraoperatif zorlukları değerlendirmektir.

**Gereç ve Yöntem:** 2014-2018 yılları arasında hafif AGP nedeniyle LC uygulanan ardışık tüm hastaların tek bir merkezde retrospektif analizi yapıldı. Alkol kötüye kullanımı olduğu bilinen hastalar, Endoskopik retrograd kolanjiyopankreatikografi (ERCP) ile indüklenen pankreatit ve kronik pankreatiti olanlar hariç tutuldu. Dört zorluk derecesi (DoD 1-4) arasındaki ortalama mesafe olarak tanımlanan doğrusal bir eşik sınırı ile 11 faktörle tek değişkenli ağırlıklı analiz yapıldı.

**Bulgular:** Altmış altı hasta (Erkek= 33, medyan yaş= 56; Kadın = 63, medyan yaş= 52) analiz edildi. Hastaların çoğunluğu, medyan BMI 28 (aralık 18-50) olan 2 ASA (N= 50; %52) idi. Sadece bir hastada DoD 4 vardı ve açık operasyona dönüştürüldü. Tek değişkenli analiz, pankreatit süresinin >6 gün (p= 0,002) ve akut kolesistit kanıtının (p< 0,05) DoD> 3 veya dönüşüm ile ilişkili olduğunu gösterdi.

**Sonuç:** Bu sonuca dayanarak, hafif AGP için LC'nin nadiren zor olduğunu ve bu bulgunun pratikte bu hastaların eğitim listeleri için seçilmesinde kullanılabileceğini önermekteyiz.

**Anahtar Kelimeler:** Akut safra taşı pankreatiti, zorluk derecesi, laparoskopik kolesistektomi

**DOI:** 10.47717/turkjsurg.2021.5084





# Serial estimation of serum C-reactive protein and procalcitonin for early detection of anastomotic leak after elective intestinal surgeries-prospective cohort study

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## ABSTRACT

**Objective:** Anastomotic leak can adversely affect the outcome of surgery especially if detected late. The present study was carried out to detect anastomotic leak early in the postoperative period using serial estimation of procalcitonin (PCT) and C-reactive protein (CRP).

**Material and Methods:** A single centre prospective cohort study was done on patients undergoing elective gastrointestinal surgery with anastomosis. Serial estimation of serum procalcitonin and C-reactive protein was done on the first five postoperative days. Other parameters such as hemoglobin, total protein, albumin and WBC counts were noted perioperatively. Patients were followed up to 60. postoperative day to assess for anastomotic leak, wound infection and other septic foci.

**Results:** Eighty-four patients were included in the study. Anastomotic leak rate was 26.19% (22/84) and 3/22 patients died in anastomotic leak group. Wound infection rate was 23.81%. The cut off value of CRP on third postoperative day in detecting anastomotic leak was 44.322 mg/dl with sensitivity of 72.73%, specificity of 66.13% and accuracy of 59.52%. The cut off value for WBC count measured perioperatively in detecting anastomotic leak was 9470 cell/mm<sup>3</sup> with sensitivity of 72.73%, specificity of 56.45% and accuracy of 59.74%. Serum procalcitonin, haemoglobin, total protein and albumin measured were not sensitive enough to detect the anastomotic leak early.

**Conclusion:** Measuring CRP on the third postoperative day can predict anastomotic leak with a cut off value of 44.32mg/dl. Patients with raised CRP need careful evaluation to rule out anastomotic leak before deciding on early discharge.

**Keywords:** C-reactive protein, procalcitonin, anastomotic leak

## INTRODUCTION

Anastomotic leak (AL) is the most dreadful complication, which can occur following all intestinal anastomotic surgeries. The incidence of AL following intestinal surgeries is 2-20% (1). The incidence is high in esophagectomy and colorectal surgeries and was reported as 10% and 2-19% respectively (2,3). Mortality following AL after colorectal and esophageal surgeries are 30% and 30-60% respectively (4,5) 70 patients undergoing colorectal surgery were prospectively analyzed in a single-center tertiary teaching hospital. Demographic and surgical data were obtained. Serum procalcitonin was taken before surgery and at day three (72 hours). AL can present early or late. It is usually diagnosed between 7 to 12 days postoperatively. Late AL presents after one-month postoperatively (6). It is always the priority of any surgeon to identify these ALs at the earliest possible so as to avoid mortality and morbidity.

AL will lead to bacterial contamination of the peritoneal cavity, which leads to rise in inflammatory mediators such as C-reactive protein (CRP) and procalcitonin (PCT) before it presents clinically. AL can be detected early in elective cases, where wound infection and peritoneal contamination are less due to preoperative bowel preparation and prophylactic preoperative antibiotics. Some studies have reported the role of PCT and CRP for early detection of AL in a group of specific surgery

**Cite this article as:** Aaron DJ, Anandhi A, Sreenath GS, Sureshkumar S, Shaikh OH, Balasubramaniyan V, et al. Serial estimation of serum C-reactive protein and procalcitonin for early detection of anastomotic leak after elective intestinal surgeries-prospective cohort study. Turk J Surg 2021; 37 (2): 109-115.

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Received: 15.11.2020

Accepted: 03.05.2021

Available Online Date: 30.06.2021

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DOI: 10.47717/turkjsurg.2021.5102

like colorectal and oesophageal surgery (3,4,7-10) it is clinically valuable to detect anastomotic leak early after esophagectomy in esophageal cancer. The purpose of this study is to investigate the associations between routine postoperative laboratory findings and anastomotic leak and to analyze the laboratory findings to find out an independent predictive marker for anastomotic leak. In addition, this study compares cases treated with neoadjuvant therapy (NT). However, there are not many reports documenting the efficacy of these parameters in overall alimentary tract surgery.

This study was carried out to determine the role of PCT and CRP plasmatic concentration as an early detector of AL following elective gastrointestinal surgery.

## MATERIAL and METHODS

This study was a prospective cohort study carried out in a tertiary center in India. Institutional ethics committee approval was obtained (JIP/IEC/201/1040). Written Informed consent was taken from all the participants in this study and patients were given full freedom to withdraw at any point of time during the study.

### Patients and Data Collection

All patients aged more than or equal to 18 years, who had undergone elective gastrointestinal surgery with an anastomosis, were included in the study. Patients with fever or focus of sepsis preoperatively, patients who had received intraperitoneal chemotherapy and in patients in whom, covering stoma was done with anastomosis were excluded from the study.

All patients, who had fulfilled the inclusion and exclusion criteria, were included in the study after taking informed written consent. Following surgery on the first five postoperative days blood was collected daily at 8 a.m. for PCT and CRP measurement.

The CRP levels were estimated using ELISA kit manufactured by Calbiotech USA® (11). The PCT levels were estimated using ELISA kit manufactured by Raybiotech® (12). The normal reference value of PCT as per the kit was less than 0.15 ng/ml and the normal reference value of CRP was less than 3 mg/l.

The patient's data, such as age, sex, telephone number, diagnosis, indication for surgery, previous surgical history, perioperative hemoglobin, total leucocyte counts (TLC), total protein and albumin were recorded. Hemoglobin and TLC were measured using Sysmex Xt-2000i which works on Coulter principle (13). Albumin was measured in Beckman-Coulter AU5800 using spectrophotometry method and bromocresol green was used as dye. Total protein was measured in Beckman-Coulter AU5800 using photometric biuret end point method (14). Confounding variables such as surgical site infection and any other postoperative septic foci were also noted. Patients were followed up postoperatively for any signs and symptoms of leak and any other postoperative complications.

AL was defined as any clinical signs of leakage, confirmed by radiological examination, endoscopy, clinical examination of the anastomosis (i.e, palpation of the anastomosis), or reoperation (15). The patient was labeled as having AL if he/she had clinical evidence of leak like peritoneal signs, bile or faecal content in the drain or if ultrasound guided aspiration of the free fluid or localized collection at the anastomotic site reveals bile or faecal matter or if water soluble contrast leak is seen on fluoroscopy or computed tomography.

Serum PCT, CRP, haemoglobin, TLC, total protein and albumin were analysed for the predictability of AL. The incidence of leak following elective intestinal anastomosis in this hospital, the risk factors associated with leak in the population studied, the sensitivity and specificity of serial estimation of serum CRP and PCT to detect leak early were calculated. The patients were followed up on post-operative day (POD) 60 over telephonic interview and development of enterocutaneous fistula or late post-operative leak were recorded.

### Sample Size

Sample size was calculated using the formula,  $N = \frac{Z^2 \times P(1-P)}{[d^2 \times (1-\text{prevalence})]}$  when p was specificity. The sensitivity of PCT measured for five post-operative days to predict AL was 100% and specificity was 72%. The specificity of CRP measured for five post-operative days to predict AL was 83% (8). With expected specificity of 72% and expected prevalence of AL as 9.4%, the sample size was calculated as 84 with 95% confidence interval, 10% relative precision. The specificity of PCT was lower than that of CRP. Hence sample size was calculated using the specificity of PCT. Power of the study was kept at 80%.

### Statistical Analysis

All statistical analysis was done using SPSS version 20. Categorical variables such as presence of AL were expressed as proportions. Continuous variables such as PCT, CRP, haemoglobin, total protein, albumin and TLC levels were expressed as mean (SD) or median (IQR) depending upon the normality of distribution. The total protein, albumin, haemoglobin and TLC showed normal distribution. CRP and PCT levels measured on all five days, did not follow normal distribution. Receiver Operating Characteristic (ROC) curve was plotted between day specific PCT, CRP, perioperative haemoglobin, total protein, albumin, TLC and the presence of AL, to determine optimum cut-off value for early detection of AL, using sensitivity and specificity. The differences in haemoglobin, total protein, albumin and TLC between the AL and NAL patients were analysed using student t test. PCT and CRP was analysed using Mann-Whitney U test. p value less than 0.05 was taken as significant.

## RESULTS

This study was carried out from January 2017 to December 2018. A total of 84 patients were included in the study. Surgical

**Table 1.** Demographic and clinical parameters studied in AL and NAL groups

Patient characteristics	AL group (N= 22)	NAL group (N= 62)	p*
Sex			0.138
Female (n= 31)	11 (35.48%)	20 (64.52%)	
Male (n= 53)	11 (20.75%)	42 (79.25%)	
Age groups			0.074
18-45 years (n= 27)	11 (40.74%)	16 (59.26%)	
45-60 years (n= 27)	7 (25.93%)	20 (74.07%)	
More than 60 years (n= 29)	4 (13.79%)	25 (86.21%)	
Mortality	3 (13.64%)	2 (3.22%)	0.076
Wound infection	6 (27.27%)	14 (22.58%)	0.657

AL: Anastomotic leak, Non AL group: Non-anastomotic leak group.  
\*Chi-square test.

**Table 2.** Comparison of procalcitonin and CRP between AL and NAL groups

Test	POD	Non-AL group Median (IQR)	AL group Median (IQR)	p*	AUC
Procalcitonin	1	210.98 (32.43-657.05)	22.06 (11.54-206.44)	0.009	0.312
Procalcitonin	2	16.27 (49.60-652.02)	26.2 (15.98-212.99)	0.013	0.322
Procalcitonin	3	176.72 (39.17-582.03)	7.55 (7.4-198.45)	0.002	0.274
Procalcitonin	4	216.35 (51.82-625.56)	20.456 (7.25-261.48)	0.017	0.328
Procalcitonin	5	162.64 (33.03-450.16)	15.63 (7.23-352.36)	0.009	0.315
CRP	1	25.04 (16.24-35.14)	34.89 (29.15-54.89)	0.041	0.647
CRP	2	27.82 (16.54-41.61)	34.39 (27.16-38.08)	0.137	0.607
C RP	3	27.09 (16.34-53.98)	44.32 (35.28-61.37)	0.033	0.654
CRP	4	34.90 (16.30-58.07)	51.23 (30.19-51.23)	0.148	0.604
CRP	5	29.44 (16.23-48.98)	45.68 (32.57-48.51)	0.104	0.617

POD: Post operative day, on AL group-non anastomotic leak group, AL group-anastomotic leak group, AUC: Area under the curve, IQR: Interquartile range.  
\*Mann-Whitney U test.

procedures done for the patients were gastric (42), colonic (13), pancreaticobiliary (20), esophageal (3), stoma closure (4) and small bowel surgeries (2). AL developed among 22/84 patients (26.19%). The distribution of anastomotic leak among various procedures were 12, 3, 6, and 1 in gastric, colonic, pancreaticobiliary and oesophageal anastomosis respectively. AL did not show any statistical difference between the sex and different age groups (Table 1). Overall mortality in the study was 5.95% (5/84). The mortality in the AL group (3/22; 13.64%) when compared to the mortality in the NAL group (2/62; 3.22%) although higher, the difference was not significant ( $p=0.076$ ). The overall incidence of postoperative surgical site infection was 20/84 (23.81%). The incidence of wound infection in the AL group was 27.27% and for the NAL group was 22.58%. The difference in distribution of wound infection was not statistically significant ( $p=0.657$ ). The clinical demographic parameters studied in AL and NAL groups were shown in Table 1.

The median and interquartile range for serum CRP and procalcitonin for all five postoperative days, were calculated. The area under the curve calculated for CRP on all five postoperative days was above 0.500 (Table 2).

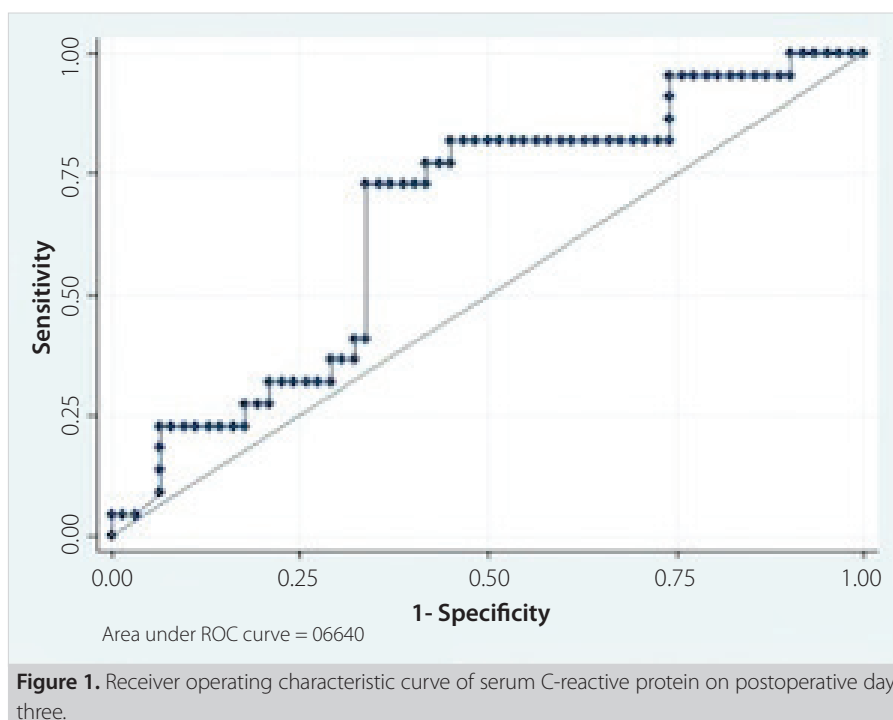
The mean and standard deviation of haemoglobin, TLC, total protein and albumin were calculated. The area under the curve of TLC was found to be significant (Table 3).

The AUC for serum CRP was 0.654 on day three reaching the maximum, than other postoperative days. The cut off value was taken as more than 44.32 mg/dl with sensitivity of 72.73% and specificity of 66.13% (Figure 1) (Table 4). When the cut off value of the perioperative TLC count was taken as more than 9470cells/mm<sup>3</sup>, the sensitivity was 72.73% and the specificity was 56.45%, (Figure 2) (Table 4). The AUC was found to be 0.641.

**Table 3.** Comparison of hemoglobin, total protein, albumin and TLC between AL and NAL groups

Test	Non AL group Mean (SD)	AL group Mean (SD)	p*	AUC
Hemoglobin	10.27 (1.81)	11 (1.76)	0.108	0.355
Total protein	5.6 (1.11)	5.62 (0.92)	0.945	0.452
Albumin	2.96 (0.59)	3.06 (0.63)	0.541	0.417
TLC	10131.94 (4468.81)	12203.64 (4472.41)	0.009	0.641

Non AL group: Non anastomotic leak group, AL group: Anastomotic leak group, AUC: Area under the curve, SD: Standard deviation, TLC: Total leucocyte counts.  
\*Student t-test.

**Figure 1.** Receiver operating characteristic curve of serum C-reactive protein on postoperative day three.**Table 4.** Best cut off value of CRP and TLC along with AUC, sensitivity and specificity for detecting anastomotic leak

Test	POD	AUC	Cut off	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
CRP	3	0.654	44.32 mg/dl	72.73%	66.13%	30%	75.93%	59.52%
TLC		0.641	9470 cells/mm <sup>3</sup>	72.73%	56.45%	28.95%	89.74%	59.74%

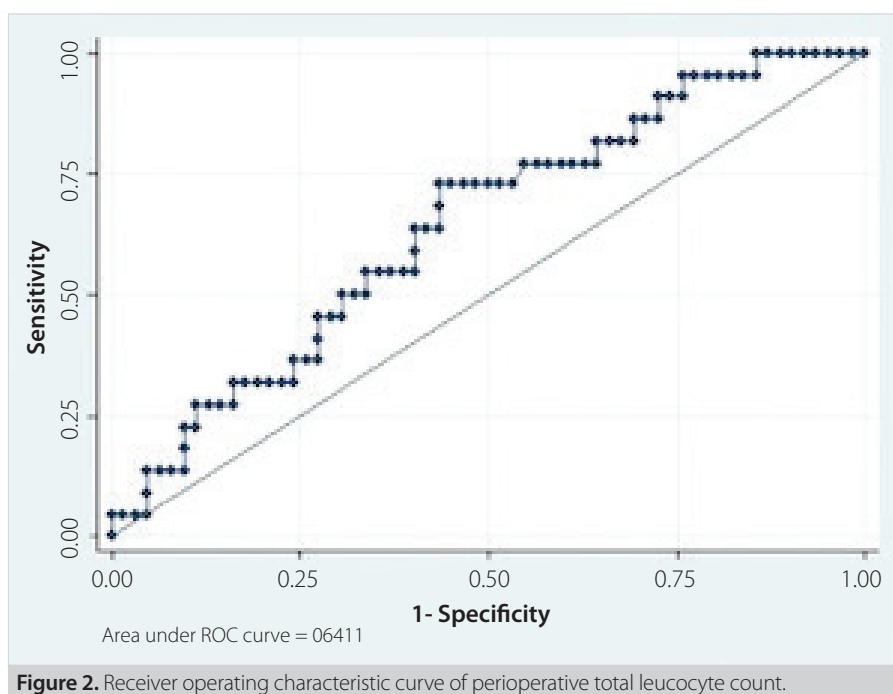
CRP: C-reactive protein, POD: Post operative day, AUC: Area under the curve, TLC: Total leucocyte counts.

## DISCUSSION

AL is a serious life-threatening complication that can occur after a gastrointestinal anastomosis. It is associated with high mortality and morbidity due to the sepsis it causes. Also, overall survival reduces, as the chance of recurrence of malignancy increases due to delay in adjuvant therapy. Early diagnosis of AL can reduce the mortality and morbidity significantly. CRP is an acute phase reactant produced by liver, in response to infection, ischemia and tissue damage (10). It starts to rise two hours following insult

and peaks at 48 hours (3). In normal circumstances, C cells of the thyroid gland produce PCT. In sepsis, white blood cells, pancreas, spleen, kidney, colon, adipocytes and the brain produce PCT. It starts rising at 3-4 hours and peaks at 8 to 24 hours (4). In the present study, the aim was to determine whether serological analysis could detect AL, prior to its clinical presentation.

The present study showed that the plasmatic concentration of CRP on third POD with the cut off value of more than 44.32 mg/dl was significantly associated with AL. The perioperative TLC,



**Figure 2.** Receiver operating characteristic curve of perioperative total leucocyte count.

more than  $9470 \text{ cells/mm}^3$  had predicted AL early. Postoperative serum PCT was not an early predictor of AL. The total protein, albumin and hemoglobin level measured perioperatively had no association with AL.

Garcia-Granero et al. have reported about early prediction of AL after colorectal resection using PCT and CRP (8). The study have shown that CRP and PCT were reliable predictors from third to fifth postoperative days with AUC more than 0.800. The best predictor was PCT on day five with the cutoff of 0.31 ng/ml, with sensitivity of 100%, specificity of 72%, and negative predictive value of 100% and positive predictive value of 17%. Aiolfi et al. have reported a systematic analysis and Bayesian meta-analysis on five studies including 850 patients on early prediction of esophageal AL using CRP (9). This study have demonstrated that CRP values on POD three and five had very good diagnostic accuracy with the AUC of 0.800. The cut off values derived for POD three and five were 17.6 mg/dl and 13.2 mg/dl respectively. Hayati et al. have reported on early prediction of colorectal AL using serum PCT on POD 3 (4). The study have shown that PCT cut off value was 5.29 ng/ml with sensitivity of 100%, specificity of 85%, the positive predictive value of 23% and the negative predictive value of 100%. The early predictor of AL associated with pancreaticoduodenectomy surgery was analyzed only in very few studies (16,17). The studies mentioned above showed that the sensitivity and negative predictive value of CRP and PCT in predicting AL of various surgeries was 100%. So, these serological tests can be used to rule out AL, postoperatively. The present study showed that the plasmatic concentration of CRP on third POD was significantly increased in patients with AL and the se-

rial estimation of serum PCT postoperatively was not associated with AL. This may be because of raised postoperative wound infection rate, which is an important confounding factor.

A meta-analysis showed that the overall incidence of AL was 9% (18). In the present study, it was found that the incidence of AL was 26.19%, which was high as many of the patients in present study had hypoalbuminemia, though it is not showing any statistical significance. The mean value of albumin in the present study was 2.96 mg/dl and 3.05 mg/dl in NAL and AL groups respectively.

Zarnescu et al. have reported the risk factors related to AL in colorectal surgery (19). The general factors which were associated with increased chance of AL in colorectal surgery were male sex, malnutrition, serum total protein less than 6 g/dl and albumin less than 3.5 g/dl, hemoglobin less than 9.9g%, blood transfusions, American Society of Anesthesiologists (ASA) score more than or equal to three, prolonged operating time and chronic steroid therapy. Local factors, associated with increased chance of AL, are low rectal anastomosis, less than 6 cm from anal verge, neoadjuvant radiotherapy, intraperitoneal chemotherapy, Hyperthermic intraperitoneal chemotherapy and bevacizumab. In the present study, it was found that risk factors, which reflect the general nutritional status of the patient such as hemoglobin, total protein, albumin had no association with the AL. Other risk factors such as neoadjuvant radiotherapy or chemotherapy, surgical techniques, duration of surgery, chronic kidney disease were not studied in our study.

The present study showed that the serum CRP value above 44.32 mg/dl on POD three can detect AL with sensitivity of

72.73%, specificity of 66.13%, positive predictive value of 30%, negative predictive value of 75.93% and accuracy of 59.52%. Since the negative predictive value of CRP was more (75.93%), it can be used as a tool to rule out AL. The present study also showed that raised peri-operative TLC is also associated with AL.

The merits of this study are the risk factors associated with AL such as hemoglobin, total protein and albumin were also analyzed. Other causes of raised CRP and PCT such as wound infection was also considered and analyzed. Duration of follow up was also long i.e, 60 days to include delayed postoperative complications.

The limitation of this study is the high wound infection rate in the study population, which may be because of poor nutritional status of the patients and the malignant nature of the disease.

## CONCLUSION

The plasmatic concentration of more than 44.32 mg/dl of CRP on POD three, and >9470 cells/mm<sup>3</sup> of postoperative TLC were found to detect the AL early with a high negative predictive value. So, this can be utilized for discharging patients early after elective gastrointestinal surgeries. However, serum procalcitonin was not found to be a predictor of anastomotic leak. Risk factors such as low serum total protein, albumin and hemoglobin were not associated with anastomotic leak.

**Ethics Committee Approval:** The approval for this study was obtained from Jawaharlal Institute of Postgraduate Medical Education and Research Ethics Committee (Decision No: JIP/IEC/2016/1040, Date: 16.02.2017).

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - A.A., G.S.S., V.K.; Design - A.A., S.S., V.K.; Supervision - A.A., G.S.S., V.K.; Materials - D.J.A., O.H.S., V.B.; Data Collection and/or Processing - D.J.A., O.H.S.; Analysis and/or Interpretation - D.J.A., O.H.S., V.B.; Literature Review - D.J.A., S.S., V.B.; Writing Manuscript - A.A., G.S.S., V.K.; Critical Reviews - A.A., G.S.S., S.S., V.K.

**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

Türk J Surg 2021; 37 (2): 109-115

## Elektif bağırsak ameliyatlarından sonra anastomoz kaçağının erken tespiti için serum c-reaktif protein ve prokalsitonin seri tahmini prospektif kohort çalışması

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### ÖZET

**Giriş ve Amaç:** Özellikle geç fark edildiğinde anastomoz kaçağı cerrahi sonucunu kötü bir şekilde etkileyebilir. Bu çalışma, prokalsitonin (PCT) ve C-reaktif protein (CRP) sıralı tahmini kullanılarak anastomoz kaçağının postoperative dönemde erken tespit edilmesi için yürütüldü.

**Gereç ve Yöntem:** Anastomozlu elektif gastrointestinal cerrahi operasyonu olan hastalarda tek merkezli prospektif kohort bir çalışma yürütüldü. İlk beş postoperative günde, serum prokalsitonin (PCT) ve C-reaktif protein (CRP) sıralı tahmini uygulandı. Hemoglobin, total protein, albümin ve akyuvar sayısı gibi diğer parametreler perioperatif olarak kaydedildi. Hastalar; anastomoz kaçağı, yara enfeksiyonu ve diğer septik odaklar açısından postoperative 60. güne kadar takip edildi.

**Bulgular:** Çalışmaya 84 hasta dahile dildi. Anastomoz kaçağı oranı %26,19 idi ve anastomoz kaçağındaki 3/22 hasta kaybedildi. Yara enfeksiyon oranı %23,81 idi. Üçüncü postoperative günde anastomoz kaçağının tespiti için CRP eşik değeri 44,322 mg/dl olarak bulunurken duyarlılık, özgüllük ve doğruluk oranları sırasıyla %72,73, %66,13 ve %59,52 idi. Anastomoz kaçağının tespiti için perioperative ölçülen akyuvar sayısının eşik değeri 9470 hücre/mm<sup>3</sup> olarak bulunurken duyarlılık, özgüllük ve doğruluk oranları sırasıyla %72,73, %56,45 ve %59,74 idi. Ölçülen serum prokalsitonin, hemoglobin, total protein ve albumin, anastomoz kaçağının erken dönemde tespiti açısından yeterince duyarlı değildi.

**Sonuç:** Postoperatif üçüncü günde CRP ölçümü, 44,32 mg/dl eşik değeri iel anastomoz kaçağına öngörebilir. CRP yüksek hastalar, erken taburculuk öncesi anastomoz kaçağı açısından değerlendirilmelidir.

**Anahtar Kelimeler:** C-reaktif protein, prokalsitonin, anastomoz kaçağı

**DOI:** 10.47717/turkjsurg.2021.5102



# Citation classics: the 50 most cited articles in surgery in Asia

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## ABSTRACT

**Objective:** The term 'citation classics' is used for highly cited papers in the scientific literature. It was aimed to understand the current landscape of academic surgery and the quality of the scientific contribution of authors belonging to Asia using citation classics.

**Material and Methods:** We searched the WoS core collection database under the category 'surgery' to include the 50 most cited articles whose lead author was affiliated to an Asian country during the research period. We noted the following characteristics for each article: total citations, average citations per year, year of publication, publishing journal, institution and country, journal quartile and impact factor, authorship, field of surgical research. Results were analyzed using IBM SPSS Statistics v26.

**Results:** The number of citations ranged from 447 to 1170 (mean  $\pm$  SD is 616.9  $\pm$  150.16) and citations per year ranged from 10.04 to 98.17 (mean  $\pm$  SD is 30.87  $\pm$  17.27). Most productive decade was 1991-2000 (n= 19 articles). Majority of the articles were published in 'Annals of Surgery' (28%). Four authors contributed two or more articles as lead author with 'Poon RTP' taking the lead. Japan's contribution was highest (60%) followed by China and its dependents' (26%). University of Hong Kong was the leading institution (n= 7). Observational study was the most commonly used design (n= 24). Most papers belonged to gastrointestinal surgery (n= 28) and surgical oncology (n= 26). 66% articles originated from a single institution, 22% had inter-institutional collaboration and 12% had national collaboration from countries outside Asia.

**Conclusion:** The study identified the most influential papers in surgery from Asia. This should provoke interest in academic surgery and research collaboration with other nations in Asia and the rest of the world.

**Keywords:** Citation classics, citations, bibliometrics, surgery, Asia

## INTRODUCTION

Asia harbors 60% of the world's population and carries a substantial burden for surgically treatable disorders (1). Moreover, the distribution of currently available surgical services is inequitable. A good way to approach this problem is to understand the current situation of academic surgery in Asia.

The term 'citation classics' was coined by Garfield who used the term for highly cited papers in the Web of Science (WoS) database (2). Bibliometric study using citation counts is an important tool to measure scientific impact and/or significance of the published literature from an individual or a region (3,4). Citation classics help in understanding the current research status and serve as a guide for future direction in a field. They can also estimate the quality of research output from a region, which can influence decisions regarding the allocation of funds and research priorities (5).

Previous reviews have looked at citation classics in different surgical specialties such as general surgery (6), plastic surgery (7,8), gastrointestinal surgery (9), neurosurgery (5), orthopedic surgery (4) et cetera. However, there has been no previous report of citation classics in surgery originating from Asia. It was aimed to understand the current landscape of academic surgery and the quality of the scientific contribution of authors belonging to Asia using citation classics determined through the Web of Science core collection database.

## MATERIAL and METHODS

Our study was based on the Science Citation Index Expanded (SCI-EXPANDED) database of the Clarivate Analytics (formerly known as the Thomson Reuters and the

**Cite this article as:** Aggarwal V. Citation classics: the 50 most cited articles in surgery in Asia. Turk J Surg 2021; 37 (2): 116-125.

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Received: 16.11.2020

Accepted: 07.03.2021

Available Online Date: 30.06.2021

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DOI: 10.47717/turkjsurg.2021.5106

Institute for Scientific Information) Web of Science (WOS) Core Collection database. According to the Journal Citation Reports (JCR) of 2019 (InCites Journal Citation Reports dataset updated June 20<sup>th</sup>, 2019), it indexes 11,877 journals with citation references across 236 disciplines. Search conducted in May, 2020 revealed a total of 1,911,690 documents in the WOS category of 'surgery'. This search was further refined by countries to include at least one author from Asian countries and their dependencies: Afghanistan, Armenia, Azerbaijan, Bahrain, Bangladesh, Bhutan, Brunei, Cambodia, China, Cyprus, Georgia, India, Indonesia, Iran, Iraq, Israel, Japan, Jordan, Kazakhstan, Kuwait, Kyrgyzstan, Laos, Lebanon, Malaysia, Maldives, Mongolia, Myanmar, Nepal, North Korea, Oman, Pakistan, Philippines, Qatar, Saudi Arabia, Singapore, South Korea, Sri Lanka, State of Palestine, Syria, Tajikistan, Thailand, Timor-Leste, Turkey, Turkmenistan, United Arab Emirates, Uzbekistan, Vietnam, Yemen, Taiwan, Hong Kong, Macao revealing a total of 349,326 documents. Search results were then arranged in descending order of the total number of citations received from WOS core collection.

These results were manually searched by the author to include only those publications whose lead author was affiliated to one of these Asian countries during the period of research. Results related to dental surgery were excluded. We selected the top 50 most cited papers which satisfied the above criteria. We searched the PubMed or Google Scholar database to obtain the full texts/abstracts of these articles. For each article, we extracted the following characteristics: article title, total number of citations in WoS core collection, average citations per year, year of publication, publishing journal, publishing institution, publishing country, journal quartile, journal impact factor (IF), authorship, area of surgical research and type of research. We inserted all data for each included article into a spreadsheet software and used descriptive statistics to quantitatively describe the features of the sample using IBM SPSS Statistics v26.

## RESULTS and DISCUSSION

Our analysis of the citation classics of surgical research originating from Asia revealed the following findings.

### Citation and Timeline Characteristics

The list of top 50 articles is provided in Table 1. The number of citations ranged from 447 to 1170 (mean  $\pm$  SD was 616.9  $\pm$  150.16). Eight papers were cited more than 800 times. The average number of citations per year ranged from 10.04 to 98.17 (mean  $\pm$  SD was 30.87  $\pm$  17.27). The paper published by Shigeyuki et al. (10) received the highest number of total citations (1170 times). It was entitled, "Mesenchymal Cell-based Repair of Large, Full-thickness Defects of Articular-cartilage." published in 1994. This basic science study attempted to repair articular cartilage defects using osteochondral progenitor cells in rabbits. This is the only paper in the list which has been cited >1000 times.

The paper ranked lowest in this list (cited 447 times) was, "Intrahepatic recurrence after curative resection of hepatocellular carcinoma – Long-term results of treatment and prognostic factors" published in 1999 (11).

All papers in the list were published between 1976 to 2015. Figure 1 depicts this timeline trend. Highest number of articles were published in 1991-2000 decade ( $n=19$  articles) followed by the 2001-2010 decade ( $n=15$  articles). The most productive decade for citation classics has been variable in medical literature (1980s in Hand surgery (12), 1990s in Aesthetic surgery, Neurosurgery and Otolaryngology (5,7,13), 2000s in Ophthalmology and GI surgery (9,14) et cetera. In the list of 35 most cited articles in surgery published by Long et al., the most productive decade was 1970 (15). Since citations take time to accumulate, it is expected that even the 'landmark' papers recently published will not be able to make it into this list. According to Garfield et al. even older papers are cited less often as they become 'common concept' over time. This is termed as Obliteration by incorporation (2). Thus, when we looked at the number of citations per year, it produced significant shifts in rank when compared to the rank based on the total number of citations (mean absolute rank change  $14.44 \pm 10.07$ ; range -33 to +32). The paper with the highest number of average annual citations among the top 50 list was produced by Wakabayashi et al. (16) This was a consensus statement on laparoscopic liver resection.

### Journals and Authors

Journals publishing top 50 cited papers are listed in Table 2. These include a total of 25 journals. Largest number of top-cited papers were published by 'Annals of Surgery' ( $n=14$  articles) followed by 'Journal of Bone and Joint Surgery-American Volume' ( $n=4$  articles). Impact factors of these journals varied from 1.29 to 10.13 according to JCR 2019. Most of these journals belong to the 1. quartile in surgery and related sub-specialties. Six journals belong to the 2. quartile and two journals 'Acta Neurochirurgica' and 'Aesthetic Plastic Surgery' belong to the 3. quartile. Top cited articles are more likely to be published in journals of high impact. This in turn increases the impact factor of these journals (17). On the other hand, landmark papers, even if published in journals with low impact, could be highly cited if they are considered important in the field. Most of the journals in our list have an origin in the US or UK. There is a reluctance of highly cited authors to publish papers in native journals as many of them are not included in major bibliographic databases.

