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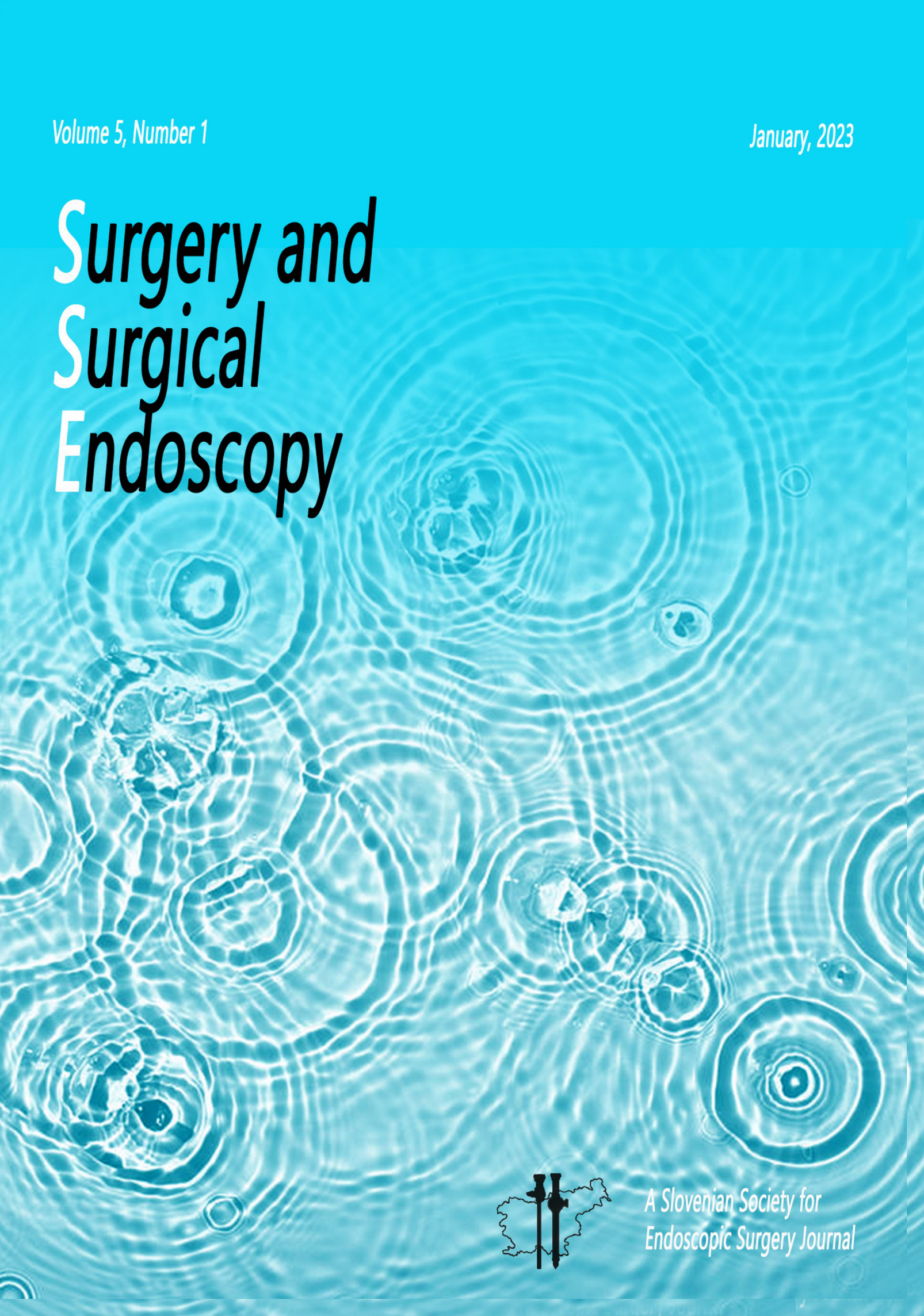

A Slovenian Society for Endoscopic Surgery Journal

January 2023

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Impressum

ABOUT THE JOURNAL

Surgery and Surgical Endoscopy is a fully open acces, peer-reviewed journal that aspires to publish articles relevant to surgery, surgical oncology, and surgical endoscopy from researchers worldwide. The journal accepts research articles, review-articles, case reports, letters to the editors, study protocols, and “How I do it” submissions. We also publish submissions that accompany educational videos, which are published on our official YouTube site.

