SURGERY and SURGICAL ENDOSCOPY

Official Journal of the Slovenian Society for Endoscopic Surgery

Vol. 2, No. 1, Jan. 2020

January 2020 ISSN 2591-2275 (print edition), ISSN 2670-5443 (electronic edition)

Surgery and Surgical Endoscopy

Official Journal of the Slovenian Society for Endoscopic Surgery

Slovenian Society
for Endoscopic Surgery

Surgery and Surgical Endoscopy is a fully open acces, peer-reviewed journal that aspires to publish articles relevant to surgery, surgical oncology as well as surgical endoscopy from researchers worldwide. The journal accepts review articles, research articles, case reports, letters to the editors, study protocols and "How I do it" submissions.

Publisher
Slovenian Society for Endoscopic Surgery

Address of the Editorial Office and Administration
Založka cesta 7, 1000 Ljubljana, E-mail: info@zeks.si

Reader for English
DEKS, d.o.o.

Layout
Jan Grosek

Graphic design
GALdesign

Printed by
Tiskarna Januš, Ljubljana

Issue frequency
2 isssues/year

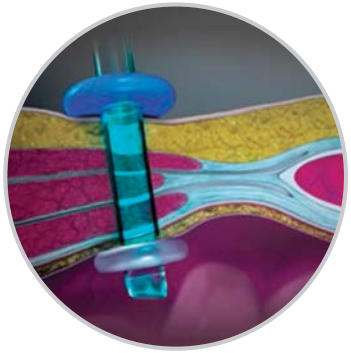
Circulation
100

Indexed and/or abstracted
Digitalna knjižnica Slovenije (dLib)

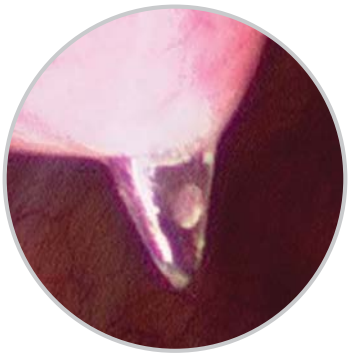
Applied Medical

A New Generation Medical Device Company

Kii Fios
First Entry System



THE ONLY INSUFFLATING OPTICAL PORT



MINAMed d.o.o. | Leskoškova cesta 9e, 1000 Ljubljana
+386 41 799 119 | +386 51 323 767 | info@mina-med.com

MINAMed

Contents

RESEARCH ARTICLES

SHORT COMMUNICATIONS

CASE REPORTS

STUDY PROTOCOLS

Editorial

Tomaž Jagrič, *University Medical Centre Maribor*
Jan Grosek, *University Medical Centre Ljubljana*

Correspondence

Tomaž Jagrič
tomaz.jagric@gmail.com

Jan Grosek
jan.grosek@kclj.si

Dear Colleagues,

Allow us to offer you a brief tour through this issue of the journal.

Arpad Ivanecz et al. have written an excellent research article analyzing complications after laparoscopic liver resection (LLR). They analyzed 128 consecutive patients after LLR, operated on between April 2008 and February 2019. Their results confirm LLR as a valid alternative to an open approach at their tertiary referral center. Early recognition of complications also allows for the timely provision of appropriate and targeted therapies in gastric surgery. Tomaž Jagrič analyzed the results of 1,211 gastric cancer patients operated on at the Maribor University Clinical Center in a 27-year period. Their excellent results show that centralization of these patients in high-volume centers not only lowers morbidity and mortality but also ensures long-term survival.

Jan Grosek et al. performed a retrospective analysis of patients that underwent preoperative endoscopic retrograde cholangiopancreatography with endoscopic papillotomy (ERCP/EPT) followed by laparoscopic cholecystectomy. The aims of their study were evaluation of their current clinical practice as well as trying to determine the optimal timing for cholecystectomy after ERCP/EPT.

Postoperative complications represent a potentially avoidable cause of morbidity and mortality. Moreover, they can also have a significant impact on health-related quality of life (QoL) of patients. QoL is increasingly recognized as an important aspect of cancer care. Jurij Aleš Košir et al. evaluated the extent of bowel disfunction in their first 11 rectal cancer patients operated on using a novel transanal approach (TaTME, or transanal total mesorectal excision). The Slovenian version of the low anterior resection syndrome score was completed by 10 out of 11 patients contacted. The preliminary results show that

the TaTME technique results in acceptable impairment of anorectal function comparable to standard laparoscopy or even the open approach.

Urška Kmetec and Mirko Omejc present an extraordinary case of a female patient that sustained a gunshot injury, was hemodynamically unstable, and had to be operated on. Fortunately, the projectile hit a silicone breast implant, causing a change in its trajectory. Because of this, the injuries sustained were not immediately fatal and the patient's life was saved with an emergency operation.

Peter Spazzapan et al. write about posthemorrhagic hydrocephalus in the setting of intraventricular hemorrhage, which is a frequent problem especially in preterm infants and as such remains an important cause of neurological impairment. The authors describe a neonate patient with such hydrocephalus that was treated with neuroendoscopic ventricular lavage.

Finally, describing the protocol of their new prospective non-randomized longitudinal clinical study, Jurij Janež assesses the role of inflammatory biomarkers, lactate, and carcinoembryonic antigen as possible markers for early recognition of patients with anastomotic leakage after colorectal resections.

We sincerely hope you enjoy reading this issue as much as we did. Let us finish by encouraging you to consider the journal Surgery and Surgical Endoscopy for publishing your work.

Best regards, and stay safe in these extraordinary times!

Jan Grosek** and **Tomaž Jagrič
Editors-in-chief

Editorial

Optimized perfusion.[1] Reduced leaks at the staple line.[2]

ECHELON CIRCULAR™ Powered Stapler

2 new technologies only in the ECHELON CIRCULAR™ Powered Stapler

The ECHELON CIRCULAR™ Powered Stapler is designed to reduce leaks without compromising perfusion—**which can result in 61% fewer leaks at the staple line.**[3]

- 3D Stapling Technology **evenly distributes compression**[4]
- Gripping Surface Technology provides **gentler handling** which has resulted in a 33% reduction in compressive forces on tissue[5]
- The combination of 3D Stapling Technology and Gripping Surface Technology **can optimize perfusion and reduce leaks at the staple line**[3]

Built on a powered firing platform, the ECHELON CIRCULAR Powered Stapler had 37% less movement at the distal tip for **increased stability.**[6]

Examples of applicable procedures

Designed specifically for creating the anastomosis in colorectal, gastric and thoracic procedures.

Colon resection

Gastrectomy

Esophagectomy

ETHICON
PART OF THE Johnson & Johnson FAMILY OF COMPANIES

Shaping the future of surgery

Echelon Circular™

Claims compared to the Medtronic manual DST Series™ EEA™ Stapler. Based on benchtop testing.

Prevention of Complications Related to Laparoscopic Liver Resection

Arpad Ivanecz, Irena Plahuta, Tomislav Magdalenić, Tomaž Jagrič, Bojan Krebs
Department of Abdominal and General Surgery, Maribor University Medical Center

Correspondence

Asst. Prof. **Arpad Ivanecz**
arpad.ivanecz@ukc-mb.si

Key words

liver resection, laparoscopic, morbidity, mortality

Research Article

SURGERY SURG ENDOS 2020; 2(1): 7-12

Abstract

Background. Laparoscopic liver resection (LLR) has been accepted as an attractive alternative to open liver resection. In determining the appropriateness of a minimally invasive approach, the primary consideration is patient safety. This study analyzes complications related to LLR.

Methods. A prospectively maintained database of all consecutive LLRs in a tertiary referral center specializing in hepato-pancreato-biliary surgery was retrospectively reviewed. The first 128 patients that underwent pure LLRs between April 2008 and February 2019 were analyzed. Intraoperative complications were defined as major blood loss, unintentional damage to surrounding structures, and conversion to an open approach. Postoperative complications were defined and graded according to the Clavien–Dindo classification.

Results. Altogether, 23 of the 128 LLR procedures (17.9%) were associated with intraoperative complications. Median estimated blood loss was 110 ml (range: 0–2,200 ml). Seventeen (13.2%) patients received perioperative blood transfusion. Blood loss of more than 775 ml occurred in eight (6.2%) patients (conversion to laparotomy was required in three of them). No unintentional damage to surrounding structures occurred in any patients. Conversion to laparotomy was required in 18 (14.0%) patients. The overall incidence of postoperative complications was 38 (29.7%). The incidence of postoperative major morbidity and mortality were 9.3% (n = 12) and 0.8% (n = 1), respectively. Four patients (3.1%) required reoperations. Three patients (2.3%) were readmitted after discharge from the hospital.

Conclusion. Only the subset of surgeons that are dually trained in hepatobiliary surgery and minimally invasive surgery are adequately equipped to safely perform LLR. Surgeons should recognize the increased risk they assume by taking on more complex procedures.

Introduction

In the previous century, minimally invasive surgery was introduced to minimize trauma in gastrointestinal operations. After the first laparoscopic cholecystectomy, the indications for a laparoscopic approach increased significantly (1). Liver surgery was initially thought to be unsuitable for laparoscopic techniques due to the difficulties of safe mobilization and exposure. As a result, a significant number of experts in open liver surgery were reluctant to incorporate a laparoscopic approach into their practice. Because of advances in radiology, anesthesiology, and surgical techniques that allowed for safer open liver surgery, these advances rarely became the bases for investigating how to make liver surgery less invasive. This reluctance was rooted in the fear of losing the improvements that the community of open liver surgeons had achieved (2).

However, early case reports and subsequent cohort studies confirmed the feasibility and safety of laparoscopic liver resection (LLR) (3). This surgical innovation was primarily proposed for peripherally located and small benign tumors. To date, two consensus conferences have been held on LLR. One of the conclusions from the first consensus conference, held in 2008, was that laparoscopic resection of segments II and III should be considered the standard of care (4). The second conference, in 2014, indicated that major resections were an innovative procedure but still in an exploratory phase (5).

In determining the appropriateness of any treatment or approach, the primary consideration is patient safety. The aim of this study was to analyze the complications related to LLR.

Methods

A retrospective review was performed of a prospectively maintained database of patients that underwent LLR at the Department of Abdominal and General Surgery, Maribor University Medical Center, Slovenia. At this institution LLR was first performed in April 2008. Patients that underwent laparoscopic cyst fenestration, liver biopsies, and radiofrequency ablation were excluded. Data were collected until February 28th, 2019.

Only pure LLR was performed; no hand-assisted or hybrid procedures were used. All LLRs were performed using techniques as reported previously (6–8).

Intraoperative complication (IOC), described as an objective marker of a complex operation (9), was used as a primary endpoint of the study. Key markers were blood loss over 775 ml, unintentional damage to surrounding structures, and conversion to an open approach.

Postoperative complications (POC), including 90-day morbidity and its grade, 90-day mortality, and the 30-day readmission rate, were secondary endpoints of the study. Postoperative complications were defined as any deviation from the normal course of recovery with the need for pharmacological, surgical, radiological, or endoscopic intervention, and they were based on the most severe complication that occurred. Postoperative morbidity was graded according to the Clavien–Dindo (CD) classification (10). Grades ≥ 3 represent a major complication requiring invasive intervention, the use of organ support, and fatality.

IBM SPSS for Windows Version 21.0 (IBM Corp., Armonk, NY, USA) was used for statistical computations. Statistical analysis was performed by using descriptive statistical methods.

Results

From April 2008 to February 2019, a total of 128 consecutive patients underwent pure LLR and were enrolled in the study. The number of patients treated by LLR progressively increased, but the total number of liver resections performed at our center showed no considerable variations, and thus the average number of open and laparoscopic liver resections per year was 69 (range: 60–86). Ten or more LLRs per year have been performed since 2013. The number of LLRs per year gradually increased to 20 in 2016, and this growing trend has been further observed in the most recent periods (Figure 1).

Indications for LLR were malignant disease in 89 (69.5%) patients, including colorectal liver metastases in 42 (32.8%), hepatocellular carcinoma (HCC) in 28 (21.9%), intrahepatic cholangiocarcinoma in 11 (8.6%), and other types of malignancy in eight (6.2%). The most commonly in-

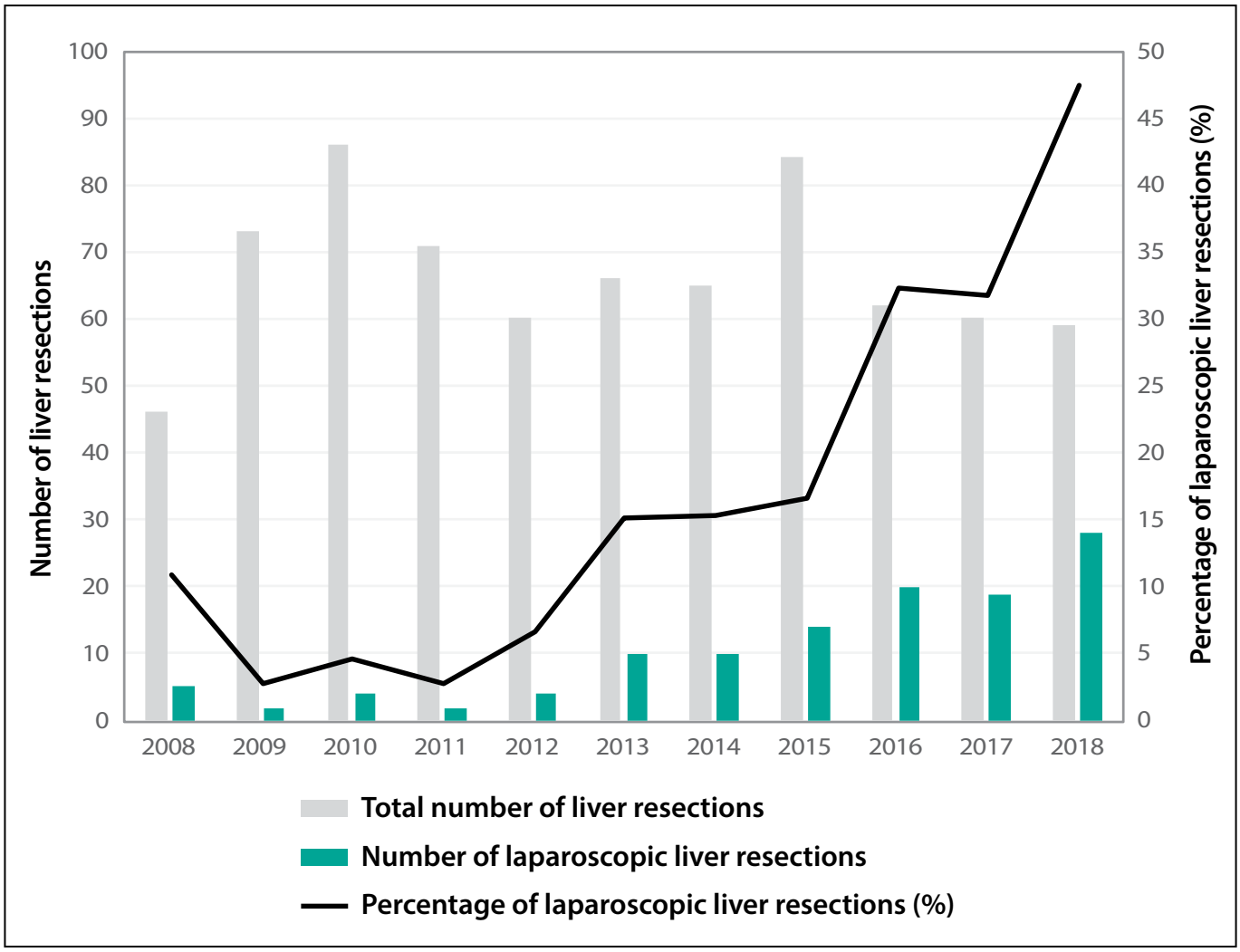


Figure 1. Number and proportion of laparoscopic liver resections per year compared to open liver resections in an 11-year period from April 2008 to 2019.

filtrated liver area was anterolateral segments in 100 (78.1%) patients. The median tumor size and number were 38.5 mm (range: 11–163 mm) and 1 (range: 1–4), respectively. Anatomical resections were performed in 70 (54.7%) patients, including 13 (10.2%) that underwent major liver resections. The median operative time of all procedures was 155 minutes, ranging from 25 to 360 minutes. An R0 resection of 97.7% for the malignant tumors with a median closest resection margin of 9.0 mm (range: 1.2–35.1 mm) was achieved.

Intraoperative Complications

IOC was present in 23 (17.9%) patients. Median estimated blood loss was 110 ml (range: 0–2,200 ml). Seventeen (13.2%) patients received perioperative blood transfusion. Blood loss of > 775 ml occurred in eight (6.2%) patients (conversion to laparotomy was required in three of them). There was no unintentional damage to surrounding structures in any of the patients. Conversion to laparotomy was required in 18 (14.0%) patients.

The need for conversion included unfavorable intra-operative findings (inability to proceed) or events (oncological concern during resection or bleeding). Reasons for inability to proceed were as follows: poor access due to dense adhesions (n = 2), difficult exposure of large, fatty liver (n = 2), inability to locate the tumor (n = 1), and slow progression of liver transection (n = 2). Unfavorable intra-operative events were as follows: oncological concern due to uncertain localization of tumor margins (n = 9), the need for diaphragm resection to ensure radical resection (n = 1), and diffuse parenchymal bleeding (n = 1). In none of these

cases was the decision to proceed to conversion made in an emergency situation caused by severe life-threatening bleeding.

Postoperative Complications

The overall incidence of POC was 38 (29.7%). The 90-day major morbidity (≥ grade 3), mortality rate, and readmission rates were 9.3%, 0.8%, and 2.3%, respectively. A detailed analysis is shown in Table 1.

Ninety-day major morbidity (≥ grade 3) occurred in 12 (9.3%) patients. Seven patients experienced grade 3a complications and were treated successfully by percutaneous drainage of pleural effusion and bile collections. Four patients required reoperations (grade 3b complication). One postoperative bleeding with hemoperitoneum occurred on the 1st postoperative day. The bleeding source from the port site in the abdominal wall was identified and managed laparoscopically. The second patient developed anastomotic leakage from a colorectal anastomosis after simultaneous laparoscopic liver and colorectal surgery and was managed laparoscopically by drainage of pelvic abscess and loop ileostomy. The third patient was readmitted after port site omental protrusion and was urgently operated on with a mini-incision and direct suturing of the abdominal wall defect. The last patient, with a biliary leak and imminent diffuse biliary peritonitis, was treated by laparotomy, evacuation of bile, and suturing of the defect on the left bile duct on postoperative day 2. One patient with liver cirrhosis (Child-Pugh A) that underwent resection of HCC experienced grade 4 complication with multi-organ dysfunction and prolonged intensive care hospitalization.

Mortality was 0.8% with one postoperative death within 90 days. In this patient with alcoholic liver cirrhosis Child–Pugh A, massive unstoppable bleeding from ruptured esophageal varices occurred on postoperative day 10 after segmentectomy VI of large (7 cm) HCC.

The 90-day readmission rate was 2.3%, with three patients readmitted after discharge from the hospital. Two patients presented with subphrenic abscesses and were treated by percutaneous drainage. The third readmission was a patient with a port site omental protrusion managed by repeated surgery.

Table 1. The 90-day overall morbidity, major morbidity (≥ grade 3), mortality, and readmission rates were 29.7%, 9.3%, 0.8%, and 2.3%, respectively. CD = Clavien–Dindo grade.

Overall morbidity (CD 1–5)	**38 (29.7%)**
CD 1	7
Wound infection	1
Ascites	6
CD 2	18
Blood transfusion	6
Fever + antibiotics	5
Pneumonia	2
Pulmonary embolism	1
Hypertensive crisis	1
Transient liver failure	1
Tachyarrhythmia	1
Brain transient ischemic attack	1
Major morbidity (CD ≥ 3)	**12 (9.3%)**
CD 3a	7
Bile collection	3
Subphrenic abscess	2
Pleural effusion	2
CD 3b	4
Biliary peritonitis	1
Hemoperitoneum	1
Port site hernia	1
Anastomotic leak	1
CD 4b	1
Liver failure and multiple organ failure	1
CD 5 (mortality)	1 (0.8%)
Bleeding from ruptured esophageal varices	1
Readmission rate	**3 (2.3%)**

Discussion

The past 20 years have seen a rapid expansion of the indications for minimally invasive approaches to liver surgery. The increased utilization of minimally invasive approaches to liver resection has paralleled improvements in open surgical technique, anesthetic management, and multidisciplinary care that have combined to greatly improve the safety of liver surgery (2). Surgical experience and skills are baseline requirements to achieve safe minimally invasive liver resections. Many have advocated that only the subset of surgeons that are dually trained in hepatobiliary surgery and minimally invasive surgery are adequately equipped to safely perform these operations (3–5). Given the technical rigor of these cases, one study estimated that the slope of the learning curve for LLR may not level off until over 60 cases were performed (11), potentially limiting the indications for major LLR to a small subset of high-volume centers.

This study was designed specifically to investigate complications related to LLR. The results of this case series study are strengthened by a 100% capture of consecutive patients undergoing LLR by a surgeon, starting at the institution from the very first case performed. All patients undergoing LLR (n = 128) over an 11-year period were included in the analysis with the exception of those undergoing cyst fenestration, liver biopsies, and radiofrequency ablation. When studying complex surgical procedures, both hospital and surgeon volume have been shown to affect the outcome (12). Importantly, as recommended by others (3–5, 11–12), in the current series laparoscopic competencies have been developed upon a foundation of open liver surgery. Prior to embarking on LLR, the surgeon was trained and experienced in open liver surgery techniques. Furthermore, only pure LLRs have been performed and, to be defined as such, the entire procedure was performed laparoscopically and an auxiliary incision was made at the end of the surgery only for specimen retrieval.

The current study is important because the utilization and growth trend of LLR since the first consensus on laparoscopic liver surgery in 2008 using a single-center database was defined. The annual volume of LLR progressively increasing since 2008 was documented. The proportion of LLR gradually increased and reached up to 45% in the most recent period. The very slow growth of liver resections performed by laparoscopy in the early periods clearly demonstrates the strict selection criteria applied at that time. Because our experience with LLR has improved over time, we have been able to embark on more complicated procedures. The substantial learning curve should be overcome in a stepwise fashion, requiring the initial mastery of simple tasks with the addition of increasingly complex steps to achieve proficiency to perform the most challenging procedures.