### Authors

Four authors contributed two or more articles as a lead author. The list was led by Poon RTP who contributed to four articles as a lead author. This was followed by Makuuchi T ( $n=3$  articles), Naruke, T and Kitano S ( $n=2$  articles each).

**Table 1.** The 50 most cited surgery articles from Asian surgeons

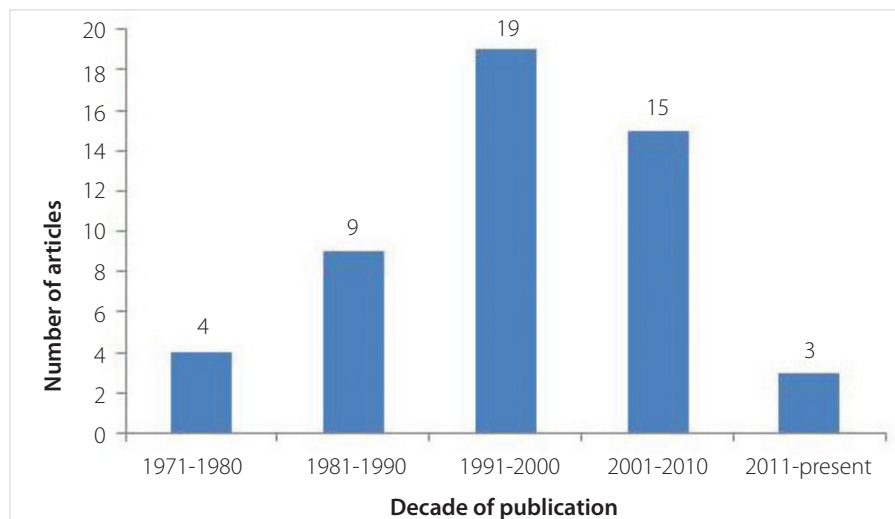
Rank	Lead author (year of publication)	Title	Total number of citations in WoS core collection	Average citations/year
1	Wakitani, Shigeyuki (1994)	Mesenchymal cell-based repair of large, full-thickness defects of articular-cartilage	1170	43.33
2	Chen, Ms (2006)	A prospective randomized trial comparing percutaneous local ablative therapy and partial hepatectomy for small hepatocellular carcinoma	910	60.67
3	Kitano, S (1994)	Laparoscopy-assisted billroth-I gastrectomy	892	33.07
4	Inoue, K (1984)	Clinical-application of transvenous mitral commissurotomy by a new balloon catheter	859	23.22
5	Inoue, H (2010)	Peroral endoscopic myotomy (POEM) for esophageal achalasia	839	76.27
6	Makuuchi, M (1990)	Preoperative portal embolization to increase safety of major hepatectomy for hilar bile-duct carcinoma - a preliminary-report	819	26.42
7	Todani, T (1977)	Congenital bile-duct cysts-classification, operative procedures, and review of 37 cases including cancer arising from choledochal cyst	811	18.43
8	Benabid, Al (1996)	Chronic electrical stimulation of the ventralis intermedius nucleus of the thalamus as a treatment of movement disorders	809	32.36
9	Song, Ye-Guang (1984)	The free thigh flap - a new free flap concept based on the septocutaneous artery	792	21.41
10	Atiyeh, Bishara S (2007)	Effect of silver on burn wound infection control and healing: review of the literature	748	53.43
11	Wei, FC (2002)	Have we found an ideal soft-tissue flap? An experience with 672 anterolateral thigh flaps	740	38.95
12	Koshima, I (1989)	Inferior epigastric artery skin flaps without rectus abdominis muscle	687	21.47
13	Akiyama, H (1994)	Radical lymph-node dissection for cancer of the thoracic esophagus	686	25.41
14	Kiuchi, T (1999)	Impact of graft size mismatching on graft prognosis in liver transplantation from living donors	650	29.55
15	Kajitani, T (1981)	The general rules for the gastric-cancer study in surgery and pathology. 1. clinical classification	648	16.2
16	Makuuchi, M (1985)	Ultrasonically guided subsegmentectomy	629	17.47
17	Poon, RTP (2002)	Long-term survival and pattern of recurrence after resection of small hepatocellular carcinoma in patients with preserved liver function - implications for a strategy of salvage transplantation	621	32.68
18	Nakajima, T (1982)	An Immunoperoxidase study of s-100 protein distribution in normal and neoplastic tissues	618	15.85
19	Poon, RTP (2000)	Risk factors, prevention, and management of postoperative recurrence after resection of hepatocellular carcinoma	611	29.1
20	Maruyama, K (1987)	Progress in gastric-cancer surgery in Japan and its limits of radicality	609	17.91
21	Kudo, S (1993)	Endoscopic mucosal resection of flat and depressed types of early colorectal-cancer	603	21.54
22	Naruke, T (1978)	Lymph-node mapping and curability at various levels of metastasis in resected lung-cancer	595	13.84

**Table 1.** The 50 most cited surgery articles from Asian surgeons (continue)

Rank	Lead author (year of publication)	Title	Total number of citations in WoS core collection	Average citations/year
23	Fan, ST (1999)	Hepatectomy for hepatocellular carcinoma: toward zero hospital deaths	592	26.91
24	Wakabayashi, GO (2015)	Recommendations for laparoscopic liver resection a report from the second international consensus conference held in Morioka	589	98.17
25	Jaffe, ES (1996)	Report of the workshop on nasal and related extranodal angiocentric t natural killer cell lymphomas-definitions, differential diagnosis, and epidemiology	584	23.36
26	Naruke, T (1988)	Prognosis and survival in resected lung-carcinoma based on the new international staging system	580	17.58
27	Imamura, H (2003)	One thousand 56 hepatectomies without mortality in eight years	578	32.11
28	Goel, A (1994)	Plate and screw fixation for atlantoaxial subluxation	576	57.5
29	Ando, Nobutoshi (2012)	A randomized trial comparing postoperative adjuvant chemotherapy with cisplatin and 5-fluorouracil versus preoperative chemotherapy for localized advanced squamous cell carcinoma of the thoracic esophagus (Jcog9907)	561	62.33
30	Yoshimura, Kotaro (2008)	Cell-assisted lipotransfer for cosmetic breast augmentation: supportive use of adipose-derived stem/stromal cells	557	42.85
31	Makuuchi, M (1993)	Surgery for small liver cancers	550	19.64
32	Wong, Ch (2003)	Necrotizing fasciitis: clinical presentation, microbiology, and determinants of mortality	538	29.89
33	Kim, Hyung-ho (2010)	Morbidity and mortality of laparoscopic gastrectomy versus open gastrectomy for gastric cancer an interim report-a phase iii multicenter, prospective, randomized trial (klass trial)	536	48.73
34	Minagawa, M (2000)	Extension of the frontiers of surgical indications in the treatment of liver metastases from colorectal cancer-long-term results	527	25.1
35	Wada, N (2003)	Lymph node metastasis from 259 papillary thyroid microcarcinomas-frequency, pattern of occurrence and recurrence, and optimal strategy for neck dissection	524	29.11
36	Yoo, Ch (2000)	Recurrence following curative resection for gastric carcinoma	523	24.9
37	Kitano, Seigo (2007)	A multicenter study on oncologic outcome of laparoscopic gastrectomy for early cancer in Japan	522	37.29
38	Yang, Zhe (2011)	Overexpression of long non-coding RNA HOTAIR predicts tumor recurrence in hepatocellular carcinoma patients following liver transplantation	514	51.4
39	Ko, Yc (1995)	Betel quid chewing, cigarette-smoking and alcohol-consumption related to oral-cancer in Taiwan	512	19.69
40	Poon, RTP (2004)	Improving perioperative outcome expands the role of hepatectomy in management of benign and malignant hepatobiliary diseases-analysis of 1222 consecutive patients from a prospective database	502	29.53
41	Utsunomiya, J (1980)	Total colectomy, mucosal proctectomy, and ileoanal anastomosis	492	12
42	Jayne, Dg (2002)	Peritoneal carcinomatosis from colorectal cancer	490	25.79

**Table 1.** The 50 most cited surgery articles from Asian surgeons (continue)

Rank	Lead author (Year of publication)	Title	Total number of citations in WoS core collection	Average citations/year
43	Tanaka, K (1993)	Surgical techniques and innovations in living related liver-transplantation	469	16.75
44	Milgrom, C (1995)	Rotator-cuff changes in asymptomatic adults-the effect of age, hand dominance and gender	463	17.81
45	Itoi, E (2000)	The effect of a glenoid defect on anteroinferior stability of the shoulder after bankart repair: a cadaveric study	459	21.86
46	Matsutani, M (1997)	Primary intracranial germ cell tumors: a clinical analysis of 153 histologically verified cases	457	19.04
47	Sugaya, Hiroyuki (2007)	Repair integrity and functional outcome after arthroscopic double-row rotator cuff repair-a prospective outcome study	456	32.57
48	Harii, K (1976)	Free gracilis muscle transplantation, with microvascular anastomoses for treatment of facial paralysis-preliminary-report	452	10.04
49	Poon, RTP (2001)	Improving survival results after resection of hepatocellular carcinoma: a prospective study of 377 patients over 10 years	449	22.45
50	Poon, RTP (1999)	Intrahepatic recurrence after curative resection of hepatocellular carcinoma-long-term results of treatment and prognostic factors	447	20.32

**Figure 1.** Number of highly cited papers published by decade.

### Countries and Institutions

A total of six countries in Asia contributed these top 50 papers (Figure 2). Japan's contribution was the highest (60% of total papers) followed by China and its dependent's Taiwan and Hong Kong (26% of total papers). Next in line were Singapore and South Korea (4% each) and India, Israel and Lebanon (2% each). The institutions producing three or more papers are enlisted in Table 3. University of Hong Kong produced the highest number of articles (n= 7) followed by National Cancer Center Hospital in

Japan (n= 6) and University of Tokyo in Japan (n= 3). The remaining institutions produced one article each. These findings are similar to citation classics in other specialties where the top-cited papers are concentrated in a few institutions and countries (5,7,8,12,14). The US predominates in the world's quality research output (18,19). The reason for this has been attributed to large research funding and diverse scientific community and also in part due to bias of American authors and reviewers towards the articles published locally which falsely amplifies citation counts



**Table 2.** Journals in which 50 most cited surgery papers of Asian origin were published

Journal name	Journal impact factor (IF)	Number of papers published
Annals of Surgery	10.13	14
Journal of Bone and Joint Surgery-American Volume	4.578	4
Journal of Thoracic and Cardiovascular Surgery	4.451	3
American Journal of Surgical Pathology	4.958	2
Annals of Surgical Oncology	4.061	2
British Journal of Plastic Surgery	1.291	2
British Journal of Surgery	5.676	2
Endoscopy	7.341	2
Journal of Neurosurgery	3.968	2
Plastic and Reconstructive Surgery	4.209	2
Acta Neurochirurgica	1.817	1
Aesthetic Plastic Surgery	1.798	1
American Journal of Surgery	2.125	1
Archives of Surgery	4.926	1
Burns	2.066	1
Diseases of the Colon & Rectum	3.991	1
Japanese Journal of Surgery 1	1.878	1
Journal of Bone and Joint Surgery-British Volume 2	4.306	1
Journal of Oral Pathology & Medicine	2.495	1
Seminars in Surgical Oncology*	2.05	1
Surgery	3.356	1
Surgery Gynecology & Obstetrics 3	4.59	1
Surgical Laparoscopy & Endoscopy 4	1.36	1
Transplantation	4.264	1
World Journal of Surgery	2.234	1

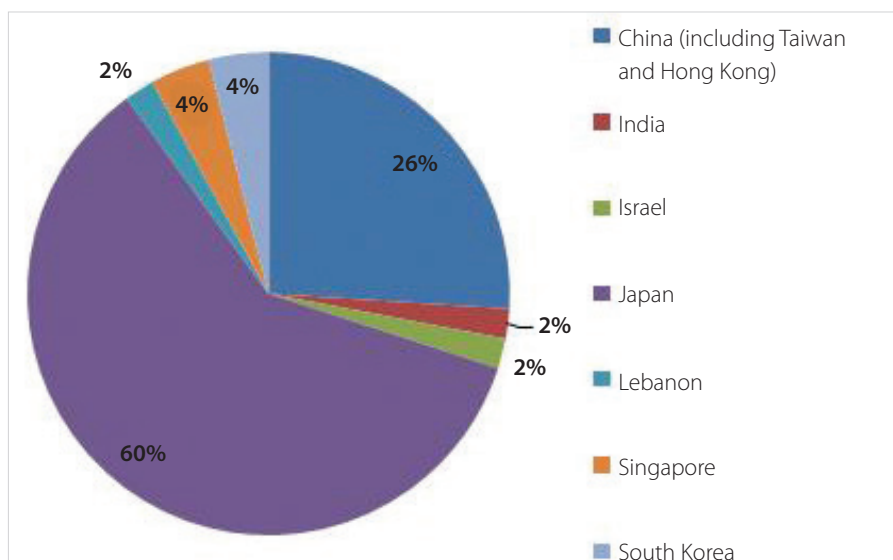
\*The names of these journals have been changed. 1, 2, 3 and 4 are now called 'Surgery Today', 'The Bone & Joint Journal', 'Journal of American College of Surgeons' and 'Surgical Laparoscopy Endoscopy & Percutaneous Techniques' respectively.

Impact factor values are based on Journal Citation Reports (JCR) of 2019 except \*. 'Seminars in Surgical Oncology' has ceased to exist. Its IF value is based on JCR of 2002.

(20,21). It has also been found that even among top journals, papers published by high-income countries are more frequently cited than low and middle-income countries (22).

Japan and China are the main contributors to classical surgical research output from Asia. This is also observed for other medical disciplines such as Ophthalmology (14), Orthopaedics (23,24) and Transplantation (25). This could be largely attributed to their better research and development expenditure compared to other Asian countries and their focus on basic science research lately. Favorable national policies in Japan for healthcare research and high productivity of human resources have contributed to its success in academic surgery across the globe (26). However, none of the papers in the list were able to make it to the list of the top 35 cited papers in surgery by Long et al. (15). This could be due to a few reasons. First, studies have shown a strong positive correlation between GDP and

number of publications (25,27). While the US spends 17% of its GDP on healthcare, Japan and China spend 11 and 5% respectively according to the World Bank (28). This amounted to 120 billion dollars spent on biomedical research by the US alone compared to only 62 billion dollars spent in Asia in 2012 (29). However, the amount of GDP spent on healthcare research has grown significantly in the last two decades in some of the Asian countries (29,30). The effect of this measure is beginning to be seen. Second, English is being used for the majority of scientific publications and bibliometric search engines. This becomes a problem particularly for Asian non-native English-speaking countries such as China where most of the papers are published in Chinese. Besides, papers written in English from these countries take more time to publish and incur higher costs due to language editing services. This could deter young academic surgeons from publishing in these journals. Third, lack of com-



**Figure 2.** Contribution of countries to the Asian Surgical research output.

**Table 3.** Institutions which contributed 3 or more of the 50 most cited surgery articles of Asian origin.

Institution (country)	Number of articles
University of Hong Kong (Hong Kong)	7
National Cancer Center Hospital (Japan)	6
University of Tokyo (Japan)	3

prehensive national healthcare databases in many low and middle-income countries in Asia(1) do not encourage research for endemic surgically treatable diseases in Asia.

### Type of Research and Surgical Field

A total of seven different study designs/research types were included in the top 50 list (Figure 3). Observational study was the most commonly used design (n= 24). Three papers reported interventional studies (randomized trials). The predominance of observational studies have been observed in other surgical disciplines' classics as well including aesthetic surgery (7), Urogynaecology (31) and eye surgery (14). The reason for such observation could be due to their role in hypothesis testing (14) and ethical concerns with interventional studies. Of note, only 4 review articles were present in our list contrary to the expectation since reviews are more likely to be cited by authors (32).

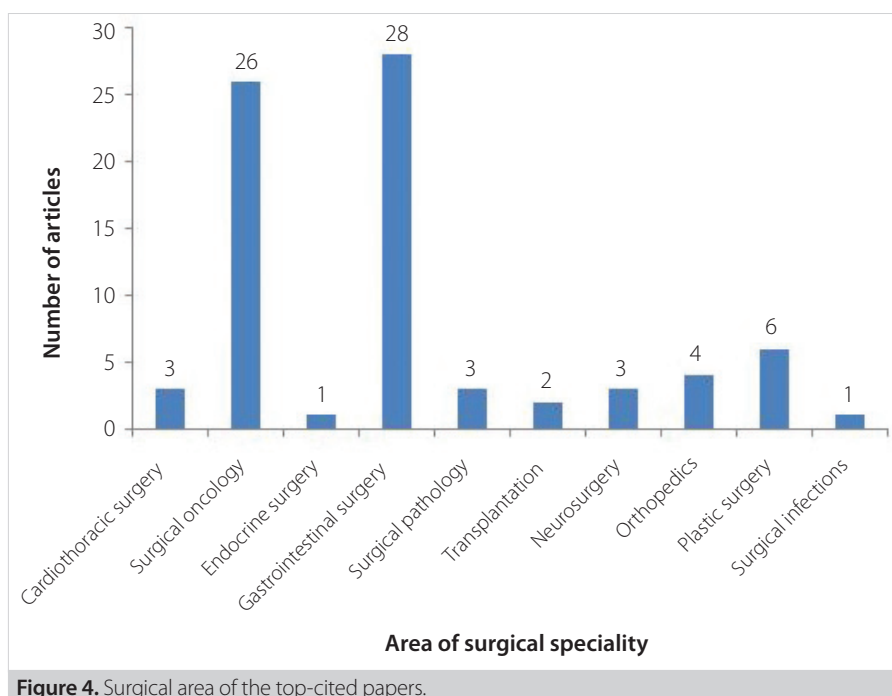
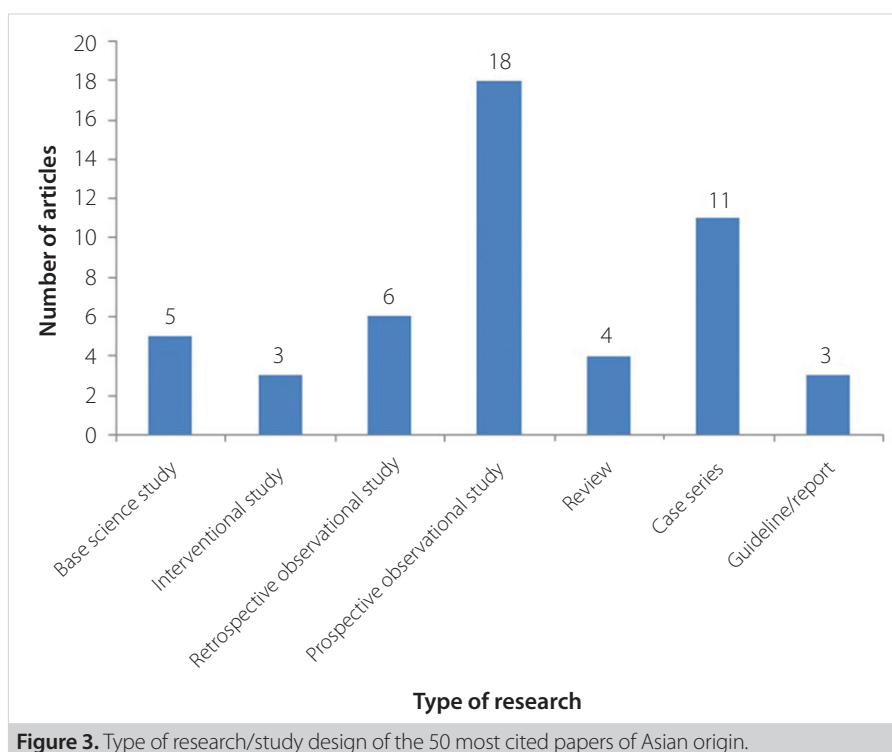
The most common studied topics was gastrointestinal (GI) surgery (n= 28) and surgical oncology (n= 26) (Figure 4). GI surgery and GI cancer remain the most studied topics even among top cited surgical and gastroenterology literature in the world respectively (6,33). This is not surprising, since the incidence of gastrointestinal cancer is highest in Asia (34) and it is the fifth most frequently diagnosed cancer worldwide (35). Japan has been a pioneer in the development of GI surgery. The con-

cept of Billroth gastrectomy, extended lymphadenectomy and lymph node metastasis in gastric cancer and right hepatectomy for hepatocellular carcinoma were all developed in Japan (36).

### Research Collaboration

Thirty-three articles (66%) in this list originated from a single institution, 11 (22%) had inter-institutional collaboration and 6 (12%) had national collaboration from countries outside Asia. None of the articles in this list had solely intra continental collaboration. These numbers are similar when compared to citation classics from surgery and its subspecialties around the world (6,8,15). It is widely accepted that international collaboration in surgical research can facilitate the conduction of research studies and improve the generalizability and applicability of the results (37). Asian countries should look at strengthening international research cooperation particularly with low and middle-income Asian countries to establish global standards for surgically treatable diseases.

There are limitations to this research. First, we used the WoS database to determine citation classics but excluded PubMed and Scopus, where the results may vary. Second, we did not correct for self-citations. However, self-citations have been shown to account for only <1% of total citations among top-cited papers (38). In addition, biases such as journal bias and omission bias



exist in this type of study which may exclude deserving articles. Third, citation classics exclude recently published landmark papers as accumulation of citations takes time, so the results may vary over time. Despite these limitations, we believe this analysis gives a fair idea about the history and landscape of Academic surgery in Asia.

## CONCLUSION

Citation classics remain the best way of looking at the most influential papers in the field of surgery. This paper highlights some of the most important contributions from the academic surgeons of Asia to the world. It offers an insight into the deve-

lopment of surgical specialty in Asia over time. This list should help early career surgeons for classical reading and experts in the field for having working knowledge of seminal contributions. In addition, this list should provoke interest in academic surgery and research collaboration with other nations in Asia and the rest of the world.

**Ethics Committee Approval:** Ethics committee approval is not required for this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - V.A.; Design - V.A.; Supervision - V.A.; Materials - V.A.; Data Collection and/or Processing - V.A.; Analysis and/or Interpretation - V.A.; Literature Review - V.A.; Writing Manuscript - V.A.; Critical Reviews - V.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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### ORJİNAL ÇALIŞMA-ÖZET

Türk J Surg 2021; 37 (2): 116-125

## Alıntı klasikleri: Asya'da cerrahide en çok alıntı yapılan 50 makale

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### ÖZET

**Giriş ve Amaç:** "Alıntı klasikleri" terimi, bilimsel literatürde çok alıntı yapılan makaleler için kullanılmaktadır. Atıf klasiklerini kullanarak akademik cerrahinin mevcut manzarasını ve Asya'ya ait yazarların bilimsel katkılarının kalitesini anlamayı amaçladık.

**Gereç ve Yöntem:** WoS çekirdek koleksiyon veritabanını "cerrahi" kategorisi altında araştırarak baş yazarı araştırma döneminde bir Asya ülkesine bağlı en çok alıntı yapılan 50 makaleyi dahil ettik. Her makale için şu özellikleri not ettik: toplam alıntılar, yıllık ortalama atıflar, yayın yılı, yayın yapan dergi, kurum ve ülke, dergi çeyreği ve etki faktörü, yazarlık, cerrahi araştırma alanı. Sonuçlar IBM SPSS Statistics v26 kullanılarak analiz edildi.

**Bulgular:** Alıntı sayısı 447 ile 1170 (ortalama  $\pm$  SD 616.9  $\pm$  150.16) ve yıllık atıflar 10.04 ile 98.17 (ortalama  $\pm$  SS 30.87  $\pm$  17.27) arasında değişmiştir. En verimli on yıl 1991-2000 yıllarıydı (n= 19 makale). Makalelerin çoğu "Annals of Surgery"de yayınlandı (%28). Dört yazar, baş yazar olarak iki veya daha fazla makaleye katkıda bulundu ve "Poon RTP" başı çekti. Japonya'nın katkısı en yüksek (%60) oldu ve onu Çin ve bakmakla yükümlü olduğu kişiler (%26) izledi. Hong Kong Üniversitesi lider kurumdur (n= 7). Gözlemsel çalışma en yaygın kullanılan tasarımdır (n= 24). Makalelerin çoğu gastrointestinal cerrahiye (n= 28) ve cerrahi onkolojiye (n= 26) aitti. Makalelerin %66'sı tek bir kurumdan geliyor, %22'si kurumlar arası işbirliğine ve %12'si Asya dışındaki ülkelere ulusal işbirliğine sahipti.

**Sonuç:** Çalışma, Asya'dan cerrahide en etkili makaleleri belirledi. Bu, akademik cerrahiye ve Asya'daki ve dünyanın geri kalanındaki diğer ülkelerle araştırma işbirliğine olan ilgiyi uyandırmalıdır.

**Anahtar Kelimeler:** Alıntı klasikleri, alıntılar, bibliyometri, cerrahi, Asya

**DOI:** 10.47717/turkjsurg.2021.5106



# The effect of obesity in laparoscopic transperitoneal adrenalectomy

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## ABSTRACT

**Objective:** Laparoscopic adrenalectomy is the gold standard for the resection of adrenal tumors. However, there are some technical difficulties, which may be due to the fact that adrenalectomy is rarely encountered in general surgery practice and has a high learning curve. In addition to these, obesity is another problem in laparoscopic adrenalectomies. In the present study, it was aimed to evaluate whether obesity affects perioperative and postoperative complications after laparoscopic adrenalectomy.

**Material and Methods:** This is a retrospective comparative study carried out between December 2008 and June 2018. A total of 65 patients who underwent laparoscopic transperitoneal adrenalectomy were divided into two groups according to their Body Mass Index (BMI). Patients' demographic data, perioperative and postoperative results were analyzed from hospital medical records.

**Results:** There were 30 non-obese and 35 obese patients. There was no significant difference between obese and non-obese patients in terms of operation time, perioperative complications and length of hospital stay. However, there was a statistically significant difference between the two groups for postoperative complications ( $p < 0.031$ ). There was conversion to open surgery in four obese patients and in one patient in the non-obese group.

**Conclusion:** In obese patients, technical difficulties may be encountered during surgery due to increased adipose tissue, and postoperative complication rates may increase. Nevertheless, laparoscopic transperitoneal adrenalectomy can be performed safely paying attention to the management of obesity-related complications.

**Keywords:** Adrenalectomy, body mass index, laparoscopy, obesity

## INTRODUCTION

Since the first laparoscopic adrenalectomy (LA) was done by Gagner et al. in 1992, laparoscopic removal of adrenal lesion has become the gold standard for the surgical management of most adrenal tumors (1). Current indications for LA are similar to open adrenalectomy and include all functional adrenal tumors; pheochromocytoma, aldosteronoma, cortisol producing adenoma (Cushing syndrome), bilateral adrenal hyperplasia secondary to Cushing's disease or ectopic ACTH production. Suspicious malignant tumors of the adrenal gland smaller than 5-6 cm in diameter, adrenal metastasis, primary adrenocortical carcinoma, symptomatic angiomyolipomas or cysts, and incidentalomas are the other indications of LA (2). Diagnosis of adrenal masses have increased with the advancement of diagnostic modalities in the last few decades. Laparoscopic adrenalectomy has gained popularity as time passed due to favorable operative field, fewer complications, decreased morbidity, better cosmetic result, less postoperative pain, faster recovery, shorter hospital stay and earlier return to daily activities (3). Several techniques have been described, the most popular are laparoscopic lateral transabdominal approach, posterior retroperitoneoscopic adrenalectomy and robotic adrenalectomy (4-6). Adrenalectomies are not common operations in general practice, so the surgery should be performed in centers with endocrine surgery experience.

Worldwide, it is estimated that there are approximately 1.9 billion overweight people, and of these, more than 650 million are obese. The prevalence of obesity approximately tripled between 1979 and 2016. Body mass index (BMI) is generally used for the diagnosis of obesity, a person's weight (in kilograms) divided by

**Cite this article as:** Altın Ö, Sari R. The effect of obesity in laparoscopic transperitoneal adrenalectomy. Turk J Surg 2021; 37 (2): 126-132.

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**Received:** 05.06.2020

**Accepted:** 07.03.2021

**Available Online Date:** 30.06.2021

© Copyright 2021 by Turkish Surgical Society Available online at  
www.turkjsurg.com

**DOI:** 10.47717/turkjsurg.2021.4901



the square of height (in meters). The diagnostic criteria of World Health Organization (WHO) for obesity is defined as  $BMI \geq 30 \text{ kg/m}^2$  (7). Obesity is often considered as a main factor for prolonged operation time, increased blood loss, septic complications and wound infection (8-10). In open surgery, visualization of the surgical field in obese patients is a major problem due to extensive of adipose tissue. In order to overcome this problem, larger incision is required. Obese patients suffer more pain and restriction for longer time due to large abdominal incision. Therefore, there is increased risk of atelectasis and other pulmonary complications in these patients (11,12). Moreover, obesity causes increased risk of wound infections as adipose tissue is hypoperfused and poorly oxygenated (13). Prolonged hospitalization is mostly due to worse perioperative and postoperative complications.

The aim of this study was to evaluate surgical outcomes of laparoscopic transperitoneal adrenalectomies performed in obese and non-obese patients.

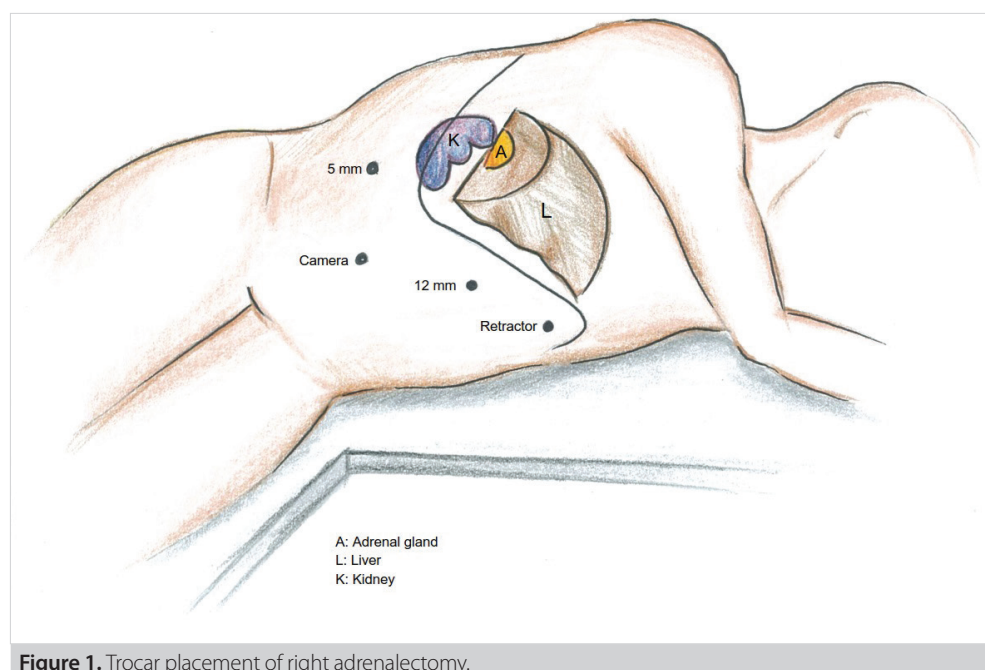
## MATERIAL and METHODS

In all patients, indications for surgery were according to the American Endocrine Surgeons and Endocrinologists guidelines; adrenal incidentalomas larger than 4 cm in diameter, functional tumors of any size (Cushing's syndrome, pheochromocytoma, Conn's syndrome or sex hormone producing tumor), and solitary adrenal metastases. Exclusion criteria included patients deemed high risk for laparoscopy by anesthesia and malignant tumors with radiological evidence of invasion of surrounding organs and tissues.

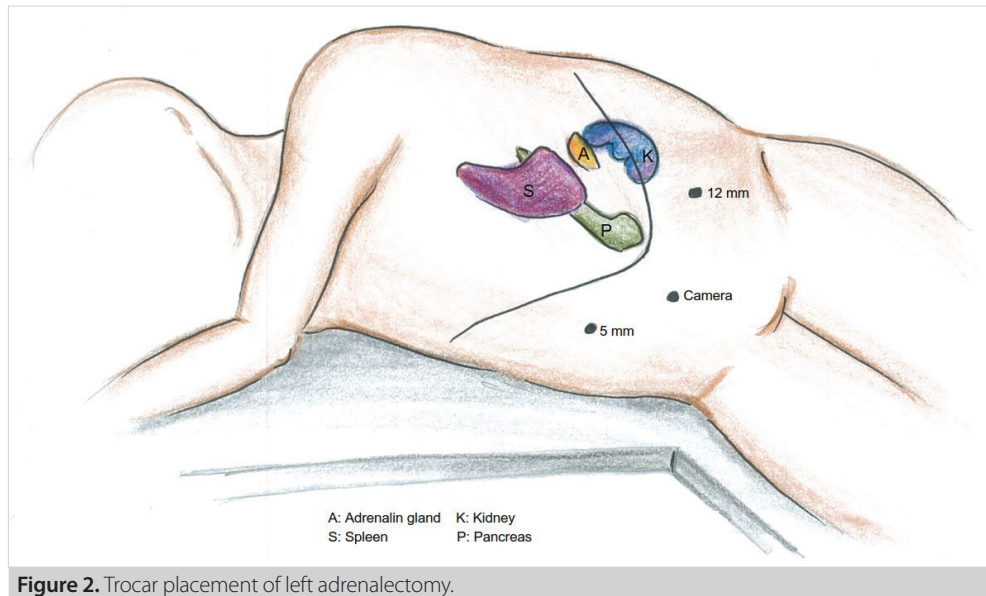
In this study, we divided the patients into 2 groups according to BMI: non-obese group ( $BMI < 30 \text{ kg/m}^2$ ) and obese group ( $BMI \geq 30 \text{ kg/m}^2$ ). All patients were assessed for the following parameters: demographics, indication for operation (preoperative diagnosis), tumor location, size, operation time, peroperative complications, conversion to open surgery, postoperative complications, hospital stay and postoperative histology.