SSE is the official Journal of the Slovenian Society of Endoscopic Surgery.

A signed authorship declaration form must accompany all manuscripts. Instructions for authors, instructions for submitting videos, the authorship declaration form, and the description of the peer review process can be found below.

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Surgery and Surgical Endoscopy

January 2023

Editorial

Prof. Stojan Potrc, MD, PhD

Dear colleagues,

I am pleased to introduce this Surgery and Surgical Endoscopy issue as we celebrate the fifth anniversary of its uninterrupted publication. I would like to take this opportunity to thank all Slovenian and foreign surgeons for their support and contribution. However, we could not celebrate without the sacrifice and enthusiasm of the editors-in-chief Jan Grosek and Tomaz Jagric. I would like to congratulate them on the work they have done. The reader should be aware that Surgery and Surgical Endoscopy is the first and only exclusively Slovenian surgical journal; therefore, it is of great importance to the Slovenian surgical society. The advantage of the journal is that it combines publications on open and minimally invasive surgical procedures, which makes it easier for the reader to compare both approaches with their advantages and disadvantages.

We are proud to inform readers that we have expanded the editorial board with international members and are on the verge of Pubmed indexing. These achievements have been made possible by the publication of several articles in different surgical fields.

In the upcoming issue, we will present articles from different surgical disciplines. We begin with the treatment options for loss of domain hernias, which are a general surgeon's nightmare since patients are usually obese, suffer from concomitant diseases, and have a hernia defect that is difficult to reconstruct without complications. We continue with surgery for herniated discs, essential for relieving spinal pain and restoring normal function in those affected. Later, we will present a case report of video-assisted thoracoscopic and laparoscopic surgery for gastric cardia cancer that enables less trauma, better visibility, reduced bleeding, fewer complications, and earlier ambulation after surgery when performed by an experienced surgeon, compared to the open technique. We will then discuss the impact of the COVID-19 pandemic on mortality and its role in halting modern medicine. We will close this issue with medical treatment options for obesity, which is an alarmingly increasing global public health issue affecting together with overweight almost 60% of adults and nearly one in three children in the WHO European Region.

To conclude, I want to encourage you to stay and become an active member of the Slovenian Society for Endoscopic Surgery member.

Surgery and Surgical Endoscopy

January 2023

Original article

The impact of the COVID-19 pandemic-driven institutional reorganization on the emergency surgery mortality

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Keywords: COVID-19; emergency surgery; mortality; morbidity and mortality meetings

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Abstract

Background: The reorganization of the surgical program by postponing elective surgery and reducing hospital beds impacted the number of emergency procedures and the type of procedures performed. We designed a retrospective study to evaluate the impact of COVID-19-related institutional reorganizations on the incidence and mortality of emergency surgical operations between 2015 and 2021. Methods: We used the SOP and the hospital's data registry to collect additional demographic data like comorbidity, previous medical history, and histology results. We analyzed the incidence and mortality of surgical emergencies between 2015 and 2021. Results: For most of the studied surgical emergencies, the incidence fell between 2019 and 2020. During the pandemic years 2019 and 2020, we had the lowest incidence in thirteen of the included emergency categories. The overall mortality was the highest in the year 2020. In the pandemic years, we had the highest mortality of the nine surgical emergencies included in this report. Conclusion: The COVID-19-related reorganizations have led to poorer access to medical care and have resulted in later and more complex presentations of the pathology leading to higher mortality that was far greater than what we would expect to form COVID-19-related pneumonia.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel coronavirus that was first recognized in the Hubei province of China [1]. Since its first outbreak, it has spread rapidly across the world. The World Health Organization declared a pandemic in March 2020 [1, 2]. The spread of COVID-19 has significantly impacted the healthcare system in the following years and has only recently been under control. The healthcare system has been put under severe strain in the three years of the pandemic crisis.