The conversion rate is commonly considered a criterion of quality in laparoscopic surgery. In the literature, the reported conversion rate for LLR ranges from 1 to 17% (11–13). Although defined as an IOC, we did not consider conversion to be a failure, and hence a higher overall conversion rate (14.0%) was observed compared to others. It has been highlighted that not delaying conversion may allow reduced blood loss and operative time (14). Importantly, among 18 patients requiring conversion in this study, no cases were related to severe, life-threatening bleeding, and the most common reasons for conversion were the inability to proceed and oncological concern.

The hemostatic issues with liver surgery fall into two categories: sudden large-volume blood loss from vascular injury and general hemostasis along the cut surface of the liver. In this study, catastrophic bleeding events have not been observed. The median blood loss of 110 ml and blood transfusion rates (13.2%) are comparable with other reports (3, 9, 11–14).

Inadvertent vascular, bowel, or other organ injury is a well-recognized complication of laparoscopic surgery that can have profound influences not only on postoperative morbidity and recovery but also on the intraoperative course to treat the injury (9). In this study, there was no unintentional damage to surrounding structures in any of the operated patients.

The overall major morbidity and mortality rates of 9.3% and 0.8% are in accordance with the reports in the literature (11–14), and the rate of reoperations and readmissions were low. An important issue regarding the safety of minimally invasive liver surgery is the ability to prevent postoperative bile leak. Despite a better understanding of liver anatomy and transection techniques, postoperative bile leak continues to be a frequent and significant complication in liver surgery (15). Because this is largely related to the magnitude of liver resection, observational studies addressing mainly

minor LLRs have reported low rates (1.4%) of this complication (3). As minimally invasive liver surgery is expanded to more substantial resections with broad transection surface areas and division of larger bile ducts deeper within the liver parenchyma, it is anticipated that the bile leak rate will rise. For LLR, most surgeons including our group use a vessel sealing device, endovascular staplers, or a combination to transect the liver parenchyma. Few reports exist comparing biliary complications after major transections using these devices and techniques (16). In practice, the bile leak rate should be less than 5% for major resection. Given the significant impact that postoperative bile leak has on related morbidity, including venous thromboembolism, delayed recovery, delayed discharge, the need for additional procedures, and costs of care, minimally invasive techniques that result in a bile leak rate in excess of this number may signal a contraindication to these approaches on a center-by-center basis (15). In this series, four patients (3.1%) developed major complications related to biliary leaks: three of them (CD grade 3a) were successfully treated by ultrasound-guided percutaneous drainage. Only one patient (CD grade 3b) required reoperation to prevent the devastating consequences of biliary peritonitis.

In conclusion, the adoption of LLR has been growing since the first consensus on laparoscopic liver surgery in 2008. The shift from laparoscopic, non-anatomical peripheral wedge resections through left lateral sectionectomy to major liver resections over the last 11 years in this institution has been documented. Our findings highlight the importance of patient selection and a cautious approach in the implementation of complex laparoscopic techniques.

References

1. Litinsky GS. Erich Mühe and the rejection of laparoscopic cholecystectomy (1985): a surgeon ahead of his time. JSLS. 1998;2:341–6.
2. Bismuth H, Eshkenazy R, Arish A. Milestones in the evolution of hepatic surgery. Rambam Maimonides Med. 2011;J2:e0021.
3. Nguyen KT, Gamblin TC, Geller DA. World review of laparoscopic liver resection – 2804 patients. Ann Surg. 2009;250:831–41.
4. Buell JF, Cherqui D, Geller DA, et al. The international position on laparoscopic liver surgery: The Louisville Statement, 2008. Ann Surg. 2009;250:825–30.
5. Wakabayashi G, Cherqui D, Geller DA, et al. Recommendations for laparoscopic liver resection: a report from the second international consensus conference held in Morioka. Ann Surg. 2015;261:619–29.
6. Ivanecz A, Krebs B, Stozer A, et al. Simultaneous pure laparoscopic resection of primary colorectal cancer and synchronous liver metastases: a single institution experience with propensity score matching analysis. Radiol Oncol. 2017;52:42–53.
7. Ivanecz A, Pivec V, Ilijevec B, et al. Laparoscopic anatomical liver resection after complex blunt liver trauma: a case report. Surg Case Rep. 2018;4:25.
8. Moris D, Tsilimigras DI, Machairas N, et al. Laparoscopic synchronous resection of colorectal cancer and liver metastases: a systematic review. J Surg Oncol. 2019;119:30–9.
9. Halls MC, Berardi G, Cipriani F, et al. Development and validation of a difficulty score to predict intraoperative complications during laparoscopic liver resection. Br J Surg. 2018;105:1182–91.
10. Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien–Dindo classification of surgical complications: five-year experience. Ann Surg. 2009;250:187–96.
11. Vigano L, Laurent A, Tayar C, et al. The learning curve in laparoscopic liver resection: improved feasibility and reproducibility. Ann Surg. 2009;250:772–82.
12. Kluger MD, Vigano L, Barroso R, et al. The learning curve in laparoscopic major liver resection. J Hepatobiliary Pancreat Sci. 2013;20:131–6.
13. Nomi T, Fuks D, Kawaguchi Y, et al. Learning curve for laparoscopic major hepatectomy. Br J Surg. 2015;102:796–804.
14. Costi R, Scatton O, Haddad L, et al. Lessons learned from the first 100 laparoscopic liver resections: not delaying conversion may allow reduced blood loos and operative time. J Laparoendosc Adv Surg Tech. 2012;22 425–31.
15. Zimmitti G, Roses RE, Andreou A, et al. Greater complexity of liver surgery is not associated with an increased incidence of liver-related complications except for bile leak: an experience with 2,628 consecutive resections. J Gastrointest Surg. 2013; 17:57–65.
16. Buell JF, Gayet B, Han HS, et al. Evaluation of stapler hepatectomy during a laparoscopic liver resection. HPB (Oxford). 2013;15:845–50.

Complications in Gastric Cancer Surgery: 27 Years of a Single Center Experience

Tomaž Jagrič
Department of Abdominal and General Surgery, Maribor University Medical Center

Correspondence

Asst. Prof. **Tomaž Jagrič**, MD, PhD
tomaz.jagric@gmail.com

Key words

gastric cancer, perioperative, morbidity, mortality

Research Article

SURGERY SURG ENDOS 2020; 2(1): 13-22

Abstract

Backgrounds. Knowledge of complications is of paramount importance when treating gastric cancer patients. We determined the factors that predisposed morbidity and mortality.

Methods. We analyzed the results of 1,211 patients with gastric cancer operated on with curative intent.

Results. Cumulative perioperative morbidity in the 27-year period was 22.5%. Cumulative perioperative mortality in the 27-year period was 4%. Age (HR 1.017; 95% CI 1.003–1.032; p = 0.019) and tumor grade (HR 1.002; 95% CI 1.001–1.004; p = 0.008) were significantly associated with perioperative morbidity. Perioperative mortality was significantly associated with perioperative chemoradiotherapy (HR 0.183; 95% CI 0.042–0.797; p = 0.024), American Society of Anesthesiologists score (HR 1.873; 95% CI 1.076–3.261; p = 0.026), and the period of operation. Perioperative mortality decreased from 8.6% in the first 3-year period to 0% in the last 3-year period. The mortality rate fell below 4% after 6 years or 361 patients operated on.

Conclusion. Our analysis showed that apart from factors that indicate the general state of the patient only the experience of a center has an impact on perioperative morbidity and mortality. Centralization of patients in a high-volume center can therefore be the only means of ensuring the best results for gastric cancer patients and excellent long-term survival.

Introduction

Gastric cancer surgery is still considered a high-risk operation by many authors (1–9). The nature of surgery, extensive and technically demanding lymph node dissection, and difficult anastomosis at the level of the diaphragm contribute to the level of difficulty that these operations are associated with (5, 8). However, the technically demanding operation is not the only factor that predisposes gastric cancer patients to complications. Patients with gastric cancer are usually affected in the 6th

or 7th decade of life and have at least one additional comorbidity that predisposes them to general complications (9, 15). These patients might also suffer from long-term malnutrition and wasting due to anorexia or dysphagia, leading to muscle weakness, lower immune response, and a higher likelihood of perioperative morbidity (9, 15). Perioperative treatment is an additional factor that can cause complications and mortality after gastric cancer surgery.

Knowledge of complications is of paramount importance when treating gastric cancer patients. It is therefore important to identify potential factors associated with morbidity and mortality to potentially correct them and prevent complications. To access the morbidity and mortality of gastric cancer surgery in a 27-year period, we analyzed patients that were operated on at our center. We determined the factors that predisposed morbidity and mortality.

Methods

Patients

Data for all patients that were operated on at our center were prospectively stored in our database. A total of 1,546 patients were operated on for gastric cancer from 1991 onward. Among these patients, only patients operated on with curative intent were selected for this study. For the final analysis, 1,211 patients remained.

Statistical Analysis

All data are presented as mean ± standard deviation (*SD*) for continuous normally distributed predictors or median ± interquartile range (IQR). Discrete variables are expressed as number and percentage. Continuous data were compared with Student's *t*-test or one-way ANOVA, and for data without a normal distribution the Mann–Whitney *U* test was used. Discrete variables were compared with a χ^2 test. We used Pearson's correlation to determine which predictors have a significant impact on perioperative morbidity and mortality. Factors with a *p*-value of < 0.5 on univariate analysis were tested with logistic regression to determine the significant predictors for morbidity and mortality. For the survival analysis, the Kaplan–Meier method was used. For the level of significance, a *p*-value of < 0.05 was selected.

Perioperative morbidity was defined as any complication of Clavien–Dindo grade 1a or higher, and perioperative major morbidity was defined as a complication of Clavien–Dindo grade 3b or higher. Perioperative mortality was defined as patient death from any cause within 30 days from the operation.

Results

Patients' Characteristics, Perioperative Complications, and Perioperative Mortality

The characteristics of the patients included and the characteristics of patients with perioperative morbidity and mortality are presented in Table 1. Patients with complications were significantly older compared to patients without complications (67.4 ± 11 years vs. 64 ± 12 years; $p < 0.0001$). Only 22.7% of patients with American Society of Anesthesiology (ASA) score I had complications, whereas 55.3% of patients with ASA score II and 22% with ASA score III had complications ($p = 0.002$). Patients with total gastrectomy and transhiatal extended total gastrectomy had higher complication rates ($p = 0.023$). We observed an inverse relationship with perioperative chemotherapy and complications. Patients that received perioperative treatment had complications in only 18.3% of cases compared to 24.6% in patients without perioperative treatment ($p = 0.014$). However, patients that received perioperative treatment were in better general condition. Patients with perioperative treatment were 7 years younger ($p < 0.0001$), without accompanying diseases ($p < 0.0001$), and had significantly lower ASA scores ($p < 0.0001$). Patients with complications had a higher-grade tumor compared to patients without complications, and more patients with tumors other than adenocarcinoma had complications compared to patients with adenocarcinoma ($p = 0.003$). D2 lymphadenectomy influenced neither morbidity nor mortality.

Perioperative mortality increased with older age, associated illness, and a higher ASA score. The mean age of patients with perioperative mortality

was 71.7 ± 10 years compared to 64.6 ± 12 years in patients without mortality ($p < 0.0001$). Patients with perioperative mortality had two accompanying diseases in 61.2% of cases, whereas most patients without perioperative mortality only had one or no accompanying disease ($p < 0.0001$). Among the patients with perioperative mortality, 57.1% had an ASA score of II and 36.7% an ASA score of III ($p < 0.0001$). Among patients without perioperative treatment, 95.6% did not have perioperative mortality ($p < 0.0001$).

The most frequent surgical complications were abscess and bleeding, and the most common general complications were respiratory distress and cardiac complications. The distribution of these complications is presented in Figure 1.

Correlations Between Predictors and Morbidity and Mortality

Cumulative perioperative morbidity in the 27-year period was 22.5%. Significant correlations were found between age, number of comorbidities, ASA score, perioperative chemotherapy, distal border length, proximal border length, tumor grade, and

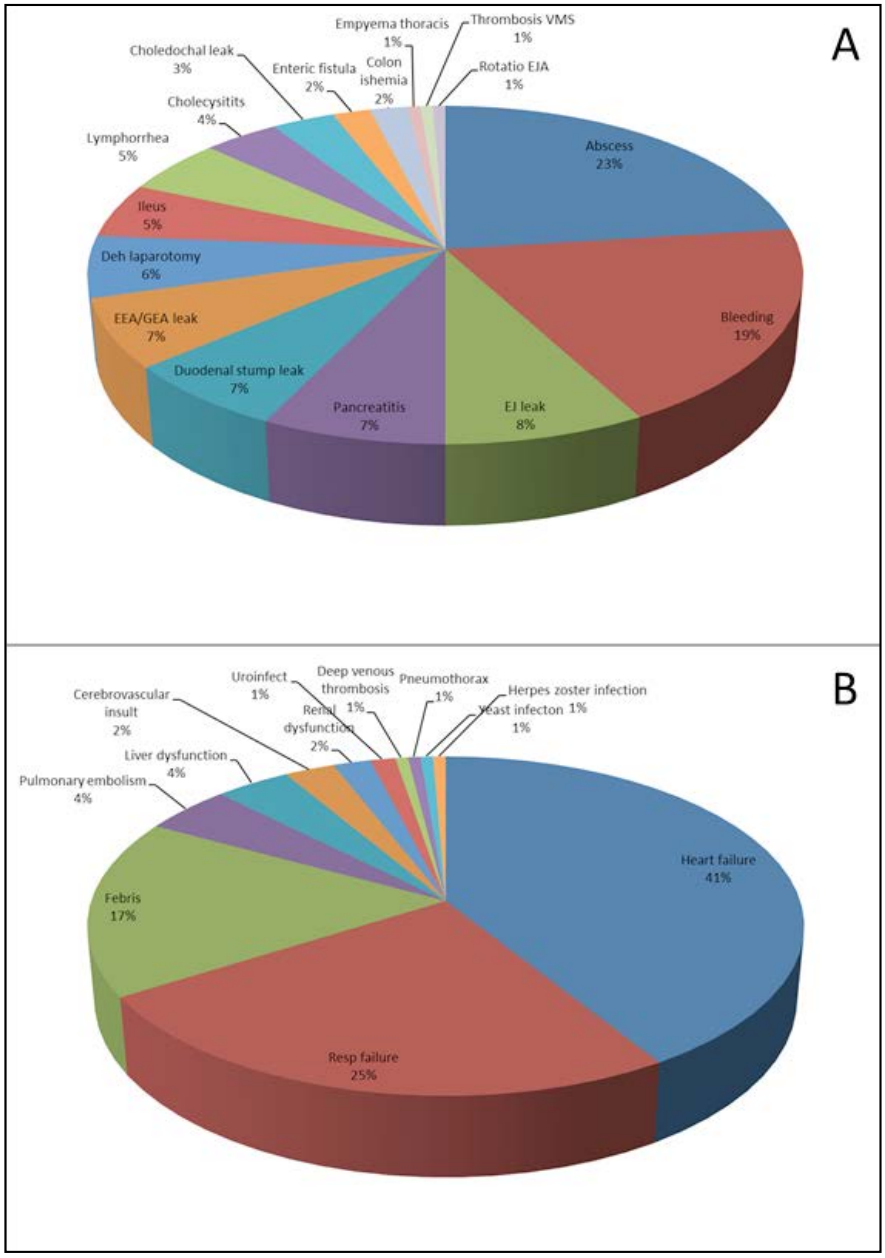


Figure 1. Distribution of surgical and general complications. A = surgical complications, B = general complications.

Table 1. Patient characteristics. ASA = American Society of Anesthesiologists score, CEA = carcinoembryonic antigen, CA 19-9 = carbohydrate antigen 19-9, Hb = hemoglobin levels, CRT = chemoradiotherapy, UICC = Union for International Cancer Control staging system, N = nodes.

	All patients	Morbidity			Mortality		
		No	Yes	*p*-value	No	Yes	*p*-value
Age, years ± *SD*	64.8 ± 12	64.1 ± 2	67.4 ± 11	< 0.0001	64.6 ± 12	71.7 ± 10	< 0.0001
Sex, *n* (%)				NS			NS
Male	785 (64.8)	598 (63.8)	187 (68.5)		756 (65.1)	29 (59.2)	
Female	426 (35.2)	340 (36.2)	86 (31.5)		406 (34.9)	20 (40.8)	
Number of comorbidities, *n* (%)				0.003			< 0.0001
0	381 (28.5)	316 (34.1)	65 (24.5)		374 (32.7)	7 (14.3)	
1	393 (32.9)	306 (33)	87 (32.8)		386 (33.7)	7 (14.3)	
2	340 (28.5)	251 (27)	89 (33.6)		310 (27.1)	30 (61.2)	
3	63 (5.3)	42 (4.5)	21 (7.9)		59 (5.2)	4 (8.2)	
4	6 (0.5)	5 (0.5)	1 (0.4)		5 (0.4)	1 (2)	
5	4 (0.3)	2 (0.2)	2 (0.8)		4 (0.3)	0 (0)	
6	6 (0.5)	6 (0.6)	0 (0)		6 (0.5)	0 (0)	
ASA, *n* (%)				0.002			< 0.0001
I	361 (29.8)	299 (31.9)	62 (22.7)		358 (30.8)	3 (6.1)	
II	636 (52.5)	485 (51.7)	151 (55.3)		608 (52.3)	28 (57.1)	
III	214 (17.7)	154 (16.4)	60 (22)		196 (16.9)	18 (36.7)	
CEA, ng/ml ± *SD*	6.2 ± 24	6 ± 23	7 ± 28	NS	6 ± 24	9 ± 30	NS
CA 19-9, ng/ml ± *SD*	137 ± 817	160 ± 913	55 ± 255	0.006	137 ± 827	97 ± 256	NS
Hb, g/ml ± *SD*	122.2 ± 21	122 ± 21	121 ± 22	NS	122 ± 21	119 ± 18	NS
Protein, g/ml ± *SD*	69.4 ± 23	69.6 ± 25	68.7 ± 7	NS	69 ± 23	67.6 ± 10	NS
Perioperative CRT, *n* (%)				0.008			< 0.0001
Yes	394 (32.5)	322 (34.3)	72 (26.4)		392 (33.7)	2 (4.1)	
No	817 (67.5)	616 (65.7)	201 (73.6)		770 (66.3)	47 (95.9)	
Lymphadenectomy, *n* (%)				NS			NS
D0	9 (0.8)	5 (0.5)	4 (1.5)		9 (0.8)	0 (0)	
D1	344 (28.5)	278 (29.7)	66 (24.2)		321 (27.7)	23 (46.9)	
D2	856 (70.8)	653 (69.8)	203 (74.4)		830 (71.6)	26 (53.1)	
Splenectomy, *n* (%)				NS			NS
Yes	350 (28.9)	259 (27.6)	91 (33.3)		334 (28.8)	16 (32.7)	
No	860 (71.1)	678 (72.4)	182 (66.7)		827 (71.2)	33 (67.3)	
Additional resections, *n* (%)				NS			NS
Yes	111 (9.2)	87 (9.3)	24 (8.8)		110 (9.5)	1 (2)	
No	1099 (90.8)	850 (90.7)	249 (91.2)		1051 (90.5)	48 (98)	
Clavien–Dindo, *n* (%)				< 0.0001			< 0.0001
0	938 (77.5)	938 (100)	0 (0)		935 (80.5)	3 (6.1)	
I	1 (0.1)	0 (0)	1 (0.4)		1 (0.1)	0 (0)	
II	120 (9.9)	0 (0)	120 (44)		119 (10.2)	1 (2)	
IIIa	25 (2.1)	0 (0)	25 (9.2)		25 (2.2)	0 (0)	
IIIb	60 (5)	0 (0)	60 (22)		60 (5.2)	0 (0)	
IV	6 (0.5)	0 (0)	6 (2.2)		6 (0.5)	0 (0)	
V	61 (5)		61 (22.3)		16 (1.4)	45 (91.8)	

Tumor site, *n* (%)				NS				NS
Proximal	190 (15.7)	132 (14.1)	58 (21.2)			185 (15.9)	5 (10.2)	
Middle	484 (40)	372 (39.7)	112 (41)			465 (40)	19 (38.8)	
Distal	465 (38.4)	374 (39.9)	91 (33.3)			444 (38.2)	21 (42.9)	
Whole stomach	39 (3.2)	32 (3.4)	7 (2.6)			38 (3.3)	1 (2)	
Stump	33 (2.7)	28 (3)	5 (1.8)			30 (2.6)	3 (6.1)	
Diameter, mm ± *SD*	60.6 ± 58	58.8 ± 35	66.6 ± 104	NS		60.7 ± 59	55.7 ± 32	NS
Proximal border, mm ± *SD*	59.3 ± 100	54.3 ± 74	75.8 ± 158	NS		60 ± 101	36.2 ± 26	0.001
Distal border, mm ± *SD*	62.3 ± 102	57.6 ± 82	78.9 ± 154	NS		62.7 ± 103	50.7 ± 31	NS
Grade, *n* (%)				0.003				NS
Well	531 (48.8)	115 (16.6)	23 (10.7)			131 (15)	7 (21.9)	
Moderate	331 (30.4)	185 (26.7)	76 (35.5)			253 (28.9)	8 (25)	
Poor	218 (20)	381 (55)	110 (51.4)			474 (54.2)	17 (53.1)	
Other	8 (0.8)	12 (1.8)	5 (2.3)			17 (1.9)	0 (0)	
UICC, *n* (%)				NS				NS
0	8 (0.7)	7 (0.8)	1 (0.4)			8 (0.7)	0 (0)	
Ia	171 (15)	139 (15.5)	32 (13.1)			164 (14.9)	7 (16.3)	
Ib	112 (9.8)	84 (9.4)	28 (11.4)			105 (9.6)	7 (16.3)	
IIa	149 (13.1)	112 (12.5)	37 (15.1)			146 (13.3)	3 (7)	
IIb	162 (14.2)	120 (13.4)	42 (17.1)			153 (14)	9 (20.9)	
IIIa	194 (17)	148 (16.5)	46 (18.8)			187 (17)	7 (16.3)	
IIIb	150 (13.1)	123 (13.7)	27 (11)			144 (13.1)	6 (14)	
IIIc	95 (8.3)	84 (9.4)	11 (4.5)			93 (8.5)	2 (4.7)	
IV	100 (8.8)	79 (8.8)	21 (8.6)			98 (8.9)	2 (4.7)	
Positive, *n* ± *SD*	6.4 ± 30	7 ± 34	4.2 ± 7	0.017		6.5 ± 31	4.1 ± 6	NS
Total, *n* ± SD	23 ± 32	23.9 ± 35	20.7 ± 12	0.023		6.5 ± 30	4 ± 6	< 0.0001
Hospital stay, days ± *SD*	15 ± 10	12 ± 3	25 ± 17	< 0.0001		14.9 ± 10	11.3 ± 2	0.015

perioperative morbidity. Major morbidity defined as complications with Claven–Dindo score > 3b was associated with the same predictors (Table 1).