## Surgical Technique

A lateral transabdominal technique was used for all laparoscopic adrenalectomies. The patients were placed in a lateral decubitus position with the tumor side up and the table flexed between the 12. rib and iliac crest. Four trocars were used for right-sided adrenalectomies (Figure 1), three trocars were used in almost all patients for left-sided adrenalectomies (only one patient needed four trocars) (Figure 2). A thirty-degree laparoscope was used in all the cases and pneumoperitoneum was maintained at 12-14 mmHg by insufflation with carbon dioxide ( $\text{CO}_2$ ). On the right side, the right lobe of the liver was mobilized to expose the inferior vena cava, and the triangular ligament was divided before placement of a liver retractor. Sharp and blunt dissection starts at the medial to the lateral edge of liver. Precaution is necessary to the vena cava inferior due to short course of adrenal vein. For the left sided adrenal gland tumor, the spleen, splenocolic ligament, and splenorenal ligament were dissected, and the tail of pancreas was mobilized to the medial on left side. Care is necessary to differentiate (not confuse) adrenal with the tail of pancreas because of similar tissue appearance, especially in obese patients. All specimens were placed in an endobag to be removed.



**Figure 1.** Trocar placement of right adrenalectomy.



**Figure 2.** Trocar placement of left adrenalectomy.

### Statistical Analysis

Data analysis and management were performed using SPSS for Windows ver. 21.0 software program (SPSS Inc., Chicago, IL). The data are expressed as mean  $\pm$  standard deviation or number (%). Differences between parameters were compared with the Fisher's exact test, Chi-square test ( $\chi^2$ ) and Mann-Whitney U test. All p values  $<0.05$  were considered statistically significant.

### RESULTS

A total of 65 patients (44 females and 21 males) underwent laparoscopic transperitoneal adrenalectomy. Patients were divided into two groups according to the BMI; non-obese (BMI  $< 30$ ) and obese group  $\geq 30$  kg/m<sup>2</sup>. The study included thirty (46.1%) patients in the non-obese group and 35 (53.9%) patients in the obese group. Mean age of the obese and non-obese group were 53 ( $\pm 9.9$ ) and 47.6 ( $\pm 14.7$ ) years, respectively. Mean tumor size of the obese group was 4.7 ( $\pm 1.8$ ) cm and 4.7 ( $\pm 2.8$ ) cm of the non-obese group. Preoperative diagnoses were Conn's and Cushing's syndrome (41 out of 65, 63%) in most of the patients. There were 25 and 32 comorbidities in the non-obese and obese group respectively, most of these comorbidities were hypertension and diabetes mellitus (Table 1).

There was no statistically significant difference between the obese and non-obese groups when we compared operation time, peroperative complication and length of hospital stay. Mean operative time was 90.5  $\pm$  21.4 minutes in the non-obese group and 100  $\pm$  24 minutes in the obese group. In the non-obese patients group, four peroperative complications (major bleeding from surgical field) occurred, and in one patient conversion to laparotomy was needed due to bleeding from right median adrenal vein. Major bleeding from surgical field was seen in five patients from the obese group and in two patients (of these

patients) we performed laparotomy due to inferior vena cava injury and intractable adrenal artery bleeding. The rate of conversion to laparotomy was 11.4% in the obese group and 3.3% in the non-obese group. The reasons of conversion to laparotomy were dense adhesions in two patients, profuse bleeding in two patients (one in non-obese and the other in obese group) and inferior vena cava injury in one patient. In patients who were converted to laparotomy, surgery was completed without any intraoperative mortality. In four obese patients, pleural effusion (two patients), deep vein thrombosis, and major postoperative hemorrhage requiring blood transfusion were seen as postoperative complications. Only one patient in the non-obese group needed blood transfusion postoperatively.

There was a statistically significant difference between two groups for postoperative complications ( $p < 0.031$ ). Postoperative complications were classified according to the Clavien-Dindo classifications. According to Clavien-Dindo classification; in the non-obese group, one patient had class 2 (blood transfusion), in the obese group, seven patients had class 2 (three blood transfusions, two pleural effusions, one upper extremity micro-emboli and one deep vein thrombosis) and one patient had class five complication. Although all patients were given deep vein thrombosis prophylaxis and anti-embolic stockings, one patient in the obese group died due to cardiopulmonary arrest (Table 2).

Postoperative histopathological diagnoses are listed in Table 3. Cortex adenoma was reported in most of patients (17 patients (56.6%) in non-obese and 28 patients (80%) in obese group). There was a case of cortex carcinoma in each group. Three patients, who previously underwent pneumonectomy for lung cancer, had radiologically confirmed isolated adrenal metastasis. These three patients were in the non-obese group, and their

**Table 1.** Patients' characteristics

	<30 kg/m <sup>2</sup>	≥30 kg/m <sup>2</sup>	p
	(n= 30)	(n= 35)	
Age	47.6 ± 14.7	53.0 ± 9.9	0.097
Female	15	29	0.007
Male	15	6	
ASA			0.072
ASA 2	14	23	
ASA 3	11	17	
Tumor location			
Right	17	14	0.218
Left	13	21	
Tumor size	4.7 ± 2.8	4.7 ± 1.8	0.993
Conn	8	9	
Cushing	4	18	
Cushing + hyperandrogenism	0	1	
Cushing + cholelithiasis	1	0	
Pheochromocytoma	4	2	
Pheochromocytoma + myolipoma	1	0	
Hyperandrogenism	1	0	
Incidentoloma	8	5	
Metastasis	3	0	
Morbidity			0.455
No	5	3	
Yes	25	32	

ASA: American society of anesthesiologist.

**Table 2.** Perioperative and postoperative results

	Non-obese (n= 30)	Obese (n= 35)	p
Operation time	90.5 ± 21.4	100 ± 24.0	0.100
Perioperative complications			1.000
No	26	30	
Yes	4	5	
Bleeding	4	4	
Vena cava inferior injury	0	1	
Conversion to open surgery	1	4	0.362
Right	1	3	
Left	0	1	
Postoperative complications			0.031
No	29	27	
Yes	1	8	
Clavien-Dindo Class 2	1	7	
Blood transfusion	1	3	
Pleural effusion	0	2	
Microembolism of Upper extremity	0	1	
Deep vein thrombosis	0	1	
Clavien-Dindo Class 5	0	1	
Length of hospital stay, mean ± SD (days)	2.5 ± 1.3	3.1 ± 1.3	0.089

**Table 3.** Postoperative histopathology

	<30 kg/m <sup>2</sup> (n= 30)	≥30 kg/m <sup>2</sup> (n= 35)
Cortical adenoma	17	28
Cortical adenoma + myolipoma	0	1
Metastasis	3	0
Ganglioneuroma	2	0
Pheochromocytoma	4	2
Pheochromocytoma + Ganglioneuroma	0	1
Cyst	1	1
Cystic lymphangioma	1	0
Myolipoma	1	0
Cortex carcinoma	1	1
Nodular hyperplasia	0	1

adrenal metastasis were resected laparoscopically without any complication.

## DISCUSSION

Over the last few decades, obesity has increased in the world posing new surgical difficulties. Obesity is commonly regarded a risk factor for surgical complications, even though many studies have shown contradicting results (14-19).

The difficulties of surgical procedures in obese patients have been previously described. There are concerns regarding laparoscopic adrenalectomy (LA) in morbidly obese patients because of the associated limited working space and increased risk of postoperative complications (20). Studies have shown comparable perioperative and postoperative results in obese versus non-obese patients after laparoscopic operations (laparoscopic appendectomy, cholecystectomy, hernia surgery, colorectal surgery and antireflux surgery) (21-25). It is unclear why complication incidences vary in LA, this difference may be due to specific organs that are manipulated in the course of operation. Particularly, in left-sided adrenal tumors, splenic flexure mobilization is required, which may lead to spleen injury. This maneuver may be more difficult in obese patients due to increased adipose tissue.

In our study, we used the lateral transabdominal technique. The most important advantages of this surgical approach are wide surgical field visualization and allowing for the resection of larger adrenal tumors.

The aim of this study was to evaluate perioperative and postoperative LA results in obese and non-obese patients. In 51 consecutive patients, Erbil et al have found a positive correlation between BMI and operating time, postoperative complications and hospital stay, suggesting that increased amount of adipose tissue is responsible for these findings (26). On the other side, Inaishi et al. have found that there were not statistically significant

differences between obese and non-obese patients in operation time, length of hospital stay, conversion to open surgery (16). They have also determined that there were no statistically significant differences in perioperative and postoperative results of obese and non-obese patients; however, BMI ≥ 25 kg/m<sup>2</sup> was the obesity criterion in their study which was a limiting factor (16). Dancea et al. have showed no statistically significant difference regarding age and operating time, but showed statistically significant difference in perioperative and early postoperative complications between obese and non-obese groups. (27). In our study, there was no statistically significant difference between groups in operating time, perioperative complications and length of hospital stay, but for the postoperative complications there was statistically significant difference between the two groups. In the obese group, three patients required blood transfusion postoperatively (two patients whose operation were completed laparoscopically and one patient who needed conversion to open) due to massive hemorrhage during operation. There was pleural effusion in two patients whose operations were completed through conversion to laparotomy (right subcostal incision). These patients reported more pain that limited effective respiratory exercise. One of the laparotomy patients had deep vein thrombosis possibly due to immobility. One laparoscopy patient had unexplained microembolism of the upper extremity. In the obese group, one patient whose operation was completed laparoscopically, had Clavien-Dindo class 5 (patient died due to cardiopulmonary arrest) complication.

In this study, conversion to open surgery was high in the obese group, but with rates similar to conversion rates in other related studies. In the literature, the most common perioperative complication of LA is bleeding, which is also the most common reported reason for conversion to open surgery (27-29). In our study, the reasons of conversion were dense adhesions in two

patients who had previously undergone abdominal surgery, laparoscopically intractable hemorrhage in two patients (one patient in each of the groups) and one case of inferior vena cava injury. In one patient, it was difficult to differentiate the separate the tail of the pancreas from left-sided adrenal tumor (2.1 cm). Before the surgery, surgeons should carefully evaluate the patients for previous laparotomies and the adrenal mass size. In obese patients, the surgeon may face the challenge of differentiating small size adrenal mass from adipose tissue or may even confuse the tail of the pancreas with the adrenal tissue of similar appearance. Before the resection of the adrenal tumor, anatomic landmarks such as pancreatic tail, aorta, medial and inferior adrenal artery, renal artery, renal vein should be well mapped for left-sided resection. For the right-sided resection, inferior vena cava, median, superior and inferior adrenal artery and vein should be exposed as important anatomic landmarks.

Although the rate of conversion to laparotomy was higher in the obese group ( $n=4$ , 11.7%) when compared to the non-obese group ( $n=1$ , 3.3%), the reasons for conversion to laparotomy were not directly related to obesity. Conversion to laparotomy was directly linked to obesity in only one patient, in whom it was difficult to tell apart the tail of the pancreas and a small mass of the adrenal gland obscured by dense adipose tissue. In our study, most of the perioperative complications were due to previous laparotomy not obesity.

Our study has several limitations. First, this was a single-center study with a retrospective design. Second, there were small number of patients causing relatively high conversion rate in the obese group.

## CONCLUSION

Obesity has no influence on operation time, preoperative complication and length of hospital stay. In obese patients, technical difficulties may be encountered during surgery due to increased adipose tissue, and postoperative complication rates may increase. Nevertheless, laparoscopic transperitoneal adrenalectomy can be performed safely in obese patients paying attention to the management of obesity-related complications.

**Ethics Committee Approval:** This approval for this study was obtained from Kartal Dr. Lütfi Kırdar Training and Research Hospital Clinical Research Ethics Committee (Decision No: 2019/514/146/4, Date: 28.01.2019).

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - Ö.A.; Design - R.S.; Supervision - Ö.A.; Data Collection and/or Processing - Ö.A.; Analysis and/or Interpretation - R.S.; Literature Review - Ö.A.; Writing Manuscript - R.S.; Critical Reviews - Ö.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 (2): 126-132

## Laparoskopik transperitoneal adrenaletomide obezitenin etkisi

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### ÖZET

**Giriş ve Amaç:** Laparoskopik adrenaletomi adrenal tümörlerin rezeksiyonu için altın standarttır. Ancak genel cerrahi pratiğinde nadiren rastlanması, öğrenim eğrisinin yüksek olması gibi bazı teknik zorlukları vardır. Bunlara ek olarak, obezite de laparoskopik adrenaletomide bir başka sorundur. Biz bu çalışmamızda obezitenin laparoskopik adrenaletomide perioperatif ve postoperatif komplikasyonlara olan etkisini değerlendirmeyi amaçladık.

**Gereç ve Yöntem:** Çalışmaya Aralık 2008 ve Haziran 2018 tarihleri arasında opere edilen hastalar dahil edildi. Laparoskopik transperitoneal adrenaletomi uygulanan toplam 65 hasta vücut kitle indeksine (VKİ) göre iki gruba ayrıldı. Hastaların demografik verileri, perioperatif ve postoperatif sonuçlarının kayıtları analiz edilerek gruplar karşılaştırıldı.

**Bulgular:** Toplam 35 obez ve 30 obez olmayan hasta değerlendirildi. Obez ve obez olmayan hastalar arasında ameliyat süresi, perioperatif komplikasyonlar ve hastanede kalış süreleri açısından anlamlı fark yoktu. Ameliyat sonrası komplikasyonlar açısından ise iki grup arasında istatistiksel olarak anlamlı bir fark gözlemlendi ( $p < 0,031$ ). Obez grubunda dört hastada, obez olmayan grupta ise bir hastada açık cerrahiye geçildi.

**Sonuç:** Obez hastalarda artan yağ dokusu nedeniyle ameliyat sırasında teknik zorluklarla karşılaşılabilir ve postoperatif komplikasyonlarda artış görülebilir. Buna rağmen obeziteye bağlı komplikasyonların yönetimine dikkat edilerek laparoskopik transperitoneal adrenaletomi güvenli bir şekilde uygulanabilir.

**Anahtar Kelimeler:** Adrenaletomi, vücut kitle indeksi, laparoskopi, obezite

**DOI:** 10.47717/turkjsurg.2021.4901





# Awareness and wound assesment decrease surgical site infections

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## ABSTRACT

**Objective:** Various surveillance methods have been described for surveillance of surgical site infections (SSI). The aim of this study was to examine practicality of SSI risk assessment methods (SENIC and NNIS) with a postoperative wound monitoring scale (ASEPSIS) as an outcome assessment measure and evaluation of the contribution of wound assesment to the reduction of wound infection.

**Material and Methods:** Patients were followed with a prospective data chart through four year. Correlation of SENIC and NNIS together with ASEPSIS were performed.

**Results:** During the study period, 275 SSI occurred. SSIs were determined within the 21 days-period after operations. Correlation between SENIC with ASEPSIS ( $rs=0.41$ ,  $p<0.001$ ) was found better than that for NNIS with ASEPSIS ( $rs=0.37$ ,  $p<0.001$ ). Type of operation (emergency vs. elective), body mass index, operation class and American Society of Anesthesiologists scores were found independently predictive factors for SSI. The forth year SSI rate was found to be significantly lower than the other years ( $p<0.001$ ).

**Conclusion:** This study indicates weak but significant correlation between preoperative risk assessment methods for SSI and ASEPSIS method. In addition, surgical wound assesment and awarness of the wound infection rates, have decreased the SSI rates over the years.

**Keywords:** Asepsis, senic, SSI, nnis

## INTRODUCTION

Surgical site infection (SSI) continue to be the one of the most common nosocomial infection, accounting for more than 20% of all hospital-acquired infections (1). The incidence of SSI is 2% to 5% in patients undergoing surgery, which is the most common nosocomial infection in surgical patients, accounting for 38% of nosocomial infections in this patient population (2,3). Surgical site infections are associated with increased length of stay results in an additional cost and a 2- to 11-fold increase in the risk of mortality. Since SSIs can be preventable up to 60% by using evidence-based measures, accurate surveillance of wound complications has become a pay-for-performance metric and a target of quality-improvement efforts.

For this purpose, The Study on the Efficacy of Nosocomial Infection Control (SENIC) and the National Nosocomial Infections Surveillance (NNIS) system methods have been used predominantly for risk assessment of surgical wounds postoperative wound monitoring (4,5). Since the most important step in surgical site infections is the recognition and definition of the infection; standardized, objective, traceable and easily applicable surveillance systems are required. It has been revealed that the scoring system with all these features is the "ASEPSIS" scoring defined by Wilson (6,7). The main objective of this study was to examine corelation of NNIS and SENIC methods with ASEPSIS wound scoring method as an outcome assessment measure. In addition, factors affecting development of SSIs in different types of general surgical operations were investigated.

**Cite this article as:** Akin M, Topaloğlu S, Özel H, Avşar FM, Akin T, Polat E et al. Awareness and wound assesment decrease surgical site infections. Turk J Surg 2021; 37 (2): 133-141.

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Received: 21.09.2020

Accepted: 13.03.2021

Available Online Date: 30.06.2021

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DOI: 10.47717/turkjsurg.2021.5059

## MATERIAL and METHODS

A total of 2339 surgical procedures, excluding local and proctological procedures, were performed in our clinic (First Department of Surgery) in Ankara Numune Training and Research Hospital within four years. Prospective wound surveillance has been practiced for all patients having a surgical operation. The study protocol was approved by the local ethics committee.

A data chart including patient's risk index and postoperative wound monitoring is used to follow all surgical wounds. All charts are followed and completed by a senior resident and a senior staff surgeon in our department.

SENIC and NNIS indexes were used together for risk assessment of SSI. The SENIC risk index includes measurement of wound contamination and a proxy for the patient's susceptibility to infection. The NNIS risk index quantifies intrinsic and extrinsic measures of patient risk for developing an SSI. Both SENIC and NNIS indexes were evaluated according to the Table 1 and 2.

During wound surveillance, operations are classified into four categories according to their invasiveness. Surgical procedures in which the abdominal cavity is not entered (group 1); abdominal operations (excluding liver and major retroperitoneal operations) (group 2); thoracic operations (group 3); liver surgery and retroperitoneal operations (group 4) (9).

SSIs were evaluated according to the latest modifications of the Centers for Disease Control and Prevention (CDC) and ASEPSIS method (6,7,10). The wound of each patient was evaluated daily by the surgeon and recorded. The wound was evaluated at 14., 17. and 21. days postoperatively in the absence of significant wound infection. Patients discharged without SSI, were checked by the resident surgeon in the postoperative first month and third month at the outpatient clinic.

Postoperative wound evaluation was made using the ASEPSIS method (Table 3). While scores between 0 and 5 were given for erythema and serous discharge in the wound; Scores between 0 and 10 were given for purulent discharge and wound dehiscence. Scoring was made according to the ratio of the present symptom to the wound area. This scoring was made for five days of the first seven days postoperatively. Extra points for five-day scoring in cases of antibiotic use (10 points), drainage with local anesthesia (5 points), debridement under general anesthesia (10 points), wound culture positiveness (10 points) and no wound healing in 14 days (5 points) was added (6,7,11). The wounds are classified into five categories according to overall scores (Table 3). When the total score score was above 20, it was considered to have wound infection. Infected wounds were followed up until surgical infection regressed.

**Table 1.** SENIC SSI risk index

Variable	SENIC risk index criteria for presence of a risk factor*
Wound class, i.e., clean, clean-contaminated, Contaminated or dirty	Contaminated or dirty infection. If present, scores 1 point
Type of operation	Abdominal operation. If present, scores 1 point
Duration of operation	Operation lasting longer than 2 hours. If present, scores 1 point
Discharge diagnosis	Patient having $\geq 3$ discharge diagnoses. If present, scores 1 point
*Risk index is obtained by summing the scores of the individual variables. Ranges from 0 to 4.	

**Table 2.** NNIS SSI risk index

Category	Variable	NNIS risk index criteria for presence of a risk factor*
Intrinsic degree of microbial contamination of the surgical site	Wound class, i.e. clean, clean-contaminated, contaminated or dirty	Contaminated or dirty infection. If present, scores 1 point
Duration of an operation	Time, in hours, of the duration of the surgical procedure from skin incision to skin closure	Length of operation $>T$ hours where T is the approximate 75. percentile of the duration of the surgical procedure. T is a surgical procedure-specific parameter. If present, scores 1 point
Makers for host susceptibility	American Society of Anesthesiologists (ASA) Physical Status Classification	ASA score 3, 4, or 5 If present, scores 1 point
*Risk index is obtained by summing the scores of the individual variables. Ranges from 0 to 3.		

**Table 3.** Brief description of the ASEPSIS method

Points scale for the daily wound inspection						
	Proportion of wound affected (%)					
Wound characteristic	0	<20	20-39	40-59	60-79	>80
Serous exudate	0	1	2	3	4	5
Erythema	0	1	2	3	4	5
Purulent exudate	0	2	4	6	8	10
Separation of deep tissues	0	2	4	6	8	10
The wound score: ASEPSIS						
Criterion points	Points					
Additional treatment						
Antibiotics	10					
Drainage of pus under local anesthesia	5					
Debridement of wound (general anesthesia)	10					
Serous discharge*	Daily 0-5					
Erythema*	Daily 0-5					
Purulent exudate*	Daily 0-10					
Separation of deep tissues*	Daily 0-10					
Positive culture	10					
Length of stay over 14 days	5					
Classification of SSI according to ASEPSIS method						
Category of infection	Total score					
Satisfactory healing	0-10					
Disturbance of healing	11-20					
Minor wound infection	21-30					
Moderate wound infection	31-40					
Severe wound infection	>40					

\* Given score only on 5 of first 7 postoperative days.

### Statistical Analysis

Patients were divided into two groups as those with and without SSI, and bivariate analysis was performed, and all significance tests were performed with two-tailed. Comparative analysis of variables was done using the  $\chi^2$  test. Correlation analysis between SENIC, NNIS, ASEPSIS methods was performed using Spearman correlation coefficient. The development of SSI was accepted as the dependent variable and multivariate analysis was performed by applying logistic regression using Wald statistics. In the multivariate analysis, those with a p value under 0.25 among the independent variables effective in the development of SSI, which were previously determined in the bivariate analysis, were used. All logistic regression results are given as odds ratio (OR) and with a 95% confidence interval (CI). All p values were two-tailed and  $p \leq 0.05$  values were considered significant.

### RESULTS

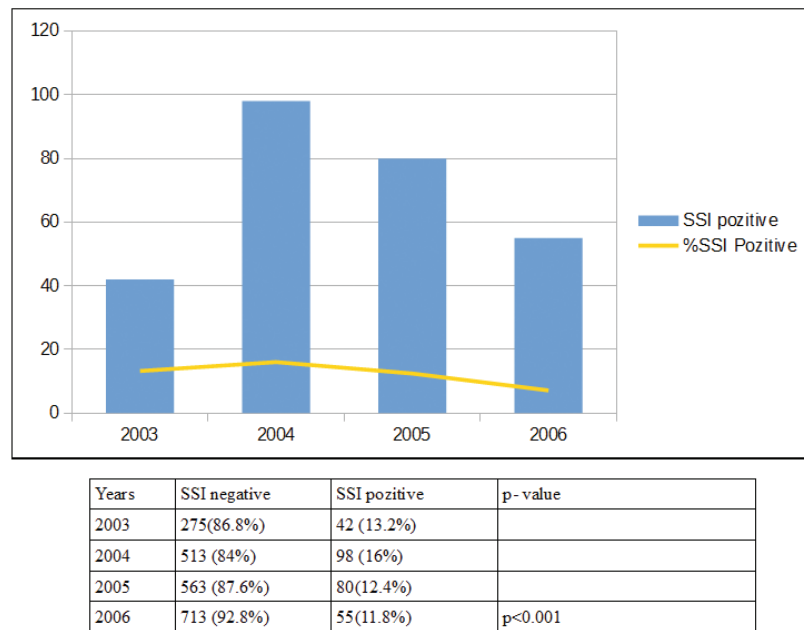
During the study, a total of 2339 patients, 1108 (47.4%) male and 1231 (52.7%) female, were operated. The average age of the patients was 47.9 (range 6 to 95) years. All patients were followed

for 21 days. This rate was 95% at 30-day follow-up, and 86% at three-month follow-up. Average BMI was 25.9 (range 15.6 to 55.5). Of all operations, 88.4% were elective. During the study, 19 different operations were performed. Most operations were included in group 2 (49%,  $n=1147$ ) (Table 4).

Approximately 90% of the patients were scored as ASA II or ASA III. 84.7% of the operations were performed under general anesthesia. During the study, 275 SSIs were occurred (11.8% of 2339 operations). All SSIs developed within the postoperative 21-day period. SSI rates through years has shown at figure 1 and the decrease at forth year was statistically significant. While the SSI rate was 9.5% at elective operations, it was 28.3% for emergency operations ( $p < 0.001$ ). SSI occurred in 1.7% in group 1 operations, 16.4% in group 2 operations, and 37.2% in group 4 operations ( $p < 0.001$  among all groups). 134 of 275 patients had culture positive SSI (48.7%). While this rate was 4.6% in elective operations, it was 13.6% in emergency operations. In general, a single microorganism isolated from the wound (75.1%), and most of them were *Escherichia coli* (45.5%) (Table 5).

**Table 4.** Class of operation

Operation	Group	n, (%)
Thyroidectomy	Group 1	376 (16.1)
Pilonidal sinus surgery	Group 1	139 (5.9)
Modified radical mastectomy	Group 1	45 (1.9)
Inguinal hernia repair	Group 1	450 (19.2)
Inguinal hernia repair and Umbilical hernia repair	Group 2	6 (0.3)
Incisional hernia repair	Group 2	134 (5.7)
Incisional hernia repair and Cholecystectomy	Group 2	18 (0.8)
Umbilical hernia repair	Group 2	71 (3)
Umbilical hernia repair ve Cholecystectomy	Group 2	30 (1.3)
Appendectomy	Group 2	133 (5.7)
Gastrectomy and Repair of peptic ulcer perforation	Group 2	123 (5.2)
Splenectomy	Group 2	18 (0.8)
Colon resection and cholecystectomy (excluding retroperitoneal resection)	Group 2	20 (0.1)
Cholecystectomy	Group 2	579 (24.8)
Small intestine operations	Group 2	14 (0.6)
Liver hydatid cyst surgery	Group 4	68 (2.9)
Colon or rectum resection (including retroperitoneal resection)	Group 4	107 (4.6)
Pancreatectomy	Group 4	8 (0.3)
Liver hydatid cyst surgery and cholecystectomy	Group 4	9 (0.4)

**Figure 1.** SSI rates through years.

Patients were compared as with and without SSI. As BMI, age, and ASA scores increased, SSI rates also increased (Table 6). However, there was no difference in SSIs between men and women. Class of operation (group 1, 2 or 4), type of operation (elective or emergency), and type of anesthesia also affected the development of SSI. NNIS and SENIC risk indexes were as-

signed in the preoperative period. Correlation between the SENIC risk index with the ASESIS ( $r_s = 0.41$ ,  $p < 0.001$ ) and a correlation between the NNIS risk index with the ASESIS ( $r_s = 0.37$ ,  $p < 0.001$ ) were found to be statistically significant.

After bivariate analysis, BMI, age, ASA score, type and class of operation were selected as variables, since p values were  $< 0.25$

**Table 5.** Microbial isolates from surgical wound infections

Species	Isolates (%)
<i>Escherichia coli</i>	61 (30.3)
MRSA*	21 (10.4)
Group D <i>enterococcus</i>	21 (10.4)
<i>Pseudomonas aeruginosa</i>	19 (9.4)
<i>Bacteriodes fragilis</i>	17 (8.4)
<i>Klebsiella pneumoniae</i>	17 (8.4)
Coagulase-negative <i>Staphylococcus</i>	14 (6.9)
<i>Fusobacterium</i> species	11 (5.4)
$\alpha$ -Hemolytic <i>streptococcus</i>	10 (4.9)
<i>Proteus mirabilis</i>	9 (4.4)
<i>Acinetobacter</i> species	8 (3.9)
<i>Candida albicans</i>	1 (0.4)

\* MRSA: Methicillin-resistant *Staphylococcus aureus*.

in the SSI development association, for logistic regression analysis. In this study, type of operation (emergency versus elective), BMI, operation class and ASA score were found to be independent variables in SSI development (Table 7).

## DISCUSSION

Postoperative SSI is the most serious cause of morbidity and sometimes mortality. Comparison of the quality of surgical care provided among all health institutions is often made by considering the infection rates. Such comparisons are only valid if standard SSI definitions are made and permanent follow-up methods are used. Indexes indicating the risk of developing SSI, such as SENIC and NNIS, have been developed to compare patients' intrinsic and extrinsic risk factors between hospitals (12,13). The SENIC risk index alone determines SSI risk better than wound classification. However, the SENIC index alone cannot determine the risk according to the type of operation. The NNIS risk index is a modification of the SENIC risk index. Some deficiencies in the SENIC system are corrected with the NNIS index. These two indexes can be used individually in studies on SSI or together, as in this study (14,15).

The diagnosis of SSI is a routine part of clinical practice. However, it is much more important to determine the severity of the infection. Recognizing the wound infection alone may be sufficient to treat the patient, but some standard criteria are needed in order to be able to take prophylactic measures and to be objective in wound follow-up. In the surgical ward, many wounds that drain "serous fluid" with wound edge separation may not be recorded as SSIs, particularly if no cultures were taken. Therefore, more objective and realistic wound assessment methods were needed. The advantages of the ASEPSIS method are that it is objective, realistic and productive, and can determine the severity of the SSI. A valid infection comparison between hospitals can be made with the ASEPSIS method (11,16).

The infection rate seen in group 1 (1.68%) can be compared with other reports. In the report published by NNIS in 2001, median rates of wound infection for mastectomy ranged from 0.72% to 1.65%, and those for herniorrhaphy ranged from 0.64% to 3.33% (3). In group 2 operations, the SSI rates (16.4%) in this study were found to be higher than the NNIS reports. According to NNIS, the lowest infection rate in this group was seen in cholecystectomies (0.00%-3.08%), whereas the highest rate was observed in colon surgery (3.57% -12.88%). In group 4 operations, the rate of SSI was found higher than both NNIS and other reports (37.2%) (3,18).

During the study, all SSI's occurred within 21 days. In the literature, follow-up time varies in different studies. Some authors recommend at least 30 days for a close follow-up period (18,19). Others propose limited surveillance of wound status (20–22). In this study, ASEPSIS method was applied according to Wilson's original definition (7). The main reason of our limited follow-up period is the improvement on the cost-effectiveness of wound surveillance. The patient concordance to the follow-up program is also another problem, as observed in our study. A similar description of SSI status, after percutaneous endoscopic gastrostomy, was reported in a recent study from United Kingdom (20). In this report, the authors followed surgical wounds up to 28 days using the ASEPSIS method, which has been discussed in the surgical literature since the first report in 1986. In the articles published by Smyth and Emmerson (21) and another one published by Mangram (22) the follow-up period was proposed 21 days, (3-weeks). Therefore, the time points for wound control in the current study were chosen based on these papers (23). A 21-day surveillance period for SSIs seems adequate for a wide range of general surgical procedures.

In this study, the significance of age, BMI, ASA score, class and type of operation and type of anesthesia in relation to the de-

**Table 6.** Bivariate analysis of the parameters according to status of infection

Characteristic	No wound infection (ASEPSIS ≤20)	Wound infection (ASEPSIS ≥21)	p
Number	2064	275	
Age	46.2 ± 16.16	54.5 ± 15.98	<0.001
Gender			0.714
Female	1090 (52.8)	142 (51.6)	
Male	974 (47.2)	133 (48.4)	
BMI	25.6 ± 3.57	27.0 ± 5.57	<0.001
NNIS			<0.001
0	1286 ( 62.3)	53 (19.3)	
1	690 (33.4)	111 (40.4)	
2	72 (3.5)	71 (25.8)	
3	16 (0.8)	40 (14.5)	
SENIC			<0.001
0	991 (48.0)	16 (5.8)	
1	931 (45.1)	118 (42.9)	
2	123 (6.0)	97 (35.3)	
3	19 (0.9)	40 (14.5)	
4	0	4 (1.5)	
ASA			<0.001
I	189 (9.2)	8 (2.9)	
II	1135 (55.0)	76 (27.7)	
III	704 (34.1)	164 (59.6)	
IV	36 (1.7)	27 (9.8)	
Class of operation			<0.001
Group 1	989 (47.9)	17 (6.2)	
Group 2	958 (46.4)	189 (68.7)	
Group 3	1 (0.1)	-	
Group 4	116 (5.6)	69 (25.1)	
Type of operation			<0.001
Elective	1869 (90.6)	198 (72)	
Emergency	195 (9.4)	77 (28)	
Type of anesthesia			<0.001
General	1719 (83.3)	262 (95.4)	
Spinal	245 (11.9)	11 (4.0)	
Epidural	83 (4.0)	1 (0.3)	
Spinal and epidural	17 (0.8)	1 (0.3)	

\*Values of age and BMI were expressed as mean ± SD. Percentages were shown in parenthesis.  
 BMI: Body mass index, ASA: Anesthesia Society of America.

velopment of SSI was clearly shown in bivariate analysis. BMI, ASA score and class and type of operation were found as independent risk factors for according to logistic regression analysis. These results are concordant with other studies. The relationship between emergency operations and SSI has been also shown in a study from Denmark (24). In their study, less SSI (6%) was found in elective GIS operations compared to emergency GIS operations (16%) . The relationship between obesity and SSI is well doc-

umented (25,26). Age and ASA score are considered as independent variables in the development of SSI (18). The role of general anesthesia on SSI pathogenesis is not fully understood yet. Until recent studies, a negative effect of general anesthesia on wound healing was not shown, however, recent studies have shown that general anesthesia may be a risk factor for the development of SSI (27,28). In this study, the low number of patients undergoing regional anesthesia led to bias among type of anesthesia.



**Table 7.** Multivariate logistic regression analyses of output parameters (SSI)

Independent predictors	OR	CI	p
AGE	0.99	0.98-1.00	0.426
BMI	1.06	1.03-1.10	<0.001
ASA Score (I-IV)	2.59	1.89-3.55	<0.001
Type of operation (elective or emergency)	3.06	2.13-4.42	<0.001
Operation class*			<0.001
Group 2	7.8	4.46-13.88	<0.001
Group 4	28.5	15-18-53.72	<0.001

BMI: Body mass index, ASA: Anesthesia Society of America, OR: Odds ratio, CI: Confidence interval.  
 \* 1 patient of group 3 is excluded from multivariate analysis.

With the SENIC project that started in 1974, it has been shown that nosocomial infections decreased by one third by following up nosocomial infections and informing the hospital staff of their results (6). As in the study of Haley et al., in our study comparing the SSI rates of first year with the increased rates of second and third year was because of the correct recognition of SSI; And the decrease in the fourth year has been thought as a result of the clinical physicians' more careful, in terms of SSI in the perioperative period. During this study we also recognised that especially at education hospitals postoperative wound assessment must be the one of the main subjects to be taught to surgical residents, as SSIs can be preventable more than 50% just with assessment. In this sense, we believe that it will be beneficial for surgical units to share their own SSI results with clinical or hospital staff, and to reduce SSI rates by both continuing awareness and monitoring risk factors by reminding them.