Worldwide, healthcare services had to cope with higher coronavirus-associated diseases hospitalization, reducing the number of available beds for elective patients. This has led to postponing elective surgeries when feasible. The European Association for Trauma and Emergency Surgery (ESTATES) has recommended postponing elective cases to later [2,3]. Despite the never-before-seen reallocation of resources to cope with emergency operations in Slovenia, there has probably been a general shortage of emergency procedures due to later presentation, social distancing, or unavailability of primary care healthcare practitioners. The reorganization of the surgical program by postponing elective surgery and reducing hospital beds impacted the number of emergency procedures and the type of procedures performed. Late presentations might have led, in some cases, to a more complex and morbid disease course, eventually leading to higher mortality unrelated to COVID-19 infection. Our department continually follows the results of elective and emergency surgery and has had monthly morbidity and mortality meetings since 2010. This has the benefit of allowing continuous comparison and reappraisal of surgical quality. We believe that the systematic reorganizations demanded by the pandemic have led to a shift to more complex and morbid emergency surgery and a resulting increase in surgical morbidity unrelated to the COVID-19 infection. Epidemiological studies can better appreciate the socio-economical impact of environmental factors. Therefore, we designed a retrospective study to evaluate the impact of COVID-19-related institutional reorganizations on the incidence and mortality of emergency surgical operations between 2015 and 2021.

METHODS

Patients

Since 2015 6994 patients have been admitted and operated on for surgical emergencies. For this study, we analyzed the 18 most prevalent surgical emergencies and have categorized them into the following groups: cholecystectomy, choledochotomy, choledocho-jejunostomy, hernia with bowel incarceration, appendectomy, perforated colon cancer, obstructing colon cancer, perforated colon, perforated diverticulitis, ischemic bowel resection, adhesive ileus, small bowel gangrene, and peptic ulcer. The data was prospectively stored in our department database. The names of the patients were blinded. We collected only information regarding their disease, operation, and mortality. All patients underwent a fast swab and a PCR test at admission. In all patients, a routine chest X-ray was performed before surgery.

Surgery of COVID-19-positive patients

Between 2019 and 2020, all elective surgery was postponed, and only cancer patients were scheduled for elective operations. These patients have been excluded from the study. COVID-19 serological testing was performed in all emergency cases presented at our hospital, in addition to PCR tests. Those patients who tested negative for COVID-19 infection were then worked up at the emergency department under strict contact isolation protocol until the final PCR results came

in. Patients who tested positive for COVID-19 disease were isolated while their work-up continued until the definitive diagnosis. If a surgical emergency was suspected, a general surgeon was consulted. The final decision on how to proceed with the surgery was held until the final PCR results in stable patients. Unstable patients who had signs of peritonitis or were in septic shock in whom the operation could not be postponed were operated on before the results of the PCR test in special operating rooms under quarantine conditions. PCR-positive patients were operated on in a special operating room designed for COVID-19 patients only. The surgical team wore N95/FFP3 mask, protective overalls, and eye visors during the operation. After the surgery, the unstable PCR-positive patients were relocated to isolation in an intensive care unit, while stable PCR-positive patients were relocated to an isolation ward. Patients who tested negative on PCR for COVID-19 were admitted to a surgical ward.