In 111 (9.2%) patients an additional resection had to be performed because of invasion of the tumor into other organs. The distribution of the additional resections is presented in Table 2. Left splenopancreatectomy (n = 33, 2.7%), bursectomy (n = 26, 2.1%), and liver resection (n = 18, 1.5%) were most frequently performed. There was no significant difference in perioperative morbidity and mortality between patients with additional resections and with no additional resections (Table 2).

Cumulative perioperative mortality in the 27-year period was 4%. The 30-day mortality was associated with age, number of comorbidities, ASA score, the period of operation, and perioperative therapy. Perioperative mortality was significantly associated with the period of operation. Figure 2 shows perioperative morbidity and mortality during the 27-year span. Although the morbidity rate was steady during the years with only minor fluctuations around 20%, perioperative mortality decreased from 8.6% in the first 3-year period to 0% in the last 3-year period. The mortality rate fell below 4% after 6 years or 361 patients operated on.

Multivariate Analysis

Among the factors included, only age (HR 1.017; 95% CI 1.003–1.032; p = 0.019) and tumor grade (HR 1.002; 95% CI 1.001–1.004; p = 0.008) were

significantly associated with perioperative morbidity. Perioperative mortality was significantly associated with perioperative chemoradiotherapy (HR 0.183; 95% CI 0.042–0.797; p = 0.024), ASA score (HR 1.873; 95% CI 1.076–3.261; p = 0.026), and the period of operation (HR 0.794; 95% CI 0.672–0.938; p = 0.007).

Survival Analysis

The cumulative 5-year survival of the patients included was 43.4%, with a median survival of 37.2 months. The cumulative 30-day mortality over the 27 years was 3.8%. Perioperative morbidity had a significant impact on long-term survival

Table 2. Additional oncological operations with perioperative morbidity and mortality.

Additional operation	n (%)	Morbidity (%)	Mortality (%)
Adrenalectomy	1 (0.1)	0	0
Resection of the falciform ligament	1 (0.1)	0	0
Liver resection	18 (1.5)	11.1	0
Peritonectomy	2 (0.2)	0	0
Diaphragmatic resection	1 (0.1)	0	0
Bursectomy	26 (2.1)	15.4	0
Colon resection	12 (1)	33.3	0
Jejunal resection	2 (0.2)	0	50
Left splenopancreatectomy	33 (2.7)	24.2	0
Left splenopancreatectomy and colon resection	7 (0.6)	42.9	0
Left splenopancreatectomy and adrenalectomy	3 (0.2)	33.3	0
Total pancreatectomy	1 (0.1)	100	0
Whipple's resection	3 (0.2)	0	0
Total	**112 (9.2)**	**21.4**	**0.9**

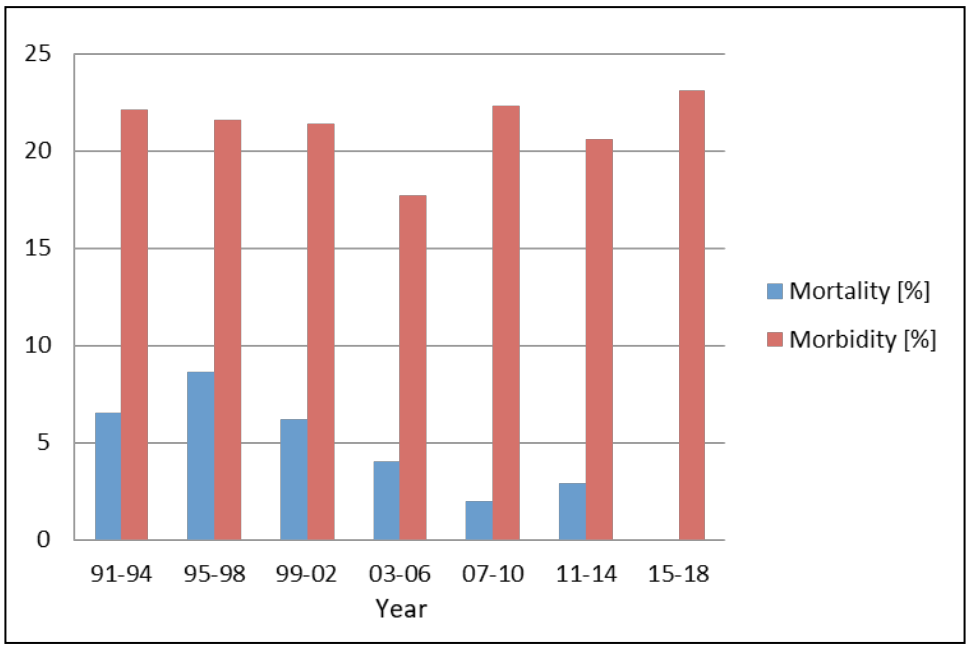


Figure 2. Perioperative morbidity and mortality in the 27-year period.

($p < 0.0001$). The 5-year survival was 45.3% and 36.2% in the group without complications and with complications, respectively. The perioperative mortality in the group without complications was 0.1%. Perioperative complications increased the 30-day mortality 100-fold to 10.6%.

The 30-day mortality and 5-year survival of individual complications is presented in Table 3. Esophago-jejunostomy leak, duodenal leak, gastro-jejunostomy, entero-enterostomy leak, and ileus had the highest perioperative mortality. None of the patients with enteric fistula, gastro-jejunostomy, and jejuno-jejunostomy leak or thrombosis of the superior mesenteric vein survived 5 years.

Figure 4 shows the cumulative survival curve and the survival of patients with and without complications.

Discussion

It has been long acknowledged that perioperative complications have a major impact on long-term survival in gastric cancer patients (7). It is therefore important that any surgeon dealing with gastric cancer surgery be aware of possible complications and risk factors that predispose patients to complications. To determine predisposing factors for perioperative morbidity and mortality, we conducted an analysis of a 27-year period of gastric cancer surgery at the Department for Abdominal and General Surgery at the Maribor University Medical Center.

The cumulative 5-year survival of patients operated on at our center was 43.4%. These results compare favorably to other high-volume centers, which report survivals from 36 to 70% (1–8, 10–14). Complications have been shown to significantly influence long-term survivals (7). In our study patients with complications had significantly shorter long-term survival compared to patients with uneventful recovery with up to 10% shorter long-term survivals. The perioperative mortality in those patients increased 100-fold to 10.6% (compared to 0.1% in the uneventful group). A profound knowledge of possible perioperative complications and their predisposing factors is hence imperative. Perioperative morbidity was 22.5% in the 27-year period and remained unchanged during the years. Although our perioperative morbidity is similar to other western centers reporting incidences from 20% to 55% (1, 3–5, 9, 10–14), eastern centers stand out with a somewhat lesser morbidity (16–20%) (2, 6, 8, 10–14). This might be due to the fact that patients operated on in the west suffer from gastric cancer on average 10 years later (9, 15) and have more additional comorbidities, which predisposes western patients to perioperative complications (9, 15).

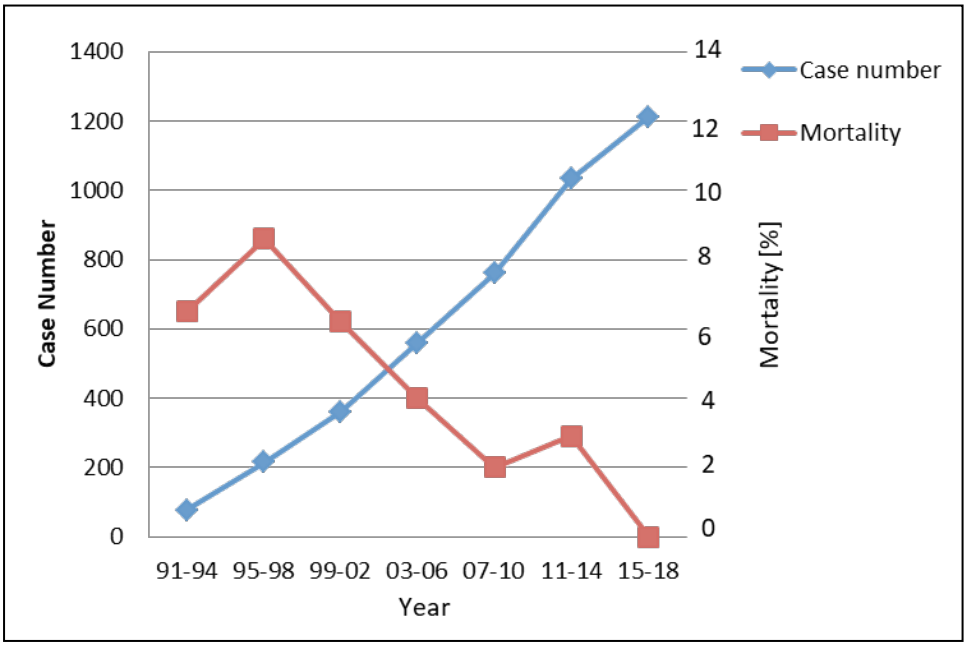
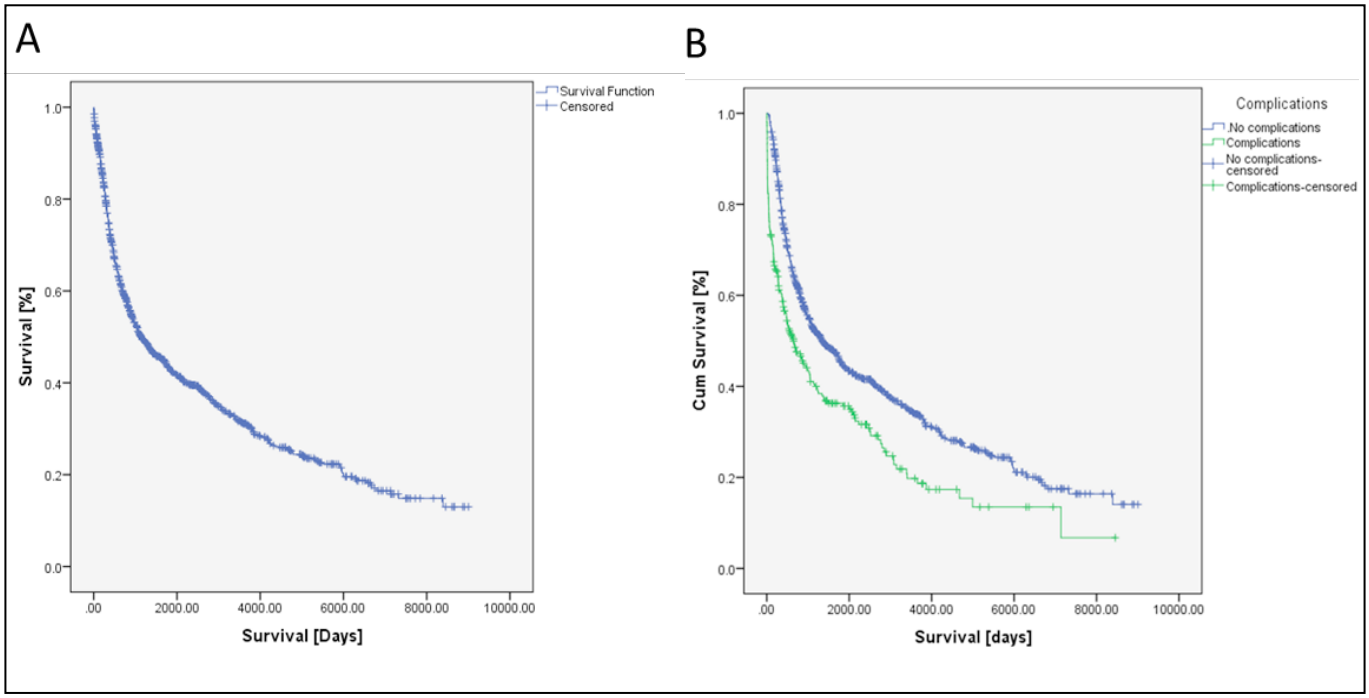


Figure 3. Perioperative mortality and case numbers in the 27-year period.

Table 3. Thirty-day mortality and 5-year survival of individual complications.
EJ = esophago-jejunostomy, EEA = entero-enterostomy, GEA = gastro-enterostomy, VMS = superior mesenteric vein.

Complication	Morbidity (%)	Mortality (%)	5-year survival (%)
All patients	22.5	4	43.4
EJ anastomosis leak	–	41.7	9.7
Enteric fistula	–	0	0
Duodenal stump leak	–	40	12
EEA/GEA leak	–	60	0
Laparotomy dehiscence	–	0	18.8
Abscess	–	14.3	36.1
Bleeding	–	3.4	46.1
Pancreatitis	–	8.2	18.2
Ileus	–	50	33.3
VMS thrombosis	–	0	0
Lymphorrhea	–	0	62.5
Ischemic colitis	–	33.3	0
Cholecystitis	–	0	66.7
Choledochal duct perforation	–	0	53.3

Figure 4. Survival curves. A = cumulative survival, B = comparison of survival of patients with and without complications.



The most frequent complications at our center were abscess (2.9%) and bleeding (2.4%). Fortunately, these two complications did not have any impact on either mortality or long-term survival. According to other studies, the most lethal complications are esophago-jejunostomy leak and duodenal stump leak. Reported mortality of esophago-jejunostomy leak and duodenal stump leak are up to 67 and 50%, respectively (16, 17). Patients with those two complications at our center also had high perioperative mortality of 41.7% for esophago-jejunostomy leak and 40% for duodenal stump leak, but these life-threatening complications were exceedingly rare. The routine over suturing of the esophago-jejunostomy and duodenal stump, reduction of tension on the anastomosis, and Kocherization of the duodenum are the main means of combat against these complications. In this manner we reduced overall mortality by reducing the incidence of these complications to less than 1%, which in turn had a beneficial impact on long-term survival.

Other factors significantly related to morbidity on univariate analysis were age, number of comorbidities, ASA score, perioperative chemotherapy, distal border length, proximal border length, and tumor grade. Factors found to be significantly associated with perioperative mortality on univariate analysis were age, number of comorbidities, ASA score, the period of operation, and perioperative therapy. Many papers have found that additional resections increase morbidity (3, 4). Resections of the tail of the pancreas therefore resulted in unacceptable morbidity and mortality in the D2 groups of the Dutch and MRC trials (3, 4). We use multivisceral resections of the adjacent organs only in cases of tumor infiltration to achieve R0 resection. Because pancreato-biliary surgery and hepatic surgery are also performed at our center, these resections could be performed without any significant increase in morbidity or mortality.

Among the factors mentioned above, the multivariate analysis determined only age and chemotherapy as significant predictors for perioperative morbidity in our analysis. Advanced age is the most powerful predictor for perioperative complications. Older patients have a higher likelihood of developing perioperative complications than their younger counterparts. This correlation was also found by other authors (9, 15). Because patients in the west are usually older than those in the east, this might explain the higher morbidity of gastric cancer surgery in western centers compared to the east (9, 15). Similarly, among the factors included, only age and the period of operation remained significant predictors for perioperative morbidity. Because perioperative morbidity and mortality are closely related, it is not surprising that age also predisposes patients for perioperative mortality. However, the strongest predictor for perioperative mortality was the period in which patients were operated on. The lowest hazard for perioperative mortality was among patients that were operated on after the 6th year since the introduction of gastric cancer resection at our center. This shows that with the accumulation of case numbers a significant impact can be expected on perioperative mortality rates. Experience of a center was found to be a significant predictor for morbidity and mortality by many authors (2, 7). Sano et al. concluded that excellent results in terms of perioperative complications, mortality, and long-term results could be achieved because only experienced surgeons with a track record of gastrectomy with lymphadenectomy were included in the study. In addition, he stressed the importance of experience of a center in perioperative treatment (2).

Our analysis showed that only factors that indicate the general state of the patient have an impact on perioperative morbidity and mortality. Unfortunately, we cannot influence the age at which patients in a region suffer from gastric cancer, or the comorbidities that these patients might have. We can, however, precondition high-risk patients with preoperative optimization and ensure intensive care monitoring after the operation for these high-risk patients. With these measures, general complications leading to higher mortality could be effectively reduced. The major determinant of mortality, apart from patients' general state, is the experience of a center in the treatment of gastric cancer. This article clearly shows how accumulation of experience effectively reduced the incidence of life-threatening complications to less than 1% and perioperative mortality to 0%. Centralization of gastric cancer patients at a high-volume center can therefore be the only mean of ensuring the best results for gastric cancer patients and excellent long-term survival.

References

1. Claassen ZHM, Hartgrink HH, Dikken JL, et al. Surgical morbidity and mortality after neoadjuvant chemotherapy in the CRITICS gastric cancer trial. Eur Surg Oncol. 2018;44:613–9.
2. Sano T, Sasako M, Yamamoto S, et al. Gastric cancer surgery: morbidity and mortality results from a prospective randomized controlled trial comparing D2 and extended para-aortic lymphadenectomy – Japan Clinical Oncology Group Study 9501. Am Soc Clin Oncol. 2004;22(14):2767–73.
3. Cuschieri A, Fayers P, Fielding J, et al. Postoperative morbidity and mortality after D1 and D2 resections for gastric cancer: preliminary results of the MRC randomised controlled surgical trial. Lancet. 1996;347:995–9.
4. Bonenkamp JJ, Songun I, Hermans J, et al. Randomized comparison of morbidity after D1 and D2 dissection for gastric cancer in 996 Dutch patients. Lancet. 1995;345:745–8.
5. Degiuli M, Sasako M, Ponti A. Morbidity and mortality in the Italian Gastric Cancer Study Group randomized clinical trial of D1 versus D2 resection for gastric cancer. Brit J Surg. 2010;97:643–9.
6. Kinoshita T, Maruyama K, Sasako M, et al. Treatment results of gastric cancer patients: Japanese experience. Gastric Cancer. 1993;319–30.
7. Begg CB, Cramer LD, Hoskins WJ, et al. Impact of hospital volume on operative mortality for major cancer surgery. JAMA. 1998;280:1747–51.
8. Wu CW, Hsiung CA, Lo SS, et al. Randomized clinical trial of morbidity after D1 and D3 surgery for gastric cancer. Brit J Surg. 2004;91:283–7.
9. Kelly KJ, Selby L, Chou JF, et al. Laparoscopic versus open gastrectomy for gastric adenocarcinoma in the west: a case-control study. Ann Surg Oncol. 2015;22:3590–6.
10. Jeremiasen M, Linder G, Hedberg J, et al. Improvements in esophageal and gastric cancer care in Sweden—population-based results 2007–2016 from a national quality register. Dis Esophagus. 2020;33(3).
11. Leiting JL, Grotz TE. Advancements and challenges in treating advanced gastric cancer in the west. World J Gastrointest Oncol. 2019;11(9):652–64.
12. Li P, Huang CM, Zheng CH, et al. Comparison of gastric cancer survival after R0 resection in the US and China. J Surg Oncol. 2018;118:975–82.
13. Cats A, Jansen EPM, van Grieken NCT, et al. Chemotherapy versus chemoradiotherapy after surgery and preoperative chemotherapy for resectable gastric cancer (CRITICS): an international, open-label, randomised phase 3 trial. Lancet Oncol. 2018;19:616–28.
14. Wanebo HJ, Kennedy BJ, Chmiel J, et al. Cancer of the stomach. A patient care study by the American College of Surgeons. Ann Surg. 1993;218:583–92.
15. Maezawa Y, Aoyama T, Kano K, et al. Impact of the age-adjusted Charlson comorbidity index on the short- and long-term outcomes of patients undergoing curative gastrectomy for gastric cancer. J Cancer. 2019;10(22):5527–35.
16. Hummel R, Bausch D. Anastomotic leakage after upper gastrointestinal surgery: surgical treatment. Visc Med. 2017;33(3):207–11.
17. Bandar A, Jin Won L, Kyo Young S. Duodenal stump leak post curative gastrectomy for early gastric cancer patient treated with endoscopic stent which complicated by migration and perforation. J Oncol Transl Res. 2016;2–4.

Timing of Cholecystectomy After Endoscopic Retrograde Cholangiopancreatography and Papillotomy

Jan Grosek,[1,2] Miha Petrič,[1,2] Danaja Plevel,[2] Aleš Tomažič[1,2]

[1] *Department of Abdominal Surgery, Ljubljana University Medical Center*
[2] *Medical Faculty, University of Ljubljana*

Correspondence

Asst. Prof. **Jan Grosek**, MD, PhD
jan.grosek@kclj.si

Key words

choledocholithiasis, endoscopic retrograde cholangiopancreatography, endoscopic papillotomy, cholecystectomy

Research Article

SURGERY SURG ENDOS 2020; 2(1): 23-30

Abstract

Background. Endoscopic retrograde cholangiopancreatography with endoscopic papillotomy (ERCP/EPT) followed by cholecystectomy is a standard treatment for common biliary duct stones. It is unclear, however, what the optimal time interval is between ERCP/EPT and cholecystectomy. The primary aim of our study was to evaluate our current practice, in which patients are mostly operated on 1 to 3 months after ERCP/EPT. The secondary aim was to determine the optimal timing for cholecystectomy after ERCP/EPT.

Methods. A retrospective analysis of 117 patients that underwent a preoperative ERCP/EPT followed by a cholecystectomy was performed. Associations between demographic characteristics, type and duration of operation, conversion rate, postoperative complications, and interval time were tested using multiple linear regression. The optimal interval was studied by drawing a receiver operating curve and studying the area under curve.

Results. The time interval between cholecystectomy and ERCP/EPT was not associated with the number of conversions to open surgery, duration of the operation, or postoperative complications. There was no statistically significant association between any independent variable and time interval. No threshold interval could be found that would discriminate between whether a patient had a conversion or postoperative complications or not.

Conclusion. Our current practice is safe because the time interval in our study does not affect the rate of conversions, postoperative complications, or operation duration. Based on the results of our study, no recommendations regarding the optimal time for surgery can be given.