In our study, the SENIC risk index was found to have a better correlation with the ASEPIS wound tracking scale than the NNIS risk index. However, rs values of both indexes are below 0.75. This shows a weak relationship between parameters. New studies should be conducted to increase the sensitivity and specificity of these indexes. The number of wound infections calculated according to the ASEPIS method includes delay in wound healing, minor, moderate and severe wound infections. Depending on these differences, the calculated number of SSIs may be higher than other SSI classification systems.

In conclusion, higher than expected rate of surgical wound infection for group 2 and 4 classes of operations were found in this study. This difference is due to intrinsic and extrinsic conditions of the study era. A weak correlation was found between the preoperative risk index scales for SSI (NNIS and SENIC) and the ASEPIS method. In fact, the SENIC index has been modified with NNIS, but the fact that the ASEPIS method has a weaker correlation with NNIS has shown the necessity of developing NNIS. The application of ASEPIS method to postoperative pa-

tients is found simple and repeatable. Surveillance tasks with feedback to clinical surgery staff are considered to be important in the care of patients.

**Ethics Committee Approval:** The approval for this study was obtained from Ankara City Hospital No. 1 Clinical Research Ethics Committee (Decision No: E1-21-1643, Date: 17.03.2021).

**Peer-review:** Externally peer-reviewed.

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

**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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**ORJİNAL ÇALIŞMA-ÖZET**

Turk J Surg 2021; 37 (2): 133-141

**Farkındalık ve yara yeri takibi cerrahi alan enfeksiyonlarını azaltıyor**Merve Akin<sup>1</sup>, Serdar Topaloğlu<sup>2</sup>, Hakan Özel<sup>1</sup>, Fatih M. Avcı<sup>1</sup>, Tezcan Akin<sup>1</sup>, Erdal Polat<sup>3</sup>, Erdem Karabulut<sup>4</sup>, Süleyman Hengirmen<sup>5</sup><sup>1</sup> Ankara Şehir Hastanesi, Genel Cerrahi Kliniği, Ankara, Türkiye<sup>2</sup> Karadeniz Teknik Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalı, Trabzon, Türkiye<sup>3</sup> Kartal Koşuyolu Yüksek İhtisas Eğitim ve Araştırma Hastanesi, Gastroenterolojik Cerrahi, İstanbul, Türkiye<sup>4</sup> Hacettepe Üniversitesi Tıp Fakültesi, Biyoistatistik Anabilim Dalı, Ankara, Türkiye<sup>5</sup> Ankara Numune Eğitim ve Araştırma Hastanesi, Genel Cerrahi Kliniği, Ankara, Türkiye**ÖZET**

**Giriş ve Amaç:** Yara yeri enfeksiyonları için birçok takip metodu tanımlanmıştır. Bu çalışmanın amacı cerrahi alan enfeksiyonlarının da (CAE) risk belirleme metodları olan SENIC ve NNIS ile postoperatif yara takip skalası olan ASEPSIS'in karşılıklı olarak değerlendirmesi ve yara takibinin yara yeri enfeksiyonun azalmasına katkısının değerlendirilmesi

**Gereç ve Yöntem:** Kliniğimizde dört yıl boyunca ameliyat olan hastalar prospektif olarak izlendi. SENIC, NNIS, ve ASEPSIS metodlarına göre kayıtlar tutuldu.

**Bulgular:** Çalışma süresince 275 CAE oluştu. CAE operasyondan sonraki 21 günlük süre içinde belirlendi. SENIC ve ASEPSIS arasındaki ilişki ( $rs=0,41$ ,  $p<0,001$ ); NNIS ile ASEPSIS arasındaki ilişkiden ( $rs=0,37$ ;  $p<0,0001$ ) daha uyumlu bulundu. Operasyon tipi (acil ve elektif), vücut-kitle indeksi (BMI), operasyon sınıfı ve Amerikan Anestezyoloji Derneği (ASA) skoru CAE için bağımsız faktörler olarak belirlendi. Dördüncü yıl CAE oranı diğer yıllara göre anlamlı olarak az bulundu ( $p<0,001$ ).

**Sonuç:** Bu çalışma preoperatif risk belirleme skalaları ile ASEPSIS metodu arasında zayıf ama anlamlı bir ilişki olduğunu belirtmektedir. Ayrıca yara takibinin yapılması ve yara yeri enfeksiyon oranlarının bilinmesi yıllar içinde CAE oranlarını azaltmıştır.

**Anahtar Kelimeler:** Asepsis, senic, cae, nnis

**DOI:** 10.47717/turkjsurg.2021.5059



# Minimally invasive versus open surgery for gastric cancer in Turkish population

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## ABSTRACT

**Objective:** In this study, it was aimed to compare short-term outcomes of minimally invasive and open surgery for gastric cancer in the Turkish population carrying both European and Asian characteristics.

**Material and Methods:** Short-term (30-day) outcomes of the patients undergoing minimally invasive and open gastrectomy with D2 lymphadenectomy for gastric adenocarcinoma between January 2013 and December 2017 were compared. Patient demographics, history of previous abdominal surgery, comorbidities, short-term perioperative outcomes and histopathological results were evaluated between the study groups.

**Results:** There were a total of 179 patients. Fifty (28%) patients underwent minimally invasive [laparoscopic (n= 19) and robotic (n= 31)] and 129 (72%) patients underwent open surgery. There were no differences between the two groups in terms of age, sex, body mass index and ASA scores. While operative time was significantly longer in the minimally invasive surgery group (p< 0.0001), length of hospital stay and operative morbidity were comparable between the groups.

**Conclusion:** While both laparoscopic and robotic surgery is safe and feasible in terms of short-term outcomes in selected patients, long operating time and increased cost are the major drawbacks of the robotic technique preventing its widespread use.

**Keywords:** Gastric cancer, laparoscopic surgery, robotic gastrectomy, D2 dissection, minimally invasive

## INTRODUCTION

Radical surgery is the gold standard treatment for a majority of patients with gastric cancer (1). Minimally invasive surgery (MIS) has gained much popularity in the treatment of gastric cancer after Kitano et al. reported the first conventional laparoscopic gastrectomy in 1994 (1). Proposed advantages of minimally invasive techniques are better visualization of the anatomy, less surgical trauma on the abdominal wall and better cosmesis (2). Since its first description, MIS has evolved within a wide scope from standard laparoscopy to robotics in order to improve operative outcomes (3).

The incidence and characteristics of upper gastrointestinal disorders of the Turkish people differ from the European residents (4). The features of gastric cancer vary depending on the geographic location and characteristics of the patient population. (5) MIS for the treatment of gastric cancer have been constantly used and developed in years, especially in Eastern countries (6). There are limited studies evaluating patient characteristics and outcomes of MIS for the radical treatment of gastric cancer from the Western world. Turkey is a country in which patient population exhibits characteristics of both Eastern and Western populations due to its geographic location and genetically heterogenic Eurasian population that carries both European and Asian traits (7). In this study, it was aimed to compare short-term outcomes of MIS and open surgery for gastric cancer in the Turkish population.

## MATERIAL and METHODS

After obtaining the Institutional Review Board approval (2018.221.IRB1.026), outcomes of the patients who underwent MIS (laparoscopic or robotic) and open

**Cite this article as:** Ağcaoğlu O, Şengün B, Tarcın S, Aytaç E, Bayram O, Zenger S, et al. Minimally invasive versus open surgery for gastric cancer in Turkish population. Turk J Surg 2021; 37 (2): 142-150.

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Received: 09.04.2019

Accepted: 02.04.2021

Available Online Date: 30.06.2021

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DOI: 10.47717/turkjsurg.2021.4506

gastrectomy with D2 lymphadenectomy by two surgical teams between January 2013 and December 2017 for gastric adenocarcinoma were reviewed. Patients with distant organ metastasis, presence of a previous or concurrent cancer, history of surgical or medical cancer treatment, hereditary cancer syndromes and emergent operations were excluded. Age, sex, body mass index (BMI), ASA (American Society of Anesthesiologists) score, diagnosis, tumor size, history of previous abdominal surgery, comorbidities, operative time, estimated blood loss, the number of harvested lymph nodes, additional resections, perioperative complications, length of hospital stay and interventions within the postoperative 30 days were evaluated and compared based on intent to treat whether MIS or open technique was used. Staging was performed based on the Union for International Cancer Control's TNM-7 guideline (8).

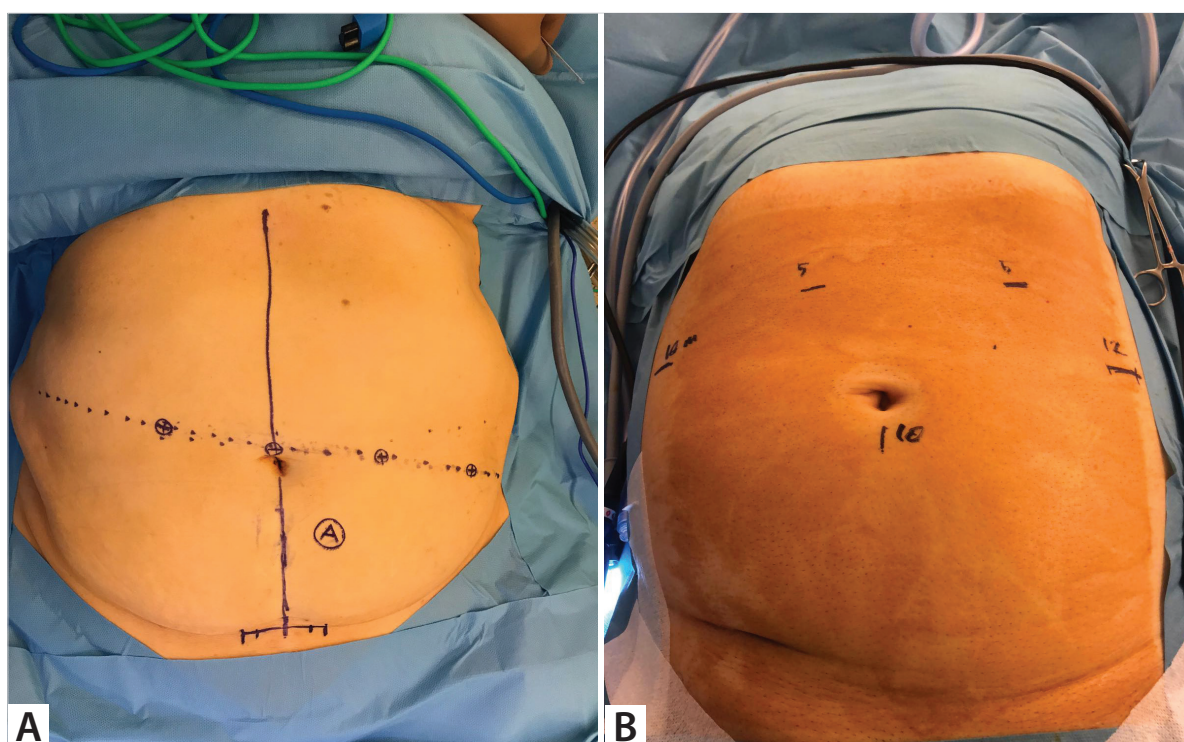
Data were retrieved from prospectively maintained institutional databases. The da Vinci Xi® Surgical System (Intuitive Surgical Inc., Sunnyvale, CA, USA) was used to perform all robotic procedures. Depending on the location of the tumor, a distal subtotal or a total gastrectomy with D2 lymph node dissection was performed based on the surgeons' discretion.

Anastomotic leak was defined as a break in the integrity of the anastomosis documented by a combination of clinical, endoscopic, radiologic, and operative findings. Bowel obstruction/ileus was defined as the presence of at least three of the following five symptoms: nausea, abdominal pain, vomiting, abdomi-

nal distension, absence of flatus and/or stool within the last 24 hours, findings indicating obstruction upon plain radiographic or contrast studies, or a diagnosis of intestinal obstruction as confirmed by surgery. Conversion to open surgery was defined as the completion of any part of the procedure with open technique, excluding the delivery of the specimen. Operative time was defined as the time from the first skin incision to final closure of the abdominal wall. Overall morbidity rate was calculated by considering the number of patients who had at least one postoperative complication. Similar discharge criteria including tolerating meals without nausea or vomiting, afebrile for more than a day, adequate pain control with oral medication, and independent ambulation was applied to two study groups.

### Operative Technique

For both laparoscopic and robotic procedures, after induction of general anesthesia, patient is placed in a supine position on a split table with each leg abducted at an angle of 30 degrees. Surgeon is positioned between the patient's legs; first assistant is on the right side and the second assistant on the left side of the patient. Blind technique with Veress needle is used to establish pneumoperitoneum of 12-15 mmHg unless there is a history of prior abdominal operation. The Hasson technique is used if blind entrance in to the abdominal cavity is contraindicated. A 10-mm camera port (an 8 mm port for robotic technique) is inserted in the supraumbilical region. A standard 5-port technique is used for the whole laparoscopic procedure (Figure 1A, 1B).



**Figure 1.** Intraoperative photos showing port placements used for the robotic technique **A.** and laparoscopic technique **B.**





**Figure 2.** Intraoperative photo showing the position of the Xi robot after docking.

In the initial phase of the procedure, the liver is retracted with a Nathanson retractor to achieve optimal view. On the left side, a 5-mm port is used for assistance and surgeon uses two 12-mm ports on each side of the camera port in laparoscopic surgery. An AirSeal® port is used as an assistant port in robotic gastrectomy (Figure 2). After port placement, patient is placed in a 20° reverse Trendelenburg position. The abdominal cavity is explored to detect the presence of any metastases. The same operative steps are followed in open, laparoscopic and robotic procedures.

First, the gastrocolic ligament is divided with an energy device toward the lower pole of the spleen exposing the omental bursa. After dividing the right gastric and gastroepiploic vessels, the pylorus is dissected to the right and the first portion of the duodenum is transected just distal to the pylorus with a staple. Dissection is then continued distally to the left side of the stomach and the short gastric and left gastroepiploic vessels are divided. The splenic lymph node station is included into the specimen and fundus is totally mobilized. The lymph nodes located at the periceliac, left gastric and porta hepatis are included in the specimen to achieve a D2 dissection.

After dissection of the first four lymphatic stations, an endo-staple is used to transect the stomach from the esophagus. After introduction of a robotic stapler in the year of mid-2015, a robotic staple is used in robotic operations for duodenal, gastric and esophageal transections. In robotic operations, specimen ex-

traction is performed via a Pfannenstiel incision. In laparoscopic operations, 12-mm port opening on the left side, which is used by the surgeon, is enlarged to 6 cm to get the resected specimen out of the abdomen. A standardized Roux-En-Y esophago-jejunostomy or gastro-jejunostomy is performed in total and distal gastrectomy procedures, respectively by transecting the jejunum at a length of 20 to 30 cm from the Treitz's ligament for anastomosis. While an OrVil® is (Medtronic, CT, USA) inserted from the patient's mouth and placed to the distal end of esophagus for esophagojejunostomy in laparoscopic procedures, a hand-sewn intracorporeal end-to-side anastomosis is performed in robotic technique. A side-to-side stapled jejunajejunostomy is performed as the distal anastomosis of the Roux-En-Y reconstruction in both laparoscopic and robotic operations. A Jackson Pratt drain is left into the lesser sac before abdominal closure.

For the open technique, patient lies in supine position. First, median upper gastric laparotomy is established from xyphoid to umbilicus. After initial exploration and evaluation of resectability, the greater omentectomy is performed. For dissection, both sonar and electrical energy-based devices were used. Later, the gastrocolic ligament is dissected, exposing the spleen in the left upper abdominal plane. If the lymph nodes at splenic hilus and preoperative evaluation suggests spread of cancer, then oncological splenectomy is performed. At the pancreas stations 7, 8 and 11, lymphadenectomy is performed in the upper border.



**Table 1.** Patient demographics and co-morbidities for the minimally invasive and open surgery groups

	Minimally invasive group (n= 50)	Open group (n= 129)	p
Age, years	56.1 ± 10.8	58.9 ± 12.6	0.929
Sex ratio, M/F	31(62%)/19(38%)	90(69.8%)/39(30.2%)	0.319
BMI kg/m <sup>2</sup>	26.1 ± 4.5	25.9 ± 4.5	0.432
ASA <sup>T</sup> , 1/2/3	22(44%)/25(50%)/3(6%)	49(38%)/65(50.4%)/15(11.6%)	0.493
Co-morbidity, n (%)			
Hypertension	14 (28%)	24 (18.6%)	0.167
Diabetes mellitus	6 (12%)	10 (7.8%)	0.371
Cardiac	8 (16%)	10 (7.8%)	0.099
Obesity	10 (20%)	22 (17.1%)	0.644
Pulmonary	3 (6%)	6 (4.7%)	0.711
Endocrine	3 (6%)	4 (3.1%)	0.401
Liver	1 (2%)	5 (3.9%)	0.999
Stage distribution <sup>ψ</sup>			0.128
I	20 (40%)	32 (24.8%)	
II	11 (22%)	33 (25.6%)	
III	19 (38%)	64 (49.6%)	
T classification <sup>ψ</sup>			0.412
pT1	19 (38%)	30 (23.3%)	
PT2	5 (10%)	17 (13.2%)	
pT3	10 (20%)	29 (22.5%)	
pT4	16 (32%)	42 (32.6%)	
Metastatic LN	3.5 ± 5.4	6.3 ± 9.7	0.991
N classification			0.101
pN0	25 (50%)	46 (35.7%)	
pN1	10 (20%)	22 (17.1%)	
pN2	9 (18%)	24 (18.7%)	
pN3	6 (12%)	37 (28.7%)	
Neoadjuvant radiotherapy	4 (8%)	6 (4.7%)	0.744
Neoadjuvant chemotherapy	16 (32%)	51 (39.5%)	0.874
Previous history of abdominal surgery	16 (32%)	40 (31%)	0.897

BMI : Body mass index.  
T: American Society of Anesthesiologists (ASA) score.

Later, we focus on duodenum. Following lymphadenectomy at station 6, gastroepiploic vessels are transected close to origin. Then, central lymphadenectomy is performed at 5, 7, 8, 9 and 12. Left and right gastric arteries are displaced, duodenum is transected 3-5 cm distal to the pylorus. Lymphadenectomy at para-aortic station 16 is performed if proximal carcinomas were found. Tumor location determines whether the tubular resection on the esophageal side is performed with a purse string clamp. Staplers are utilized similar to minimally invasive technique described above. For reconstruction, a side-to-side stapled jejunojejunostomy is performed as the distal anastomosis

of the Roux-En-Y. The operation is ended after an intraabdominal drain is placed on the subhepatic side. The aponeurosis is sutured followed by stapling of the skin.

### Statistical Analysis

Categorical variables were expressed as frequency (%) and continuous variables as mean ± standard deviation (SD) unless otherwise stated. Categorical variables were compared with Fisher's exact test or Chi-square test. Continuous variables were compared with independent t test or Mann-Whitney U test considering the normality. SPSS 18 (IBM Corp. Armonk, NY) was

**Table 2.** Surgical outcomes and postoperative complications for the minimally invasive and open surgery groups

	Minimally Invasive group (n= 50)	Open group (n= 129)	p
Operative time, min	339.6 ± 113.7	195.6 ± 76.2	<b>&lt;0.001</b>
Blood loss, ml	164.5 ± 128.2	124.5 ± 64.4	0.198
Harvested LN	31.5 ± 11.1	34.6 ± 12.0	0.946
Largest tumor diameter, mm	38.1 ± 24	43.3 ± 24.2	0.850
Additional resections (e.g. spleen, pancreas)	4 (8%)	28 (21.7%)	<b>0.031</b>
Intraoperative complications, n (%)	4 (8%)	8 (6.2%)	0.675
Overall morbidity, n (%)	17 (34%)	42 (32.6%)	0.769
Anastomotic leakage, n (%)	3 (6%)	3 (2.3%)	0.350
Anastomotic stenosis, n (%)	1 (2%)	1 (0.8%)	0.481
Intraperitoneal abscess, n (%)	2 (4%)	4 (3.1%)	0.672
Intraperitoneal hematoma, n (%)	4 (8%)	2 (1.6%)	0.052
Pancreas fistula, n (%)	0 (0%)	1 (0.8%)	0.999
Pneumothorax, n (%)	2 (4%)	0 (0%)	0.999
Pleural effusion, n (%)	1 (2%)	4 (3.1%)	0.999
Pulmonary emboli, n (%)	1 (2%)	1 (0.8%)	0.486
Wound site infection, n (%)	0 (0%)	5 (3.9%)	0.323
Subcutaneous seroma, n (%)	0 (0%)	2 (1.6%)	0.999
Subcutaneous hematoma, n (%)	1 (2%)	3 (2.3%)	0.999
Atelectasis, n (%)	2 (4%)	12 (9.3%)	0.355
Pneumonia, n (%)	0 (0%)	2 (1.6%)	0.999
Urinary tract infections, n (%)	0 (0%)	2 (1.6%)	0.999
Hospital stay, days	9.5 ± 5	9.3 ± 6.6	0.835
Mortality within postop. 30-days, n (%)	0 (0%)	0 (0%)	

LN: Lymph nodes.

used for statistical analyses. Statistical significance was accepted when  $p < 0.05$ .

## RESULTS

### Patient Demographics and Comorbidities

One hundred and seventy-nine patients were included in the study. Fifty patients (27.9%) underwent MIS (laparoscopic,  $n=19$  and robotic,  $n=31$ ) and 129 patients (72.1%) underwent open surgery. Age, sex, BMI, ASA scores, disease stage, history of previous abdominal surgery, use of neoadjuvant treatment and medical comorbidities were comparable between the two groups (Table 1).

### Surgical Outcomes and Postoperative Complications

Total gastrectomy was performed in 130 (72.6%) patients [MIS, 34 (68%) vs open, 96 (74.4%);  $p=0.387$ ], and subtotal gastrectomy was performed in 49 (27.4%) patients [MIS, 16 (32%) vs open, 33 (25.6%);  $p=0.746$ ]. While operative time was longer in the MIS group ( $339.6 \pm 113.7$  versus  $195.6 \pm 76.2$ ,  $p < 0.001$ ),

estimated blood loss was similar between the groups ( $164.5 \pm 128.2$  vs.  $124.5 \pm 64.4$  ml,  $p=0.198$ ). The number of patients requiring additional resections was higher in the open group [ $n=4$  (8%) vs.  $n=28$  (21.7%),  $p=0.031$ ]. Histopathologic outcomes were similar between the groups (Table 2).

Conversion to open surgery was required in 7 (14%) patients in the MIS group (Robotic= 3, laparoscopic= 4). Causes of conversion were insufficient exploration ( $n=3$ ), intra-abdominal adhesions ( $n=1$ ), uncontrolled bleeding ( $n=1$ ) and technical difficulties ( $n=2$ ). No differences were observed with respect to intra- and postoperative complications between the groups. Intraoperative complications were vascular injury ( $n=5$ ), splenic injury ( $n=5$ ), ischemia of gastroenterostomy anastomosis ( $n=1$ ), and pancreas injury ( $n=1$ ). There were no re-operations in both groups. Hospital stay was similar between the two study groups ( $9.5 \pm 5$  versus  $9.3 \pm 6.6$  days;  $p=0.835$ ) (Table 2).

A subgroup analysis comparing laparoscopic versus robotic surgery was performed to reveal the differences and basic

**Table 3.** Patient demographics, co-morbidities and perioperative outcomes for laparoscopic and robotic surgeries

	Laparoscopic (n= 19)	Robot (n= 31)	p
Age, years	57.2 ± 11.8	55.5 ± 10.5	0.822
Gender ratio, M/F	11 (57.9%)/8 (42.1%)	20 (64.5%)/11 (34.5%)	0.640
BMI kg/m <sup>2</sup>	26.3 ± 4.6	26 ± 4.7	0.592
ASA <sup>T</sup> , 1/2/3	5 (26.3%)/12 (63.2%)/2 (10.5%)	17 (54.8%)/13 (41.9%)/1 (3.2%)	0.117
Stage distribution			0.723
I	10 (52.6%)	10 (32.2%)	
II	2 (10.5%)	6 (19.4%)	
III	7 (36.8%)	15 (48.4%)	
Previous history of abdominal surgery, n (%)	8 (42.1%)	8 (25.8%)	0.297
Neoadjuvant chemotherapy	7 (36.8%)	9 (29%)	0.566
Operative time, min.	244.7 ± 60.6	404.1 ± 94.5	<b>&lt;0.001</b>
Blood loss, ml	221.5 ± 225.5	181.3 ± 183.9	0.575
Harvested LN	30.2 ± 11.7	32.3 ± 10.9	0.529
Intraoperative complications, n (%)	3 (15.8%)	1 (3.2%)	0.112
Postoperative complications, n (%)	9 (47.4%)	8 (25.8%)	0.118
Hospital stay, days	10.1 ± 5	9.1 ± 5	0.493
Mortality within postop. 30-days, n (%)	0 (0%)	0 (0%)	

LN: Lymph Nodes, BMI: Body mass index.  
T: American Society of Anesthesiologists (ASA) score.

perioperative parameters regarding these two groups. Overall, between the laparoscopic and robotic subgroups, no differences were found except for the operative time which was significantly longer in the robotic group (Table 3).

## DISCUSSION

The present study revealed that minimally invasive gastrectomy with D2 lymphadenectomy seemed to provide equal perioperative and short-term oncological outcomes as open radical surgery for gastric cancer in selected cases. While our results lacked to reveal presumed benefits of MIS over open surgery, the characteristics of our patient population and structural differences between our study and prior studies provided remarkable information regarding current status of MIS for gastric cancer in Turkey. Even though they were suitable for major curative surgery, our patients had advanced disease at the time of diagnosis. Majority of our cases undergoing radical gastric surgery had T3-T4 tumors, while the main studies evaluating the value of MIS and D2 lymphadenectomy for gastric cancer treatment included less advanced disease compared to our series (9). Secondly, average BMI of our patients in this study seemed to be higher than the patients included in a vast majority of the prior studies evaluating the outcomes of laparoscopic and robotic surgery for gastric cancer (10). A Korean study has reported promising results with robotic technique in patients with high body mass compared to laparoscopic distal subtotal gastrectomy with D2

lymphadenectomy (11). This is a very good example to reveal the differences in terms of patient characteristics between the Korean and Turkish patients. Mean value of the Korean patients in the high BMI group (26.9 kg/m<sup>2</sup>) was similar to the overall BMI (26.1 kg/m<sup>2</sup>) of our patients. Operating patients with increased body weight and advanced staged cancer possibly complicates the course of surgery.

Efficacy of MIS for the management of advanced gastric cancers is still controversial (12). Nevertheless, complex features of our population did not worsen the outcomes of MIS compared to open surgery. Some of the prior studies evaluating the value of MIS included patients who underwent D1 and D2 lymphadenectomy with gastrectomy as a combined group (13). This heterogeneity may deeply impact operative outcomes. A D2 lymphadenectomy with gastric resection is an extensive procedure performed to increase the number of harvested lymph node numbers. Harvesting increased number of lymph nodes has been shown to improve staging. Besides providing an accurate staging, a proper lymphadenectomy potentially reduces the risk of local recurrence and may provide better survival (14). While D2 lymphadenectomy has been the standard in Asia, associated operative morbidities and lack of survival benefits of D2 dissection in early Western trials (15) have prevented European and American surgeons from performing D2 as a standard procedure. The Italian Gastric Cancer Study Group has reported comparable morbidity after D1 and D2 lymphadenectomy

with radical gastrectomy (9). The long-term results of the Dutch Gastric Cancer Trial have revealed better survival and decreased local recurrence in patients undergoing D2 lymphadenectomy group (16). Currently, the European Society for Medical Oncology (ESMO) and other main Western guidelines recommend D2 lymphadenectomy for physically fit patients currently (17). Gastric resection with D1 lymphadenectomy is performed for palliation or for wide T1 gastric tumors in our practice. Otherwise, a gastrectomy with D2 lymphadenectomy is our standard surgical approach for the radical treatment of gastric adenocarcinoma (18).

The number of harvested lymph nodes with MIS radical gastrectomy seems acceptable (19). There are reports showing that the number of harvested lymph nodes is greater in minimally invasive procedures, while some studies comparing minimally invasive and open procedures report significantly less total number of dissected lymph nodes in MIS groups (20). Laparoscopy seems to provide comparable or poorer retrieval of lymph nodes when compared to open and robotic surgery in some series (21). Robotic surgery has been introduced to overcome limitations of laparoscopic procedures especially to improve efficacy of lymphadenectomy and intracorporeal suturing (22). While our results were statistically similar for lymphadenectomy in our open and minimally invasive gastrectomy groups, the mean numbers of harvested lymph nodes were 35, 32 and 30 for open, robotic and laparoscopic operations respectively. The surgeons are relatively less experienced on laparoscopic and robotic surgery compared to open radical gastrectomy, which has been the mainstay treatment for years. Robotic technique seems to provide some improvement in terms of the number of harvested lymph nodes, but low patient numbers possibly result statistical insignificance. On the other hand, the open technique was preferred in cases where an additional organ resection is required. This situation reveals selection bias in decision making for the type of surgery whether to perform an open or minimally invasive gastric resection. Technical difficulties, potential intraoperative and postoperative complications are the major factors preventing surgeons from robotic or laparoscopic gastrectomy. Relatively high conversion rate in our patients undergoing a laparoscopic resection compared to prior laparoscopic series seemed remarkable (6-7%) (23). Although conversion is not a parameter effecting operative quality in terms of oncological and postoperative outcomes, conversion to open surgery can be related to emerging operative experience, aggressive characteristics of the disease and relatively high BMI of our patients compared to their Asian counterparts (19,20). The number of patients with advanced gastric cancer at the time of diagnosis seems high in Turkey, which may complicate planning of treatment strategy and surgical performance (24). Longer operating time in the MIS group was in accordance with prior studies (25). The role of caseload in reducing the time

spend in the operating room has been well documented previously (13). Duration of procedure is expected to be shorter in the future with increasing experience on MIS gastrectomy.

Anastomotic leak is one of the major complications of gastric surgery (26). Previously published studies report a leakage rate of 1-10% (27). Furthermore, the results of a meta-analysis published by Kostakis et al. have shown no significant difference in anastomotic leakage between MIS and open groups (23). Our operative morbidity was similar with prior reports for both MIS and open surgery (28,29). This reflects and is related to comparable duration of hospital stay following MIS and open surgery for gastric cancer in our series (30). While there are some comprehensive reports on planning treatment strategy for gastric cancer, lack of a national consensus results remarkable heterogeneities in the treatment of gastric cancer in Turkey (24). Non-randomized and retrospective nature are the major limitation of the study. Inclusion of the MIS cases which were performed within the learning curve period may have an impact on the outcomes. Increased cost is still the major drawback of the robotic technique preventing its widespread use expectedly. However, we can report that minimally invasive procedures including both laparoscopy and robotics are feasible and safe for the treatment of gastric cancer, yielding similar short-term results compared to open surgery.

Due to our study being retrospective and having limited number of patients, patient selection criteria were not established in the beginning, laparoscopic and robotic groups could not be analyzed separately. Therefore, further prospective studies with increased number of patients and strict patient selection criteria, quality of life and survival outcomes will provide clearer data on the role of MIS for gastric cancer.

**Ethics Committee Approval:** The approval for this study was obtained from Koç University Ethics Committee (Decision No: 2018.221.IRB1.026, Date: 02.10.2018).

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - E.B., B.B.; Design - E.B., B.B.; Supervision - D.B., T.K., İ.H.; Data Collection and/or Processing - V.Ö.; Analysis and/or Interpretation - O.B., S.Z., Ç.B.; Literature Review - O.A., B.S., S.H.T., E.A.; Writing Manuscript - O.A., B.S., S.H.T., E.A.; Critical Reviews - D.B., T.K., İ.H.

**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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## ORJİNAL ÇALIŞMA-ÖZET

Türk J Surg 2021; 37 (2): 142-150

**Mide kanseri tedavisinde minimal invazif cerrahi ile açık cerrahinin karşılaştırılması: Türk popülasyonu sonuçları**

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**ÖZET**

**Giriş ve Amaç:** Bu çalışmada mide kanseri tedavisinde minimal invaziv cerrahinin (MİC) rolü, hem MİC hem de açık teknikte öğrenme eğrisini tamamlamış cerrahlar tarafından uygulanan radikal cerrahi olgularının sonuçları karşılaştırılarak değerlendirilmesi amaçlanmıştır.

**Gereç ve Yöntem:** Ocak 2013-Aralık 2017 tarihleri arasında, iki cerrahi ekip tarafından radikal cerrahi tedavi uygulanan ardışık 199 mide adenokanseri hastası çalışmaya dahil edildi. Hastaların demografik bilgileri, geçirilmiş karın ameliyatları, komorbid faktörler, perioperatif, kısa dönem postoperatif ve histopatolojik sonuçları değerlendirildi. Postoperatif komplikasyonlar Clavien-Dindo sınıflamasına göre skoru  $\geq 3$  veya  $<3$  olarak sınıflandırıldı.

**Bulgular:** Toplam 179 hastanın 53 (%28)'üne MİC (Laparoskopik 19, Robotik 31), 129 (%72)'una açık radikal cerrahi uygulandı. Gruplar arasında yaş, cins, vücut kitle indeksi ve ASA skorları açısından fark saptanmadı. Ameliyat süresi MİC grubunda açık cerrahi grubuna göre istatistiksel anlamlı olarak daha uzun bulundu ( $p < 0,0001$ ). Çıkarılan toplam lenf nodu sayısı, ortalama hastanede kalış süresi ve perioperatif komplikasyonlar gibi diğer sonuçlar arasında farklılık saptanmadı.

**Sonuç:** Mide kanserinin radikal cerrahi tedavisinde geçirilmiş karın ameliyatlarından daha çok radikal mide cerrahisi ile birlikte uygulanacak işlemler MİC'nin tercihinde etkilidir. Ameliyat süresi daha uzun olmasına karşın, MİC tecrübeli ellerde standart açık cerrahinin güvenli sınırlarıyla uygulanabilir ve açık cerrahiye benzer onkolojik etkinlik sunar.

**Anahtar Kelimeler:** Mide kanseri, laparoskopik cerrahi, robotik gastrektomi, D2 disseksiyonu, minimal invaziv cerrahi

**DOI:** 10.47717/turkjsurg.2021.4506





# An experimental study on the pathophysiology of rectal prolapse

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## ABSTRACT

**Objective:** For decades, rectal prolapse has been hypothesized to be caused due to laxity or weakness of the pelvic floor muscles which is often supposed to be related to childbearing in females. However, 50% of females with rectal prolapse have been reported to be nulliparous and this hypothesis does not explain the incidence of rectal prolapse in males. The aim of this study was to evaluate the role of rectal redundancy in rectal prolapse pathophysiology.

**Material and Methods:** Nineteen female Sprague Dawley rats (250-300 g) at 16 weeks of age were obtained from the animal center. Rats were divided into two groups as rectal mobilization (study) group (n= 9) and sham-operated control (n= 10) group. In the study group, soft dissection was applied and rectum were mobilized up from the pelvic floor to create a redundant or hypermobilized rectum. The primary outcome was the rate of rectal prolapse after rectal mobilization.