Data sources

The primary data source was the Surgical operation planner program (SOP) for scheduling the operations and reporting patients' emergency admissions. At the clinical department for Abdominal and general surgery, it is compulsory that every admitted patient has to be registered in our SOP database. The data collected with the SOP can be easily recalled by the type of admission and procedure performed. Besides these data, it is also possible to collect demographic data and the physicians' names that performed any intervention.

In addition to the SOP, we used the hospital's data registry to collect additional demographic data like comorbidity, previous medical history, and histology results. All data is stored prospectively and under strict central supervision. Only the permanent employees of the Clinical department for abdominal and general surgery had access to these databases. For this study, all data has been blinded. The study was approved by a local ethics committee.

Data processing

The retrieved data is coded and analyzed by a designated surgeon responsible for the monthly Morbidity and mortality meetings (MH). MH grouped the patients by pathology and performed the surgery. He collected data on the preoperative mortality for each surgical procedure and the total number of procedures performed in a specific period. In addition, he separately analyzed the patients' disease after surgical procedures and organized separate meetings that discussed the treatment of the diseased patients. All data was analyzed, and the results were presented with Microsoft Excel for Windows (Microsoft, Washington, USA).

RESULTS

Incidence

Although there has been a slight fall in 2019 and a rise above the average in 2021, the overall incidence of surgical emergencies has not changed since 2015. For most of the studied surgical emergencies, the incidence fell between 2019 and 2020. During the pandemic years 2019 and 2020, we had the lowest incidence in thirteen of the included emergency categories (Figure 1). These were the years with the lowest number of emergency surgical procedures. The lowest incidence of cholecystectomies was in 2019 and 2020; conversely, the highest incidence of choledochojejunostomies was in 2020, while most of the emergency choledochotomies were performed in 2015.