Introduction

Up to 33% of patients with gallstones also have gallstones present in the common bile duct (CBD) (1, 2). There are no clear evidence-based recommendations for the management of patients with choledocholithiasis (3). The management of CBD stones includes clearance of both bile duct and gallbladder stones. Cholecystectomy and one of the methods of bile duct clearance must be performed. Bile duct clearance is achieved through endoscopic retrograde cholangiopancreatography (ERCP) or surgical common bile duct exploration (2–9).

Two-stage management, which consists of pre-operative (or post-operative) ERCP and endoscopic papillotomy (EPT) with CBD clearance followed by laparoscopic cholecystectomy, is the most commonly used minimally invasive technique. This approach has some setbacks because some patients will be submitted to an unnecessary ERCP and some others will develop complications, mainly pancreatitis but also other adverse events, such as bleeding, perforation, infection, and sedation-related events (10). Apart from that, there is also the issue of residual stones following endoscopic treatment in up to 35% of patients (11). The one-step approach, in which ERCP/EPT is performed during cholecystectomy, is performed less often. Some authors argue that it decreases the length of stay and costs, and is more comfortable for the patients. On the other hand, others report no differences in length of stay and operation time, with most noting the one-step approach being technically and organizationally more challenging, and therefore requiring a high level of experience (12–26).

The primary aim of our study was to evaluate our current practice, in which patients are mostly operated on 1 to 3 months after ERCP/EPT. The secondary aim was to try to determine the optimal timing for cholecystectomy after ERCP/EPT.

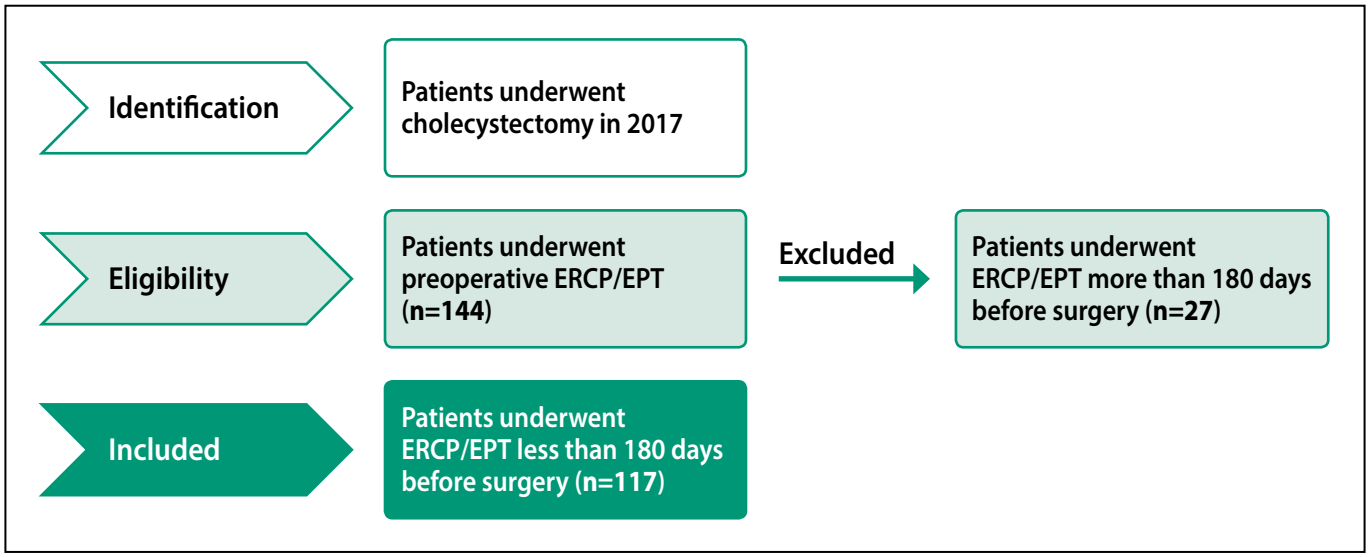
Patients and methods

In our institution the current standard of care for the treatment of patients with CBD stones is ERCP/EPT and extraction of stones followed by laparoscopic cholecystectomy. The operation date is scheduled after discussion at a multidisciplinary team meeting. Patients are mostly operated on within 3 months from the index procedure (ERCP/EPT).

Participants

The electronic database of a tertiary referral medical center was searched for patients that underwent cholecystectomy between January 1st, 2017 and December 31st, 2017 at the Department of Abdominal Surgery, Ljubljana University Medical Center. Patients that had undergone a preoperative ERCP/EPT were intended to be included. All

Figure 1. Participant selection.



the patients with ERCP/EPT performed more than 180 days before the cholecystectomy were excluded from our study (Figure 1).

Data regarding the surgery (date, type of surgery, approach, duration, and postoperative complications) were gathered with a quality control (Q1) form, and the rest of the patient data (sex, age, body mass index (BMI), and American Society of Anesthesiologists (ASA) score) were collected from patient records. Data regarding ERCP/EPT procedures (date, indication, concretions extraction, stent placement, and complications) were collected from the procedure notes.

Statistical Tools

Means and standard deviations were calculated for numerical variables, and frequencies and percentages for categorical variables. Median and interquartile range (IQR) was calculated for non-normally distributed numerical variables. For testing the normality of distribution, the Shapiro–Wilk test was used. The relationship between demographic characteristics, illness severity, type, duration of operation, conversion to open surgery, postoperative complications, and time interval from index procedure to the operation were tested using multiple linear regression. The optimal interval of time between ERCP/EPT and cholecystectomy that would discriminate between patients having conversion to open surgery or not was studied by drawing a receiver operating curve (ROC) and studying the area under the curve (AUC). ROC and AUC was also used to find the optimal interval of time between ERCP/EPT and cholecystectomy that would discriminate between patients with postoperative complications and those without. The significance level was set to $\alpha = 0.05$. The analysis was performed using SPSS v. 23.0.

Our study was approved by the National Medical Ethics Committee (MZ 0120-436/2018), and all the procedures performed in our study were in accordance with the Declaration of Helsinki (1964) and its later amendments or comparable ethical standards. Informed consent was obtained from all participants in the study.

Results

A total of 117 patients were included in the statistical analysis. Clinical and demographic data are shown in Table 1. For 107 (91.5%) patients, the indication for ERCP/EPT was choledocholithiasis, whereas 10 (8.5%) had undergone the procedure due to biliary pancreatitis. All the patients had an EPT performed during the ERCP. During the procedure, stones were extracted in 100 (85.5%) patients. Stent placement was necessary in 10 patients. Apart from small bleeding in 24 patients, there were no other complications during the ERCP. The range of the interval between ERCP/EPT and cholecystectomy was 0 to 179 days, with

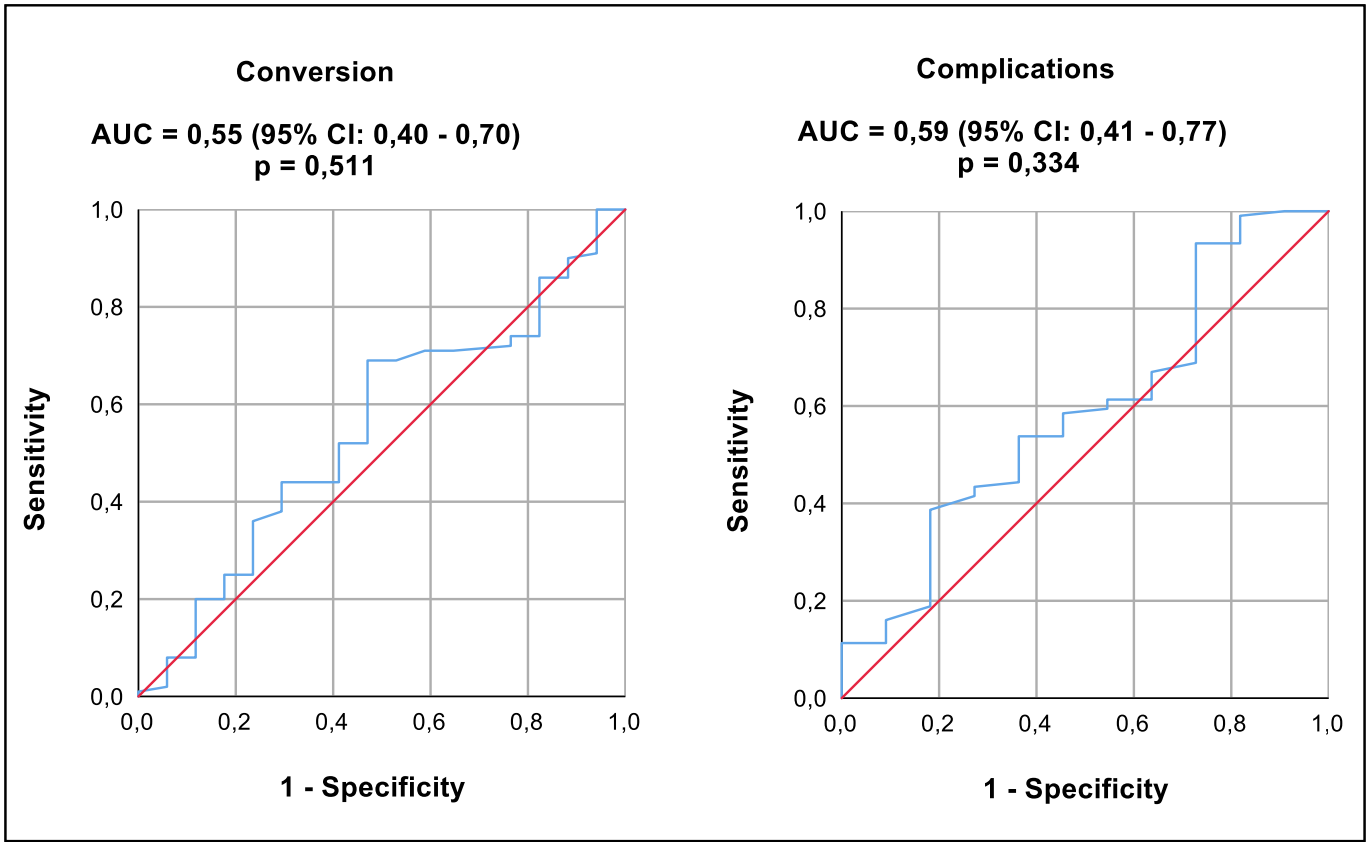
Table 1. Patient characteristics. IQR = interquartile range, BMI = body mass index, ASA = American Society of Anesthesiologists score, ERCP = endoscopic retrograde cholangiopancreatography.

Measure	Std. reg. coef. (*p*-value)
Sex	-0.03 (0.759)
Age	0.17 (0.202)
BMI	0.11 (0.370)
ASA I	0.12 (0.447)
ASA II	-0.15 (0.302)
ASA III or IV	ref.
Choledocholithiasis	0.13 (0.276)
Open surgery	-0.05 (0.652)
Conversion to open surgery	-0.06 (0.653)
Complications	-0.03 (0.798)
Operation duration	0.01 (0.967)

Measure	Value
Sample size	117
Male sex	61 (52.1%)
Median age (IQR)	67 (range 52–75)
Median BMI (IQR) (*n* = 91)	26.9 (range 24.7–30.3)
ASA	
I	16 (13.7%)
II	67 (57.3%)
III	33 (28.2%)
IV	1 (0.9%)
Indication for ERCP	
Choledocholithiasis	107 (91.5%)
Acute pancreatitis	10 (8.5%)
Conversion	17 (14.5%)
Complications	11 (9.4%)
Median number of days until operation (IQR)	56 (range 21–92)
Median length of operation in minutes (IQR)	57 (range 40–82)

Table 2. Relationship between time interval and patient characteristics, type of operation, duration of operation, conversion to open surgery, and postoperative complications (results of multiple linear regression). Std. reg. coef. = standardized regression coefficient, ref. = reference group, BMI = body mass index, ASA = American Society of Anesthesiologists score.

Figure 2. Receiver operating curve and area under the curve with 95% confidence interval for two binary classifiers with different thresholds of time until operation. AUC = area under the curve, CI = confidence interval.



a median of 56 days and an IQR between 21 and 92 days. Surgery was performed in an elective setting in 81 (69.2%) patients, and the rest were operated on as an emergency. Laparoscopic cholecystectomy was performed in 114 (97.4%) patients. Among those, there were 17 (14.5%) conversions to open surgery, most of them (64.7%) due to unclear anatomy, and the rest due to adhesions. The range of operating time was 15 to 190 min, with a median of 57 min and an IQR of 40 to 82 min. Postoperative complications occurred in 11 (9.4%) patients, five patients had a Clavien–Dindo score of 2, and six patients had a Clavien–Dindo score of 3a. There was no mortality in the group.

No statistically significant associations between any independent variable and time until operation were found, and all the *p*-values for the calculated standardized regression coefficient were significantly higher than 0.05 (Table 2). When controlling for other variables in the model, conversion to open surgery, complications, and operation duration were still not associated with the time interval from ERCP/EPT to the operation. To find the threshold of time until operation that best discriminates between conversion to open surgery or postoperative complications, the ROC was plotted and the AUC was calculated (Figure 2). In both instances, the AUC was not statistically significantly different from 0.05. No threshold value of the time interval to operation could be found that would discriminate between whether a patient had a conversion or postoperative complications or not.

Discussion

ERCP with EPT, followed by a subsequent laparoscopic cholecystectomy (a two-step approach), is currently the gold standard for treatment of patients with CBD stones. However, there is no consensus in the literature on what the time interval from the index procedure to the operation should be.

The results of our study show no statistical differences in the number of conversions to open surgery, duration of the operation, or postoperative morbidity regardless of the time interval between cholecystectomy and ERCP/EPT.

Based on the results of our study, our current practice, in which patients are usually operated on 1 to 3 months after ERCP/EPT, is safe. There was no mortality in our group and the rate of postoperative complications was 9.4%, which is similar to those reported by other authors (5.3–14%) (2, 9, 27–29). The rate of conversion to open cholecystectomy is higher (8–55%) in patients with a complicated gallstone disease (e.g., gallstones present, previous ERCP/EPT, urgent surgery) compared to the conversion rates (3–5%) in uncomplicated cholecystectomies (7, 16, 27, 30–31). In our study the conversion rate was 14.5%, which is comparable to the reported conversion rates in the literature.

Nevertheless, the optimal timing of cholecystectomy after ERCP/EPT remains unclear. Despite the fact that an early cholecystectomy is recommended, there are no clear guidelines on how long the time interval should be (2, 10–13). The recommendations put forth in many guidelines are conflicting and often very unspecific, as is clearly shown in the review article by van Dijk et al. (3). Literature recommendations for the time interval differ from a few hours to a few months. Moreover, some authors even favor single-step management, in which ERCP/EPT is performed during the cholecystectomy (3, 6–7). It is hypothesized that ERCP/EPT causes inflammation in the gallbladder area, thus making the subsequent cholecystectomy more difficult. Therefore, surgery is often delayed, presumably allowing the area to settle. The delay also allows the patient to recover from initial illness. Such a delay, however, causes an increased risk of biliary symptom reoccurrence and disease progression, hence complicating the following surgery (10, 15–16, 27). However, there appears to be no single factor related to ERCP that makes laparoscopic cholecystectomy more difficult. Inflammatory gall bladder pathology, rather than ductal pathologies, seems to be the determining factor that makes the operation more or less difficult (32).

In a two-step approach, a very early or somewhat delayed laparoscopic cholecystectomy can be performed. The early procedure avoids the risk of symptoms recurring, and the delayed procedure allows the gallbladder area to settle. Several published studies confirm the equivalency of both therapeutic strategies, including the results of our study (12, 15, 17, 22, 27). In contrast, some studies favor either one approach or the other. An article by Salman et al. recommends a very short time interval (< 72 hours) due to a presumably decreased risk of conversion, shorter duration of surgery

and length of stay, and fewer postoperative complications. The same approach is recommended by Borreca et al., mainly due to a decreased risk of symptom recurrence. An early cholecystectomy does seem to decrease the risk for recurrence of biliary complications. Postponing the operation for about 6 weeks, on the other hand, provides for better operating conditions due to less inflammation in the gallbladder area (2, 23). Mann et al. argue that a 6-week delay is safe for the patients and does not increase the risk of symptoms recurring, postoperative complications, operation duration, or conversion rates (22). In contrast, Schiphorst et al. believe that an operation performed within the 1st week after ERCP/EPT leads to a decreased rate of symptom recurrence, length of stay, and rate of conversion (7). This is backed by a study by de Vries et al., which shows that patients operated on less than 2 weeks after ERCP/EPT have a lower conversion rate than those operated on within 2 to 6 weeks (12).

Some authors argue that ERCP/EPT should be performed during the operation itself, when the gallbladder is removed (33–34). During such a one-step approach, the intraoperative ERCP can even be facilitated through the so called laparo-endoscopic rendezvous procedure. Sahoo et al. have compared this method to standard two-stage management in a prospective randomized trial. Their results show that the rendezvous approach increases selective cannulation of the CBD, reduces post-ERCP pancreatitis, and prevents unnecessary intervention into the CBD (35).

Our study has some limitations. First of all, it has all of the inherent biases of a retrospective study. Second, only a few patients (n = 3) were operated on within a very short period of time (< 72 hours), in an interval that many authors argue decreases the rate of conversions, postoperative morbidity, and length of stay, outweighing the risk of early surgery (2, 23, 30). On the other hand, even though most of our patients were in fact operated on in a somewhat delayed fashion (a median of 56 days), our analysis did not find any statistical significance of such an approach, positive or negative. This is not in line with a review performed by Friis et al., in which the authors argue that a delayed cholecystectomy increases the risk of conversion to open surgery (27).

Furthermore, there are other variables that could affect the rate of conversions (patient conditions, previous abdominal surgeries, adhesions, and experience of the surgeon), duration of operation (preoperative diagnosis, intraoperative complications, anatomical differences, and surgeon experience), and postoperative complications, and these were not included in the analysis.

Based on the results of our study, the interval of 1 to 3 months between ERCP/EPT and laparoscopic cholecystectomy is safe because it did not affect the rate of conversions, duration of the operation, or postoperative complications in our group of patients. However, no recommendations regarding the optimal time for the surgery can be given. With the lack of clear guidelines and conflicting recommendations for the optimal time interval in the literature, it is evident that further research is necessary, probably through larger prospective randomized studies.

Acknowledgements

The authors wish to thank Vanja Erčulj, the statistician that performed all the necessary statistical calculations.

Funding

No specific funding was received for this study.

Transparency declarations

The authors declare that they have no competing interests.

References

1. Sarli L, Iusco D, Sgobba G, et al. Gallstone cholangitis: a 10-year experience of combined endoscopic and laparoscopic treatment. Surg Endosc Other Interv Tech. 2002;16(6):975–80.
2. Salman B, Yilmaz U, Kerem M, et al. The timing of laparoscopic cholecystectomy after endoscopic retrograde cholangiopancreaticography in cholelithiasis coexisting with choledocholithiasis. J Hepatobiliary Pancreat Surg. 2009;16(6):832–6.
3. van Dijk AH, de Reuver PR, Besselink MG, et al. Assessment of available evidence in the management of gallbladder and bile duct stones: a systematic review of international guidelines. HPB (Oxford). 2017;19(4):297–309.
4. Cai JS, Qiang S, Bao-Bing Y. Advances of recurrent risk factors and management of choledocholithiasis. Scand J Gastroenterol. 2017;52(1):34–43.
5. Shaffer EA. Epidemiology of gallbladder stone disease. Best Pract Res Clin Gastroenterol. 2006;20(6):981–96.
6. Gurusamy K, Sahay SJ, Burroughs AK, et al. Systematic review and meta-analysis of intraoperative versus preoperative endoscopic sphincterotomy in patients with gallbladder and suspected common bile duct stones. Br J Surg. 2011;98(7):908–16.
7. Schiphorst AHW, Besselink MGH, Boerma D, et al. Timing of cholecystectomy after endoscopic sphincterotomy for common bile duct stones. Surg Endosc Other Interv Tech. 2008;22(9):2046–50.
8. Zang J, Yuan Y, Zhang C, et al. Elective laparoscopic cholecystectomy without intraoperative cholangiography: role of preoperative magnetic resonance cholangiopancreatography – a retrospective cohort study. BMC Surg. 2016;16(1):45.
9. Zhang W, Xu G, Huang Q, et al. Treatment of gallbladder stone with common bile duct stones in the laparoscopic era. BMC Surg. 2015;15(1):7.
10. Rustagi T, Jamidar PA. Endoscopic retrograde cholangiopancreatography-related adverse events: general overview. Gastrointest Endosc Clin N Am. 2015;25(1):97–106.
11. Tranter SE, Thompson MH. Comparison of endoscopic sphincterotomy and laparoscopic exploration of the common bile duct. Br J Surg. 2002;89:1495–504.
12. De Vries A, Donkervoort SC, Van Geloven AAW, et al. Conversion rate of laparoscopic cholecystectomy after endoscopic retrograde cholangiography in the treatment of choledocholithiasis: does the time interval matter? Surg Endosc Other Interv Tech. 2005;19(7):996–1001.
13. Sahoo MR, Kumar AT, Patnaik A. Randomised study on single stage laparo-endoscopic rendezvous (intra-operative ERCP) procedure versus two stage approach (preoperative ERCP followed by laparoscopic cholecystectomy) for the management of cholelithiasis with choledocholithiasis. J Minim Access Surg. 2014;10(3):139–43.
14. Golub R, Brodsky N, Cantu R, et al. Same-session endoscopic retrograde cholangiopancreatography and cholecystectomy. Surg Laparosc Endosc Percutan Tech. 2000;10(5):272–4.
15. Siert J, Reinders K, Goud A, et al. Early laparoscopic cholecystectomy improves outcomes after endoscopic sphincterotomy for choledochocystolithiasis. YGAST. 2010;138:2315–20.
16. Boerma D, Rauws EA, Keulemans YC, et al. Wait-and-see policy or laparoscopic cholecystectomy after endoscopic sphincterotomy for bile-duct stones: a randomised trial. Lancet. 2002;360(9335):761–5.
17. Kwon YH, Cho CM, Jung MK, et al. Risk factors of open converted cholecystectomy for cholelithiasis after endoscopic removal of choledocholithiasis. Dig Dis Sci. 2015;60(2):550–6.
18. Lu J, Cheng Y, Xiong XZ, et al. Two-stage vs single-stage management for concomitant gallstones and common bile duct stones. World J Gastroenterol. 2012;18(24):3156–66.
19. Clayton ESJ, Connor S, Alexakis N, et al. Meta-analysis of endoscopy and surgery versus surgery alone for common bile duct stones with the gallbladder in situ. Br J Surg. 2006;93(10):1185–91.
20. Rogers SJ, Cello JP, Horn JK, et al. Prospective randomized trial of LC+LCBDE vs ERCP/S+LC for common bile duct stone disease. Arch Surg. 2010;145(1):28–33.
21. Liberman MA, Phillips EH, Carroll BJ, et al. Cost-effective management of complicated choledocholithiasis: laparoscopic transcystic duct exploration or endoscopic sphincterotomy. J Am Coll Surg. 1996;182(6):488–94.
22. Mann K, Belgaumkar AP, Singh S. Post-endoscopic retrograde cholangiography laparoscopic cholecystectomy: challenging but safe. J Soc Laparoendosc Surg. 2013;17(3):371–5.
23. Borreca D, Bona A, Bellomo MP, et al. "Ultra-rapid" sequential treatment in cholecystocholedocholithiasis: alternative same-day approach to laparoendoscopic rendezvous. Updates Surg. 2015;67(4):449–54.
24. Schachter MDP, Peleg MDT, Cohen MDO. Interval laparoscopic cholecystectomy in the management of acute biliary pancreatitis. HPB Surg. 2000;11(5):319–23.
25. van Baal MC, Besselink MG, Bakker OJ, et al. Timing of cholecystectomy after mild biliary pancreatitis: a systematic review. Ann Surg. 2012;255(5):860–6.
26. Morino M, Baracchi F, Miglietta C, et al. Preoperative endoscopic sphincterotomy versus laparoendoscopic rendezvous in patients with gallbladder and bile duct stones. Ann Surg. 2006;244(6):889–93.
27. Friis C, Rothman JP, Burcharth J, et al. Optimal timing for laparoscopic cholecystectomy after endoscopic retrograde cholangiopancreatography: a systematic review. Scand J Surg. 2018;107(2):99–106.
28. Bostanci EB, Ercan M, Ozer I, et al. Timing of elective laparoscopic cholecystectomy after endo-

scopic retrograde cholangiopancreaticography with sphincterotomy: a prospective observational study of 308 patients. Langenbeck's Arch Surg. 2010;395(6):661–6.