**Results:** As compared to the sham-operated control group, in which none of the rats had rectal prolapse throughout the post-surgical period, rectal prolapse was observed in four of the rats in the rectal mobilization group (0% vs. 44%; p= 0.006). Being unable to increase the length of the rectums of the rats, but using only mobilization to create the redundancy, and the lack of data regarding any adhesions after surgery are the main limitations of this study.

**Conclusion:** This study showed the role of rectal redundancy on the rectal prolapse pathophysiology.

**Keywords:** Rectal prolapse, pathophysiology, redundancy

## INTRODUCTION

Although rectal prolapse affects relatively few people (2.5 cases/100,000 people) and is very rarely life-threatening, symptoms can be debilitating if left untreated (1,2). Rectal prolapse is generally more common in elderly women, but it may occur at any age and in either sex. While a number of factors have been shown to be associated with the development rectal prolapse, there is no clear cut "cause" of rectal prolapse. Chronic constipation is present in 30-67% of patients, while an additional 15% experience diarrhea. Some have assumed that the development of rectal prolapse is a consequence of multiple vaginal deliveries (1). Other risk factors of prolapse include long-term diarrhea, long-term straining during defecation, previous surgery, cystic fibrosis, chronic obstructive pulmonary disease, whooping cough, multiple sclerosis, and paralysis (3). However, the precise cause of rectal prolapse is still unknown (4-6). Few theories have been proposed regarding the pathophysiology of rectal prolapse. For decades, rectal prolapse has been hypothesized to be caused due to laxity or weakness of the pelvic floor muscles (7). Although the development of pelvic floor laxity in females is often supposed to be related to childbearing, 50% of females with rectal prolapse have been reported to be nulliparous (8). Furthermore, this hypothesis does not explain the incidence of rectal prolapse in males. On the other hand, rectal prolapse has also been suggested to be associated with psychiatric disorders (1,2).

We recently suggested a novel hypothesis to explain the pathophysiology of rectal prolapse (9). Our suggestion is that the etiology behind rectal prolapse lies in the

**Cite this article as:** Attaallah W, Menek G, Erdaş FA, İnceoğlu İY, Kankılıç MP, Yilmazer AH, et al. An experimental study on the pathophysiology of rectal prolapse. Turk J Surg 2021; 37 (2): 151-155.

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Received: 06.01.2021

Accepted: 02.04.2021

Available Online Date: 30.06.2021

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www.turkjsurg.com

DOI: 10.47717/turkjsurg.2021.5188

rectal anatomy itself rather than in an intrinsic dysfunction of the pelvic floor muscles. We believe that the pelvic floor weakness may not be fully responsible of rectal prolapse, but an anatomic variation of a redundant rectum in some individuals may predispose for rectal prolapse. In support of our hypothesis, we used a virtual simulator to demonstrate the process of rectal prolapse (Video 1) and explained this theory by an illustration showing the possible mechanism of rectal prolapse (Figure 1). In order to evaluate this hypothesis in an in vivo model, we also designed an animal study. Thus, the aim of this experimental study was to evaluate the role of rectal redundancy in rectal prolapse pathophysiology by observing the occurrence of rectal prolapse in response to rectal mobilization.

## MATERIAL and METHODS

### Animals

Female Sprague Dawley rats (250-300 g) at 16 weeks of age were obtained from the Marmara University Animal Center and were housed in cages (one rat/cage) and maintained in an air-conditioned room with controlled humidity (65-70%), temperature ( $22 \pm 2^\circ\text{C}$ ) and 12-h light-dark cycles. Rats were fed with commercial rat chow and received tap water ad libitum. All the experimental protocols used in this study were approved by the Marmara University Animal Ethical Committee.

### Surgery and Experimental Design

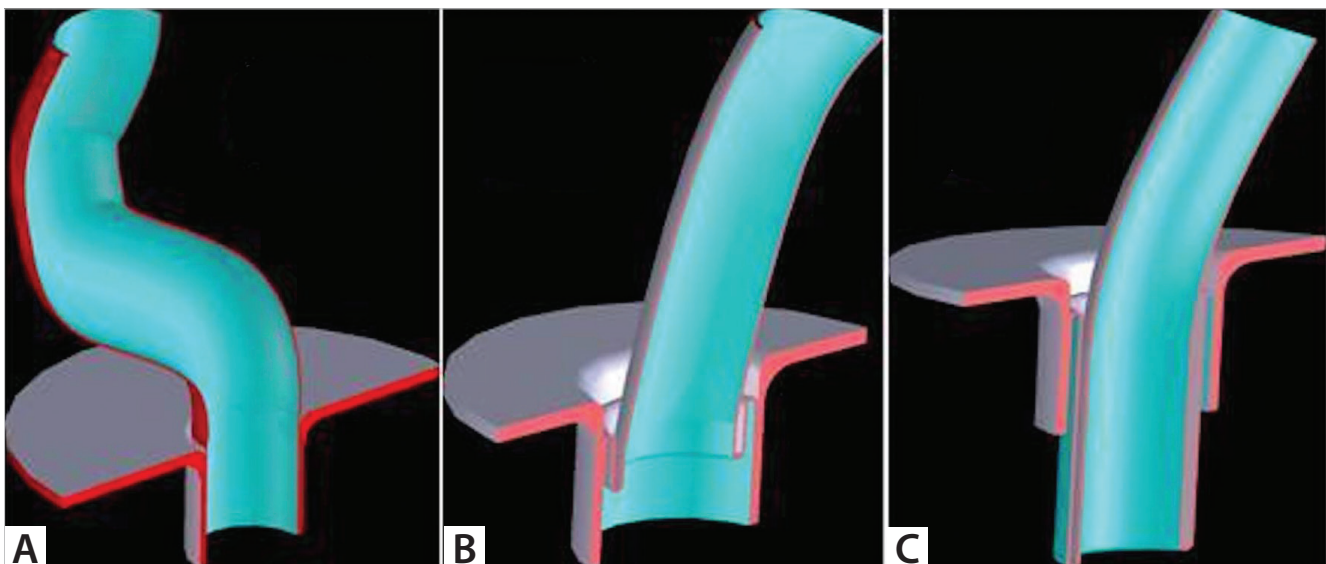
Rats were divided into two groups as rectal mobilization group ( $n=9$ ) and sham-operated control ( $n=10$ ) group. Under general anesthesia induced by intraperitoneal (i.p.) injection of ketamine (100 mg/kg) and xylazine (10 mg/kg), laparotomy was performed by transverse incision of the shaved lower abdomen. In

the rectal mobilization group, soft dissection was applied using a mosquito clamp and rectum were mobilized up (by cutting the ligaments) from the pelvic wall to create a redundant or hypermobile rectum (Figure 2). Circumferential dissection was performed along the rectum up to pelvic floor in the rectal mobilization group. The dissection was stopped at the pelvic floor. To prevent adhesions, hyaluronic acid gel was then applied to whole areas of dissection and along the rectum. In the sham-operated control group, laparotomy was performed without any dissections. Anti-adhesive material was not applied to the sham group since no any dissection was done and the rectum already fixed by its peritoneal ligaments. Abdominal incisions in both groups were closed by simple continuous sutures and subcutaneous saline (1 ml/kg; i.p.) was injected to prevent any fluid loss.

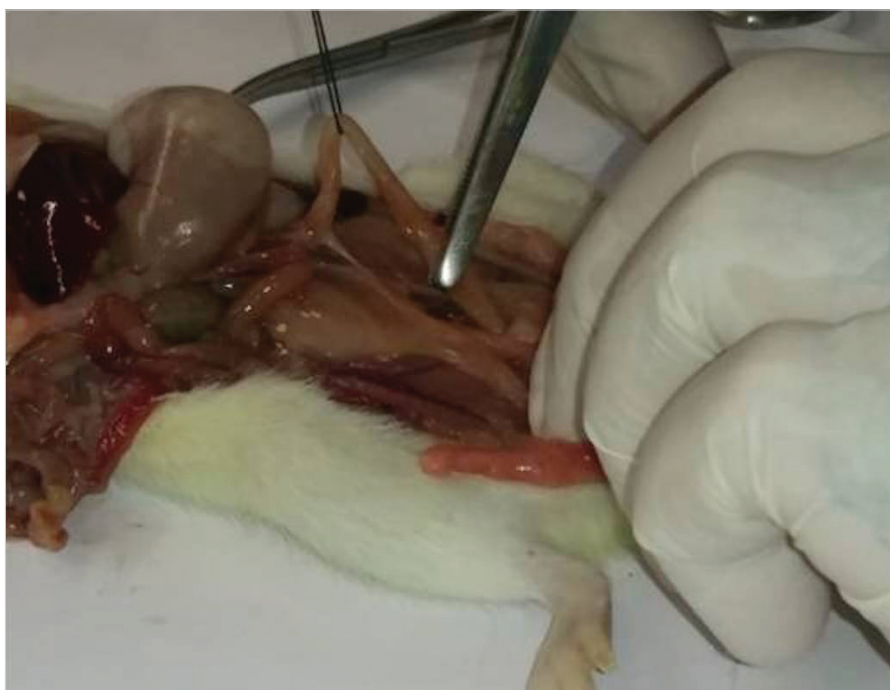
After a two-week recovery period, rats in both groups were given loperamide hydrochlorid (0.15 mg/kg/day; Ali Raif ilaç, İstanbul) in their drinking water in order to induce constipation and thereby, straining during defecation. During the follow-up period, rats were checked every day, on two occasions, by lifting their tails and observing the anal openings during defecation. It was recorded as "complete prolapse" when the entire layer of the rectum with its visible concentric folds has protruded to the outside of the anus. At the end of the post-surgical 15. week, rats were sacrificed by decapitation. The primary outcome of this study was the rate of rectal prolapsed after rectal mobilization.

### Statistical Analysis

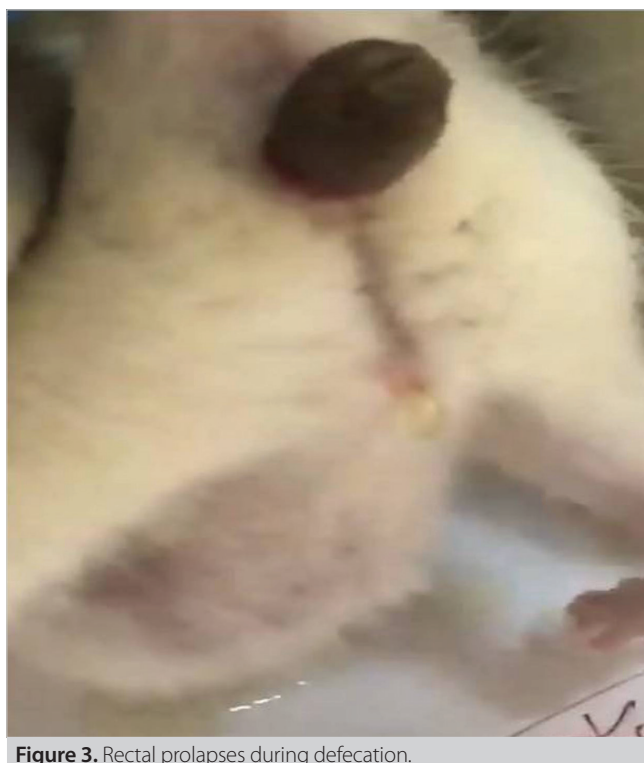
Data were analyzed using the Statistical Package for Social Sciences for Windows version 23 (SPSS Inc.; Chicago, IL, USA). Analysis was performed using Chi-square test and p values  $<0.05$  were considered statistically significant.



**Figure 1.** An illustration showing the possible mechanism of rectal prolapsed. **A.** A redundant rectum, **B.** Intussusception during straining, **C.** Complete prolapse.



**Figure 2.** Rectum were mobilized up (by cutting the ligaments) from the pelvic wall to create a redundant or hypermobilized rectum.



**Figure 3.** Rectal prolapses during defecation.

## RESULTS

All the rats in both groups survived during the follow-up period. As compared to the sham-operated control group, in which

none of the rats had rectal prolapse throughout the post-surgical period, rectal prolapse was observed in 4 of the rats in the rectal mobilization group (0% vs. 44 %;  $p=0.006$ ). Rectal prolapses in these rats were initially observed at the 3, 6, 7 and 12 weeks following surgery and recurrent prolapses were consistently observed in these rats throughout the follow-up period (Figure 3). The presence of sustained prolapses in these rats ruled out that the observed prolapses have not occurred coincidentally.

## DISCUSSION

Today, the most relevant explanations of rectal prolapse are still controversial. These explanations include anatomic dispositions, such as pelvic floor laxity, and predisposing factors, such as multiparity; but none of them are sufficient to explain the mechanism of prolapse and the definite cause is still unknown (10). In order to search the pathophysiology of rectal prolapse we established an animal model. All rats were nulliparous, and were operated to mobilize their rectum (by cutting ligaments in laparotomy) and given a constipation-inducing drug to cause severe straining during defecation. Nearly half of the rats developed rectal prolapses throughout the experimental period. Since the rats were all nulliparous, results show that rectal prolapse cannot be solely associated with giving birth. Furthermore, we also showed that mobilization of the rectum can by itself lead to rectal prolapse in some of the rats, suggesting that elongated and freed rectum could protrude repetitively as a result of defecation effort due to constipation. Changes in the timings of prolapse could be attributed to possible variations in rectal lengths. Since not all of

the rats that had constipation and mobilized elongated rectum have developed rectal prolapse, it may be suggested that other additional causative factors could be responsible in exaggerating the mobility of rectum. Since most patients with rectal prolapse have a long history of constipation (5), it is thought that prolonged, excessive and repetitive straining during defecation may predispose to rectal prolapse (4,6-10). However, we believe that rectal intussusceptions or prolapse lead to obstructive defecation which subsequently may be the cause of severe straining during defecation. In 1912, Moschcowitz has proposed that rectal prolapse was a sliding hernia through a deficient pelvic floor which the rectum herniates (11). This theory was based on the observation that a hernia sac of peritoneum from the Pouch of Douglas and rectal wall can be seen (2). Although this theory still seems valid, we do not think that the pelvic floor weakness could lead to rectal prolapse. For example, the weakness of the abdominal wall around colostomy leads to parastomal hernia but not to stoma prolapse. However, an elongated non-fixed bowel may cause stoma prolapse without any weakness of the abdominal wall. In the same way, we think that an anatomic variation of a redundant (elongated) rectum may predispose for rectal prolapse without weakness of pelvic floor. Another concept suggested that rectal prolapse was actually a circumferential 2° or 3° intussusception (12). Complete circumferential intussusception usually starts 6-8 cm from the anal verge but can continue through the anal canal (13). This seems to be more reasonable and partially appropriate with our theory. Furthermore, in our theory we have explained the cause of intussusceptions by the redundancy of the rectum. Surgery is the mainstay of rectal prolapse treatment. Until today over one hundred surgical modalities were identified. Transabdominal or Perineal procedures are performed to repair a rectal prolapse. Transabdominal repairs involve rectal fixation, rectal resection or a combination of resection and fixation. Attachment of the rectum to the sacrum can be performed using foreign material or sutures although the lateral rectal attachments can be achieved to the sacral periosteum without foreign material. Perineal procedures including Altemeier operation (perineal proctosigmoidectomy) and Delorme Procedure in which transanal resection of the rectum or rectal plication method is also used to shorten the length of rectum (13-17). As transabdominal repairs involve sacro-promontory fixation of the rectum without any intervention to the pelvic floor or muscles, giving us a hint that rectal prolapse may not be the result of a pelvic floor or muscle pathology. Thus, rectal prolapse etiology may lie within its mobile state. Being unable to increase the length of the rectums of the rats, but using only mobilization to create the redundancy, and the lack of data regarding any adhesions after surgery are the main limitations of this study. On the other hand, observation of the rats during defecation was done only twice a day, but a 24-h video monitoring could be used to gather more convincing results.

Since there are no similar studies and not enough knowledge in this field, this study introduced a new reasonable explanation on the pathophysiology of rectal prolapse and proved that using a new experimentally model of rectal prolapse, which may be a premise for future studies. We think that this theory has a significant value in clinical practice since the parity and pelvic floor weakness seem to be less important than the redundancy of the rectum. The redundancy is common and well-defined in the human colon; that is, an individual with a redundant colon has an abnormally long colon, especially in the final section (the descending colon). A redundant colon often has additional loops or twists. Other names for a redundant colon include tortuous colon or elongated colon. We think that this definition can be applied to the rectum. Therefore, this variation of the rectum may lead to the clinic of obstructive defecation, which also includes the rectal prolapse. Furthermore, this diagnosis is usually underestimated, particularly in cases of internal intussusceptions. By using our hypothesis, in which we defined the variation of redundant rectum, we think that the prevalence of rectal prolapse among both genders should also be re-evaluated. Further studies including clinical studies are needed to definitely prove our theory in explaining the pathophysiology of rectal prolapse.

## CONCLUSION

This study showed the role of rectal redundancy on rectal prolapse pathophysiology. We believe that the pelvic floor weakness may not be fully responsible of rectal prolapse, but an anatomic variation of a redundant rectum in some individuals may predispose for rectal prolapse.

**Ethics Committee Approval:** The approval for this study was obtained from Marmara University Animal Experiments Local Ethical Committee (Decision No: 08.2019.mar, Date: 08.02.2019).

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - A.A., G.S.S., V.K.; Design - A.A., S.S., V.K.; Supervision - A.A., G.S.S., V.K.; Materials - D.J.A., O.H.S., V.B.; Data Collection and/or Processing - D.J.A., O.H.S.; Analysis and/or Interpretation - D.J.A., O.H.S., V.B.; Literature Review - D.J.A., S.S., V.B.; Writing Manuscript - A.A., G.S.S., V.K.; Critical Reviews - A.A., G.S.S., S.S., V.K.

**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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## ORJİNAL ÇALIŞMA-ÖZET

Turk J Surg 2021; 37 (2): 151-155

### Rektal prolapların patofizyolojisi üzerine deneysel bir çalışma

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#### ÖZET

**Giriş ve Amaç:** Yıllardır, rektal prolapsusun, genellikle kadınlarda çocuk doğurma ile ilgili olduğu düşünülen pelvik taban kaslarının gevşekliği veya zayıflığından kaynaklandığı varsayılmaktadır. Ancak rektal prolapsusu olan kadınların %50'sinin nullipar olduğu bildirilmiştir ve bu hipotez erkeklerde rektal prolapsus etiolojisini açıklamamaktadır. Bu çalışmanın amacı, rektal prolapsus patofizyolojisinde rektal fazlalığın rolünü değerlendirmektir.

**Gereç ve Yöntem:** Hayvan merkezinden 16 haftalık 19 dişi Sprague Dawley sıçanı (250-300 g) elde edildi. Sıçanlar, rektal mobilizasyon (çalışma) grubu (n= 9) ve kontrol (n= 10) grubu olarak iki gruba ayrıldı. Çalışma grubunda fazlalık veya hipermobilize bir rektum oluşturmak için yumuşak diseksiyon uygulandı ve rektum mobilize edildi. birinci çıkım rektal mobilizasyon sonrası rektal prolapsus oranıydı.

**Bulgular:** Ameliyat sonrası dönem boyunca kontrol grubundaki sıçanların hiçbirinde rektal prolapsus görülmezken, mobilizasyon grubundaki sıçanların dördünde rektal prolaps gözlemlendi (%0'a karşı %44; p= 0,006). Sıçanların rektumlarının uzunluğunu uzatamamak, sadece mobilizasyon kullanmak ve ameliyat sonrası herhangi bir yapışıklığa ilişkin veri eksikliği bu çalışmanın ana kısıtlamalarıdır.

**Sonuç:** Bu çalışma, rektal prolapsus patofizyolojisinde rektal redundancy'nin rolünü göstermiştir.

**Anahtar Kelimeler:** Rektal prolapsus, patofizyoloji, redundancy

**DOI:** 10.47717/turksurg.2021.5188



# How can surgical continuity be maintained during the COVID-19 pandemic? A quality improvement study in the pre-vaccination period

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## ABSTRACT

**Objective:** During the COVID-19 pandemic, most of the elective surgeries had to be postponed. However, it is not possible to delay the surgical treatment of cancer patients for a long time. The aim of this study was to present how gastrointestinal system surgery operations are managed without delay and how employee safety is ensured, together with the results of the last five months. For this purpose, a preclinical and clinical screening system was created.

**Material and Methods:** Data of the patients who presented to our outpatient clinic between April 1<sup>st</sup> 2020 and August 31<sup>st</sup> 2020 were retrospectively reviewed.

**Results:** During the last five months of the pandemic, a total of 387 patients were hospitalized and 309 of these patients underwent surgical procedures. 165 of the patients who underwent surgery were newly diagnosed malignancy patients. All patients who were hospitalized were subjected to a screening for COVID-19 during the preclinical, clinical and surgical period. In the preclinical period, five patients were found positive and were directed to COVID-19 treatment without hospitalization. In the clinical period, six patients were isolated by showing symptoms during the hospitalization period. Only one of these patients received surgical treatment. The remaining five patients underwent endoscopic and interventional procedures. In this process, COVID-19 positivity was detected in a total of five healthcare workers.

**Conclusion:** With this preclinical and clinical screening method, it is shown that a COVID-19 sterile environment can be provided by early detection of positive cases in both patients and healthcare workers. In this way, the possibility of surgical continuity was demonstrated.

**Keywords:** COVID-19, pandemic, pre-vaccination period, surgery

## INTRODUCTION

Respiratory track-related cases that emerged in the Wuhan province of China in December 2019 rapidly spread worldwide and caused radical changes in the field of health care together with all living spaces. Three months after the first appearance, along with the pandemic declaration of the World Health Organization (WHO) (1) on 11<sup>th</sup> March 2020, the first cases started to emerge also in Turkey, and through a rapid response, the health system has been tried to be adapted to the pandemic period. The experience in China and then in Europe where the number of patients has seen a rapid rise contributed much to shape this adaptation. The increase in the need for hospital beds, intensive care beds and ventilators has led to the allocation of these resources for COVID-19 infected patients also in Turkey, and other non-compulsory health services have been delayed.

Surgeons and surgical patients have also been affected by this forced attitude. During the early phase of the pandemic, the results of the national survey that we conducted among the general surgeons in Turkey showed that a large majority of the surgeons were able to operate emergency cases, and elective cases were delayed as much as possible (2). Because of the intense and variable information

**Cite this article as:** Pişkin E, Çolakoglu MK, Öter V, Özgün YM, Aydın O, Güven A, et al. How can surgical continuity be maintained during the COVID-19 pandemic? A quality improvement study in the pre-vaccination period. Turk J Surg 2021; 37 (2): 156-161.

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Received: 26.01.2021

Accepted: 02.04.2021

Available Online Date: 10.05.2021

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DOI: 10.47717/turkjsurg.2021.5226



flow during the first phase of the pandemic, approaches about malignant patients varied and the main point became whether to delay such patients or not.

Until today, the total number of infected patients in Turkey has been reported as 351413, the number of recovering patients as 306939, and the total number of deaths as 9445, and these numbers continue to increase (3). It is highly doubtful how long we can postpone the treatment of patients who need surgical treatment, and especially oncological patients, in a process that is uncertain when it will end, and it is a big question mark that needs to be answered. Surgical continuity should be ensured for these patients at some point.

In Ankara City Hospital, which has the largest bed number in Europe and the third largest in the world, during the COVID-19 pandemic period, the surgical management of oncological patients continues uninterruptedly from the first day of the process, and our center is a tertiary reference center where advanced digestive system surgery and liver transplantation are performed. A pre-clinic and clinical screening algorithm is established by our clinic with reflexes taken from the beginning of the pandemic period. This study aimed to define the reorganization of our department concerning methods with which we maintain surgical continuity in the center providing services as a pandemic hospital during the COVID-19 pandemic period by using a pre-clinic and clinical screening algorithm, and to report the results of all patients admitted to and hospitalized in our service in this five-month pre-vaccination period.

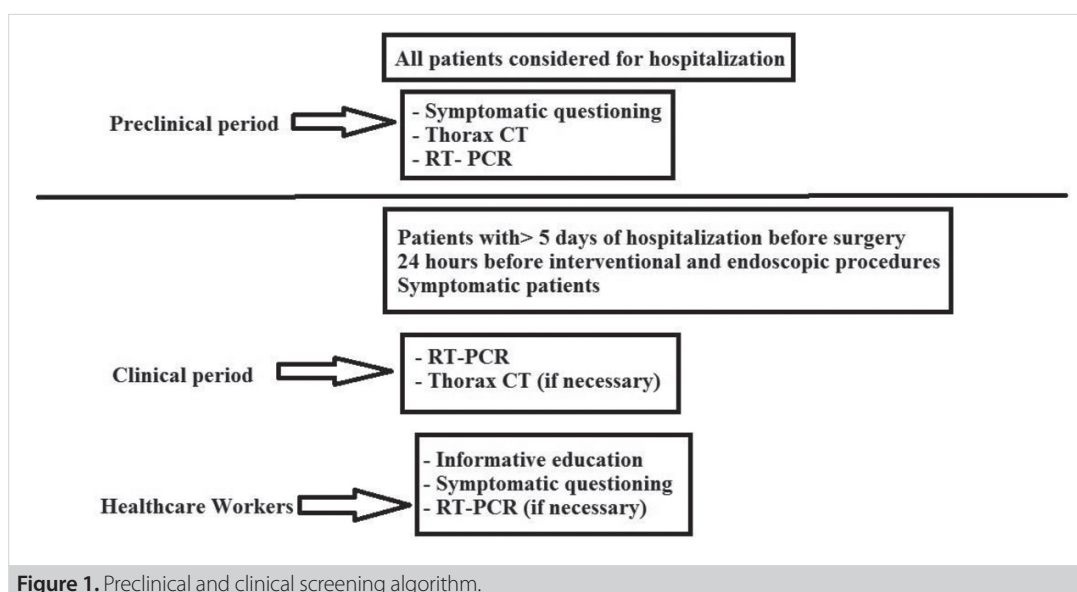
## MATERIAL and METHODS

This retrospective quality improvement study is registered with the Ministry of Health form number 2020-08-18T14\_08\_35, and scientific research approval was obtained. Then, the study was

evaluated and approved by the ethics board of our center. (Ethics board number: E1-20-1120)

Data of all patients who applied to surgical polyclinics and those admitted to the service for the need of surgical, interventional or endoscopic therapy between the date of April 01, 2020, when the first peak period started after the emergence of the initial cases, and August 31, 2020, including the second peak, were reviewed over digital records. After recording the number of month-to-month polyclinic and the number of patients admitted to and hospitalized in the service, the age, sex and reason for admission in the service for the patients who required admittance were evaluated. A screening algorithm was planned covering the pre-clinic and clinical period in order to minimize the COVID-19 risk (Figure 1), and all patients were subjected to that algorithm.

COVID-19 assessment procedure for the patients who required to be hospitalized for surgical, interventional or endoscopic therapy was completed in the polyclinics before the patients were admitted. During this process, primarily symptoms evaluation of the patients was conducted and they were physically examined. Patients who had anamnesis or any COVID-19 findings or suspects (fever  $\geq 38^\circ$ , dyspnea, respiration rate  $>22$ /minute, general status disorder etc.) found during the examination were referred to the infectious diseases, and they were accepted to the service after their evaluation procedures had been completed. And for all patients who were not symptomatic, during the beginning of the pandemic process, radiological visualization with Thorax computed tomography (CT), and after the test became widespread, again for all patients, reverse transcriptase- polymerase chain (RT-PCR) test together with CT was conducted. The patients who were found positive in one of the methods were referred again to the infectious diseases, and they were



accepted to the service after their evaluation or treatment for COVID-19 was completed. Those patients who had negative results obtained from both of the methods were hospitalized. Informed consent forms were taken from the patient and patient's relatives both for the procedure to be delivered and for COVID-19 and related risks before hospitalization. RT-PCR test was repeated 24 hours before the procedure to be delivered (surgery, intervention, endoscopic) for those patients who had a hospitalization period longer than five days, and the planned procedures were delivered for the patients with negative results. The patients who had positive results were referred to the infectious diseases, and their treatments were started. For those patients who were assessed negative before hospitalization, but became symptomatic during the hospitalization period, RT-PCR and CT were repeated when necessary. During this process, CT, RT-PCR and repeated RT-PCR results of all hospitalized patients were recorded. Treatment methods delivered for the patients were also recorded.

In addition to pre-operative COVID-19 evaluation, some changes were made in hospital and service policies. Working health staff and auxiliary staff were ensured to use masks, and personal protective equipment when necessary. Visitors' entrance was prevented and only one person was allowed for companion in compulsory cases. The patients and their companions, if any, were ensured to wear masks when health or auxiliary staff visited them. The patients with suspected findings were isolated and no one was allowed to visit them without personal protective equipment.

In our hospital, COVID-19 suspected or positive patients were followed in various services and isolated from other patients under the supervision of infectious diseases or pulmonary diseases services. The patients who had suspected findings during the hospitalization process or had test positive results were immediately transferred to these services, and their follow-ups were performed at these services when necessary. For those cases who required urgent surgery or known to be COVID-19 positive were operated in separate operation rooms by taking measures and again followed up at services allocated to COVID-19.

Through this defined algorithm, the therapies of the patients continued as both their pre-operative check-out were conducted and a COVID-19 negative environment was tried to be creat-

ed. During this five-month period, whether the surgery service and operation room staff had COVID-19 positivity was recorded by examining the staff records.

## RESULTS

A total of 5185 outpatients were admitted to our surgical polyclinics between April 1<sup>st</sup>, 2020 and August 31<sup>st</sup>, 2020. After the evaluations made for these patients, 392 (232-males and 160-females) of them were hospitalized. Median age of the patients agreed to be hospitalized was  $53.06 \pm 15.14$  (17-84 ages). While 165 of the patients (42%) were hospitalized for their newly diagnosed malignancy, the other patients were either previously operated malignant or newly diagnosed benign patients. While great majority of the cases were desired to be hospitalized for diagnosis of lower gastrointestinal system (GIS) diseases ( $n = 80$ , 20.4%), the number of the upper GIS, hepato pancreaticobiliary system, liver transplantations and other (cholelithiasis, hydatid cyst etc.) diseases were respectively as 58 (14.7%), 57 (14.5%), 35 (8.9%) and 162 (41.2%).

While PCR test was not very widespread during April and May, most of the assessments were made through CT evaluation, both methods were used together during June, July and August. During COVID-19 evaluation of the cases, before hospitalization during the polyclinic stage, COVID-19 positivity was detected in a total of five (3%) patients with CT radiological examination and RT-PCR test. CT and RT-PCR results of these five patients are presented in Table 1. According to this, while in all five patients PCR positivity was detected, CT findings appeared only in three patients. Those patients detected positive were referred to the infectious diseases department, and first their COVID-19 treatments were completed and then, as the infectious diseases department approved, their re-applications were accepted. The remaining 387 patients were hospitalized in services.

While 309 (79.8%) of the hospitalized patients had surgical intervention, 26 received (6.7%) endoscopic intervention (including endoscopic retrograde colangiopancreatography) and 22 (5.6%) interventional radiology. Thirty patients (7.7%) were followed up on medical treatment. Most of the surgical interventions were conducted for hospitalized oncological cases, five patients had liver transplantations (four living donors, one cadaveric). From the RT-PCR tests taken and repeated during

**Table 1.** Computed tomography (CT) and RT-PCR results of the patients with COVID-19 + detected in pre-clinic evaluation

	CT	RT-PCR
Patient 1	Findings consistent with COVID-19	Positive
Patient 2	Findings consistent with COVID-19	Positive
Patient 3	No findings consistent with COVID-19	Positive
Patient 4	No findings consistent with COVID-19	Positive
Patient 5	Findings consistent with COVID-19	Positive

**Table 2.** Number of outpatient clinic patients, number of hospitalized patients, treatment and COVID-19 status

	April	May	June	July	August	Total
Outpatient clinic patients (n)	414	564	1530	1431	1246	5185
Hospitalized patients (n)	19	37	106	136	94	392
Treatment method (n)						
Surgery	12	28	75	113	81	309
Endoscopy	0	4	7	2	0	13
ERCP	0	1	8	1	3	13
Interventional	3	3	4	8	4	22
Medical	3	0	9	12	6	30
Number of COVID-19 positives before hospitalization	1	1	3	0	0	5
Number of CT positive cases	1	1	1	0	0	-
Number of RT-PCR positive cases	1	1	3	0	0	-
Number of RT-PCR positive cases after hospitalization	1	1	0	2	2	6

the hospitalization process, positivity was detected only in six patients (1.5%). The test was repeated in these six patients because of resistant fever. After the identification of positivity, these patients were also referred to the infectious diseases department and their follow-ups and treatments were completed. The month-to-month hospitalization numbers, treatments delivered and COVID-19 statuses of the hospitalized patients are presented in Table 2.

During this five-month period, when the service and operation room physician and health staff records are examined, COVID-19 positivity was detected only in one operation room nurse, two service nurses and two physicians. The staff continued their duties after their treatments were completed and approval was obtained from infectious diseases department. No COVID-19 related mortality was observed in patients with detected COVID-19 positivity.

## DISCUSSION

The COVID-19 pandemic affecting the entire world has also caused important changes to be made in the health system. Because of increasing intensive care and ventilator needs and personal protective equipment requirements, as the majority of the hospital resources had to be used for these patients, dilemmas were faced with ways of managing the treatments of other patients and especially of oncological cases. Leading surgical associations in the world have declared guidelines during the beginning of the pandemic about which oncological patients' surgical treatments may be delayed in which conditions or to which alternative treatments they may be led (4-9). While the first reason for such a desire for delay was adequate and correct management of hospital resources, the real fear stemmed from the fact that mortality is higher in oncological patients infected by COVID-19 (10). During the pandemic, we have published a review about managing digestive system cancers (11). However,

the ongoing pandemic process had gone beyond such durations of delays that were seen as possible in these guidelines, and is still ongoing. Therefore, at some point, it seems no more possible to delay the surgical treatments of the oncological patients, and maintenance of surgical continuity is a requirement for not interrupting their treatment conditions.

Our study showed that surgical continuity can be achieved by presenting the number of patients, number of hospitalizations, treatment services provided and COVID-19 positive status of the patients during the pandemic period. As a reflex to the outbreak, the number of admitted patients decreased in April and May that refer to the beginning of the process; however, after completing adaptation and reorganization, the numbers returned to normal in June and July. We think that there are two basic conditions for these conditions to be achieved.

The first basic condition to manage surgical continuity, as defined in the guidelines, is to have enough resources. Surgical and especially oncological patients are the ones who may need intensive care or ventilator after the post-operative period. Also, for the health staff who will assume their care, adequate personal protective equipment should be provided. This may create problems both in COVID-19 and oncological treatment centers. For this reason, in the centers where surgical continuity should be maintained, separate and adequate operation room, intensive care and personal protective equipment support should be provided for such patients.