29. Denjalić A, Škiljo H, Bečulić H, et al. Bile duct injury during laparoscopic cholecystectomy: risk of procedure or professional negligence? Med Glas (Zenica). 2013;10(2):413–5.
30. Sarli L, Iusco DR, Roncoroni L. Preoperative endoscopic sphincterotomy and laparoscopic cholecystectomy for the management of cholecystocholedocholithiasis: 10-year experience. World J Surg. 2003;27(2):180–6.
31. Lau JYW, Leow CK, Fung TMK, et al. Cholecystectomy or gallbladder in situ after endoscopic sphincterotomy and bile duct stone removal in Chinese patients. Gastroenterology. 2006;130(1):96–103.
32. Krishnamohan N, Lo C, Date RS. Predicting the degree of difficulty of laparoscopic cholecystectomy following endoscopic retrograde cholangiopancreatography—subgroup analysis does not improve the prediction. J Min Access Surg. 2019;15:360–1.
33. Rábago LR, Vicente C, Soler F, et al. Two-stage treatment with preoperative endoscopic retrograde cholangiopancreatography (ERCP) compared with single-stage treatment with intraoperative ERCP for patients with symptomatic cholelithiasis with possible choledocholithiasis. Endoscopy. 2006;38(8):779–86.
34. Mattila A, Mrena J, Kellokumpu I. Cost-analysis and effectiveness of one-stage laparoscopic versus two-stage endolaparoscopic management of cholecystocholedocholithiasis: a retrospective cohort study. BMC Surg. 2017;17(1):79.
35. Sahoo MR, Kumar AT, Patnaik A. Randomised study on single stage laparo-endoscopic rendezvous (intra-operative ERCP) procedure versus two stage approach (preoperative ERCP followed by laparoscopic cholecystectomy) for the management of cholelithiasis with choledocholithiasis. J Minim Access Surg. 2014;10(3):139–43.

Functional Results After Transanal Total Mesorectal Excision for Rectal Cancer

Jurij Aleš Košir, Jan Grosek, Aleš Tomažič, Gregor Norčič
Department of Abdominal Surgery, Ljubljana University Medical Center

Correspondence

Jurij Aleš Košir, MD
ales.kosir@kclj.si

Key words

transanal total mesorectal excision, low anterior resection syndrome, rectal cancer, quality of life

Short Communication

SURGERY SURG ENDOS 2020; 2(1): 31-35

Abstract

Backgrounds. The main focus of treating rectal cancer is curing the disease. However, curing the disease is only one of the aspects of successful treatment. Treatment of rectal cancer can result in functional disturbances that may significantly impair the quality of patients' lives. As such, increasing emphasis is being placed on preserving the function of the pelvic organs. Our study examines the extent of bowel dysfunction and its impact on health-related quality of life after transanal total mesorectal excision (TaTME).

Methods. The Slovenian version of the low anterior resection syndrome (LARS) score was completed by rectal cancer patients that underwent TaTME between January 1st, 2017 and January 31st, 2019 at the Ljubljana University Medical Center. The questionnaire was sent to the patients and then returned via mail.

Results. Out of 11 patients that were contacted for participation, 10 (90.9%) were included in the final analysis. Four of the patients reported major LARS, four patients reported minor LARS, and two patients reported no LARS. The mean LARS score was 28.2.

Conclusion. Rectal cancer patients after TaTME seem to have acceptable impairment of anorectal function, but further studies are needed to confirm this.

Introduction

In recent decades, much progress has been made in rectal cancer surgery and non-operative therapy for rectal cancer. This has led to improved survival of patients with rectal cancer. Advances in surgery have also allowed more sphincter-preserving resections in patients with low rectal tumors. The number of patients after sphincter-preserving operations is thus increasing (1). With the improvement of survival of patients, more attention is being focused on improving functional outcomes after surgery (2). Patients may report complaints regarding their anorectal and urogenital functions, psychological aspects, and

social relationships (2). Urogenital and anorectal dysfunction is related to factors such as intraoperative damage to the anal sphincter, nerves surrounding the rectum, loss of recto-anal inhibitory reflex, and poor compliance of the neorectum (2).

Patients with anorectal dysfunction report fragmented defecation, increased stool frequency, emptying difficulties, fecal urgency, and incontinence (3). The set of these symptoms is known as low anterior resection syndrome (LARS), and it affects between 60 and 90% of patients after low anterior resection (LAR) (2–6). The main predisposing factors for developing LARS are radiotherapy of the rectum and low height of the anastomosis (3, 4). Other risk factors are the construction of a temporary ileostomy and its prolonged presence, postoperative complications, age, and female sex (2–6). In an effort to improve functional results, the construction of a side-to-end anastomosis, a J-pouch, or a coloplasty can be performed (2). Anorectal function is the worst in the first few months after surgery, and it slowly improves with time, stabilizing within the first 2 years after surgery (7).

Transanal total mesorectal excision (TaTME) is a novel surgical technique that overcomes some of the difficulties related to laparoscopic total mesorectal excision (LaTME), especially in patients with a narrow pelvis and bulky mesorectum (8). It utilizes a bottom-up approach combining the concepts of total mesorectal excision, laparoscopy, and transanal endoscopic microsurgery (8). In comparison to LaTME, TaTME is associated with fewer conversion rates, fewer anastomotic leaks, and better short-term surgical outcomes (9).

TaTME allows better visualization of the pelvic structures, which can prevent injuries to the hypogastric plexus (8, 9). With better control of the distal resection margin, this may help achieve better postoperative anorectal function (8, 9). However, TaTME may also cause sphincter damage due to stretching during the operation, which may negatively impact the anorectal function (8, 9). TaTME also allows more sphincter-sparing operations with low-lying anastomoses to be performed, which is one of the most important risk factors for the development of LARS (8, 9).

Currently, there are not many studies in the literature evaluating functional results after TaTME. The objective of this study was to evaluate the bowel function of rectal cancer patients after TaTME.

Methods

Participants

The electronic database of a tertiary medical center was searched for all patients with rectal cancer treated with TaTME from January 1st, 2017 to January 31st, 2019. All patients operated on for rectal adenocarcinoma within 15 cm of the anal verge that were 18 years old or above were included. Exclusion criteria were the presence of a stoma, known disseminated or recurrent disease, inability to read and write Slovenian, or any psychiatric conditions that might interfere with the questionnaire evaluation. Questionnaires regarding bowel function were sent in May 2019 to all 11 eligible patients identified in our database that had undergone TaTME and either had no ileostomy or already had their ileostomy closed at the time of the study. To achieve a better response rate, the patients were contacted via telephone. All patients included provided signed informed consent for participation in the study. Demographic and clinical information was obtained from the electronic database.

Low Anterior Resection Syndrome Score

Bowel function was assessed with the low anterior resection syndrome score (LARS score), a scoring instrument for evaluating bowel function after sphincter-preserving procedures for rectal cancer. This self-administered questionnaire was developed in Denmark specifically for rectal cancer patients that received curative low anterior resection with or without radiotherapy for non-disseminated disease (10). The LARS score has been validated in Denmark, Lithuania, the Netherlands, Germany, Sweden, Spain, the UK, Thailand, China, Slovenia, and several other countries (5, 11–14).

The questionnaire includes five questions that evaluate gastrointestinal symptoms. The questions and scoring algorithm of the LARS score are shown in Table 1. The score values were assigned to possible answers in order to calculate the LARS score, which was divided into “no LARS” (score of 0–20 points), “minor LARS” (21–29 points), and “major LARS” (30–42 points) (10). All questions had to be answered for inclusion in our analysis.

Table 1. Low anterior resection syndrome score (LARS score) (10).

Question	Score
1. Do you ever have occasions when you cannot control your flatus (wind)?	
No, never	0
Yes, less than once per week	4
Yes, at least once per week	7
2. Do you ever have any accidental leakage of liquid stool?	
No, never	0
Yes, less than once per week	3
Yes, at least once per week	3
3. How often do you open your bowels?	
More than 7 times per day (24 h)	4
4–7 times per day (24 h)	2
1–3 times per day (24 h)	0
Less than once per day (24 h)	5
4. Do you ever have to open your bowels again within 1 h of the last bowel opening?	
No, never	0
Yes, less than once per week	9
Yes, at least once per week	11
5. Do you ever have such a strong urge to open your bowels that you have to rush to the toilet?	
No, never	0
Yes, less than once per week	11
Yes, at least once per week	16

Table 2. Patient characteristics (n = 10).

Variable	Value
Males, n (%)	6 (60)
Age in years at time of survey, mean (*SD*)	66.3 (11.7)
Age in years at time of operation, mean (*SD*)	65.1 (12.2)
Tumor stage	
T0–T2, n (%)	8 (80)
T3–T4, n (%)	2 (20)
Months since operation, mean (SD)	13.9 (9.0)
Tumor level in cm, mean (SD)	6.2 (4.0)
Chemoradiotherapy, n (%)	4 (40.0)
Radiotherapy, n (%)	1 (10.0)
Temporary ileostomy, n (%)	7 (70.0)

Table 3. Analysis of the low anterior resection syndrome score (LARS score) questionnaires (n = 10).

Scores	Value
LARS score, mean (*SD*)	28.2 (9.7)
Major LARS, n (%)	4 (40.0)
Minor LARS, n (%)	4 (40.0)
No LARS, n (%)	2 (20.0)

Results

Out of 11 patients eligible for the study, 10 responded, yielding a 90.9% response rate. One of the patients did not respond to our mail and our telephone calls. All the respondents were included in the analysis. Clinical and demographic data are shown in Table 2. No local recurrence was noted in the patients included. The results of the questionnaires are presented in Table 3.

Discussion

To our knowledge, this is the first report of bowel function after TaTME in Slovenian rectal cancer patients.

Although the number of patients included is small, the results of bowel function are within the expected range for patients after sphincter-preserving rectal cancer surgery (5–9, 15–19). We performed end-to-end anastomoses in all our TaTME patients. Construction of side-to-end anastomoses might have even improved our results, but there are no data available yet to support this in TaTME patients (2). The average time since surgery is over a year, meaning that the bowel function has already stabilized in most patients. We observed similar results in the analysis of the bowel function of rectal cancer patients that underwent open anterior rectal resection from 2006 to 2010 at our center (5). In the open resection group, 58% of our patients experienced major LARS and 21% experienced minor LARS (5).

Other authors observed major LARS in 33 to 82% of rectal cancer patients after TaTME (15–19). Most of these authors compared TaTME patients with LaTME patients, but none of the differences between groups of patients compared were statistically significant.

This was a unicentric study and it included patients that were among the first ones operated on with the transanal approach at our center. To gain a better understanding of bowel function after TaTME, a multicentric randomized study should be performed evaluating a larger number of patients. One such study currently in progress is the COLOR III trial, comparing TaTME to LaTME (20).

Another limitation of our study is that it did not evaluate aspects of the quality of patients' lives other than bowel function. Urogenital, social, and psychological aspects of quality of life after TaTME should also be evaluated for a better understanding of these patients.

In summary, surgeons should discuss expectations regarding anorectal function and quality of life with patients undergoing rectal resections. Scoring systems exist to calculate the predicted postoperative functional results; however, none of these scores have yet been validated for TaTME (21). If there are risk factors for poor anorectal function, the construction of a permanent colostomy should be considered at the time of rectal resection.

Conclusions

Current data show acceptable impairment of bowel function in rectal cancer patients after TaTME. Results of randomized controlled trials are needed to confirm this.

Acknowledgments

The authors express their gratitude to all the participating patients.

References

1. Grosek J, Velenik V, Edhemovic I, Omejc M. The influence of the distal resection margin length on local recurrence and long-term survival in patients with rectal cancer after chemoradiotherapy and sphincter-preserving rectal resection. Radiol Oncol. 2016;51:169–77.
2. Ziv Y, Zbar A, Bar-Shavit Y, Igov I. Low anterior resection syndrome (LARS): cause and effect and reconstructive considerations. Tech Coloproctol. 2013;17:151–62.
3. Juul T, Ahlberg M, Biondo S, et al. International validation of the low anterior resection syndrome score. Ann Surg. 2014;259:728–34.
4. Ridolfi TJ, Berger N, Ludwig KA. Low anterior resection syndrome: current management and future directions. Clin Colon Rectal Surg. 2016;29:239–45.
5. Grosek J, Kosir JA, Novak J, et al. Validation of the Slovenian version of the low anterior resection syndrome score for rectal cancer patients after surgery. Zdr Varst. 2019;58(4):148–54.
6. Grosek J, Novak J, Kitek K, et al. Health-related quality of life in Slovenian patients with colorectal cancer: a single tertiary care center study. Radiol Oncol. 2019;53(2):231–7.
7. Emmertsen KJ, Laurberg S, Rectal Cancer Function Study Group. Impact of bowel dysfunction on quality of life after sphincter-preserving resection for rectal cancer. Br J Surg. 2013;100(10):1377–87.
8. Fernandez-Hevia M, Delgado S, Castells A, et al. Transanal total mesorectal excision in rectal cancer. Short-term outcomes in comparison with laparoscopic surgery. Ann Surg. 2015;261:221–7.
9. Deijen CL, Tsai A, Koedam TWA, et al. Clinical outcomes and case volume effect of transanal total mesorectal excision for rectal cancer: a systematic review. Tech Coloproctol. 2016;20:811–24.
10. Emmertsen KJ, Laurberg S. Low anterior resection syndrome score development and validation of a symptom-based scoring system for bowel dysfunction after low anterior resection for rectal cancer. Ann Surg. 2012;255:922–8.
11. Juul T, Battersby NJ, Christensen P, et al. Validation of the English translation of the low anterior resection syndrome score. Colorectal Dis. 2015;17:908–16.
12. Samalavicius NE, Dulskas A, Lasinskas M, Smailyte G. Validity and reliability of a Lithuanian version of low anterior resection syndrome score. Tech Coloproctol. 2016;20:215–20.
13. Hou XT, Pang D, Lu Q, et al. Validation of the Chinese version of the low anterior resection syndrome score for measuring bowel dysfunction after sphincter-preserving surgery among rectal cancer patients. Eur J Oncol Nurs. 2015;19:495–501.
14. Juul T, Ahlberg M, Biondo S, et al. International validation of the low anterior resection syndrome score. Ann Surg. 2014;259:728–34.
15. Pontallier A, Denost Q, Van Geluwe B, et al. Potential sexual function improvement by using transanal mesorectal approach for laparoscopic low rectal cancer excision. Surg Endosc. 2016;30(11):4924–33.
16. Kneist W, Wachter N, Paschold M, et al. Midterm functional results of taTME with neuromapping for low rectal cancer. Tech Coloproctol. 2016;20(1):41–9.
17. Koedam TWA, van Ramshorst GH, Deijen CL, et al. Transanal total mesorectal excision (TaTME) for rectal cancer: effects on patient-reported quality of life and functional outcome. Tech Coloproctol. 2017;21(1):25–33.
18. Veltcamp Helbach M, Koedam TWA, Knol JJ, et al. Quality of life after rectal cancer surgery: differences between laparoscopic and transanal total mesorectal excision. Surg Endosc. 2019;33(1):79–87.
19. Bjoern MX, Nielsen S, Perdawood SK. Quality of life after surgery for rectal cancer: a comparison of functional outcomes after transanal and laparoscopic approaches. J Gastrointest Surg. 2019;23(8):1623–30.
20. Deijen CL, Velthuis S, Tsai A, et al. COLOR III: a multicentre randomised clinical trial comparing transanal TME versus laparoscopic TME for mid and low rectal cancer. Surg Endosc. 2016;30(8):3210–5.
21. Battersby N, Bouliotis G, Emmertsen KJ, et al. Development and external validation of a nomogram and online tool to predict bowel dysfunction following restorative rectal cancer resection: the POLARS score. Gut. 2018;67:688–96.

GET MORE. **WITH LESS.**

Less sticking.[1,†] Less cleaning.[2,‡]
Less eschar buildup.[2,§]

More benefits.

MM SURGICAL

LigaSure™ Maryland jaw device
with nano-coated jaws

†Instances of tissue sticking to jaws measured over 110 seals per device.
‡Cleaning effectiveness assessed after each of two cleaning cycles.
§Eschar buildup assessed using optical imaging analysis after 60 seal and divide cycles.

Medtronic
Further, Together

Ventricular Lavage for Pediatric Hematocephalus Treatment: a Case Report and Operative Technique

Peter Spazzapan, Roman Bošnjak, Tomaž Velnar
Pediatric Neurosurgery Unit, Department of Neurosurgery, Ljubljana University Medical Center

Correspondence

Assoc. Prof. **Tomaž Velnar,** MD, PhD
tvelnar@hotmail.com

Key words

ventricular lavage, hematocephalus, pediatric surgery, neuroendoscopy

Case Report

SURGERY SURG ENDOS 2020; 2(1): 37-44

Abstract

Posthemorrhagic hydrocephalus in the setting of intraventricular hemorrhage is a frequent problem especially in preterm infants and remains a cause of severe neurological impairment. Many techniques have been used to treat intraventricular hemorrhage, ranging from fibrinolytic agents to drainages and endoscopic surgery. The technique of neuroendoscopic lavage allows a partial or complete hematoma evacuation in addition to hematocephalus washing. We describe the case of a neonate patient with hematocephalus that was treated with neuroendoscopic ventricular lavage.

Introduction

Posthemorrhagic hydrocephalus (PHH) after intraventricular hemorrhage (IVH) in preterm infants is a serious neonatological and neurosurgical pathology challenge (1). The most effective treatment modality has not yet been determined. Despite advances in intensive neonatal care, IVH remains a cause of subsequent severe neurological impairment and cognitive delay, mainly due to primary cerebral tissue damage resulting from hemorrhage and also due to the increased intracranial pressure that PHH may cause. Many techniques have been used to treat IVH (and consequent PHH), and their effectiveness is debatable. However, all are being used in clinical practice. The intraventricular administration of fibrinolytic agents has shown favorable long-term results. On the other hand, it also poses a high risk of new intracranial hemorrhage. In the belief that early removal of an intraventricular and intracerebral hematoma is favorable, however, the technique of neuroendoscopic lavage has been proposed (1, 2). This method allows the hematoma to be reduced or removed in a short time without extensive surgery or the introduction of fibrinolytic drugs, thus preventing the intraventricular inflammatory reactions that occur in response to hematoma degradation products. We

describe a neonate with hematocephalus that was successfully treated with a neuroendoscopic ventricular lavage.

Case report

The Patient

Our patent was born at 32 weeks of gestation. The birth weight was 1,740 g, the head circumference at birth measured 31 cm, and the Apgar score was rated at 9/10. After birth, he became agitated, was not feeding properly, and was showing failure to thrive. An ultrasound examination of the head and subsequently a magnetic resonance of the head revealed extensive bleeding in the ventricular system (grade IV with intraparenchymal bleeding in the left hemisphere), after which repeated head ultrasound examinations confirmed progressive expansion of the ventricular system. The head circumference increased by 2.5 cm in the first 2 weeks of age. Due to the progressive head enlargement, an external ventricular drain (EVD) was initially placed 14 days after birth in order to relieve the haematocephalus and prevent further head expansion. After 14 days of treatment with the EVD, the clot was not degrading and the cerebrospinal fluid (CSF) was hemorrhagic, and so we proposed fully neuroendoscopic clot removal and the boy underwent a neuroendoscopic lavage. The indication for the treatment of the PHH, first with the EVD and then with a neuroendoscopic lavage, was set on the basis of the gradual increase in head circumference (more than 2 mm per day in 1 week) and ultrasound-proven ventricular dilatation. The ventricular index, the width of the frontal horn, the thalamo-occipital distance, and the width of the third ventricle were above the 97th percentile. In addition, clinical signs of elevated intracranial pressure (a bulging fontanelle and bradycardia) were present.

The endoscopic procedure was successfully performed and a ventriculosubgaleal shunt was left behind as a temporary drainage device. Within a week after surgery, the ventricular system started to dilate slowly but progressively, and the patient required repeated punctures of the subgaleal pocket until the CSF became clear enough to place a permanent ventriculoperitoneal drain (VPD). No CSF infection was observed. After this treatment, the boy was discharged home.

The Operative Technique

After anesthesiologic preparation, the boy was placed supine on the operating table. Preoperative antibiotic prophylaxis with cephamezine was introduced perioperatively. The surgical field was prepped and draped, and the skin was cut in the left frontal area, next to the fontanelle (Figures 1 and 2). The bone was exposed and drilled so that a burr hole 8 mm in diameter was formed. The dura was visualized and cut. Under ultrasound guidance, visualizing the brain parenchyma and the ventricular system, a 0-degree endoscope (Karl Storz Lotta) was inserted into the frontal horn of the left lateral ventricle because the hematoma was located in the left ventricle (Figure 3).

After entering the ventricular cavity, the visualization was obscured due to the hematocephalus (Figure 4). After initial diluting and washing of the hemorrhagic CSF through the working channel of the endoscope, the left wall of the septum pellucidum was identified on the right side first, and in the lateral wall of the frontal horn a large hematoma was seen that was extending into the brain parenchyma (Figure 5). The ventricle was rinsed profusely with Ringer's solution at 37 °C in order to improve visibility by further diluting and washing the hemorrhagic CSF. An endoscope was inserted into the hematoma and a suction catheter was introduced through the working channel of the endoscope. With cautious suction, we started to reduce and gradually mobilize the coagulum. Intermittent pulsatile aspiration was used through the narrow-gauge aspiration catheter rather than constant suction in order to break the blood clot into smaller pieces. The hematoma particles were then aspirated, and the hematoma mass was gradually reduced. The inflow and outflow of washing solution into the ventricular system was carried out passively through the endoscope, so that the intraventricular volume of fluid was constant and balanced throughout the procedure. The parenchymal portion of the hematoma was not removed because new brain hemorrhages could be triggered. After the hematoma reduction, the ventricular lavage was prolonged for few more minutes and the ventricles were further flushed in order to rinse the hemorrhagic CSF and small clotted blood particles floating in the ventricular cavity. When the CSF became clear, the visibility improved and the anatomy of the left ventricle could be appreciated. The ventricular wall, especially in the left frontal area

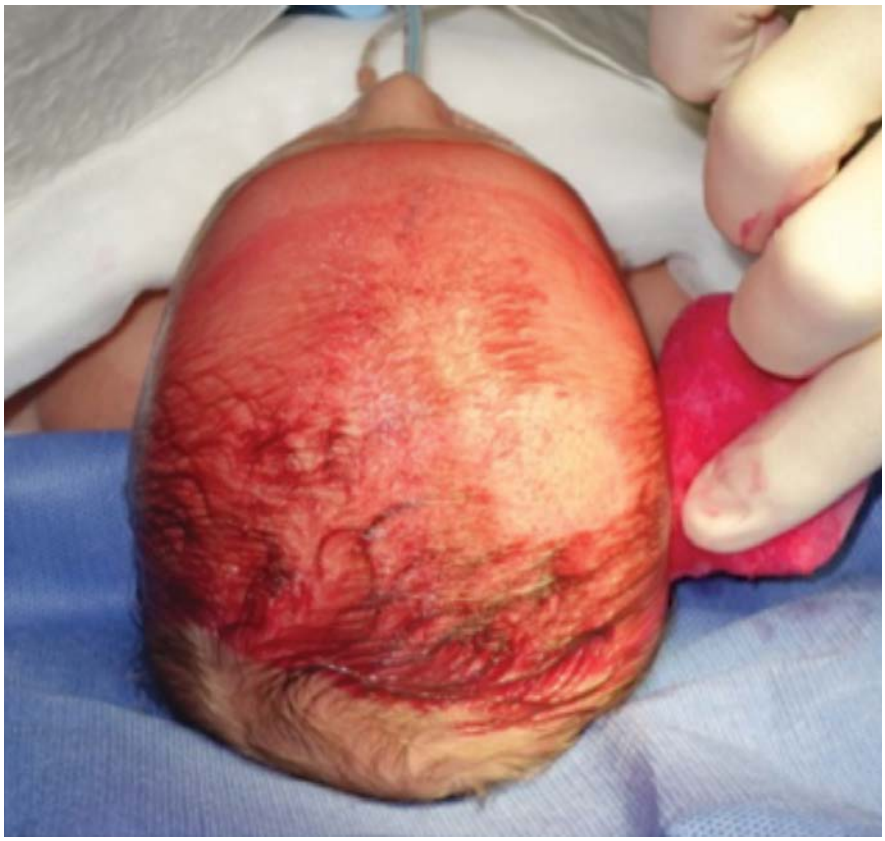


Figure 1. Positioning of the patent's head. It is vital for neuroendoscopic lavage that the head be secured in a neutral position for easier orientation during the operation.

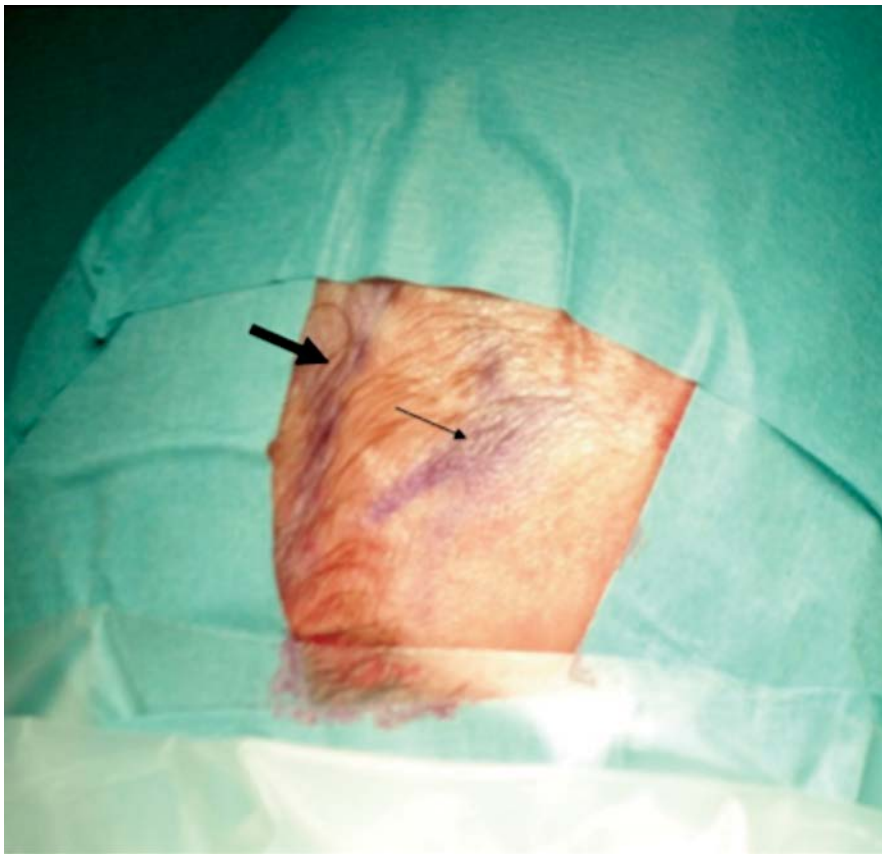


Figure 2. The surgical field is prepared. The thick arrow indicates the median line. The thin arrow is the edge of the fontanel, where the skin cut and burr hole will be located.

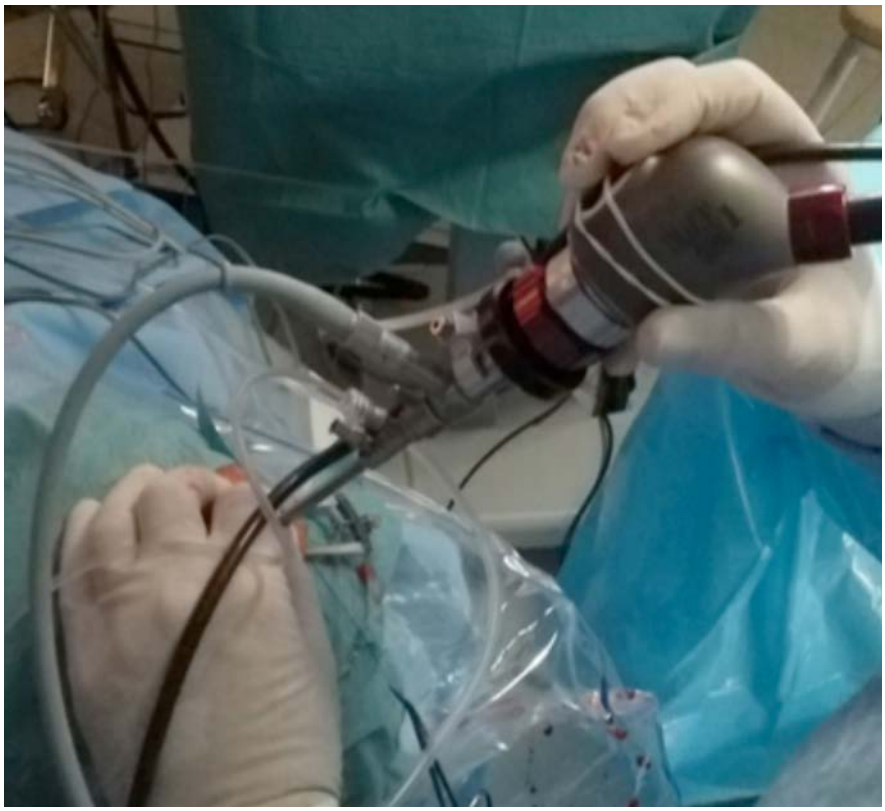


Figure 3. The endoscope advancing through the burr hole into the lateral ventricle.

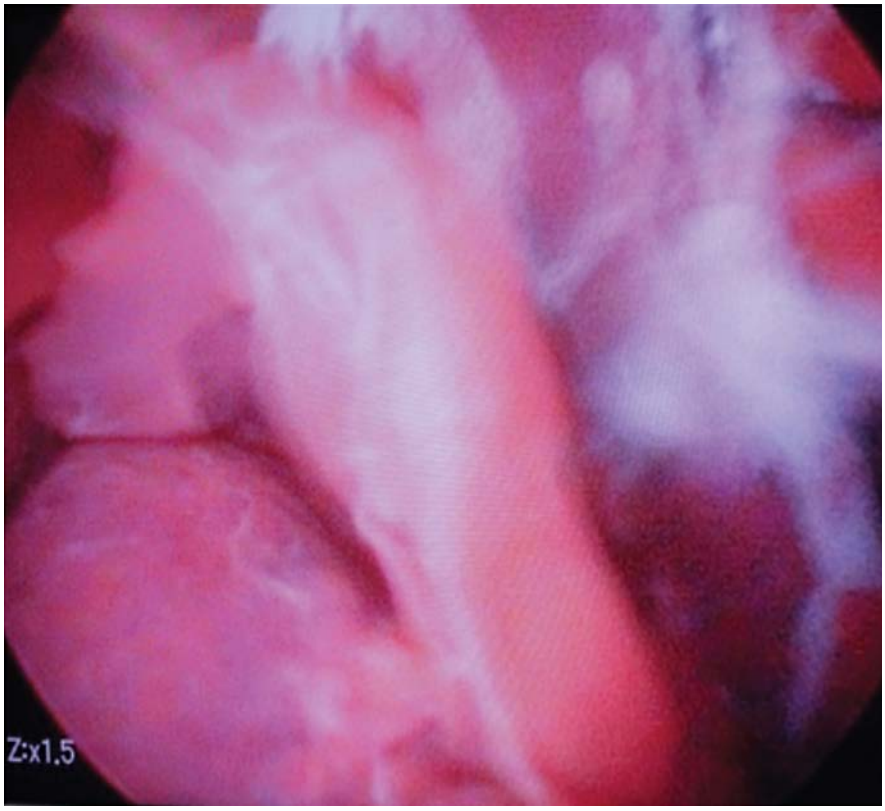


Figure 4. Endoscopic view of the hematocephalus. The ventricular cavity is filled with a blood clot and visualization is obscured.

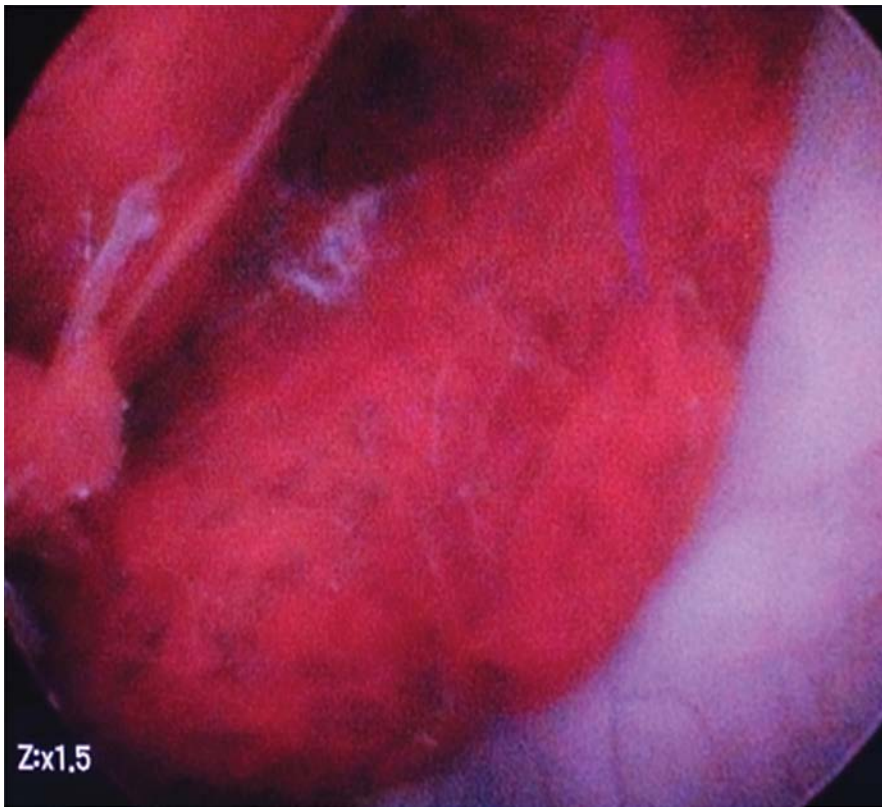


Figure 5. Ventricular view through the endoscope. On the left, a large hematoma can be seen, extending into the brain parenchyma. Part of the blood clot has been cleared and the cerebrospinal fluid has started to clear. White brain parenchyma can be seen on the right.

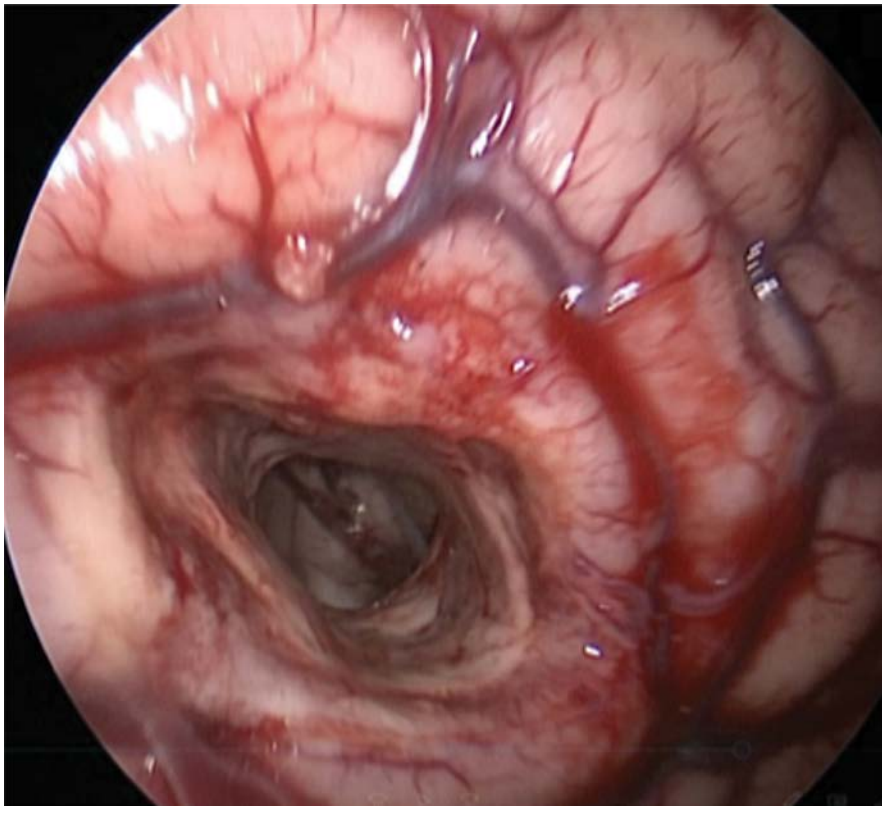


Figure 6. After removing the endoscope, the working channel is clear with no active bleeding.

surrounding the hematoma, was distorted due to the bleeding. The left foramen of Monro was patent and the hemorrhagic CFS in the third ventricle was washed. Then, we coagulated and punctured the wall of the severed septum pellucidum and inspected the right lateral ventricle. Here, the CSF was blood-stained from the previous bleeding and the ventricular anatomy was completely preserved, as was the ependymal wall. After the blood-stained CSF was cautiously flushed, the endoscope was retracted into the left ventricle and carefully removed. The working channel was inspected during the retraction and no bleeding was seen (Figure 6). In total, 2,500 ml of Ringer's solution was used during the surgery for a thorough ventricular lavage. During the course of the entire operation, ultrasound guidance showed the exact position of the endoscope and helped in orientation, especially in the areas that were obscured by bleeding.

At the end of the operation, a ventriculosubgaleal shunt was left behind in order to allow temporary drainage of a possible CSF excess. The burr hole was sealed with a fibrinogen/fibrin patch (Tachosil, Baxter, USA) and the subcutaneous tissue and skin were carefully closed. The boy was transferred to the ward, where he was continuously monitored and the ventricles were evaluated with ultrasound, every day initially and then progressively after a longer period every 2 and 4 days. After a week, all the ventricles were enlarging progressively, most probably due to hampered resorption after the hemorrhage. We evacuated the CSF excess through repeated punctures of the subgaleal pocket. The child required frequent punctures, and so a permanent VPD was inserted when the CSF became clear. The rest of the postoperative course was uneventful. A ventricular ultrasound at follow-up showed a favorable location of the ventricular catheter and ventricular width. One year after the surgery, the VPD is working normally and the child is being monitored by a neurological rehabilitation team.

Discussion

Despite recent advances in neonatal diagnostic and therapeutic care, prematurity is still a challenging medical condition associated with many and serious complications (3). IVH in preterm infants and subsequent PHH are pathologies for which the ideal treatment method has not yet been westablished and can cause marked long-term cognitive and motor impairment. About 3 to 20% of early preterm infants suffer from IVH, with 29 to 49% of them developing PHH and 38 to 92% requiring permanent CSF drainage (3–6). PHH is initially treated with temporary CSF drainage. Most commonly, EVD has been used as well as ventriculosubgaleal drainage, ventricular reservoir punctures, and occasionally lumbar punctures. Every modality has its own advantages, disadvantages, and challenges (5–7).

In order to direct the treatment straight into the reduction or removal of IVH, thrombolysis has been initiated in preterm infants (8). However, the largest prospective study involving these patients (the DRIFT Trial) has already been terminated during its implementation due to a high frequency of rebleedings, reaching a rate as high as 34%. Nevertheless, children treated successfully in the DRIFT Trial showed a favorable neurological outcome after 2 years, and therefore the evacuation of the blood clot and hematocephalus by other means was suggested (9). One reasonable option in the advent of neuroendoscopic surgery also includes ventriculoscopy and ventricular lavage. Hence, the neuroendoscopic lavage technique was developed to help in hematocephalus and IVH treatment with the reduction of IVH without risking the complications of thrombolysis. Neuroendoscopic lavage is a time-limited technique performed under sterile conditions, with direct visualization of the ventricular system and the bleeding or blood clot (3, 7). The intraventricular fluid volume is always balanced throughout the procedure, thus keeping the ventricles dilated. With this technique, liquefied blood, hematoma particles, and fibrin fragments can be removed intraoperatively and the hematoma itself can be reduced or removed through direct mobilization and aspiration. With the neuroendoscope, all ventricular compartments except the temporal horns are accessible; they can be visualized and washed, and the draining catheters can be placed when needed.

The neuroendoscopic ventricular lavage may not be always sufficient per se due to various reasons. These include partial hematoma removal (residual in the temporal horns), concomitant or acquired aqueductal stenosis or occlusion, membrane and multiloculated hydrocephalus formation, hemorrhage-induced hampered resorption of the CSF, and so on. In these cases, a postoperative alternative route for CFS drainage must be established, as was done in our patient, in whom ventriculosubgaleal drainage was inserted. In the literature, a ventricular reservoir or ventriculosubgaleal drainage is also the most frequently used temporary drainage device (5, 6). In cases in which children develop chronic hydrocephalus, a permanent VPD must be implanted. The decision for VPD placement, however, must always be carefully considered. A VPD means lifelong dependence on the drainage system and a high chance of frequent shunt revisions and infections. On the other hand, untreated hydrocephalus causes severe brain tissue damage due to increased intracranial pressure and, consequently, severe neurocognitive impairment. In the light of these results, the lavage technique in the Charité experience has been evaluated as safe and successful in the treatment of PHH in preterm infants and was also adopted in our patient (1, 2, 10). For CSF drainage, a ventriculosubgaleal shunt was placed first, immediately after the lavage, because the CSF cannot be drained normally after the majority of IVHs. This can only be a temporary treatment, and the CSF excess that is not resorbed is drained through regular punctures of the collection in the subgaleal space connected to the ventricular system. Sometimes the punctures alone are not enough and, in such instances, a VPD is the solution. Ultrasound monitoring is of vital importance and is always used to control the ventricular width (10–12).

In two experimental clinical studies from Berlin Charité Hospital, the following results after the introduction of the lavage technique were reported: 1 week after the intervention, the ventricular dimension on the ultrasound was significantly smaller than in the reservoir-treated group, which included children with a reservoir connected with a catheter to the ventricles (1, 2). There was also less necessity for relief punctures, especially in the initial weeks after the intervention. As a result, the incidence of infection and consequently the cases of multiloculated hydrocephalus have been reduced (12, 13). The long-term VPD insertion frequency was reduced from 100 to 55% after lavage treatment (2). According to the favorable results and suitable pathology, we decided on the same treatment in our patient. Especially the long-lasting EVD and refractory hematoma, which was not degrading, were problematic, and with neuroendoscopic lavage the treatment course was shortened.

Conclusion

Neuroendoscopic lavage is a safe and effective technique for treating PHH resulting from IVH in preterm infants. Considering the success of this method in the literature and in our clinical case, we have introduced this technique into regular clinical practice.