The second condition to manage surgical continuity is to provide a COVID-19 negative environment especially for oncological patients. Therefore, we believe that patients should be subjected to a detailed evaluation in terms of COVID-19 before hospitalization. For this aim, a triple evaluation was performed in polyclinic services for the patients. Although no findings were found in the patients planned to be hospitalized in their symptomatic interro-

gation or physical examination, positivity was detected in five patients. However, in two patients who were to be hospitalized, the test was repeated for resistant fever and positivity was identified. For this reason, symptomatic follow-ups of all patients should be closely observed. Although the sensitivity and specificity of the CT and RT-PCR analyses show variances, it is known that using both methods together reduces the rate of false negativity (12). As during the beginning of the pandemic process PCR usage was not widespread, CT was used alone but after then, by using both methods together, admittance of COVID-19 positive patients in the service was prevented at an early stage and they were referred to the infectious diseases department.

In order to maintain a COVID-19 negative environment, in addition to the health staff, the patients and their relatives were required to wear masks, outside of their personal areas and when health staff entered in their rooms. No companions were allowed beside the patients when it was not necessary. Also, the mobilization of the patients and their relatives out of the service was kept limited. Despite the measures taken during pre-hospitalization and hospitalization, during hospitalization periods, COVID-19 positivity was detected in six patients, and these six patients were the ones with long hospitalization periods. Only one of them had surgical treatment, and the other five patients had endoscopy or interventional treatment. For all six patients, PCR test was repeated for resistant fever and positivity was shown. These patients were isolated and then, they were referred to the infectious diseases department and their treatments were followed up there. For this reason, we think that PCR technique should be repeated, 24 hours before each invasive intervention to be made, for patients with longer hospitalization and for patients becoming symptomatic.

Although there are adequate resources and COVID-19 negative environment is maintained, as the ability of the disease to infect is high, the patients and the health staff should be closely followed up. One of the limitations of this study is that no systematic evaluation is made about the COVID-19 status of the health employees. COVID-19 positivity was detected only in one operation room nurse, two service nurses and two physicians, and after completing the treatment and approval of the infectious diseases department, service provision continued. However, we do not know whether these employees caught the disease during the working process or outside the hospital. The other limitation is that the study is a retrospective evaluation. This study evaluates clinical management in the pre-vaccination period. COVID-19 vaccination started to be performed to health-care workers in the second week of January, 2021. Not enough time has yet passed to see what might change clinically after vaccination. For this reason, we think that our recommendations may be valuable in surgical clinic management, even after vaccination, until we all enter a full normalization process.

## CONCLUSION

During the ongoing pandemic process, it is not possible to delay the surgical treatment of the oncological patients forever. Their surgical treatments should continue by taking the risk of contamination for these patients. In order to do this, the center should have adequate resources and a COVID-19 negative environment should be maintained. Surgical continuity is only possible when these conditions are met. In cases where these conditions cannot be provided, oncological patients should be directed to appropriate centers.

**Ethics Committee Approval:** The ethical approval for this study was obtained from Ankara City Hospital No.1 Clinical Research Ethics Committee Board (Decision No: E1-20-1120, Date: 02.09.2020).

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - E.P., V.Ö., M.K.C.; Design - E.P., V.Ö., M.K.C.; Supervision - M.M.Ö., E.B.B., A.A.S.; Materials - Y.M.Ö., O.A.; Data Collection and/or Processing - Y.M.Ö., O.A., A.G.; Literature Review - M.K.C., V.Ö.; Writing Manuscript - E.P., M.K.C.; Critical Reviews - E.B.B., M.M.Ö., A.A.S.

**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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### ORJİNAL ÇALIŞMA-ÖZET

Turk J Surg 2021; 37 (2): 156-161

## COVID-19 salgını sırasında cerrahi devamlılık nasıl korunabilir? Aşılama öncesi dönemde bir kalite iyileştirme çalışması

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### ÖZET

**Giriş ve Amaç:** COVID-19 salgını sırasında, elektif ameliyatların çoğu ertelenmek zorunda kalmıştır. Ancak kanser hastalarının cerrahi tedavisini uzun süre ertelemek mümkün değildir. Bu çalışmanın amacı, gastrointestinal sistem cerrahisi operasyonlarının gecikmeden nasıl yönetildiğini ve çalışan güvenliğinin nasıl sağlanacağını son beş ayın sonuçlarıyla birlikte ortaya koymaktır. Bu amaçla pre-klinik ve klinik bir tarama sistemi oluşturuldu.

**Gereç ve Yöntem:** Polikliniğimize 1 Nisan 2020 ile 31 Ağustos 2020 tarihleri arasında başvuran hastaların verileri geriye dönük olarak incelendi ve tarama sistemi oluşturuldu.

**Bulgular:** Son beş aylık pandemi döneminde toplam 387 hasta kliniğimize yatırıldı ve bu hastaların 309'una cerrahi işlem uygulandı. Ameliyat geçiren hastaların 165'i yeni tanı konulmuş malignite hastasıydı. Hastaneye yatırılan tüm hastalar yatış öncesi, yatış sonrası ve cerrahi dönemde COVID-19 taramasına tabi tutuldu. Klinik öncesi dönemde beş hastanın testi pozitif bulunarak hastaneye yatmadan COVID-19 tedavisine yönlendirildi. Klinik dönemde altı hasta yatış süresi boyunca semptomları olması üzerine izole edildi. Bu hastalardan sadece bir tanesine cerrahi tedavi uygulanmıştı. Kalan beş hastaya endoskopik ve girişimsel prosedürler uygulandı. Bu süreçte toplam beş sağlık çalışanında COVID-19 pozitifliği tespit edildi.

**Sonuç:** Bu pre-klinik ve klinik tarama yöntemi ile hem hastaların hem de sağlık çalışanlarının pozitif vakalarının erken tespiti ile COVID-19 steril ortamının sağlanabileceği gösterilmiştir. Bu şekilde cerrahi devamlılığın olabileceği gösterilmiştir.

**Anahtar Kelimeler:** COVID-19, pandemi, aşılama öncesi dönem, cerrahi

**DOI:** 10.47717/turksurg.2021.5226





# Safety of endoscopic retrograde cholangiopancreatography (ERCP) in patients aged 85 years and older: A single center experience

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## ABSTRACT

**Objective:** To evaluate the efficacy and safety of endoscopic retrograde cholangiopancreatography (ERCP) in elderly patients (≥85 years old).

**Material and Methods:** Patients who underwent ERCP for any reason within 12 months were evaluated. Patients undergoing ERCP were classified as the elderly group aged 85 years and older or the controls under the age of 85 years.

**Results:** A total of 1225 patients, 504 males and 721 females, were included in the study. Length of hospital stay, the number of patients in whom pre-cut sphincterotomy was performed in ERCP, and mortality rate showed similar characteristics compared to the control group in patients with advanced age (≥85 years old). Except for pancreatitis, there was no significant difference between the groups in terms of complications related to the procedure. Post ERCP pancreatitis was observed significantly less in the elderly group ( $p=0.042$ ). Pre-cut sphincterotomy was required in a total of 191 (15.5%) patients. In patients who underwent pre-cut sphincterotomy and patients with cholangitis, post ERCP complication rates were not significant between the groups.

**Conclusion:** ERCP is a safe procedure for older patients (≥85 years old) as well as young patients.

**Keywords:** Endoscopic retrograde cholangiopancreatography, elderly, endoscopic procedures

## INTRODUCTION

Today, the average life expectancy is increasing day by day due to the rapid development of technology and medical techniques. In some of the developed countries, people over the age of 65 make up 10% or more of the population (1). In this direction, while in the past, patients over 65 years old were considered in the advanced age category, today patients over 65 years old are classified as early-aged (65-75), middle-aged (75-85), and elderly (85 years and over) (2).

Endoscopic retrograde cholangiopancreatography (ERCP) continues to be used as the gold standard treatment method in the diagnosis and treatment of hepatobiliary diseases. Comorbid diseases that increase with advanced age raise doubts about the safety of ERCP for the patient. In this direction, this study aimed to evaluate the safety of the ERCP procedure in elderly patients (85 years and over) by taking other age groups into consideration.

## MATERIAL and METHODS

### Study Group and Endoscopic Procedure

Patients who underwent ERCP in the gastroenterology department between December 2018-2019 were included in the study. The patients included in the study were examined in detail before the procedure for comorbid diseases, anesthesia risk, the reason for the procedure, and post-operative complications. Patients with missing files were not included in the study. While evaluating the safety of the ERCP procedure in the advanced age group (85 years), those under 85 years of age were accepted as the control group.

**Cite this article as:** Baykan AR, Cerrah S, Çiftel S, Karahan B, Özdemir Y. Safety of endoscopic retrograde cholangiopancreatography (ERCP) in patients aged 85 years and older: A single center experience. Turk J Surg 2021; 37 (2): 162-168.

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Received: 01.01.2021

Accepted: 02.04.2021

Available Online Date: 30.06.2021

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www.turkjsurg.com

DOI: 10.47717/turkjsurg.2021.5166



ERCP procedure was performed in our clinic by three gastroenterologists with at least five years of ERCP experience using the brand device (Fujinon ED-450XT5). After the procedure, patients were followed for at least two days for complications.

### Descriptions

The scoring system recommended by the "American Society of Anaesthesiologists" was used for risk scoring of anesthesia applied during the procedure (3).

Post-ERCP pancreatitis diagnosis was defined as the complaint of newly developed or worsened abdominal pain and an increase in the amylase level of three times or more 24 hours after the procedure, the need for hospitalization or an extension of the planned hospital stay for at least 2-3 days (4).

In the process-related perforation classification, the classification suggested by Stapfer et al. (5) traumatic and atraumatic duodenal perforations have been managed surgically; however, in the last decade, management has shifted toward a more selective approach. Some authors advocate routine nonsurgical management, but the reported death rate of medical treatment failures is almost 50%. Others advocate mandatory surgical exploration. Those who favor a selective approach have not elaborated distinct management guidelines. Methods: A retrospective chart review at the authors' medical center from June 1993 to June 1998 identified 14 instances of periduodenal perforation related to endoscopic retrograde cholangiopancreatography (ERCP) was used. Accordingly, duodenoscope-related duodenum perforations were classified as type 1, perforations as a result of periampullary sphincterotomy or pre-cut as type 2, perforations that occurred in the bile duct and pancreatic duct while removing the materials used (guidewire), stent, or stone as type 3, and small perforations that occurred as a result of manipulations and characterized by only retroperitoneal air were classified as type 4.

Bleeding due to ERCP was graded according to the classification made by Cotton et al. (6). Accordingly, the hemoglobin value of  $<3$  g/dl and not having the need for transfusion is characterized as mild, the need for transfusion ( $\leq 4$  units) and the need for an interventional (angiographic or surgical) procedure to stop the bleeding as moderate, the need for  $\leq 5$  units of transfusion or interventional (angiographic or surgical) procedure was classified as heavy bleeding.

### Statistical Analysis

IBM SPSS Statistics 17 package program was used to statistically compare the findings. In addition, ERCP results were taken as the gold standard. Numerical variables with normal distribution were shown as mean  $\pm$  SD, while those without normal distribution were shown as mean (minimum-maximum). Categorical variables were shown as numbers and percentages. Mann-Whitney U and Kruskal-Wallis H tests were used for comparison of nu-

merical variables without normal distribution between groups. Categorical variables were compared with  $\chi^2$  and Fisher's exact  $\chi^2$  tests. The relationship between quantitative variables was examined with Pearson and Spearman correlation analyses.

### RESULTS

A total of 1225 patients (504 males, 721 females) who underwent ERCP were included in the study. When the patients were classified according to their age, a significant difference was observed in terms of ASA ( $p < 0.006$ ) and comorbid diseases ( $p = 0.001$ ). There was no significant difference between the patient groups in hospital stay ( $p = 0.325$ ) and sex ( $p = 0.953$ ) (Table 1).

Classification was made according to the coexistence of at least two of the following comorbid diseases; diabetes mellitus, hypertension, coronary artery disease, chronic obstructive pulmonary disease (COPD), cerebrovascular disease (CVD), dementia, chronic renal failure (CRF), liver cirrhosis along with the existing diseases. Comorbid disease status was found to be significantly higher in the advanced age group ( $p < 0.001$ ).

When the medications used by the patients were evaluated, a total of 232 (21.2%) patients in the control group and 87 (65.9%) patients in the elderly group had a history of using antiaggregant, anticoagulant, or both. When an evaluation was made between the groups, the use of medication was significantly higher in the elderly group ( $p < 0.008$ ).

ERCP was applied for bile duct stones frequently (1034). ERCP procedure was performed on a total of 131 patients with 60 patients due to malignancy and for other reasons (bile duct damage after cholecystectomy, parasitosis, stenosis, etc.) (Table 2).

Common bile duct cannulation could not be performed in 48 patients. Forty-one (3.8%) of these patients were in the non-elderly group, and 7 (5.3%) in the advanced elderly group.

Pre-cut was required in 191 (15.5%) patients. Cannulation was achieved by needle-tipped sphincterotome in 120 (9.7%) patients and by transpancreatic septostomy in 71 (5.7%) patients. There was no significant difference in the pre-cut application between the patient and the control group ( $p = 0.386$ ).

There was no significant difference in procedure-related complication rates among endoscopists (complication rates were 6.1%, 6.3%, and 7.1% ( $p = 0.833$ )). The most common complication due to ERCP was pancreatitis (89 patients), which was followed by bleeding after the procedure with 26 patients. There was no severe bleeding after ERCP. Twenty-two of the patients had mild bleeding, while the remaining four had moderate bleeding. Post-ERCP infectious complications were observed in 16 patients (cholecystitis, cholangitis). A total of 10 patients were affected by the cardiopulmonary system (cardiac arrhythmia, subendocardial myocardial infarction, aspiration, etc.) while perforation was observed in three patients after the procedure. There was only

**Table 1.** Demographic characteristics and hospitalization periods of the patients

	Control group (<85 y) n= 1093	Advanced age (≥85 y) n= 132	p
Sex			
Male	450 (36.7%)	54 (4.4%)	0.953
Female	643 (52.5%)	78 (6.4%)	
ASA score	2.1 ± 0.8	3.0 ± 0.5	<0.006*
Hospitalization period (day)	3.6 ± 1.5	3.7 ± 1.6	0.325
Drugs	232 (21.2%)	87 (65.9%)	<0.004*
Antiaggregant	167 (15.3%)	60 (45.5%)	
Anticoagulant	40 (3.7%)	9 (6.8%)	
Both	25 (2.3%)	18 (13.6%)	
Comorbidity	479 (43.8%)	120 (90.9%)	<0.001*
Diabetes mellitus	93 (7.6%)	15 (1.2%)	
Hypertension	80 (6.5%)	7 (0.6%)	
Coronary artery disease	72 (5.9%)	15 (1.2%)	
COPD	53 (4.3%)	9 (0.7%)	
CVD	55 (4.5%)	7 (0.6%)	
Dementia	5 (0.4%)	6 (0.5%)	
CRF	26 (2.1%)	12 (1%)	
Cirrhosis	2 (0.2%)	1 (0.1%)	
At least 2 of them together	93 (7.6%)	48 (3.9%)	

COBD: Chronic obstructive pulmonary disease, CVD: Cerebrovascular disease, CRF: Chronic renal failure.

**Table 2.** ERCP procedure details

	Control group (<85 y) n= 1093	Advanced age (≥85 y) n= 132	p
ERCP reason			
Stone	924 (84.5%)	110 (83.3%)	0.716
Malign	45 (4.1%)	15 (11.3%)	<0.001*
Other	124 (11.3%)	7 (5.3%)	0.032*
ERCP result			
Removal stone	731 (66.9%)	95 (72%)	0.234
Stent**	321 (29.4%)	30 (22.7%)	0.115
Non-cannulation	41 (3.8%)	7 (5.3%)	0.386
Pre-cut	167 (15.2%)	24 (18.1%)	0.387
Pre-cut sphincterotomy	102 (9.3%)	18 (13.6%)	0.112
Transpancreatic sphincterotomy	65 (5.9%)	6 (4.5%)	0.514
Complication	131 (12%)	13 (9.8%)	0.475
Perforation	3 (0.2%)	0	0.405
Pancreatitis	85 (7.8%)	4 (3%)	0.042*
Bleeding	22 (2%)	4 (3%)	0.448
Infectious (cholangitis, cholecystitis)	13 (1.1%)	3 (2.2%)	0.302
Cardiopulmonary	8 (0.7%)	2 (1.5%)	0.346
ERCP related mortality			0.645
During the procedure	1 (0.09%)	0	0.728
After the procedure	1 (0.09%)	1 (0.7%)	0.516

\*\* Patients with stent insertion or removal due to malignancy, stenosis, cholangitis, parasite, bile duct damage.

**Table 3.** Binary logistic regression analysis for ERCP-related complications

	Odds ratio	95% CI	p
Age	1.02	0.99-1.06	0.07
Cholangitis	1.3	0.6-2.6	0.40
Pre-cut	0.89	0.3-2.5	0.84
Comorbid diseases			
Coronary artery disease	0.48	0.7-3.0	0.44
Diabetes mellitus	0.11	0.1-0.8	0.06
Hypertension	0.15	0.2-1.2	0.07
Cerebrovascular disease	0.99	2.6-3.7	0.99
Dementia	2.9	0.5-17.4	0.22
Cirrhosis	0.62	0.1-2.5	0.5

retroperitoneal air in the CT scans of the patients who developed perforation. They were considered as type 4 perforation.

When evaluated in terms of post-ERCP pancreatitis, the incidence of pancreatitis was observed less in the elderly patient group than in the control group ( $p=0.042$ ). Death due to ERCP occurred in three patients. One of the deaths occurred during the procedure and the other two occurred during their follow-up in the hospital after the procedure.

Pre-procedure cholangitis was present in 109 patients in total. Complications related to ERCP were observed in six (6.3%) of these patients. The patients with cholangitis were similar in terms of complications between the elderly and control groups ( $p=0.687$ ).

## DISCUSSION

As the average age increases worldwide, the elderly population is increasing day by day. With increasing age, bile duct pathologies are more common. Accordingly, in our study, we evaluated the risks of ERCP, which is the gold standard in diagnosis and treatment in hepatobiliary pathologies, in elderly patients by taking other age groups into consideration. As a result, no significant difference was observed in ERCP complications between other age groups and elderly patients.

Half (50.7%) of the 1225 ERCP procedures performed in our hospital in one year consisted of patients aged 65 and over, the geriatric patient group. The elderly age group over the age of 85 made up 10.8% of all ERCP performed.

Considering the reasons for ERCP, the most common reason was bile duct stones in both groups. It was observed that performing the procedure due to malignancy was significantly more frequent in the elderly group than in the non-elderly group.

Many studies report that the patient's comorbidity, except cirrhosis, has no effect on ERCP-related complications (7,8). In our results, we determined that comorbid diseases do not cause an

increase in ERCP complications. In our study, a total of three patients had a diagnosis of liver cirrhosis. There was no post-ERCP complication in these patients with Child A cirrhosis. As a matter of fact, in some studies conducted in this direction, complications after ERCP observed in patients with cirrhosis were higher in children B and C, and there was no increase in complication rates in patients with child A cirrhosis (9,10).

An interesting result of our study is that although the ASA score is significantly higher in elderly patients, the complication rates do not make a significant difference in both groups. A similar situation was described in a study by Galeazzi et al. (11) and the ASA scoring system was evaluated as a qualitative index rather than a quantitative index, which is insufficient to define the complexity of the geriatric population, and a comprehensive geriatric assessment (CGA) was proposed to be applied to geriatric patients as an alternative.

The frequency of complications due to ERCP varies between 5-17%. (11-15). In our study, our complication rate due to ERCP was 11.8%. When studies evaluating the safety of ERCP in patients aged 90 and over are reviewed, it is seen that the overall complication rates related to ERCP vary between 5-8% (16-18). In our study, there were a total of 45 patients aged 90 years and over. In these patients, ERCP-related complications occurred in two of our patients (4.4%).

Pancreatitis is one of the most common and important complications of the ERCP procedure. It has been reported that post-ERCP pancreatitis is seen less frequently in elderly patients due to less response to traumas caused by atrophy, fatty infiltration, and fibrosis that develop in pancreatic tissue with advancing age (19,20). While Finkelmeier et al. have reported the frequency of post-ERCP pancreatitis as 5.2% in patients under 80 years of age in their study including 758 patients, they found this rate as 0.9% in patients aged 80 and over. Similarly, Han et al. (21), in their study involving 624 patients, have stated that the frequency of post-ERCP pancreatitis was lower and its severity

was lower in patients over the age of 80 compared to the young age group. In our study, we found that the rate of post-ERCP pancreatitis was significantly lower in the elderly group compared to those without advanced age (7.8% vs. 3%).

During ERCP, pre-cut is needed at a rate of 5-31.5% (22-24). We needed pre-cut at a rate of 15.6% to provide cannulation. Our pre-cut requirement was similar in the elderly and control groups ( $p=0.386$ ). We did not observe a significant difference between the patient groups in the risk of post-ERCP complications and the patients who had pre-cut. It is not clear whether pre-cut increases the risk of post-ERCP complications (25,26). Bailey et al. (27) have stated that 90% of the cases were pre-incised after cannulation failure at least 15 times during the procedure and that the high rate of post-ERCP pancreatitis in patients with pre-cut was the result of these unsuccessful trials.

Finkelmeier et al. (19) have reported procedure-related bleeding up to 3 times in patients over the age of 90, but Fritz et al. (28) have stated that there was no significant difference in post-ERCP bleeding in patients over 80 years old compared to young people. Han et al. (21), similar to our study, have found no significant difference in terms of bleeding although anti-aggregant and anticoagulant use was significantly higher in the 80-year-old group compared to the younger group. In our study, in patients using dual antiaggregant drugs before ERCP, one of the drugs was stopped if it had a high cardiac risk. Patients using Warfarin or new generation anticoagulants were switched to low molecular weight heparin.

Cholangitis is a situation where the ERCP process should be carried out urgently. Studies suggest that the mortality risk of cholangitis is related to the timing of drainage rather than age (29-33). We applied an early period (<48 hours) ERCP to our patients with cholangitis and we did not find the association of cholangitis with an increased risk of complications in the elderly patient group.

The limitation of our study is that we did not know the procedure time, and a homogeneous classification could not be made before the procedure as the study was designed retrospectively, and the patients were treated with a structured classification for the operation.

As a result, ERCP is a very safe procedure that can be applied in elderly patients by experienced hands.

**Ethics Committee Approval:** The approval for this study was obtained from Health Sciences University Erzurum Regional Training and Research Hospital Ethics Committee (Decision No: 2020/02-19, Date: 20.01.2020).

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - A.R.B.; Design -S.C.; Supervision - A.R.B.; Data Collection and/or Processing - S.Ç.; Analysis and/or Interpretation - B.K.; Literature Review - S.C., Writing Manuscript - A.R.B.; Critical Reviews - Y.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

Türk J Surg 2021; 37 (2): 162-168

**85 Yaş ve üzeri hastalarda endoskopik retrograd kolanjiyopankreatografinin (ERCP) güvenliği: Tek merkez deneyimi**Ahmed Ramiz Baykan<sup>1</sup>, Serkan Cerrah<sup>1</sup>, Sedat Çiftel<sup>1</sup>, Büşra Karahan<sup>2</sup>, Yılmaz Özdemir<sup>3</sup><sup>1</sup> Erzurum Bölge Eğitim ve Araştırma Hastanesi, Gastroenteroloji Kliniği, Erzurum, Türkiye<sup>2</sup> Erzurum Bölge Eğitim ve Araştırma Hastanesi, İç Hastalıkları Kliniği, Erzurum, Türkiye<sup>3</sup> Erzurum Bölge Eğitim ve Araştırma Hastanesi, İç Hastalıkları Kliniği, Erzurum, Türkiye**ÖZET**

**Giriş ve Amaç:** Yaşlı hastalarda (85 yaş ve üzeri) endoskopik retrograd kolanjiyopankreatografinin (ERCP) etkinliğini ve güvenliğini değerlendirmek amaçlandı.

**Gereç ve Yöntem:** 12 ay içerisinde herhangi bir nedenle ERCP uygulanan hastalar değerlendirildi. ERCP uygulanan hastalar 85 yaş ve üzeri yaşlı grubu ve 85 yaş altı kontrol grubu olarak sınıflandırıldı.

**Bulgular:** Çalışmaya 504 erkek ve 721 kadın olmak üzere toplam 1225 hasta dahil edildi. Hastanede kalış süresi, ERCP'de ön kesi yapılan hasta sayısı ve mortalite oranı ileri yaştaki (85 yaş) hastalarda kontrol grubuna göre benzer özellikler gösterdi. Prosedüre bağlı komplikasyonlar açısından gruplar arasında pankreatit dışında anlamlı fark yoktu. Yaşlı grupta post-ERCP pankreatit anlamlı olarak daha az görüldü ( $p=0,042$ ). Toplam 191 (% 15,5) hastada ön kesi gerekti. Ön-kesi ve kolanjit geçiren hastalarda görülen ERCP sonrası komplikasyonlarda, ileri yaş grubu ( $\geq 85$  yaş) ve kontrol grubu ile karşılaştırıldığında anlamlı bir fark yoktu.

**Sonuç:** ERCP, genç hastalar kadar yaşlı hastalar ( $\geq 85$  yaş) için de güvenli bir prosedürdür.

**Anahtar Kelimeler:** Endoskopik retrograd kolanjiyopankreatografi, yaşlı, endoskopik prosedür

**DOI:** 10.47717/turkjsurg.2021.5166





# Does taurolidine have any effect on liver regeneration and oxidation in the experimental hepatectomy model?

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## ABSTRACT

**Objective:** Taurolidine is a bicyclic molecule produced by the natural amino acid taurine. Antibacterial, antiendotoxic and cytoprotective effects of taurolidine have been shown experimentally. Data on the effects of taurolidine on oxidative stress and hepatic regeneration are limited. The aim of the study was to evaluate the effect of taurolidine on hepatic regeneration and oxidative stress in rats undergoing partial hepatectomy.

**Material and Methods:** Forty adult, male Wistar Albino rats were randomly divided into four equal groups: sham (S) group (n= 10), post-sham operation taurolidine administered (ST) group (n= 10), partial hepatectomy (H) group (n= 10) and post-partial hepatectomy taurolidine administered (HT) group (n= 10). 100 mg/kg/day taurolidine was administered for seven days. Blood and liver tissue samples were collected on postoperative day seven. Liver tissue malondialdehyde, glutathione and Cu-Zn superoxide dismutase activity (SOD) were measured to assess oxidative stress. Binuclear hepatocyte and Ki-67 antigen levels were measured to evaluate hepatic regeneration.

**Results:** There was no difference between the groups for malondialdehyde, Cu-Zn superoxide dismutase and glutathione levels ( $p > 0.05$ ). Binuclear nuclei levels were comparable between the H and HT groups ( $p = 0.06$ ), while taurolidine decreased binuclear hepatocyte levels in the sham operated groups ( $p = 0.02$ ). Taurolidine application decreased Ki-67 levels after partial hepatectomy ( $p = 0.001$ ).

**Conclusion:** Taurolidine may cause anti-regenerative effects after partial hepatectomy without causing oxidative damage.

**Keywords:** Oxidative stress, liver resection, hepatic regeneration, partial hepatectomy

## INTRODUCTION

Partial hepatectomy (PH) is a common procedure of liver surgery. Hepatic regeneration (HR), which almost instantly follows PH, is an exceptional response of the organ to recover to its original size and functions (1). HR is a complex process where epithelial cells, Kupffer cells and hepatocytes have significant roles (2). Remarkable biochemical changes take place during HR; the oxidative stress has a paramount role with an immediate increase after the PH and during hepatic regeneration (3-4). Moreover, free oxygen radicals arise from the partial fragmentation of molecular oxygen, and free radicals increase with tissue damage; tissue malondialdehyde (MDA) is utilized to quantify lipid peroxidation caused by free radicals (5,6). Finally, tissue glutathione (GSH) levels and superoxide dismutase (SOD) activities reveal antioxidant status (7,8).

Taurolidine (TRD) is a taurine based bicyclic molecule, and previous studies have revealed that it has antibacterial, antiendotoxic and cytoprotective effects (9,10). TRD is mostly used for the treatment of patients with sepsis. It leads to prokaryote degeneration and connects free lipopolysaccharides to exotoxins (11). TRD suppresses mitochondrial cytochrome-C and induces apoptosis in tumor cells by inhibiting protein synthesis at an early stage without adverse effects (12,13). Since there is limited data on the effects of TRD on oxidative damage and hepatic HR after PH, it was aimed to evaluate this issue in an animal model.

## MATERIAL and METHODS

The Institutional Ethics Committee of Experimental Animal Research approved the protocol of the study. Forty Wistar-Albino male rats, weighing between 250 and 350 gr, were used. Rats were housed five in per cage, under constant temperature (

**Cite this article as:** Akın E, Sarıbeyoğlu K, Esen E, Aytaç E, Özbay G, Uzun H, et al. Does taurolidine have any effect on liver regeneration and oxidation in the experimental hepatectomy model? Turk J Surg 2021; 37 (2): 169-174.

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Received: 15.12.2019

Accepted: 04.04.2021

Available Online Date: 30.06.2021

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DOI: 10.47717/turkjsurg.2021.4690

20–22°C) and humidity (50F) with an artificial 12-hour light-dark cycle and randomized into four groups. Rats were fed ad libitum with standardized industrial rat prey during the study period except 12 hours prior to operation. Rats were divided randomly into four equal weight-matched groups containing ten rats each: Group 1: Sham (S) group; Group 2: Subsequent to sham operation, intraperitoneal TRD administered (ST) group; Group 3: Partial hepatectomy (H) group (the control group); Group 4: Subsequent to partial hepatectomy, intraperitoneal TRD administered (HT) group.

A daily dose of 100-mg/kg/day (Taurolidine®, Boehringer Ingelheim, Germany) were given to the rats in the ST and HT groups. The S and H groups were administered same volume 0.9 % NaCl solution intraperitoneally daily, while the others received TRD injections.

PH was performed with general anesthesia. After shaving, the abdominal wall was cleaned with povidone iodine solution and a median abdominal incision was performed. Standard 70% PH was performed in the H and the HT groups (14), whereas laparotomy without liver resection was performed in the S and the ST groups. The abdominal incision was closed with 2/0 silk continuous sutures. On postoperative day seven, the rats were decapitated under general anesthesia [ketamine 40 mg/kg, intraperitoneal and xylazine (5 mg/kg, intramuscular)]. Liver tissue sampling was done immediately after decapitation. Oxidative stress was evaluated by measuring malondialdehyde, glutathione and Cu-Zn superoxide dismutase activity (SOD) levels in the liver tissue.

### Biochemical analyses

Tissue samples were weighed at room temperature. Ten percent homogenates were prepared by homogenization buffer with 0.15 M phosphate. Homogenization was performed at 4°C. When the homogenization was completed, supernatants were obtained by centrifuging the homogenates, which were prepared for the determination of MDA at 3000 rpm for 10 minutes and for SOD and GSH at 13000 rpm for 15 minutes. The method of Beutler and et al. (15) was used for these quantifications. SOD analysis was performed based on Sun and Oberley's method (16). In MDA analysis, a pink colored complex is formed as a result of its incubation at 95°C with thio-barbituric acid (TBA) at pH 3.5 and this complex is measured by spectrophotometer at a wavelength of 532 nm. MDA levels were given as nmol/gr tissue by using MDA's molar extinction coefficient ( $n = 1.56 \times 10^5 \text{ M}^{-1}$ ).

### Histopathological analysis

For each animal, four randomly taken tissue sections were stained with hematoxylin-eosin and examined by experienced pathologists who were unaware of the treatment groups. Dual nuclei hepatocytes located randomly selected ten different fields were counted under x400 magnification. Cells definitely defined that two nuclei in a single cytoplasm were accepted as dual nuclei and the arithmetic average of the total number of cells were considered. The number of mitosis located in the same fields was recorded.

Immunohistochemical staining procedure was applied with Ki-67 (SP6) (Neomarkes, USA) ready-to-use rabbit monoclonal antibody. Ki-67 positive hepatocyte nuclei were counted at randomly selected 10 different fields under x400 magnification on aforementioned laminas. Some cells, such as lymphocyte, Kupffer et cetera, were excluded from the count. The ratio of Ki-67 positive nuclear staining cells to total cells number was calculated by percentage (17).

### Statistics

The results were presented as mean and standard deviation. P value of <0.05 was considered to be significant used by JMP® Statistical Discovery Software and analyzing Kruskal-Wallis test. Student's t test was used in the comparison of the groups of Binuclear hepatocyte and Ki-67.

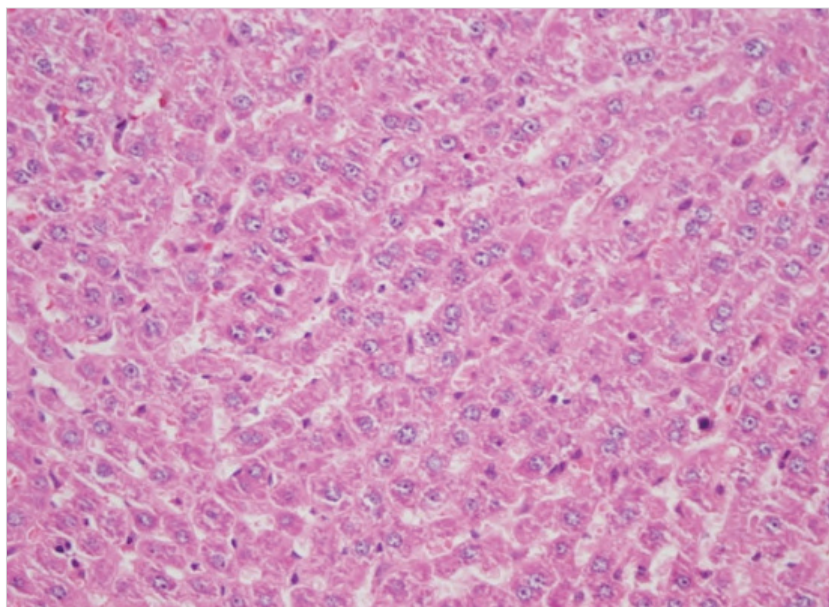
### RESULTS

All the rats completed the experiment; there was no perioperative death. There was no difference between the groups regarding the malondialdehyde, Cu-Zn superoxide dismutase and glutathione levels (Table 1). On postoperative day seven, both experimental and control groups had similar hepatic oxidant activity.

Although they were significantly close, the levels of binuclear hepatocytes were statistically comparable between the H and HT groups. ( $p = 0.06$ ). Additionally, taurolidine administration decreased binuclear hepatocyte numbers in the sham-operated group (Figure 1) and (Table 2). Further evaluation with immunohistochemical staining revealed decreased Ki-67 levels after PH with taurolidine use (Figure 2) and (Table 2).