References

1. Schulz M, Bührer C, Pohl-Schickinger A, et al. Neuroendoscopic lavage for the treatment of intraventricular hemorrhage and hydrocephalus in neonates. J Neurosurg Pediatr. 2014;13(6):626–35.
2. d'Arcangues C, Schulz M, Bührer C, et al. Extended experience with neuroendoscopic lavage for posthemorrhagic hydrocephalus in neonates. World Neurosurg. 2018;116:217–24.
3. Brouwer AJ, Brouwer MJ, Groenendaal F, et al. European perspective on the diagnosis and treatment of posthaemorrhagic ventricular dilatation. Arch Dis Child Fetal Neonatal. 2012;97:50–5.
4. Limbrick DD Jr, Mathur A, Johnston JM, et al. Neurosurgical treatment of progressive posthemorrhagic ventricular dilation in preterm infants: a 10-year single-institution study. Clinical article. J Neurosurg Pediatr. 2010;6:224–30.
5. Nagy A, Bognar L, Pataki I, et al. Ventriculosubgaleal shunt in the treatment of posthemorrhagic and postinfectious hydrocephalus of premature infants. Childs Nerv Syst. 2013;29:413–8.
6. Wellons JC, Shannon CN, Kulkarni AV, et al. A multicenter retrospective comparison of conversion from temporary to permanent cerebrospinal fluid diversion in very low birth weight infants with posthemorrhagic hydrocephalus. Clinical article. J Neurosurg Pediatr. 2009;4:50–5.
7. Brouwer MJ, de Vries LS, Pistorius L, et al. Ultrasound measurements of the lateral ventricles in neonates: why, how and when? A systematic review. Acta Paediatr. 2010;99(9):1298–306.

8. Whitelaw A, Pople I, Cherian S, et al. Phase 1 trial of prevention of hydrocephalus after intraventricular hemorrhage in newborn infants by drainage, irrigation, and fibrinolytic therapy. Pediatrics. 2003;111:759–65.
9. Whitelaw A, Jary S, Kmita G, et al. Randomized trial of drainage, irrigation and fibrinolytic therapy for premature infants with posthemorrhagic ventricular dilatation: developmental outcome at 2 years. Pediatrics. 2010;125:852–8.
10. Rahman S, Teo C, Morris W, et al. Ventriculosubgaleal shunt: a treatment option for progressive posthemorrhagic hydrocephalus. Childs Nerv Syst. 1995;11(11):650–4.
11. Mazzola CA, Choudhri AF, Auguste KI, et al. Pediatric hydrocephalus: systematic literature review and evidence-based guidelines. Part 2: management of posthemorrhagic hydrocephalus in premature infants. J Neurosurg Pediatr. 2014;14 (Suppl 1):8–23.
12. Romero L, Ros B, Ríus F, et al. Ventriculoperitoneal shunt as a primary neurosurgical procedure in newborn posthemorrhagic hydrocephalus: report of a series of 47 shunted patients. Childs Nerv Syst. 2014;30(1):91–7.
13. Srinivasakumar P, Limbrick D, Munro R, et al. Posthemorrhagic ventricular dilatation-impact on early neurodevelopmental outcome. Am J Perinatol. 2013;30(3):207–14.

Can Breast Implants Save Your Life?

Urška Kmetec,[1] Mirko Omejc[2]

[1] *Department of Urology, Ljubljana University Medical Centerr*
[2] *Department of Abdominal Surgery, Ljubljana University Medical Center*

Correspondence

Prof. **Mirko Omejc**, MD, PhD
mirko.omejc@mf.uni-lj.si

Key words

breast implant, gunshot injury, liver trauma, ballistics, surgical management, endoscopic retrograde cholangiopancreatography

Case Report

SURGERY SURG ENDOS 2020; 2(1): 45-50

Abstract

The liver is one of the most frequently injured organs in penetrating gunshot injuries. Exploratory laparotomy should be performed in all patients that are hemodynamically unstable. We present a case in which a projectile penetrated a silicone breast implant and hit the fifth rib. Because of the implant, the pathway of the projectile was changed, and it advanced through the liver, bypassing the lungs. The silicone breast implant was one of the important reasons the damage was not fatal.

Introduction

Penetrating firearm-related injuries of the abdominal cavity are rare in Slovenia. Most often they are inflicted in suicide attempts, damaging various abdominal organs. In some cases, the firearm projectile can even penetrate the diaphragm and cause damage to the thoracic cavity and its organs (1). In penetrating abdominal trauma, the most frequently injured organ is the small intestine (50%), followed by the large intestine (40%) and the liver (30%). Injuries of the genitourinary tract are less frequent, but they need to be considered especially because of the unclear path of the projectile (1, 2).

The extent of injury from a projectile is due to the mechanical shredding and crushing of tissue by the projectile as it perforates the tissue; shearing, compression, and stretching injuries to the tissue due to temporary cavity formation; secondary injuries due to breakup of the projectile; the nature of the tissue perforated by the projectile; and the length of the wound track. As a projectile travels through the body, it crushes and shreds the tissue in its path, at the same time flinging the surrounding tissue outward from the path of the projectile, producing a temporary cavity considerably larger than the diameter of the projectile. The location, size, and shape of the temporary cavity in the body depend on the nature of the projectile, the amount of kinetic energy lost by the projectile in its path through the tissue, how rapidly the energy is lost, and the elasticity and cohesiveness of the tissue. Gunshot wounds are either penetrating or perforating. Penetrating wounds occur when a projectile en-

ters an object and does not exit, whereas in perforating wounds the projectile passes completely through the object. However, a wound can be both penetrating and perforating. High- and medium-velocity firearms can cause temporary cavities that can inflict damage to the intraperitoneal structures despite the extraperitoneal tracking of the missile (3).

Case Presentation

Patient Description and Case History

A 61-year-old woman was brought by ambulance to the emergency room 30 minutes after being shot in the right breast area. Upon arrival of paramedic team, the patient was unresponsive and without measurable blood pressure. She was immediately intubated and given 1 g of tranexamic acid.

Physical Examination Results

After arrival in the emergency room, examination of the wound was performed. She has sustained a gunshot injury, with the entry wound 1 cm medially from the right nipple at the superior border of the areola. The patient had signs of peritoneal irritation. Digital rectal examination was normal. Injuries were also visible on the right palm between the thumb and the forefinger. The initial management consisted of catheterization, intravenous hydration, and analgesia.

Investigation

A chest X-ray showed no signs of hemothorax or pneumothorax, and pelvic X-ray also revealed no signs of injuries. Initial ultrasound of the abdomen showed approximately 500 ml of fluid in the upper abdominal cavity and intraparenchymal hematoma in the liver. CT scan with intravenous contrast of the abdomen cavity confirmed the ultrasound findings and revealed the path of the projectile. The projectile penetrated the right breast and continued its path through the breast implant and then hit the fifth rib (Figure 1).

The direction of the projectile then changed, and the projectile advanced through the liver, bypassing the lungs. The projectile stopped paravertebrally at the second lumbar level (L2) of the spine. Imaging also showed a large non-contrast staining area, and some small air inclusions were visible in the right liver lobe. Approximately 400 to 500 ml of blood was visible along the liver, spleen, and paracolic gutters. There were no signs of lung injury. Fluid was visible at the right breast implant, and the implant itself looked slightly emptier compared to the other one. During the diagnostic investigation, the patients' condition was worsening; she became hemodynamically unstable and prompt surgery was required.

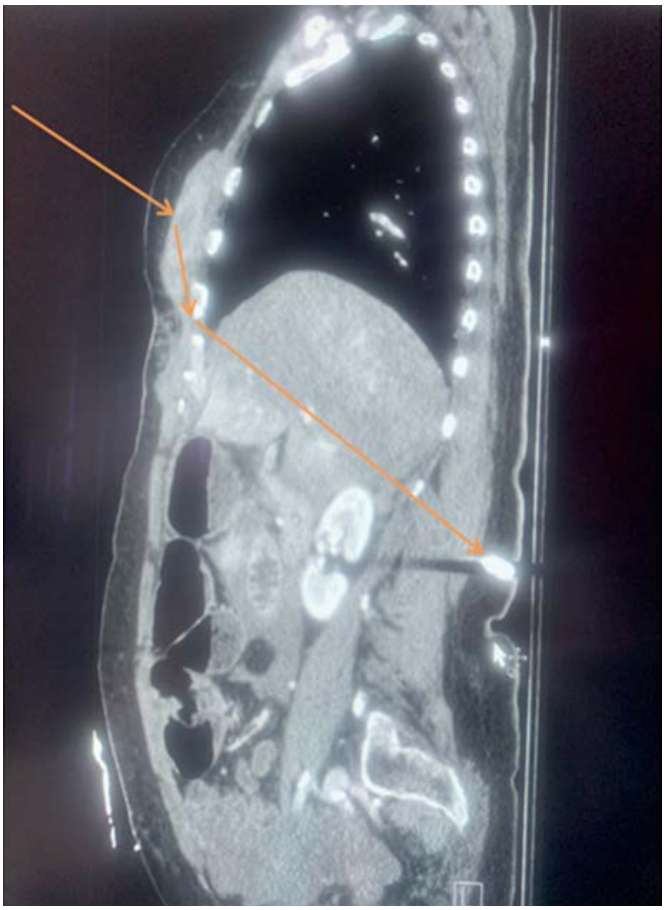


Figure 1. CT scan with the reconstruction of the projectile pathway.

Treatment

Initial management of the injured patient was carried out according the guidelines of Advanced Trauma Life Support (4). Based on the injury characteristics, presence of hematoperitoneum, and hemodynamic instability of the patient, we decided on emergency explorative laparotomy. Approximately 2 l of blood with clots was found in the

abdominal cavity. Initially, the injured liver was compressed manually to control the bleeding and subsequent packs were temporarily placed above and below the liver. Examination of the entire abdominal cavity revealed active diffuse bleeding from the perforation wound in hepatic segments IV and V, where the entry and exit wound through the liver was found, and partial fracture of the lower right rib, which probably slowed down the velocity and altered the direction of the projectile. Hemostasis was achieved with cauterization, topical sealants, and hemostatic agents. When the bleeding was controlled after temporary packing, the packs were removed during the initial operation. The small diaphragmatic injury was closed using interrupted sutures, avoiding hemodynamically important pneumothorax. During the surgery the patient received six units of red blood cells, 10 units of fresh frozen plasma, one unit of concentrated thrombocytes, and 2,000 ml of crystalloids. When the explorative laparotomy was completed and the patient was hemodynamically resuscitated, a plastic surgeon drained the hematoma from the area around the right implant, which was then removed. Both entry and exit points of the projectile were noticed on the implant (Figures 2 and 3). The empty breast cavity was irrigated. At the end of the procedure, the projectile was taken out paravertebrally.

Outcome and Follow-up

After the surgery, the patient was transferred to the intensive care unit. During the hospitalization, the patient's liver function gradually improved. On the 1st postoperative day, control ultrasound imaging was performed, showing the initial or-

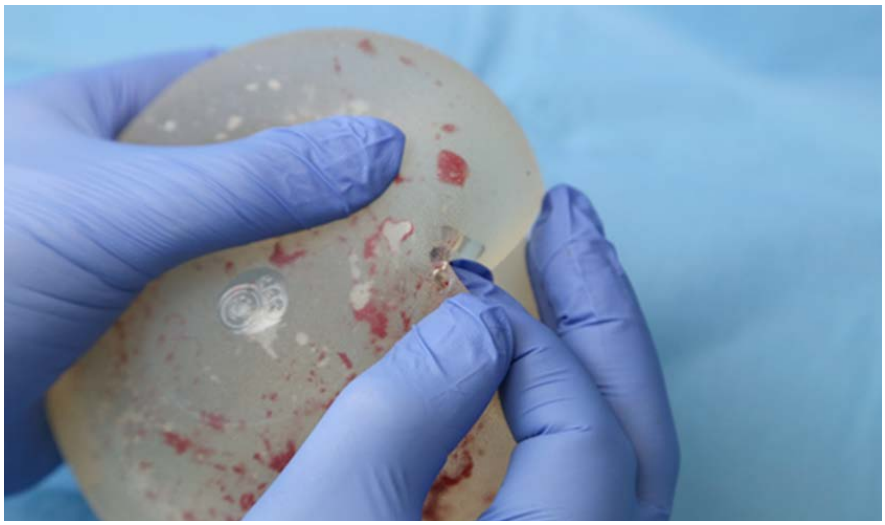


Figure 2. The entry point of the projectile in the breast implant.

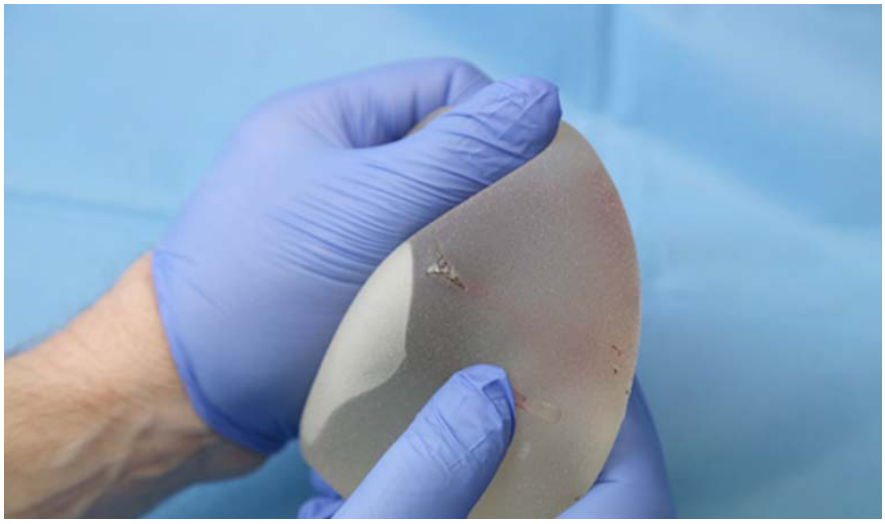


Figure 3. The exit point of the projectile in the breast implant.

ganization of hematoma at the site of the damaged liver, and no evident fluid collections or free fluid were present in the abdomen.

On the 12th and 13th postoperative days, control ultrasound imaging and CT scan of the abdomen were performed, revealing a secondary liver infection with the formation of an abscess collection measuring 16 × 6 × 7 cm (Figure 4).

An ultrasound-guided aspiration of the air-fluid collection was performed, and a drain was inserted in the abscess collection. The aspirate appeared to be a black mass containing individual clots with the appearance of an old hematoma.

On the 16th postoperative day, control ultrasound imaging and a CT scan of the abdomen were repeated, which still revealed an extensive abscess in the right lobe of the liver with surrounding edema of the hepatic parenchyma. We re-drained the abscess collection in the right lobe of the liver, where the content appeared bilious. The patient was adequately treated with supportive antibiotic therapy during the entire hospitalization period.

On the 30th postoperative day, we decided to perform an endoscopic retrograde cholangiopancreatography (ERCP) due to bile leakage through the percutaneous drain and increasing values of liver tests. In the central part of the liver, a blunt restricted area appeared at the site of the gunshot injury (Figure 5).

A choledochal sphincterotomy was performed, and a plastic stent was inserted into the bile duct. After the ERCP procedure, bile leakage through the percutaneous drain stopped. During a subsequent follow-up, the patient had multiple ultrasound-guided percutaneous abscess drainages, which eventually led to healing of the septic source.

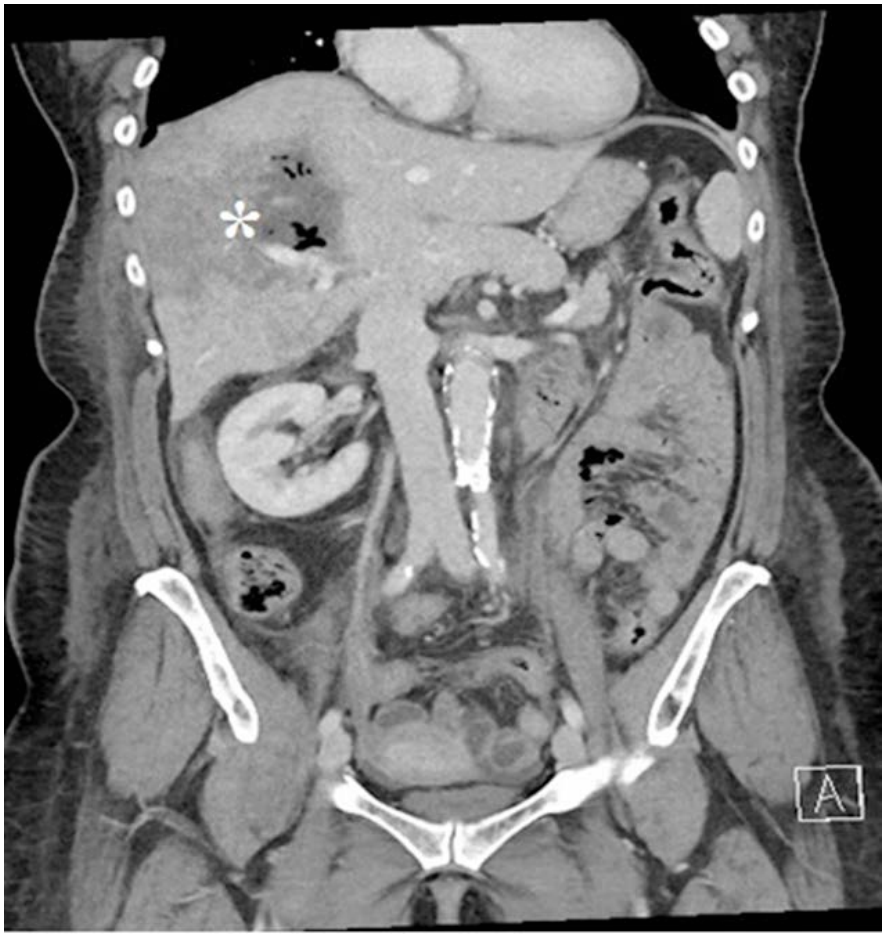


Figure 4. Fluid collection / abscess in the liver (*).

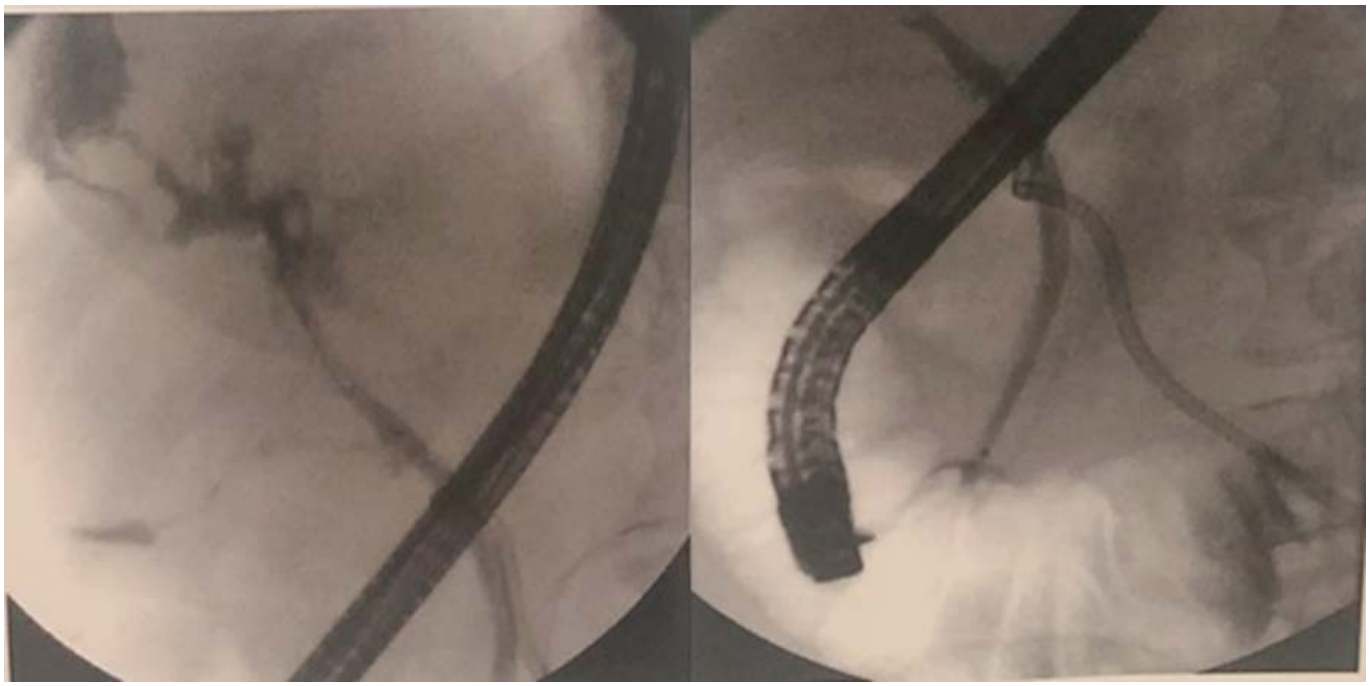


Figure 5. Cholangiogram showing a cavitation in the right liver lobe and an abscess after the inflicted gunshot injury to the liver

Discussion

We describe a case of a female patient that was shot in the thoracic region. The projectile traveled through a silicone implant in the right breast, changed its path away from the thoracic cavity, and ended up severely damaging the liver. The projectile's pathway was altered due to the silicone implant in the right breast and the fifth right rib, which decreased the projectile's velocity and direction advancing through the liver, bypassing the lungs. The broken fragment of the rib did not accompany the projectile; otherwise, it could have caused even more extensive damage to the surrounding tissue. When a projectile is traveling through the tissue, the velocity steadily slows down and its kinetic energy is transferred to the surrounding tissue. The patient was shot with a 38-calibre revolver, which is categorized as a short-barrel firearm. Handguns discharge a projectile with lower velocity, causing less trauma to the tissue upon striking the body, and their projectiles possess less kinetic energy at the time of impact (3). In our case, the projectile's primary pathway caused diffuse trauma to the right liver lobe. The projectile's secondary pathway (due to the vibration of the tissue) caused a major contusion and ischemia of the liver parenchyma. The missile that hit the patient was a full-metal-jacket bullet, which does not deform in the tissue.