**Table 1.** Groups' oxidative stress parameters levels

	Malondialdehyde $\mu \text{ mol/wet tissue}$	Superoxide Dismutase U/wet tissue	Glutathione $\mu \text{ mol/wet tissue}$
Sham (n= 10)	12.6 $\pm$ 7.7	0.9 $\pm$ 0.3	1.5 $\pm$ 0.3
Sham and taurolidine (n= 10)	12.8 $\pm$ 5.2	0.9 $\pm$ 0.1	1.3 $\pm$ 0.4
Partial hepatectomy (n= 10)	5.9 $\pm$ 0.7	0.8 $\pm$ 0.2	1.3 $\pm$ 0.2
Partial hepatectomy and taurolidine (n= 10)	6.02 $\pm$ 1.8	0.9 $\pm$ 0.2	1.5 $\pm$ 0.5
p	0.96	0.38	0.28



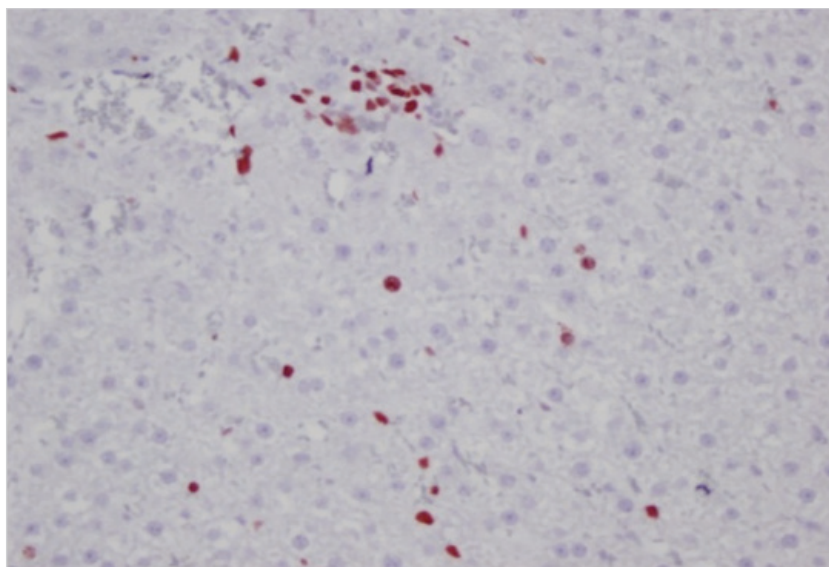
**Figure 1.** Binuclear hepatocytes after taurolidine administration.

**Table 2.** Binuclear and Ki-67 levels in groups

	Binuclear hepatocyte	Ki-67 (median)
Sham (n= 10)	15.6 ± 2.5	1
Sham and taurolidine (n= 10)	12.4 ± 2.3	1
<b>p*</b>	<b>0.002</b>	<b>1</b>
Partial hepatectomy (n= 10)	9.2 ± 2.2	10.3
Partial hepatectomy and taurolidine (n= 10)	11.2 ± 1.9	4.03
<b>p**</b>	<b>0.06</b>	<b>0.003</b>

\* p between the groups of sham with sham and taurolidine.

\*\* p between partial hepatectomy with partial hepatectomy and taurolidine.



**Figure 2.** Ki-67 levels after taurolidine administration.

## DISCUSSION

The results of the current study revealed that TRD use may reduce the ability of *in vivo* regeneration of the liver. This is a remarkable finding to consider for use of TRD after PH, especially for patients with limited functional liver capacity. TRD is commonly used for treatment of patients with sepsis (11). While we did not use any kind of septic model in our experimental study, it is well known that the toxic internal environment limits regenerative capacity of the liver and cause hepatotoxicity (18). The additional anti-proliferative effect of TRD may be an undesirable effect following liver resection. Anti-neoplastic effects of TRD against various cancer types such as mesothelioma have been shown previously (19). Prooxidant antineoplastic drugs affect cancerous tissue, but do not affect non-neoplastic tissue (20). TRD is a prooxidant antineoplastic drug with anti-regenerative effect on cancer cells and not hazardous on non-neoplastic tissues (21). TRD promotes leukopoiesis, erythropoiesis, as well as improves renal and hepatic function against systemic toxicity in severe sepsis (7). While TRD supports wound healing, it may prolong the epithelization process (22,23). Since regeneration pathways varies for different, consequences of TRD use may vary among the tissue types (24).

Hepatic regeneration is an exceptional response of the liver to recover to its original size and functions (1). In addition to hepatocytes, Epithelial cells, endothelial and Kupffer cells of the biliary tract play a role in liver regeneration (1,2). Endocrine and paracrine hormones, proto-oncogenes and transcription factors are the key points for modulating regeneration process (25). Remarkable biochemical changes take place during HR; the oxidative stress has a paramount role with an immediate increase after the PH and during hepatic regeneration (3,4). The liver tissue oxidant status was similar among study groups. The oxidant activity increases within the early phase of liver regeneration (26). Regeneration starts in 10-12 hours after hepatectomy, reaches to its maximum value at 24 hour and completes in 5-10 days (27). In rats, lipid peroxidation significantly increases 90 minutes after the generation of the liver ischemia (28). Hepatic functional tests are closely correlated with the MDA (29). Therefore, monitoring lipid peroxidation, gives a reliable impression on liver functions. We have previously reported that high oxidant activity was being maintained in the plasma but resolved in the liver tissue seven days after PH (14). Overall impression based on the results of the study is that anti-regenerative effects of TRD after PH seem non-toxic. There is no sign of oxidative damage in the biochemical and histological analyses were observed.

We need to mention the controversies on oxidative activity related to *in vivo* and *in vitro* use of TRD. Dual effect of TRD has been shown previously. While antioxidant properties of TRD

have been shown against sepsis induced oxidative stress, TRD increased production of reactive oxygen species in *ex vivo* glioma cells (7-21). Low production of oxidants and dominant antioxidant capacity of the non-malignant cells compared to the cancer cells and infectious agents may establish a selective environment for survival of healthy host tissues (30).

It has been shown that many inflammatory cytokines including TNF-alpha and IL-6 are up-regulated during hepatic regeneration (31,32). TRD increases NFkB which inhibits NFkB in esophageal cancer (33). NFkB is known as potential regulator of TNF-alpha and IL-6. Anti-inflammatory effects of TRD may indirectly contribute inhibition of hepatic regeneration (34). Angiogenesis is an important component of liver regeneration (35). Tumor-derived VEGF are blocked by TRD (29). Antiangiogenic properties of TRD can be considered as a potential drawback for hepatic regeneration.

Formaldehyde, which is a carcinogenic and toxic substance, is an *in vivo* breakdown product of TRD. In routine practice, TRD is used with polyvinylpyrrolidone, which reduces *in vivo* concentration of formaldehyde (36). No toxic effect of TRD has been reported neither in clinical practice nor in our study (37). In addition to hematoxylin and eosin dye for histological evaluation, immunohistochemical staining with Ki-67 (SP6) had performed. Ki-67 is an antigen in the nucleus of the cell and the level of the monoclonal antibody, which is produced against Ki-67, increases as the cell cycle progresses on (38,39). Ki-67 analysis is one of the most reliable immunohistochemical techniques for evaluating liver regeneration (40).

Lack of molecular markers analyzing hepatic regeneration and oxidative stress is the limitation of the study. However, our results provide a basis on taurolidine use after PH or in liver surgery for the patients with limited hepatic parenchyma reserve.

## CONCLUSION

Taurolidine may cause anti-regenerative effects after partial hepatectomy without causing oxidative damage.

**Ethics Committee Approval:** The approval for this study was obtained from Istanbul University Animal Experiments Local Ethics Committee (Decision No: 41, Date: 16.04.2009).

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - E.A., K.S., E.A.; Design - E.A., K.S., E.A.; Materials - E.A., E.E.; Data Collection and/or Processing - E.A., G.Ö., H.U.; Literature Review - E.A.; Writing Manuscript - E.A., K.S., E.A.; Critical Reviews - K.S., S.P.

**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 (2): 169-174

## Taurolidinin deneysel hepatektomi modelinde hepatik rejenerasyon ve oksidatif stres üzerine herhangi bir etkisi var mıdır?

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### ÖZET

**Giriş ve Amaç:** Taurolidin doğal bir aminoasit olan taurinden oluşan bisiklik yapıda bir moleküldür. Taurolidinin antibakteriyel, antiendotoksik ve sitoprotektif etkileri deneysel çalışmalarla gösterilmiştir. Taurolidinin oksidatif stres ve hepatik rejenerasyona etkileri için ise elimizde yeterli veri bulunmamaktadır. Çalışmanın amacı parsiyel hepatektomi yapılan ratlarda taurolidinin hepatik rejenerasyon ve oksidatif stres üzerine etkilerini ölçmektir.

**Gereç ve Yöntem:** Kırk erkek Wistar Albino rat rastgele dört eşit gruba ayrıldı: sham (S) grubu (n= 10), sham operasyonu sonrası taurolidin (ST) uygulanan grup (n= 10), parsiyel hepatektomi (H) grubu (n= 10), parsiyel hepatektomi sonrası taurolidin (HT) uygulanan grup (n= 10) 100 mg/kg/gün taurolidin yedi gün boyunca uygulandı. Kan ve karaciğer doku örnekleri postoperatif yedinci günden sonra alındı. Oksidatif stresi saptamak amacıyla karaciğer dokusunda malonaldehit, glutatyon ve Cu-Zn superoksit dismutaz (SOD) aktivitesi ölçüldü. Binükleer hepatosit ve Ki-67 anti-jen seviyeleri hepatik rejenerasyonu değerlendirmek için ölçüldü.

**Bulgular:** Gruplar arasında malonaldehit, Cu-Zn superoksit dismutaz ve glutatyon seviyeleri açısından fark yok (p> 0,05). Binükleer nükleus seviyeleri H ve HT grupları arasında karşılaştırılabilir düzeydeydi (p= 0,06), taurolidin binükleer hepatosit seviyelerini sham ve sham opere gruplarda azalttı. Taurolidin uygulaması parsiyel hepatektomi sonrası Ki-67 seviyelerini düşürdü (p= 0,001).

**Sonuç:** Taurolidin parsiyel hepatektomi sonrası oksidatif hasara yol açmadan anti-rejeneratif etki gösteriyor olabilir.

**Anahtar Kelimeler:** Oksidatif stres, karaciğer rezeksiyonu, hepatik rejenerasyon, parsiyel hepatektomi

**DOI:** 10.47717/turkjsurg.2021.4690





# A rare cause of duodenal obstruction: Bouveret syndrome

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## ABSTRACT

Gallstone ileus is a relatively rare pathology, most commonly obstructing the terminal ileum. Bouveret syndrome, leading to gastric outlet obstruction and seen with an incidence of less than 1%, is a syndrome met particularly in elderly patients and develops as the result of cholecysto-enteric fistula. In this report, it was aimed to present a 95-year-old case diagnosed with Bouveret syndrome.

**Keywords:** Obstruction, gallstone ileus, Bouveret syndrome

## INTRODUCTION

Bouveret syndrome was initially defined by Leon Bouveret and described as the gastric outlet obstruction occurring as the result of a cholecysto-duodenal or a cholecysto-gastric fistula (1). Non-specific symptoms such as nausea, vomiting, and abdominal pain are observed as the result of developing approximal obstruction in this syndrome, which is usually seen with a less than 1% incidence (2,3). Although ultrasonography is the first used imaging method for diagnosis, computerized tomography and magnetic resonance cholangiopancreatography (MRCP) can provide more precise information (4). Endoscopic, laparoscopic, and open surgical methods can be used for its treatment. In this report, it was aimed to present a 95-year-old case admitted to the emergency service with the complaint of nausea and vomiting and diagnosed with Bouveret syndrome.

## CASE REPORT

A 95-year-old female patient was admitted to the emergency service with the complaints of abdominal pain, nausea and bilious vomiting lasting for approximately two days. Her physical examination revealed tenderness at her right sub-costal region, with the absence of defense and rebound findings. Murphy finding was not present. Her bowel sounds were normal. Gas and stool discharge were absent for the last two days. In the rectal examination, the stool was present with no palpable mass. Other systemic examination findings were reported as normal. Regarding her laboratory results, liver function tests, renal function tests, and bilirubin values were interpreted as normal. Leucocyte count was measured as 8500/mm<sup>3</sup>, and other results of the complete blood count were normal. No pathology was detected on chest X-ray. Erect abdominal X-ray was obtained in the patient, and minimum amount of air-fluid levels were observed in the small bowel at the epigastric region. Abdominal tomography revealed a gallbladder stone leading to near-complete obstruction at the second portion of the duodenum. The patient was admitted to the ward, a nasogastric tube was inserted, and oral intake was discontinued. The patient was hydrated, and bilious drainage of approximately 500-750 cc/day was observed through the nasogastric tube. It was decided to remove the stone through endoscopic intervention. The patient was consulted with the Gastroenterology department, and endoscopic retrograde cholangiopancreatography (ERCP) was performed. The stone was attempted to be extracted using

**Cite this article as:** Yılmaz EM, Cartı EB, Kandemir A. A rare cause of duodenal obstruction: Bouveret syndrome. Turk J Surg 2021; 37 (2): 175-178.

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Received: 13.12.2016

Accepted: 05.05.2017

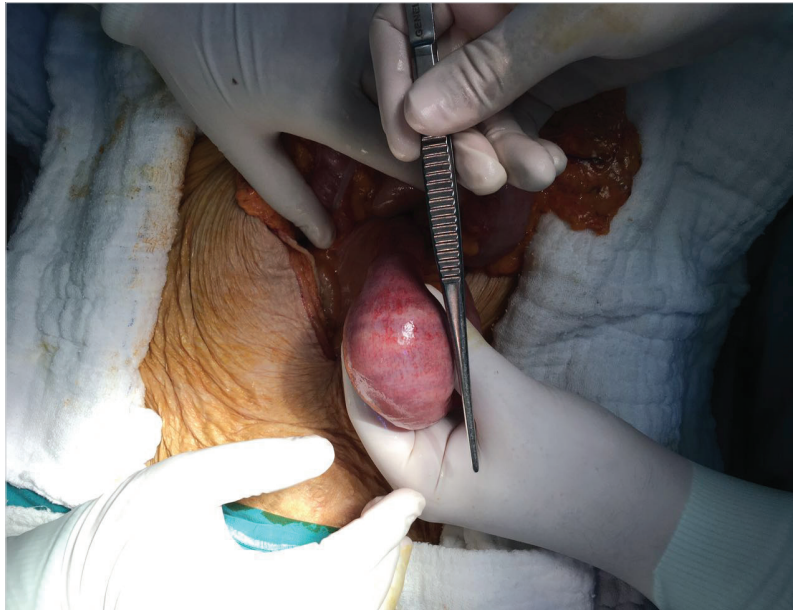
Available Online Date: 30.06.2021

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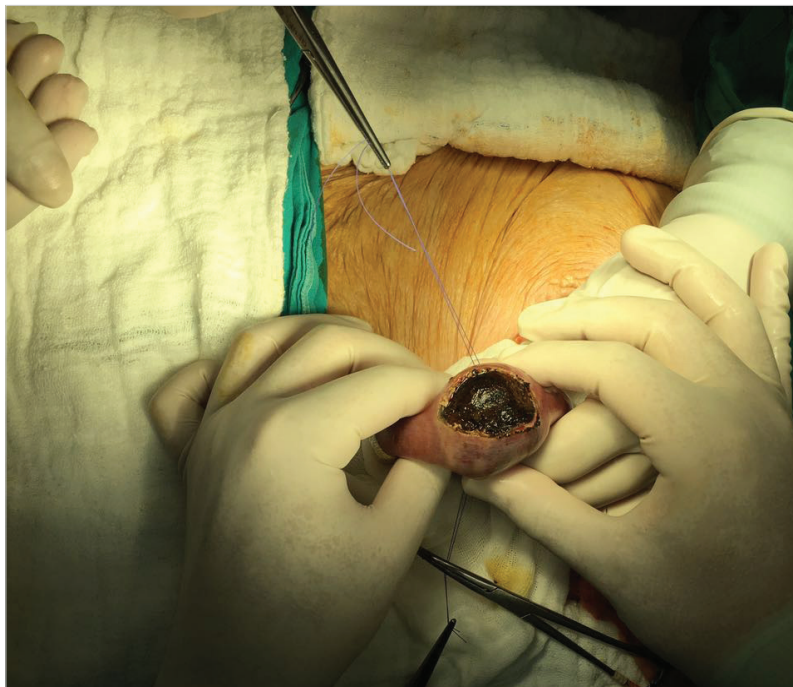
DOI: 10.47717/turkjsurg.2021.3794

the basket method, but it was observed that the size of the stone was too big. The stone was partially fragmented, and the procedure was terminated. A larger basket was brought in; however, it was observed that the stone was not in the duodenum and had moved further into the duodenum. Since ileus continued, laparotomy was decided to be performed. The patient and her relatives were informed about the disease of the patient together with its complications, and written informed

consent was obtained. The patient was taken to the operating room. Epidural anesthesia was preferred due to the advanced age of the patient. The gallstone causing complete obstruction at the location 10 cm distal to the Treitz ligament was observed (Figure 1). The attempt to move the stone to a further site by squeezing the intestine was unsuccessful. Enterotomy was made at the site of obstruction, and the stone was extracted (Figure 2). Then the enterotomy site was repaired primarily by



**Figure 1.** Gallstone causing complete obstruction.



**Figure 2.** Stone removal with enterotomy.

Gambie-type sutures, and the procedure was completed. The patient was followed postoperatively at the surgical ward. Liquid diet was started on the fourth postoperative day and was tolerated well. Then, following the gas-stool discharge, the patient's oral intake was increased, and she was discharged to follow-up on the sixth postoperative day.

## DISCUSSION

The incidence of ileus-related gallbladder stone is quite low (0.3-0.4%), and approximately 90% of these stones obstruct the terminal ileum (3,5). While a less portion of these stones obstruct the jejunum, duodenal and gastric outlet obstructions are seen with an incidence of less than 1% (1). The most typical reason of such a duodenal obstruction is the Bouveret syndrome, which is a cholecysto-enteric fistula.

Typically, abdominal pain, nausea and vomiting symptoms may be observed in Bouveret syndrome. Most of the cases are in advanced age and manifest typical gallstone symptoms (6). Our patient was 95 years old and manifested all of the typical symptoms. While these symptoms are usually confused with those of pyloric stenosis or other gastric outlet obstructions, the diagnosis can be more easily made by modern imaging methods today. In our case, making the diagnosis was also possible by performing computerized tomography. The initial attempt by endoscopic extraction of the stone was unsuccessful. The number of cases in whom endoscopic extraction of gallstone is successful is limited (7).

While surgical treatment is quite effective in Bouveret syndrome, the surgical method of choice is controversial. The main purpose should be to eliminate the symptoms with a minimal number of complications. Some authors prefer to remove the stone and close the enterotomy opening. Some others claim that the probability of recurrent ileus due to fistula is present with such a method (6); therefore, they claim that cholecystectomy and fistula repair should be performed within the same session. The risk of biliary tract injury is quite high with such a preference (8). Reisner et al., in their study (9), have reported that mortality rate reached 16.9% in single-stage, cholecystectomy + enterotomy, and fistula repair operations. In our case, we preferred to defer the cholecystectomy and fistula repair operation to a second stage due to the advanced age and extremely high amount of adhesions around the gallbladder and the biliary tract. It has been reported in the literature that recurrence may develop at a rate of 4-8% in cases in whom only enterotomy is performed (10). Fifty per cent of these recurrences develop within the following two years (11). We consider that meticulous planning should be done regarding mortality and morbidity in such cases. Since the age of our case was rather advanced, we preferred to discharge to follow-up after informing about recurrence.

## CONCLUSION

As a conclusion, gallstone ileus is a rarely met disorder, most commonly obstructing the terminal ileum whereas Bouveret syndrome is a much rarer cause of proximal mechanical gastrointestinal obstruction. It should be kept in mind as a preliminary diagnosis in advanced-aged patients admitted with typical complaints of abdominal pain, nausea, and vomiting. Various surgical methods are present and the most appropriate method that causes the least morbidity should be preferred.

**Peer-review:** Externally peer-reviewed.

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

**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**

Türk J Surg 2021; 37 (2): 175-178


**Nadir bir doudenom obstrüksiyon nedeni: Bouveret sendromu**Eyüp Murat Yılmaz<sup>1</sup>, Erdem Barış Cartı<sup>1</sup>, Altay Kandemir<sup>2</sup><sup>1</sup> Adnan Menderes Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalı, Aydın, Türkiye<sup>2</sup> Adnan Menderes Üniversitesi Tıp Fakültesi, Gastroenteroloji Bilim Dalı, Aydın, Türkiye**ÖZET**

Safra taşı ileusu oldukça nadir görülen bir olgu olup en sık terminal ileumu obstrükte etmektedir. Mide çıkış obstrüksiyonuna neden olan ve %1'den az görülen Bouveret sendromu ise özellikle yaşlılarda gözlenen bir sendrom olup kolesistoenterik fistül sonucu gelişen bir tablodur. Bu olgumuzda 95 yaşında Bouveret sendromu tanısı alan bir vakayı sunacağız.

**Anahtar Kelimeler:** Obstrüksiyon, safra taşı ileusu, Bouveret sendromu**DOI:** 10.47717/turkjsurg.2021.3794



# Pediatric abdominal chylolymphatic cysts-sneaky abdominal masqueraders

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## ABSTRACT

Chylolymphatic mesenteric cyst of the abdomen is a rare differential for cystic tumors, more so in the pediatric age group and has varied clinical presentations. There have been very few cases reported worldwide. To the best of our knowledge, a multicystic chylolymphatic cyst of the abdomen as demonstrated below is the first reported occurrence worldwide in the paediatric age group.

**Keywords:** Mesenteric cyst, chylous cyst, atypical presentation, abdominal cysts

## INTRODUCTION

Mesenteric cysts of the abdomen occur with exceedingly rare frequencies, more so in the paediatric population with an incidence of 1:100,000 in adults and 1:20,000 in children (1). They are most commonly found in the small bowel as compared to the large bowel, the ileum being the relatively more common site (2). Chylolymphatic cysts of the mesentery are chyle filled cysts characterized by the absence of smooth muscle and lymphatic spaces in the cyst wall (1,3). The exact theory of origin of these cysts is not known but a variety of possible explanations have been proposed; the most widely accepted being Gross' theory of benign proliferation of ectopic mesenteric lymphatics which have been excommunicated from the main lymphatic channels (4). They commonly present as solitary cysts or multiloculated cysts. Multiple lymphatic cysts of the small bowel arranged in a chain tightly attached to a segment of small bowel is rare as described in the case below.

## CASE REPORT

A 1-year-old male child presented to us with gradually progressing abdominal distension for the past 4-5 months with occasional episodes of vomiting which was non bilious. There was history of occasional constipation. On evaluation at his hometown, he was treated with ATT (anti tuberculous treatment) for a mistaken diagnosis of abdominal tuberculosis as his ultrasound revealed loculated ascites. After the medication, his mother did report some decrease in size. Clinical examination revealed a large mass of size 10x12 cm which was lobulated, variegated in consistency (cystic in some areas, firm in others) and partly mobile (Figure 1).

Ultrasound imaging of the abdomen revealed a well-defined large, heterogenous, predominantly multicystic lesion-9.4x12.2 cm extending from epigastrium up to the urinary bladder with no significant interval vascularity.

On a computed tomogram (CT) (Figure 2), the same lesion was found to have multiple enhancing septae within the lesion with bowel loops enmeshed within. His blood investigations were within normal limits.

Intraoperatively, he was found to have multiple cysts of varying sizes and colors, some hemorrhagic, arranged in a chain along the mesentery of the duodenum commencing at 4 cm from the duodenojejunal flexure and extending up to 20 cm. (Figure 3) An attempt was made to individually excise the cysts; however, that

**Cite this article as:** Mohamed F. Pediatric abdominal chylolymphatic cysts-sneaky abdominal masqueraders. Turk J Surg 2021; 37 (2): 179-182.

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Received: 07.02.2017

Accepted: 05.05.2017

Available Online Date: 30.06.2021

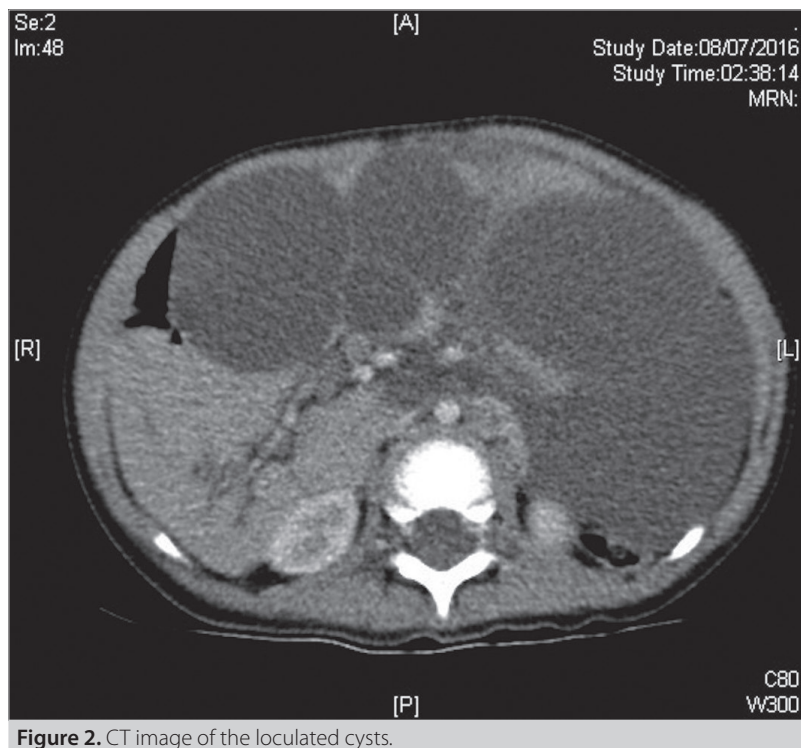
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DOI: 10.47717/turkjsurg.2021.3830





**Figure 1.** Pre-operative photograph-clinical presentation.



**Figure 2.** CT image of the loculated cysts.

caused the rupture of the cysts leading to leakage of milky chylous fluid, and proceeding would have rendered the mesenteric vascular supply precariously compromised. A resection was hence performed on the affected segment with the multiple cysts and an end to end double layer bowel closure with closure of the mesenteric defect was performed after confirming a good vascular supply to the bowel. The entire specimen was sent in total for histopathological examination which revealed

that the histopathology of the excised cyst showed the wall composed of a single layer of flattened cells with compressed connective tissue, consistent with the chylolymphatic cyst.

His postoperative period was uneventful.

#### DISCUSSION

Mesenteric cysts were first reported in the 16. century (2). They are rare with an incidence of 1:100,000 in adults and 1:20,000 in





**Figure 3.** Intra operative image of multiloculated cysts with varying appearance and sizes.

children (3). Chylolymphatic cysts comprise 7.3% of all mesenteric cysts and are characterized by the absence of smooth muscle and lymphatic spaces in the cyst wall (3-5). They are most commonly found in the small bowel as compared to the large bowel, the ileum being the relatively more common site (6). The exact theory of origin of these cysts is not known but a variety of possible explanations have been proposed; the most widely accepted being Gross' theory of benign proliferation of ectopic mesenteric lymphatics which have been excommunicated from main lymphatic channels (2). The usual occurrence is that of a solitary or multicystic lesion closely applied to the bowel wall, which to the best of our knowledge, has never been reported before. A similar case was described in an adult aged 35 years old published in 1992 (7).

Clinically, the patient may be asymptomatic or present with an abdominal mass, acute abdomen due to rupture, infection, hemorrhage into a cyst or volvulus or intestinal obstruction or other atypical presentations. Especially in endemic areas like ours, the presence of large chylolymphatic cysts can be mistaken for the more common loculated tuberculous ascites (8). Although tuberculosis would be a more common differential diagnosis to consider, emphasis has to be made that the diagnosis of these multiple chylolymphatic cysts; albeit rare; has to be kept in mind while dealing with patients who present with multiple cystic lesions in the abdomen. A Computed Tomogram is a useful adjunct in the evaluation of patients with abdominal distension.

Differential diagnoses considered in this case include mesenteric lymphangioma and MPIC (multilocular peritoneal inclusion cysts). These are distinct histologically; lack of smooth muscle and lymphatic spaces in the cyst wall seen in chylolymphatic cysts which will be demonstrated in a lymphangioma (3). An MPIC shows mesothelial cells on histopathology (4).

Current management guidelines recommend complete resection of the cyst either by enucleation or if blood supply to the bowel has to be sacrificed, resection and anastomosis of the closely applied bowel loop should be performed as in our case.

## CONCLUSION

Chylolymphatic cysts should be borne in mind as one of the differential diagnoses of cystic masses in the abdomen in the pediatric age group. Multiple chylolymphatic cysts rarely occur, but their clustered appearance with a negative work up for tuberculosis should warrant further imaging and a reconsideration of management options. In an endemic country for Tuberculosis such as India, this differential should also be borne in mind. Adequate surgical treatment includes a complete excision with resection and anastomosis of the affected bowel.

## Take Home Messages

1. Chylolymphatic cysts are a rare cause of abdominal distension in children.

2. Computed Tomogram is a useful adjunct in the evaluation of abdominal distension of unknown etiology (especially if the diagnosis is questionable).
3. En bloc bowel resection with the cyst may be required.

**Informed Consent:** Informed consent has been obtained from the patient's guardian before submission of this article.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - F.M.; Design - F.M.; Supervision - F.M.; Materials - F.M.; Data Collection and/or Processing - F.M.; Analysis and/or Interpretation - F.M.; Literature Search - F.M.; Writing Manuscript - F.M.; Critical Reviews - F.M.

**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 (2): 179-182

## Çocuk yaşta chylolenfatik mezenter kisti-sinsi abdominal taklitçiler

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## ÖZET

Abdominal chylolenfatik mezenter kisti, kistik tümörlerin nadir karşılaşılan bir türü olmakla birlikte çocuk yaş grubunda neredeyse hiç karşılaşılmamaktadır ve çeşitli klinik prezentasyonları vardır. Dünya çapında çok az sayıda olgu bildirilmiştir. Bildiğimiz kadarıyla, bu olgu sunumunda bildirdiğimiz abdominal multikistik chylolenfatik kisti, çocuk yaş grubunda dünya çapında bildirilen ilk olgudur.

**Anahtar Kelimeler:** Mezenter kisti, şilöz kisti, atipik prezentasyon, abdominal kist

**DOI:** 10.47717/turkjsurg.2021.3830



# Gastric volvulus as a deadly cause of acute abdominal pain: Presentation of three cases

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## ABSTRACT

Gastric volvulus is usually associated with non-specific abdominal pain and is a very rare condition. Diagnosis of gastric volvulus is difficult because of the lack of specific findings. Its acute form usually requires urgent surgical treatment and is associated with high mortality. In this study, gastric volvulus was diagnosed in three patients who presented with abdominal pain in the emergency department and had non-specific abdominal findings on physical examination. We evaluated this situation, which is rarely seen, on different patients.

**Keywords:** Gastric volvulus, acute, abdomen

## INTRODUCTION

Gastric volvulus is a rare condition that can occur at different degrees of rotation of the stomach along the long axis (organo-axial) on transverse plain (mesentero-axial) as combined or unclassified form, and can cause different clinical conditions. The stomach usually causes organo-axial rotation as a result of herniation of the defect of the diaphragm (1). Primary gastric volvulus is often blamed for laxity of the gastric ligaments. The Borchardt triad, which is clinically characterized by severe epigastric pain accompanied by abdominal distension, inability of vomiting despite gag reflex, and failure to insert a nasogastric tube can be seen in many patients with gastric volvulus (2). This study aimed to present three cases diagnosed with acute gastric volvulus.

## CASE 1

A 65-year-old female patient was admitted in the emergency department with complaints of sudden onset abdominal pain and distention. On physical examination, there were significant abdominal distention prominently in the epigastric region and diffuse abdominal tenderness. Patient anamnesis revealed that the patient had been suffering of dyspeptic complaints for a long time. An urgent laparotomy was performed for the lethargic patient with arterial blood pressure of 60/30 mmHg. During exploration, it was found that the stomach was expanded excessively, associated with rotation in the pylorocardic axis (organo-axial volvulus), and a necrosis has developed in an area with dimensions of 4x2 cm in the lesser curvature. In addition, the splenic capsule was observed with active hemorrhage due to laceration. No macroscopic pathology which could explain the volvulus was detected except gastrocolic and hepatogastric ligament agenesis and stenosis, which may be consistent with the fibrotic band of the pylori (Figure 1). Distal subtotal gastrectomy, Roux N-Y gastrojejunostomy and splenectomy were performed. Gastrojejunal fistula and further gastric atonia emerged in post-operative period and the patient who treated without operation was discharged on day 34 without any complaint. Pathological study was reported as 'pyloric stenosis and chronic inflammation. Informed consent was obtained from the son of the patient.

**Cite this article as:** Türkan A, Yalaza M, Akkurt G, Kafadar MT. Gastric volvulus as a deadly cause of acute abdominal pain: Presentation of three cases. Turk J Surg 2021; 37 (2): 183-187.

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Received: 01.06.2018

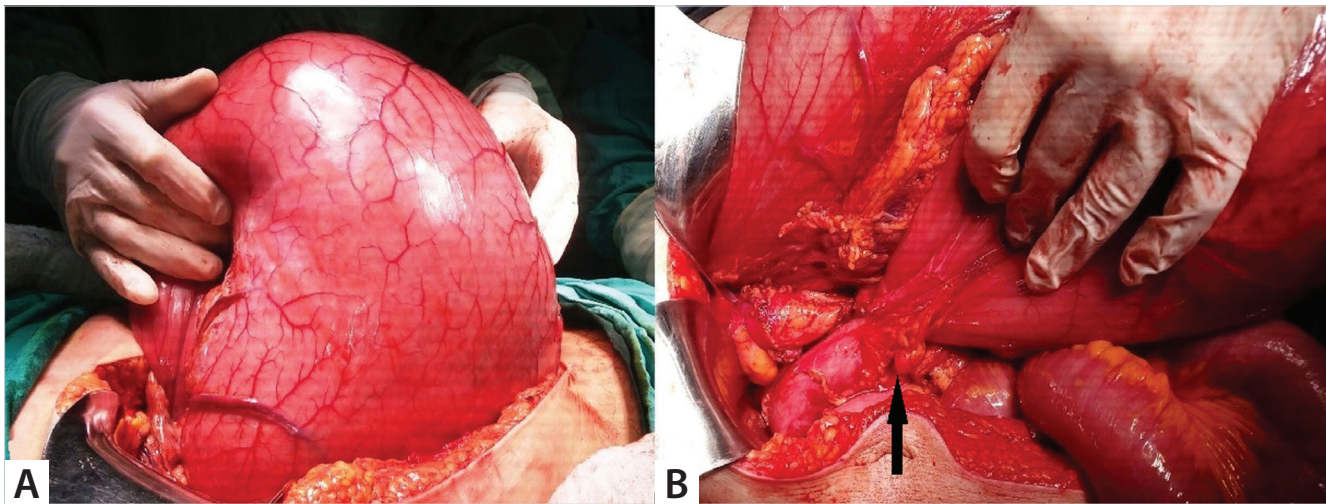
Accepted: 20.06.2021

Available Online Date: 30.06.2021

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DOI: 10.47717/turkjsurg.2021.4232





**Figure 1.** A. Gastricorgano-axial volvulus. B. Pylor (black arrow). The stomach is seen dilated due to pyloric stenosis but the duodenum is collapsed.

## CASE 2

A 78-year-old female patient was admitted in the emergency department with complaints of sudden onset abdominal pain and distention. According to anamnesis taken during the application, it was found out that she had chronic obstructive pulmonary disease (COPD) and history of gastric hemorrhage that occurred a year ago. On physical examination, there were abdominal distention, diffuse tenderness and defense. Tests resulted with white blood cell (WBC): 7.4 K/ul, hemoglobin (Hb): 11.5 g/dl, Creatinine: 1.87 mg/dl, C-reactive protein (CRP): 40 mg/L, Glucose: 130 mg/dl. Paraesophageal hernia, intraabdominal free air and fluid were detected on the abdominal computed tomography (CT) (Figure 2). Patient was preliminarily diagnosed with gastric perforation and emergency surgery was performed.

During exploration, it was found that the stomach was localized mostly in the thoracic cavity, organo-axial gastric volvulus has developed, the omentum and the transverse colon had elevated up to the diaphragm, and splenic hemorrhage had occurred due to diaphragmatic hernia. In addition, there was a post-pyloric perforation approximately 0.5 cm in diameter. Splenectomy was performed because hemorrhage could not be controlled. The stomach was taken into the abdomen and detorsed. No gastric ischemia was identified. The focus perforation of the post-pyloric region was primarily repaired by suturing and an omentopexy was performed. The diaphragmatic defect was repaired by suturing one-by-one using silk suture No. 1 after providing sufficient space in peripheral of the esophagus. The gastric corpus-anterior surface was sutured on the abdominal anterior wall



**Figure 2.** Tomographic image of the para-esophageal hernia.

using 3.0-Prolene sutures one-by-one and a gastropexy was performed. The patient had no drainage through catheters, her vital signs were stable, and she started on oral feeding on post-operative day seven and tolerated it. The patient who was known to have COPD previously was followed up by the Department of Chest Diseases with the diagnosis of post-operative pneumonia. The patient was transferred to intensive care unit and intubated on post-operative day 21 due to respiration arrest and started on mechanical ventilation support. The patient's enteral nutrition was maintained, spontaneous stool defecation occurred, and the patient died on post-operative day 51 due to respiratory problems. Informed consent was obtained from the son of the patient.

### CASE 3

A 75-year-old male patient was admitted in the emergency department with complaints of sudden onset abdominal pain and distention. It was found out that the patient was followed up for Chronic Lymphocytic Leukemia, stricture of the pylori detected during gastroscopy conducted for dyspepsia and patient had been suffering from dyspeptic complaints since then. It was further found out that the patient had relaxed spontaneously when transferring to a medical center due to the diagnosis of acute gastric volvulus six months ago. Physical examination showed abdominal distention and diffuse tenderness. Tests resulted with WBC: 11.69 K/ul, Hb: 10.1 g/dl, Creatinine: 1.69 mg/dl, CRP: 49.6 mg/L, Glucose: 190 mg/dl. Abdominal CT scan was found consistent with acute gastric volvulus (Figure 3). The patient, for whom emergency surgical treatment was planned, left the hospital voluntarily, not accepting the treatment, even though he was informed that he had a life-threatening risk. The patient was

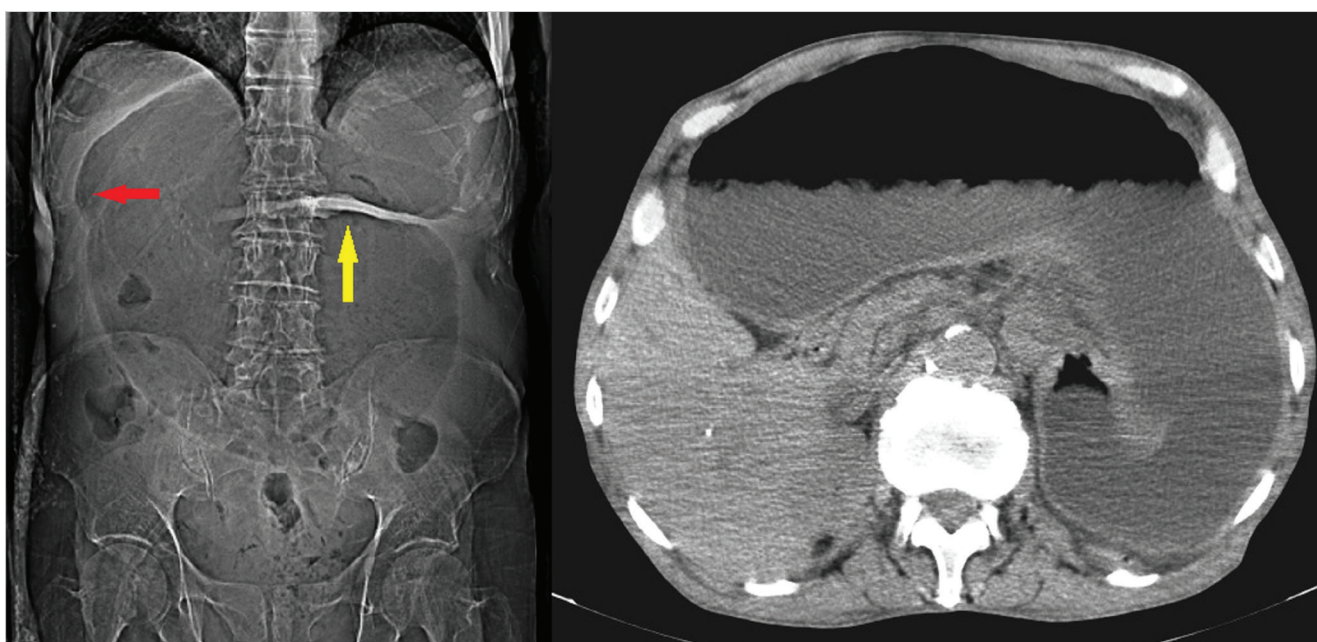
brought to the emergency department about 24 hours later in arrest condition. The patient without response to cardiac resuscitation died. Informed consent was obtained from the son of the patient.

### DISCUSSION

Gastric volvulus can occur due to the secondary causes such as diaphragmatic hernia of the stomach, pyloric stenosis, intra-abdominal adhesions, and peptic ulcers and/or tumors that cause the stomach torsion causing retraction of the minor curvature. Primary gastric volvuli are often blamed for laxity of the gastric ligaments (2,3). The first patient had collapse of the duodenum and severe gastric dilation secondary to pyloric stenosis. That patient also had gastroduodenal and hepatogastric ligament agenesis. The second patient had diaphragmatic hernia, and the third patient had known pyloric stenosis.

Gastric volvulus usually has a chronic and asymptomatic course. Symptomatic ones are associated with nonspecific dyspeptic complaints such as epigastric pain and feeling of abdominal distention. In some cases, respiratory problems due to diaphragmatic hernia can also be seen. In acute gastric volvulus, clinical picture is more complex and patients usually admit due to acute abdominal findings. Although the presence of the Borchardt triad is suggestive of gastric volvulus, its absence does not exclude the diagnosis (4). All of the patients had complaints of sudden onset severe abdominal pain and severe abdominal distention. It was found out that the first patient had been suffering from dyspeptic complaints for a long time.

Barium passage graphy and CT help the diagnosis of gastric volvulus (5). In addition, esophagogastroduodenoscopy, which can



**Figure 3.** Gastric organo-axial volvulus tomography image. Lesser curvature (yellow arrow), greater curvature (red arrow).



be used in patients with stable disease, can be used in both diagnosis and treatment to provide detorsion. CT continues to be a key diagnostic imaging for gastric volvulus because of its success in diagnosis, its rapidity, its 24-hour accessibility, its ability to assess the presence of necrosis or perforation of the gastric wall, and the possibility of planning treatment (6). The first patient, who was lethargic and hemodynamically unstable, underwent an emergency laparotomy without further tests and evaluations. CT of the second patient was consistent with para-esophageal hernia and gastrointestinal perforation, whereas CT of the third patient was consistent with acute gastric volvulus.

Although a conservative approach may be considered in selected cases, the treatment of gastric volvulus is surgery. Conservative treatment can only be considered for hemodynamically stable patients. Zuiki et al. have successfully treated a patient diagnosed with acute mesentero-axial gastric volvulus by endoscopic detorsion and gastropexy (6). Surgical treatment can be done by open or laparoscopic method. It usually includes procedures for the secondary cause leading to gastric volvulus and gastric fixation. Anterior gastroparesis or fundoplication may be preferred in gastric fixation. The results of both techniques are successful, and the technique to be applied depends on the condition of the patient (7,8). If there is gastric perforation or necrosis, resection must be performed (9). The Billroth two operation was performed for the necrosis of the gastric lesser curvature of the first patient. The second patient had no any ischemic focus. After post-pyloric perforation focus and diaphragmatic defect were repaired, anterior gastroparesis was performed.

Acute gastric volvulus should be treated without delay due to high mortality risk. Mortality level has been reported 30% in the case of presence of necrosis and perforation. The most common post-operative complication is pneumonia and long-term stay in intensive care. This is considered to be associated with the fact that patients are generally older and comorbid (8). The fistula of the patient with gastrojejunal anastomosis leakage was closed by treatment without operation. However, patient's length of stay was extended due to gastric atonia emerged accordingly. The second patient with known COPD died because of respiratory failure secondary to pneumonia that emerged within the post-operative period. The third patient, who refused the treatment and died in a short time of 24 hours, is considered a good example demonstrating the importance of quick treatment.

## CONCLUSION

While the chronic form often has an asymptomatic course, acute gastric volvulus is potentially life threatening and may be associated with high mortality rates. Early diagnosis and early surgical intervention can be life-saving for gastric volvuli.

**Ethics Committee Approval:** Retrospective case study.

**Informed Consent:** Informed consent was obtained from the son of the patients.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - A.T., M.T.K.; Design - M.Y., G.A.; Supervision - M.Y., M.T.K.; Materials - A.T., G.A.; Data Collection and/or Processing - A.T., M.Y., G.A.; Analysis and/or Interpretation - A.T., M.Y., G.A., M.T.K.; Literature Search - A.T., M.T.K.; Writing Manuscript - A.T., M.T.K.; Critical Reviews - 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 SERİSİ-ÖZET**

Türk J Surg 2021; 37 (2): 183-187

**Akut abdominal ağrının ölümcül bir nedeni olarak gastrik volvulus: Üç olgunun sunumu**

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**ÖZET**

Gastrik volvulus genellikle non-spesifik karın ağrısı ile ilişkilidir ve çok nadir bir durumdur. Gastrik volvulus tanısı, spesifik bulguların eksikliği nedeniyle zordur. Akut formu genellikle acil cerrahi tedavi gerektirir ve yüksek mortalite ile ilişkilidir. Acil serviste abdominal ağrı ile başvuran ve fizik muayenede non-spesifik abdominal bulguları olan üç hastada gastrik volvulus tanısı kondu. Bu sunumda, nadir görülen bu klinik durumu farklı hastalarda değerlendirdik.

**Anahtar Kelimeler:** Gastrik volvulus, akut, karın

**DOI:** 10.47717/turkjsurg.2021.4232



# Endoscopic parathyroidectomy via unilateral axillobreast approach

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## ABSTRACT

Endoscopic parathyroid and thyroid surgery is becoming increasingly common. In this study, we present the results of patients who underwent Endoscopic parathyroid via unilateral axillo-breast approach (EP via UABA). Three patients underwent EP via UABA. Patients were discharged on the next day after surgery, while at one month follow up all of them reported no further symptoms. Operation performed via two axillar and one areolar trochar. As different from open surgery, the strap muscles don't pulled laterally and not entered into the thyroid lobe from the midline. In this technique, the strap muscles are separated from the middle part of the strap muscles and the thyroid gland is reached from the middle of the strap muscles. In this way, N. laryngeal recurrence and parathyroid gland that usually located in the posterior aspect of the thyroid gland can be revealed clearly by reducing the risk of complications. EP via UABA can be performed safe effective procedure via good cosmetic results.

**Keywords:** Endoscopic parathyroidectomy, endoscopic surgery, parathyroidectomy

## INTRODUCTION

Primary hyperparathyroidism (PHPT) is a common endocrine disorder associated with elevated levels of serum calcium due to oversecretion of parathormone. 75%-85% of all cases are single adenomas; the remaining cases consist of multiple adenomas, hyperplastic glands, and carcinomas (1).

Bilateral neck exploration was a standart method of PHPT surgery in the past. Today, minimally invasive parathyroidectomy (MIP) has become the standard method with the use of high-resolution neck ultrasonography (US) and 99mTc-SestaMIBI scintigraphy (MIBI scan) (2). In addition to US and MIBI scan, some methods such as intraoperative rapid parathormone determination, radioguided surgery are used to increase the success of surgery in minimally invasive parathyroidectomy (3-5). Many studies have reported that MIP provides reduced operation time, length of stay and hospital costs (6). Furthermore, these studies showed that the MIP had fewer cases of permanent hypocalcemia with succesfully treatment results (95%) similar to bilateral neck exploration (7).

In past three decades, minimal access and minimally invasive techniques have become routine practice in abdominal and gynaecological surgeries. At the beginning of the 21. century, minimally invasive endoscopic techniques have been attempted in different subspecialties. Similarly, thyroid and parathyroid diseases were not excluded from these approaches.

In our country, endoscopic thyroid and parathyroid surgery has been applied in some surgical clinics. In this respect, we started to perform endoscopic thyroid and parathyroid surgery in our clinic. In this study, we presented patients who underwent endoscopic parathyroidectomy (EP) via unilateral axillobreast approach (UABA) in our clinic for parathyroid adenoma.

## CASES

Patients with a history of neck surgery or neck radiotherapy, patients with multiple adenomas compatible with surgical imaging methods, patients with ectopic

**Cite this article as:** Mayir B, Altun K, Ertürk MS, Ensari CÖ. Endoscopic parathyroidectomy via unilateral axillobreast approach. Turk J Surg 2021; 37 (2): 188-192.

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Received: 02.03.2020

Accepted: 24.04.2020

Available Online Date: 30.06.2021

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DOI: 10.5152/turkjsurg.2021.4755

parathyroid adenoma, patients with concomitant thyroid nodules, and patients who did not accept this surgical approach were not considered appropriate for EP via UABA. Except for the patients with this feature, patients who were compatible with parathyroid adenoma in the same localizations on both neck ultrasound and Tc-99m MIBI parathyroid scintigraphy were found suitable for e EP via UABA.

Three patients underwent EP via UABA. Two patients were female and one was male. The patients age were 24-67 (mean: 47.3). Preoperative blood calcium levels were 10.9-11.9 (mean: 11.5) mg/dl and parathormone levels were 99-548 (mean: 250) ng/dl preoperatively. Neck ultrasonography of these patients revealed parathyroid adenoma with a diameter of 9-30 (mean: 18) mm and located in the lower part of left thyroid lobe. Tc-99m MIBI parathyroid scintigraphy showed increased activity uptake at the same locations in all patients. All operations were completed endoscopically. The operations time was calculated

as 140-150 (mean 147 min). In all patients, N. laryngeus recurrences were seen and preserved. We did not need to use intraoperative neural monitoring in any patient.

Drains were removed in all patients one day after surgery. It was seen that blood calcium levels decreased below normal levels and parathormone levels returned to normal levels in three patients on the first postoperative day. There was no unpleasant cosmetic appearance in the neck on the first postoperative day in patients (Figure 1). Patients were discharged on the next day after surgery, while at one month follow up all of them reported no further symptoms. Histopathological examination of the parathyroid glands revealed as parathyroid adenoma.

### Surgical Technique

General inhalational anaesthesia was utilised with orotracheal intubation. Patients were placed in a supine position. The neck was slightly extended (Figure 2). A 10 mm incision was made



**Figure 1.** View of patient's neck one day after surgery.



**Figure 2.** Patient's position on the operating table.





**Figure 3.** Trochar positions.

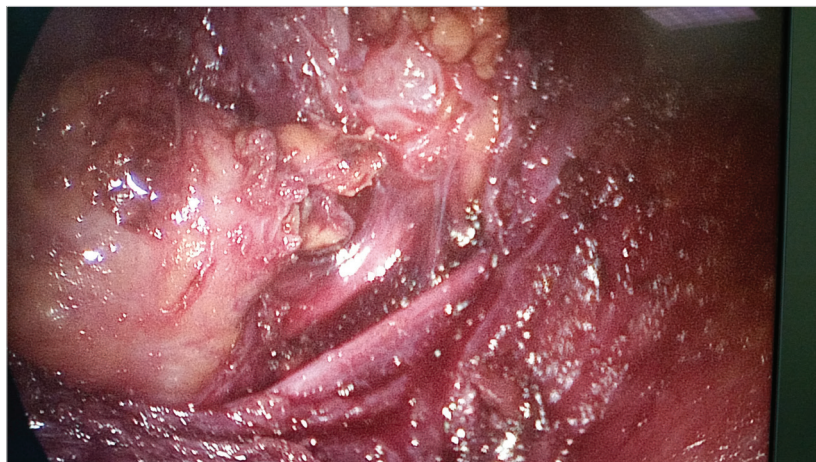
from the axillary region on the side where the parathyroid adenoma was detected. Trocar and camera were entered through this incision. 6 mm CO<sub>2</sub> insufflation was performed. 5 mm incision were made 3-4 cm above the 10 mm trocar incision and 5 mm incision were made around the breast areola on the same

side. Under the camera vision, 5 mm trocars was inserted from these incisions. (Figure 3).

No fluid or any drug injections were performed under the skin prior to flap dissection. Flap dissection was advanced from axilla to sternal notch. Than flap dissection was continued from the sternal notch to the thyroid cartilage. Thyroid strap muscles were found between the trachea and the sternocleidomastoid muscle and below the omohyoid muscle. Than strap muscles were opened parallel to the trachea with a cautery. The thyroid gland was reached through the strap muscles. The thyroid gland was separated from the muscle with blunt dissection and vascular sealing device and then lifted upwards. At this stage n. laryngeus recurrence was searched (Figure 4). Neural monitoring was not used routinely. According to preoperative imaging methods, parathyroid adenomas were found and removed. The parathyroid specimen was removed from the 10 mm trocar region in the endobag. The excised parathyroid specimen was sent for frozen section histopathological examination. After the histopathological examination confirmed the parathyroid gland, the trocars were removed following bleeding control. A hemovac was placed in the 10 mm trocar region and the operation was terminated.

## DISCUSSION

In the majority of the 20. century, a traditional approach for parathyroid exploration was done with a horizontal neck incision. The first EP was reported in 1996 by Gagner (8). Subsequently, in 1997, Husher reported the first endoscopic thyroidectomy (ET) (9). Increasing experience, gaining confidence among endocrine surgeons, and the presence of complex endoscopic equipment contributed to accelerating endoscopic thyroid and parathyroid surgery. However, this progress was more pronounced in ET than in EP. Probably, commonality of thyroid disease and more experience in open thyroid surgery compared to the less common PHPT are the most important factors for the stagnant evolution of EP. Another reason for this



**Figure 4.** View of N. laryngeus recurrence.



trend is that parathyroidectomy for solitary adenoma usually requires a small 2-3 cm incision compared to open thyroidectomy which requires a 6-10 cm incision.

Today, many EP and ET techniques have been reported. Fully endoscopic, video-assisted, robotic, transaxillary, chest wall, thoracoscopic, post-auricular, and lateral neck routes have been already attempted (10). Although none of them are universally confirmed, endoscopic parathyroid and thyroid surgery is becoming increasingly common. The goals of any ET and EP techniques are the cure with best cosmesis and low morbidity.

In this study, we present the results of patients who underwent EP via UABA. When the results were examined, it was seen that good cosmetic results, which are the most important expectations of endoscopic parathyroid surgery, were achieved. No complications were observed in any patient. In this study, the mean operation time was 147 minutes. This time seems to be long for open minimally invasive parathyroidectomy. Nuyeng et al reported that they completed thyroid lobectomy in 50 minutes by EP via UABA and operation time is same as open surgery (11). We think that operation time will be shorten as our experience increases. It is considered that after the learning curve phase, the operative times for EP via UABA will be comparable to open surgery

When compared with minimally invasive parathyroidectomy than can performe with 2-3 cm incision made with local anesthesia, it is accepted that there are disadvantages of EP via UABA such as requiring general anesthesia, requiring a total incision of 4 cm, and long operation time. The most important aspect of EP via UABA technique is that the incision made to axilla and areola, so there is no visible scar at the end of the operation and it shows a cosmetically superior result. Although the incision in the neck at the MIP is small, the scar on the neck is not considered to be cosmetic.

This technique is different from the conventional method. In this technique, as in the conventional technique, the strap muscles don't pulled laterally and not entered into the thyroid lobe from the midline. In this technique, the strap muscles are separated from the middle part of the strap muscles and the thyroid gland is reached from the middle of the strap muscles. In this way, n. laryngeal recurrence and parathyroid gland that usually located in the posterior aspect of the thyroid gland can be revealed clearly by reducing the risk of complications. Therefore, we did not need to use intraoperative neural monitoring in any patient.

Currently, the transoral vestibular approach has become very popular in endoscopic thyroid-parathyroid surgery. It has been shown that thyroidectomy and parathyroidectomy can be performed safely via this technique (12-14). Although there is no comparative study, we think that the EP via UABA have some advantages over the transoral endoscopic parathyroidectomy

vestibular approach (TOEPVA). Firstly, in TOEPVA method, some technical difficulties may arise because the trocars are very close to each other (15). This problem does not exist during endoscopic parathyroidectomy in the axillo-breast approach. Trocars can be inserted at desired distance intervals according to the patient. Secondly, if a second surgical intervention is required for thyroid or parathyroid glands after TOETPA, the second surgical approach cannot be performed endoscopically again. However, since the axillo-breast approach is performed only from the diseased side, a second surgical procedure could be performed on the opposite side via the axillo-breast approach. Thirdly, in EP via UABA, there are no risks such as mental nerve injury and infection that may occur in TOEPVA surgery.

It is demonstrated that EP via UABA for the first time in our country can be performed safely via good cosmetic results. In our country, there is increasing interest in endoscopic thyroid-parathyroid surgery in parallel via the developments in the world. Our study will further encourage surgeons to perform ET and EP. The publication of similar results in patients who underwent thyroidectomy will further demonstrate the efficacy and safety of this technique. It is demonstrated that EP via UABA for the first time in our country can be performed safely via good cosmetic results. can be recommended to patients who require parathyroidectomy and who have better cosmetic expectations than open surgery.

**Ethics Committee Approval:** The approval for this study was obtained from Health Sciences University Antalya Training and Research Hospital Clinical Research Ethics Committee (Decision No: 26/12, Date: 12.12.2019).

**Informed Consent:** Informed consents were obtained from patients.

**Peer-review:** Externally peer-reviewed.

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

**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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### CERRAHİ TEKNİK-ÖZET

Türk J Surg 2021; 37 (2): 188-192

## Aksilla meme yaklaşımı ile endoskopik paratiroidektomi

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### ÖZET

Endoskopik paratiroid ve tiroid cerrahisi giderek yaygınlaşmaktadır. Bu çalışmada aksilla meme yolu ile endoskopik paratiroidektomi tekniği ve bu hastalara ait sonuçları sunmayı amaçladık. Üç hasta bu teknik ile ameliyat edildi. tüm hastalar ameliyattan sonraki gün taburcu edildi. Birinci ay kontrollerinde hastalarda parathormon ve kalsiyum düzeyleri normal idi. Ameliyat aksiller bölgeden iki ve meme başından bir trokar girilerek yapıldı. açık cerrahiden farklı olarak strap kasları laterale ayrıldı ve tiroid lojuna orta hattan ulaşılmadı. Bu teknikte strap kasları orta kısımdan ayrılarak tiroid lojuna lateralden girildi. Böylece tiroid bezinin arka kısmında yer alan N. larengus rekürrens ve paratiroid bezleri kolaylıkla görülebiliyor ve komplikasyon riski azaltılabilir. Aksilla meme yolu ile endoskopik paratiroidektomi güvenli efektif ve kozmetik açıdan çok iyi sonuçlara sahip bir tekniktir.

**Anahtar Kelimeler:** Endoskopik paratiroidektomi, endoskopik cerrahi, paratiroidektomi

**DOI:** 10.47717/turkjsurg.2021.4755



# Letter to the editor concerning “Most cited 100 articles from Turkey on abdominal wall hernias: a bibliometric study”

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Dear Editor,

We read the article “Most cited 100 articles from Turkey on abdominal wall hernias: a bibliometric study” by Kulacoğlu et al (1). It is a very interesting, valuable and encouraging study for abdominal wall hernias especially for inguinal hernias. However, we think a highly cited article from Turkey written by Isik et al. “Metalloproteinases and Their Inhibitors in Patients with Inguinal Hernia” (Figure 1) published at World Journal of Surgery in 2017 should be ranked (2). We attached the images of citations of Web of Science/Google Scholar (Figure 2-3) for their research in our country (3,4).

**Cite this article as:** Işık A, Fırat D. Letter to the editor concerning “Most cited 100 articles from Turkey on abdominal wall hernias: a bibliometric study”. Turk J Surg 2021; 37 (2): 193-194.

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E-mail: kararda@yahoo.com

Received: 23.07.2020

Accepted: 07.04.2021

Available Online Date: 30.06.2021

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DOI: 10.47717/turkjsurg.2021.4973

> World J Surg. 2017 May;41(5):1259-1266. doi: 10.1007/s00268-016-3858-6.

## Metalloproteinases and Their Inhibitors in Patients with Inguinal Hernia

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PMID: 28050662 DOI: 10.1007/s00268-016-3858-6

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By: Isik, Arda; Gursul, Cebirail; Peker, Kemal; et al.  
WORLD JOURNAL OF SURGERY Volume: 41 Issue: 5 Pages: 1259-1266 Published: MAY 2017

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Figure 1. Published article at World Journal of Surgery in 2017 by Isik et al.



Figure 2. Citations of the "Metalloproteinases and their Inhibitors in Patients with Inguinal Hernia" at Web of Science.

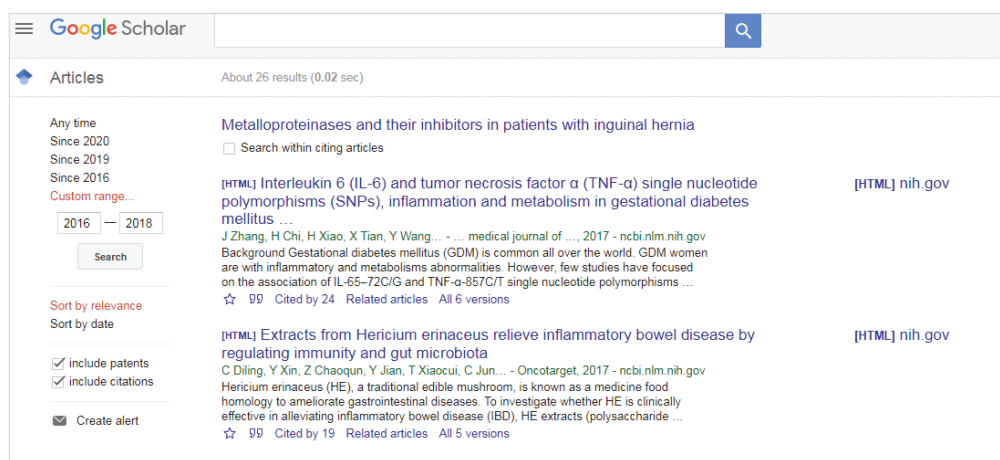


Figure 3. Citations of the "Metalloproteinases and their Inhibitors in Patients with Inguinal Hernia" at Google Scholar.

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## Letter to *A rare cause of acute abdomen: Isolated necrosis of the cecum*

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Dear Editor,

We value the article by Eyvaz et al. highlighting a rare case of isolated caecal necrosis with a classic presentation of acute appendicitis (1). It is a very interesting case as the cause of isolated necrosis of the caecum is not determined. Nevertheless, we believe that the value of this article could be improved further if certain issues are addressed. Firstly, we believe that readers will appreciate the description of the case to be made universally and widely understood. Authors have mentioned that there was no feature on direct abdominal graphy in the upright position, in which the features they meant to highlight are not grasped. Were they addressing the air-fluid level with dilated bowels as would be seen in the ileus and intestinal obstruction or features of pneumoperitoneum such as Riger's sign or gas under the diaphragm from the abdominal or chest radiograph (2)?

Secondly, we advocate that the preoperative diagnosis must be aligned to the complementary imaging modality, especially in acute surgical abdomen (3). It was presumed that he had acute appendicitis but computed tomography (CT) did not highlight such tomographic evidence. Certain diagnostic radiological features including a dilated and thickened appendix, presence of faecolith or free fluid that are pathognomonic for the diagnosis of acute appendicitis were not addressed. In fact, the CT scan showed thickening of caecal wall which could be guided towards malignancy or typhilitis. We hope that the authors could comment on the contrast uptake which suggests hollow and solid organ viability (4). In addition, radiological signs such as pneumatosis intestinalis, thumbprinting sign and pericolic fat streakiness would add to clinching a diagnosis pre-operatively. We believe the value of CT angiography of the bowel mesentery will give added value for diagnostic purposes and surgical planning in managing this patient.

Thirdly, in the era of minimally invasive surgery, such cases with a diagnostic dilemma will benefit from diagnostic laparoscopy with avoidance of unnecessary open surgery. Based on the laparoscopic findings, further interventions namely diverticulectomy and limited right hemicolectomy could follow especially in a tertiary centre with a presence of colorectal surgeon. As compared to performing an oncological resection, laparoscopic right hemicolectomy for benign cases requires less technical expertise and in return provides better surgical outcomes to the patient (5).

**Cite this article as:** Hayati F, Zakariz AD, Azizan N, Kadir F, Subramaniam S. Letter to: a rare cause of acute abdomen: isolated necrosis of the cecum. Turk J Surg 2021; 37 (2): 195-196.

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Received: 12.11.2020

Accepted: 12.03.2021

Available Online Date: 30.06.2021

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DOI: 10.47717/turkjsurg.2021.5115



Lastly, pertaining to the specimen, we reckon that there was no proper orientation of the gross specimen in addition to the lack of a gauge to objectively portray the specimen's measurement. The picture of the specimen provided depicts excision of the Meckel's diverticulum only. This is in contrast to the conventional resection of Meckel's diverticulum with a 2 to 5 cm margin of the ileum both proximally and distally to encompass the removal of ectopic gastric and pancreatic tissue, which may be present within this region and could cause complications at a later date. Despite providing the microscopic image of the histopathological examination, it is not well-magnified to be appreciated. We suggest that the provision of images with higher magnification may aid in solving this diagnostic dilemma.

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# Emergency hernia surgery during COVID-19 outbreak: delayed presentations, more resections

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Dear Editor,

The outbreak of COVID-19 pandemic has, without a doubt, affected the provision of emergency and elective surgery on a worldwide scale. In contrast to elective procedures, emergency surgery can hardly be postponed due to the associated increased morbidity and mortality risks; hence the public has been globally encouraged to seek medical attention upon the development of acute symptoms (1,2). However, in our anecdotal experience, and being in accordance to recently published data, there has been a drop in the volume of the emergency hospital admissions, with a notable increase of the complexity of the presenting problems (3). With respect to surgery, and in particular emergency hernia surgery, we have noticed a trend of delayed admission from the onset of symptoms, along with an increased percentage of non-salvageable visceral contents during emergency hernia repairs. We have therefore reviewed our operative records of emergency hernia repairs since the onset of the pandemic in our catchment area (Warwickshire, United Kingdom) between 03/2020-02/2021 (COVID-19 pandemic year) and compared them with the relevant data from 03/2019-02/2020 (pre-COVID-19 pandemic year). Of note, our hospital (district general) has been providing continuously uninterrupted emergency general surgery services in our region during the COVID-19 pandemic outbreak. However, between 03-05/2020 and 01-02/2021 there was a substantial reduction in the volume of elective operations (including hernias), with prioritization of clinically urgent cases, such as surgical oncology operations, as sole elective procedures, due to increased hospital pressures from the pandemic.

Reviewing our records for the 2020-2021 study period, we performed 46 emergency hernia operations, while 29 cases were operated between the respective 2019-2020 observation period; therefore, resulting in a more than 50% increase of our emergency hernia workload during the pandemic. Interestingly, the average time from onset of symptoms of incarceration/strangulation to the eventual assessment by the on-call surgical team increased in the COVID-19 period to 2.7 days from 1.2 days in the pre-COVID-19 year. The latter resulted in a significant increase of the need for intestinal resections due to non-viability of the herniated viscera, from 10.3% (2/29 cases) in 2019-2020 to 17.4% (8/46 cases) in 2020-2021. Although there was no major postoperative morbidity or mortality in our case series, either in 2019-2020 or 2020-2021 (only Clavien-Dindo grade II/III –wound infections, superficial post-operative collections, urinary retentions / no occurrence of anastomotic leaks, re-operations or unplanned returns to the Intensive Care Unit), there was a significant increase of the average length of stay of the patients operated during the 2020-2021 period (5.77 days in 2020-2021 vs 3.01 days in 2019-2020), to an extent expected due to the higher resection rates during the pandemic year. With

**Cite this article as:** Seretis C. Emergency hernia surgery during COVID-19 outbreak: delayed presentations, more resections. Turk J Surg 2021; 37 (2): 197-198.

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**E-mail:** babismed@gmail.com

**Received:** 06.03.2021

**Accepted:** 19.04.2021

**Available Online Date:** 30.06.2021

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**DOI:** 10.47717/turkjsurg.2021.5267

respect to possible hospital-acquired COVID-19 infection, none of our patients was tested positive (nose-throat swab for PCR) during any stage of their hospitalization, and none developed any major respiratory tract complication.

Based on our observations as a district general hospital emergency surgical service, in light of the recurrent relapses of COVID-19 infection waves in the community -and until the immunisation programmes cover the majority of the general population- we strongly advocate that patients with acutely symptomatic hernias should be encouraged to seek surgical specialist input with no delays. In our experience since the outbreak of the pandemic, emergency hernia surgery can be safely performed with very low risk for respiratory complications and postoperative care can be delivered without unplanned

intensive care admissions. We would reserve taxis of the acutely symptomatic hernias only for patients who are unfit or unwilling for surgery.

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