The main principle of surgery in patients with gunshot injuries always includes achieving adequate hemostasis, identifying life-threatening injuries, and preserving the liver parenchyma whenever possible (2). The operative management of liver injuries that require surgical intervention can be a challenge even for the most experienced surgeons due to the complex nature of the liver, its size, its vascularity, and its dual blood supply (portal and hepatic arterial) (5). Biliary tract injury, bile leakage, perihepatic abscess formation, and biloma formation are common complications of liver injury; according to the literature, the incidence of complications ranges from 0.5 to 21% (6). Management of bile leakage after penetrating liver trauma requires long and complex treatment. We treated bile leakage endoscopically with ERCP. Biliary sphincterotomy with a large-diameter endobiliary stent placement relieved the pressure gradient between the bile duct and the duodenum, resulting in an increased flow from high resistance (biliary tree) to low resistance (duodenum),

thereby allowing closure of the leak. In the setting of bile leaks involving the common duct, crossing the leak site is preferred, but this is not possible with intrahepatic leaks (7, 8). Patients' prognosis is variable and depends on the extent of the injury and the time of the arrival to the emergency unit. Mortality remains low in patients that have undergone surgical treatment in a timely manner.

Conclusion

This case drew our attention due to the specific pathway of the projectile, which changed its direction twice, apparently saving the patient's life. Based on research, the tissue penetration was decreased due to the impact of a breast implant and a piece of broken rib. This might be the reason that the trauma to our patient's tissue was not fatal.

References

1. Pleskovič A. Abdominal trauma. Zdrav vestn. 2003;72:Supl. 1:67–73
2. Colwell C, Moore EE. Initial evaluation and management of abdominal gunshot wounds in adults [internet]. In: Post TW, editor. UpToDate. Available from: https://www.uptodate.com/contents/initial-evaluation-and-management-of-abdominal-gunshot-wounds-in-adults
3. Di Maio VJM. Gunshot wounds: practical aspects of firearms, ballistics, and forensic techniques. 3rd ed. New York: CRC Press; 2015. p. 29–55.
4. Henry S, Brasel K, Stewart RM. Abdominal and pelvic trauma. In: American College of Surgeons Committee on Trauma. Advanced trauma life support program for doctors. 10th ed. Chicago: American College of Surgeons; 2018. p. 83–101.
5. Christmas BA, Jacobs GD. Management of hepatic trauma in adults [internet]. In: Post TW, editor. UpToDate. Available from: https://www.uptodate.com/contents/management-of-hepatic-trauma-in-adults
6. Saleem A, Baron HT. Endoscopic management of biliary leak following gunshot wound to the liver. J Interv Gastroenterol. 2012;2:84–85.
7. Bridges A, Wilcox CM, Varadarajulu S. Endoscopic management of traumatic bile leaks. Gastrointest Endosc. 2007;65:1081–5.
8. Tringali A, Loperfido S, Costamagna G. Endoscopic retrograde cholangiopancreatography: Indications, patient preparation, and complications [internet]. In: Post TW, editor. UpToDate. Available from: https://www.uptodate.com/contents/endoscopic-retrograde-cholangiopancreatography-indications-patient-preparation-and-complications

Early Recognition of Anastomotic Leak and Septic Complications in Patients After Colorectal Resections

Jurij Janež
Department of Abdominal Surgery, Ljubljana University Medical Center

Correspondence

Asst. Prof. **Jurij Janež**, MD, PhD
jurij.janez@kclj.si

Key words

colorectal cancer, surgery, resection, anastomotic leak, biomarkers

Study Protocol

SURGERY SURG ENDOS 2020; 2(1): 51-53

Abstract

Backgrounds. Colorectal cancer is the third most common malignancy in the world. Improvement in surgical techniques and adjuvant treatment with chemotherapy and radiation have improved overall survival. The mainstay of treatment is still surgery with radical tumor resection and adequate lymphadenectomy. The most serious surgical complication after surgery is anastomotic leakage and septic complications, which often require another surgery and stoma formation, and increase mortality, morbidity, total hospital stay, and overall costs. This prospective clinical study will evaluate some biomarkers as possible markers of early anastomotic leakage recognition and earlier intervention.

Methods. A prospective non-randomized longitudinal clinical study in patients undergoing curative resection due to colorectal cancer will be performed. The study will include approximately 100 patients in a 3-year period. Preoperative blood samples will be taken to determine the inflammatory markers (leukocytes, C-reactive protein, procalcitonin, interleukin-6, interleukin-10, tumor-necrosis factor alpha, lactate, and carcinoembryonic antigen). All these markers will be determined from blood samples and from abdominal drain fluid 6 to 8 hours after surgery and then from the 1st to 5th day after surgery.

Discussion. The aim of this study is to elucidate the role of inflammatory biomarkers, lactate, and carcinoembryonic antigen as possible biomarkers for early recognition and prompt treatment of patients with anastomotic leakage after colorectal resections. Many studies have also been published on this topic, and we believe that our study will provide new and valuable information about this important topic.

Introduction

Anastomotic leakage (AL) is the most frequent major adverse event after colorectal surgery (CRS) and remains a large burden for patients and surgeons. Despite new operation modalities and stapling techniques, the incidence of AL after CRS has not decreased over the last decade. Usually the clinical signs of AL are apparent between the 5th and 7th postoperative day (POD) and they are rare before the 5th POD. Short-term morbidity and mortality, as well as detrimental long-term effects, such as permanent stoma, might be reduced if AL is detected and treated in an early phase. Although many studies have focused on the preoperative risk factors for AL after CRS, such as age, sex, neoadjuvant therapy, emergency surgery, and distance to the anal verge, postoperative delay in diagnosis and treatment is common and harmful (1). Early recognition and treatment of AL after CRS is important because it lowers postoperative mortality and morbidity, decreases the overall hospital stay, and is also more cost-effective. Studies have been performed that evaluate various biomarkers as a tool for early recognition and treatment of AL after CRS. Among all the biomarkers investigated, the carcinoembryonic antigen (CEA) and lactate from the abdominal drain fluid have proved to be valuable biomarkers for early recognition of AL after CRS (2).

Methods

Our prospective longitudinal non-randomized clinical study will include 100 consecutive patients with diagnosed colorectal cancer. All of the patients will be at least 18 years old and will confirm their participation in the study with written informed consent. Eligible patients that decline to participate will not be included in the study. All patients included will undergo curative resection with an anastomosis. All patients with palliative resection with stoma formation or palliative intestinal bypass or only exploratory laparotomy will be excluded from the study. Patients with chronic inflammatory bowel disease (ulcerative colitis, Crohn's disease, or other forms of colitis), known immunodeficiency, or active infections will also be excluded from the study. Before the surgery, blood samples will be taken from the patients included to determine the preoperative values of serum leukocytes, C-reactive protein (CRP), procalcitonin (PCT), lactate, CEA, interleukin-6 (IL-6), interleukin-10 (IL-10), and tumor necrosis factor alpha (TNF-a). Patients that undergo a curative resection with an anastomosis will also be included in the study. Blood samples will be taken 6 to 8 hours after surgery, and samples of abdominal drain fluid will also be taken to determine these biomarkers. The study will last approximately 3 years. All the data will be gathered into Microsoft Excel tables after the study concludes, and the results will be statistically processed. The data from our study will be presented as a research article.

Discussion

Postoperative delay in the diagnosis of colorectal leakage is common and harmful. Many studies have been performed in diagnosis of early AL after CRS. The general level of evidence is relatively low. The air leak test is recommended for intraoperative assessment of AL (1). Some systematic reviews have been performed to evaluate various biomarkers for predicting early AL, although at different time points (POD 1–5). Both peritoneal and systemic biomarkers, when assessed individually, were poor predictors of AL after CRS. Combinations of these biomarkers showed improvement in predictive accuracy (2, 3). Along with clinical observation, it is important to distinguish the physiological response after CRS and the signs of a major inflammatory event, which may forecast an important complication such as AL. CRP is a non-specific acute-phase protein that can identify AL before symptoms and changes in other laboratory parameters such as white blood cell count, which can be used as markers for the systemic inflammatory response that can precede AL (4). CRP is the most common biomarker used to predict AL. It has proven to be a useful negative predictive test for AL on POD 3–5 following CRS. The downsides of CRP testing are its limited sensitivity (70%), specificity (76%), and low positive predictive value (16%) as they relate to AL (3). PCT is another marker used as an AL predictor. It has a high specificity when detecting bacterial infection and was initially used in intensive care units to monitor treatment of sepsis. More recently, PCT has been used as an AL predictor. Its advantage over CRP is not yet clear because the results of studies have

not been unified. Recently, researchers have proposed evaluation of peritoneal fluid cytokines for early detection of AL (5–7). The theory is that local inflammation at the site of anastomosis occurs before the first systemic signs of sepsis. In line with this is the concept that cytokines measured locally, in the proximity of anastomosis, can provide real-time information on its healing. Several studies have evaluated this hypothesis and have shown that levels of TNF-a, IL-1b, IL-6, and IL-10 in drain fluid were significantly higher in patients with AL (3). It is important to note that AL is not the sole factor affecting CRP and cytokine concentrations in the perioperative period. Perioperative factors, including tumor grade, stage of neoplastic disease, and the patient's general state of health, might also influence cytokine concentrations at baseline (3, 6, 7). Among useful biomarkers in detecting early AL in patients after CRS are CEA and lactate in the intraperitoneal fluid. Studies have confirmed elevated levels of CEA and lactate in peritoneal fluid in patients that had AL from POD 1–3 after CRS (8–10). Despite all these studies, there is still no universal biomarker to detect early AL, and further studies are needed to provide more information about this topic.

Conclusion

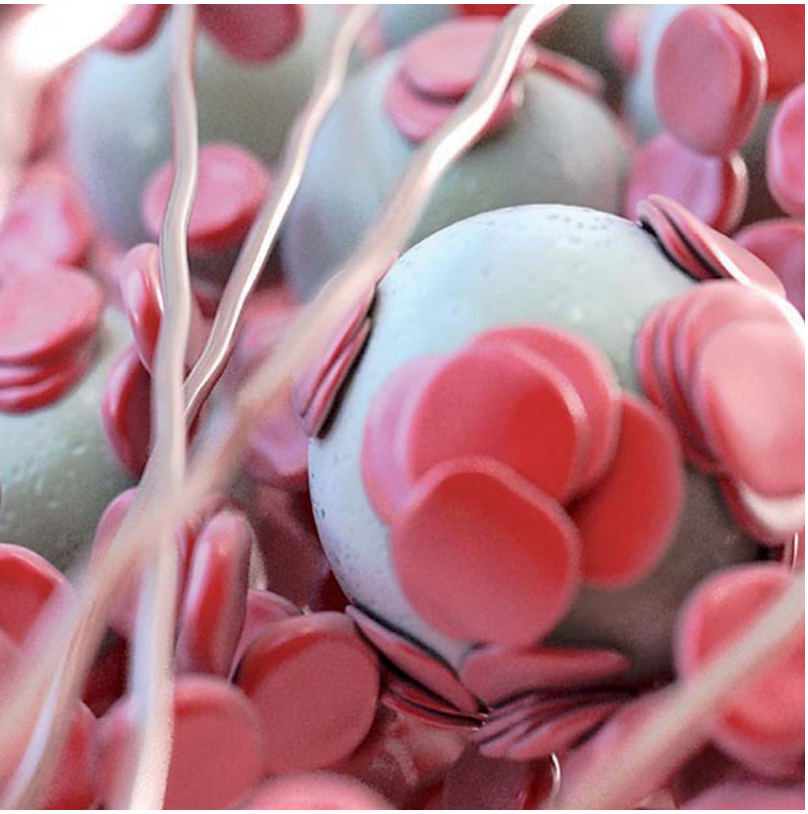
The incidence of AL after CRS varies between 1 and 40%, depending on the definition of leakage and on the type of resection performed, being higher in extraperitoneal colorectal anastomosis. This complication is associated with high mortality, accounting for more than a third of hospital deaths after CRS. Therefore, the necessity for early diagnosis of AL becomes clear. However, the diagnosis is not always easy in the early postoperative period because few clinical manifestations present at that time, which contributes to increased morbidity and mortality. We believe that our clinical study will provide new information about early recognition of AL in patients after CRS (6–10).

References

1. Daams F, Wu Z, Lahaye MJ, et al. Prediction and diagnosis of colorectal anastomotic leakage: a systematic review of literature. World J Gastrointest Surg. 2014;6(2):14–26.
2. Su'a BU, Mikaere HL, Rahiri JL, et al. Systematic review of the role of biomarkers in diagnosing anastomotic leakage following colorectal surgery. Br J Surg. 2017;104:503–12.
3. Zawadzki M, Krzystek-Korpacka M, Gamian A, et al. Serum cytokines in early prediction of anastomotic leakage following low anterior resection. Videosurgery Miniinv. 2018;13(1):33–43.
4. Popescu G, Bancu S, Sala D, et al. Prediction and early identification of anastomotic leaks after colorectal surgery. J Surg. 2018;14(1):23–7.
5. Jongen A, Bosmans J, Kartal S, et al. Predictive factors of anastomotic leakage after colorectal surgery: study protocol for a prospective observational study (REVEAL study). JMIR Res Protoc. 2016;5(2):e90.
6. Almeida AB, Faria G, Moreira H, et al. Elevated serum C-reactive protein as a predictive factor for anastomotic leakage in colorectal surgery. Int J Surg. 2012;10:87–91.
7. Ge W, Chen G. The value of biomarkers in early diagnosis of anastomotic leak following colorectal tumor resection: a review of the literature between 2012 and 2017 [internet]. Oncotarget. 2017. Available at: www.impactjournals.com/oncotarget/.
8. Lohsiriwat V. Pelvic drain after colorectal anastomosis: useful or useless. Transl Cancer Res. 2016;5(7):1404–7.
9. Hyšpler R, Ticha A, Kaška M, et al. Markers of perioperative bowel complications in colorectal surgery patients. Dis Markers. 2015;428535.
10. Hirst NA, Tiernan JP, Millner PA, et al. Systematic review of methods to predict and detect anastomotic leakage in colorectal surgery. Colorect Dis. 2013;16:95–109.

ARISTA™ AH
Absorbable Hemostatic Particles

ARISTA™ AH is more than "just a powder"



ARISTA™ AH offers a **unique method of action to achieve hemostasis. Microporous polysaccharide hemospheres (MPH):**

- Accelerate clotting process, regardless of the patient's coagulation status.
- Dehydrate and gel the blood on contact.
- Concentrate blood solids such as platelets, red blood cells and blood proteins.[1]

ARISTA™ AH provides broad area coverage on rough surfaces and in hard-to-reach areas.[1]

ARISTA™ AH is synthesized from a purified plant starch.[2]

ARISTA™ AH is **cleared by the body in 24 to 48 hours.**[4]

ARISTA™ AH is **cell saver safe.**[3]

1. ARISTA™ AH PMA P050038 Clinical Study.
2. ARISTA™ AH Instructions for Use.
3. See full Instructions for Use for detailed application instructions.
4. Because there have been reports of decreased amylase activity in newborns up to 10 months, absorption rates of ARISTA™ AH in this population may be longer than 48 hours.

CARDIO MEDICAL, d.o.o.
E: info@cardiomedical.si, T: (01) 510 74 00

BD

BARD
has joined BD

Instructions for Authors

Surgery and Surgical Endoscopy is the official journal of the Slovenian Society of Endoscopic Surgery. It is a multidisciplinary journal devoted to publishing original and high-quality scientific papers, pertinent to surgery, surgical oncology as well as surgical endoscopy.

The Editorial Board requires that the paper has not been published or submitted for publication elsewhere. The authors are responsible for all statements in their papers. Accepted articles become the property of the journal and, therefore, should not be published elsewhere without the written permission of the editors.

1. SUBMISSION OF THE MANUSCRIPT

The journal accepts *review articles, research articles, case reports, letters to the editors, study protocols and "How I do it" submissions.*

The manuscript written in English should be submitted to Editors-in-Chief, Tomaž Jagrič or Jan Grosek (tomaz.jagric@gmail.com; jangrosek@gmail.com).

All articles are subjected to the editorial review. The editorial board reserves the right to ask authors to make appropriate changes of the contents as well as grammatical and stylistic corrections when necessary.

Articles are published printed and on-line as the open access (www.zeks.si/journal). There is no publication fee.

When manuscripts are submitted under multiple authorship, it is the corresponding author who has the authority to act on behalf of all the authors in all matters pertaining to publication. Submitted manuscripts are reviewed by the editorial board on the assumption that all listed authors concur in the submission and are responsible for its content.

2. PREPARATION OF MANUSCRIPTS

The manuscript should be submitted as .doc or .docx file. It should be written in grammatically and stylistically correct language. Abbreviations should be avoided. If their use is necessary, they should be explained when first mentioned in the text. The chapter headings should not contain abbreviations. The technical data should conform to the SI system. Each section should be started on a new page, and each page should be numbered consecutively with Arabic numerals.

The Title page should include a concise and informative title, followed by the full name(s) of the author(s); the institutional affiliation of each author; the name and address of the corresponding author (including telephone, fax and E-mail). Authors should be qualified for authorship. They should contribute to the conception, design, analysis and interpretation of data, and they should approve the final version of the contribution.

This should be followed by the abstract page, summarizing in less than 250 words the reasons for the study, experimental approach, the major findings (with specific data if possible), and the principal conclusions. Three to six key words should be provided for indexing purposes. Structured abstracts are required for research articles only.

Review Articles

The Editorial Board encourages submission of review articles on topics of current interest. The manuscript should be restricted to 5000 words and up to 50 references. An abstract of no more than 250 words and up to six key words should be provided.

Research Articles

The abstract of the research article should be structured (Background, Methods, Results, Conclusions) and of no more than 250 words (Slovenian language abstracts are limited to 400 words).

Research article should be structured as well, divided into sections: Introduction, Methods, Results and Discussion. Manuscript should be restricted to 4000 words.

Introduction should summarize the rationale for the study or observation, citing only the essential references and stating the aim of the study.

Materials and methods should provide enough information to enable experiments to be repeated. New methods should be described in detail.

Results should be presented clearly and concisely without repeating the data in the figures and tables. Emphasis should be on clear and precise presentation of results and their significance in relation to the aim of the investigation.

Discussion should explain the results rather than simply repeating them as well as interpret their significance and draw conclusions. It should discuss the results of the study in the light of previously published work.

Case Reports

This section presents reports on rare or otherwise interesting case report or case series. Articles must be authentic, ethical, educational and clinically interesting to an international audience of surgeons, trainees and researchers in all surgical subspecialties, as well as clinicians in related fields.

The manuscript should be in the format:

- Introduction
- Case report/case presentation
- Discussion

Submissions to this section should carry no more than 2500 words, two figures and 20 references. An unstructured abstract of up to 200 words and six key words should be provided.

Letters to the Editor

Comment on papers recently published in the Journal. The letters should be restricted to up to 500 words and three references and should not carry any figures.

Study Protocol

Study protocol articles can be for proposed or ongoing prospective clinical research, and should provide a detailed account of the hypothesis, rationale and methodology of the study. Study protocols for pilot or feasibility studies will be treated on a case by case basis. Study protocols without ethics approval will generally not be considered. The manuscript should be structured the same way as a research article.

How I Do It?

Submissions to this section should provide description of a well-established procedure focussing on its technical aspects. The manuscript should be in the format:

- Introduction
- Preoperative preparation
- Operative steps
- Postoperative care

The operative steps should be illustrated with high-quality figures. The manuscript should be restricted to 1500 words, a 150-word abstract, six key words and may carry up to 10 figures and 10 references.

3. DECLARATIONS

All manuscripts must contain the following sections under the heading "Declarations".

- Ethics approval and consent to participate
- Consent for publication
- Competing interests
- Authors contributions
- Funding
- Acknowledgements

If any of the sections are not relevant to your manuscript, please include the heading and write "Not aplicable" for that section.

a) Ethics approval and consent to participate

Manu scripts reporting studies involving human participants, human data or human tissue must:

- include a statement on ethics approval and consent (even where the need for approval was waived), and
- include the name of the ethics committee that approved the study and the committee's reference number if appropriate.

Studies involving animals must include a statement on ethics approval. If your manuscript does not report on or involve the use of any animal or human data or tissue, please state "Not applicable" in this section.

b) Consent for publication

If your manuscript contains any individual person's data in any form (including any individual details, images or videos), consent for publication must be obtained from that person, or in the case of children, their parent or legal guardian. All presentations of case reports must have consent for publication. You should not send the form to us on submission, but we may request to see a copy at any stage (including after publication). If your manuscript does not contain data from any individual person, please state "Not applicable" in this section.

4. REFERENCES

References must be numbered in the order in which they appear in the text and their corresponding numbers quoted in the text. Authors are responsible for the accuracy of their references. References to the Abstracts and Letters to the Editor must be identified as such. Citation of papers in preparation or submitted for publication, unpublished observations, and personal communications should not be included in the reference list. If essential, such material may be incorporated in the appropriate place in the text. References follow the style of Index Medicus, DOI number (if exists) should be included. All authors should be listed when their number does not exceed six; when there are seven or more authors, the first six listed are followed by "et al.". The following are some examples of references from articles, books and book chapters:

1. Dent RAG, Cole P. In vitro maturation of monocytes in squamous carcinoma of the lung. Br J Cancer 1981; 43: 486–95. doi:10.1038/bjc.1981.71
2. Chapman S, Nakielny R. A guide to radiological procedures. London: Bailliere Tindall; 1986.
3. Evans R, Alexander P. Mechanisms of extracellular killing of nucleated mammalian cells by macrophages. In: Nelson DS, editor. Immunobiology of macrophage. New York: Academic Press; 1976. p. 45–74.

5 . CHARTS, ILLUSTRATIONS, IMAGES AND TABLES

Charts, Illustrations, Images and Tables must be numbered and referred to in the text, with the appropriate location indicated. Each of them should contain a title and an explanation of all the abbreviations and non-standard units used. Charts, Illustrations and Images, provided electronically, should be of appropriate quality for good reproduction and should be submitted as separate files. Illustrations and charts must be vector image, created in CMYK colour space, preferred font "Century Gothic", and saved as .AI, .EPS or .PDF format. Colour charts, illustrations and Images are encouraged, and are published without additional charge. Image size must be 2.000 pixels on the longer side and saved as .JPG (maximum quality) format. In Images, the identities of the patients should be masked. Tables should be typed double-spaced. The files with the figures and tables can be uploaded as separate files.

6. PAGE PROOFS

Page proofs will be sent by E-mail to the corresponding author. It is their responsibility to check the proofs carefully and return a list of essential corrections to the editorial office within three days of receipt. Only grammatical corrections are acceptable at that time.

7. OPEN ACCESS

Papers are published electronically as open access on www.zeks.si/journal.