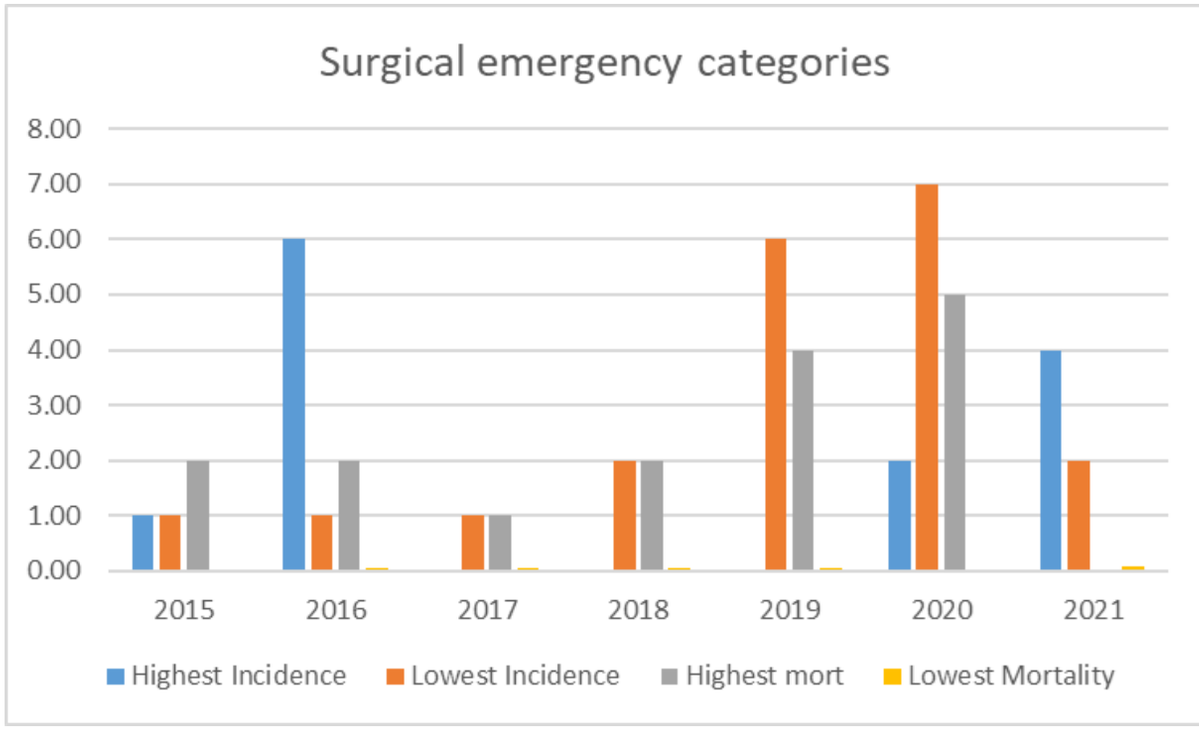

Figure 1. Surgical emergency categories

Figure 2. The incidence of surgical emergencies.

The lowest incidence of hernia with bowel incarceration operations was in 2019 and 2020. Furthermore, the lowest incidence of perforated colon cancer, obstructing colon cancer, perforated colon, perforated colon diverticulitis, ischemic bowel resections, and small bowel gangrene was in 2020. The incidence of the remaining categories remained steady during the observational period.

Meanwhile, this trend was different for perforated duodenal ulcer incidence. The number of perforated peptic ulcers was the highest in the year 2020. The highest incidence of surgical emergency procedures was noted in 2016. Choledochal explorations, ischemic colitis operations, and perforated colon cancer operations peaked in

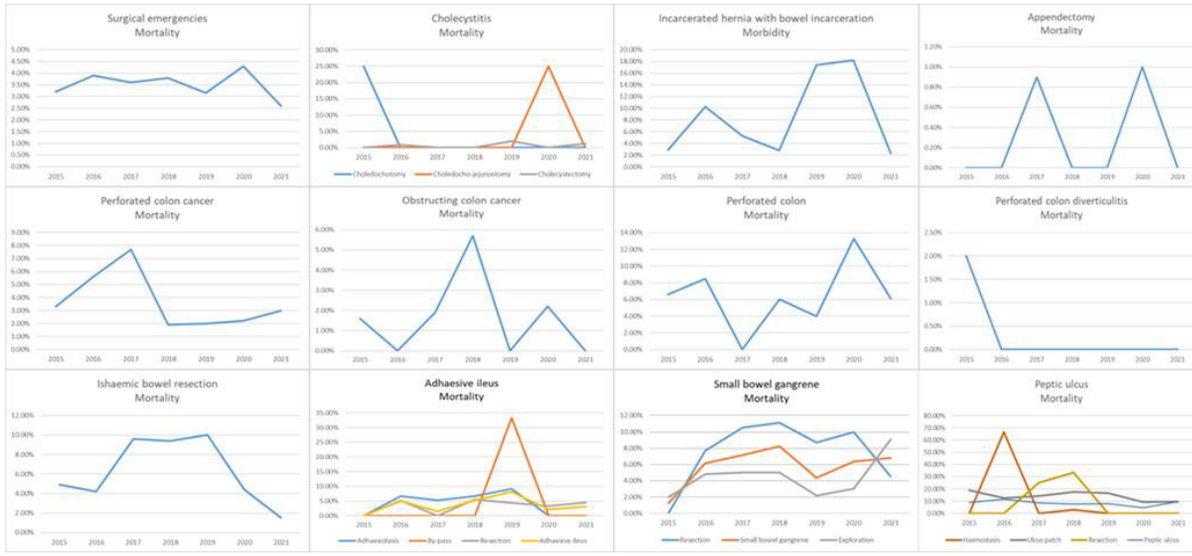

Figure 3. The mortality of emergency surgical procedures.

2016. The incidence of adhesive ileus was the highest in 2017.

Mortality

The overall mortality was the highest in the year 2020. During the pandemic years, we had the highest mortality in nine of the included surgical emergencies. The choledochojejunostomy, incarcerated hernia operation, appendectomy, perforated colon, and ischemic bowel resection had the highest mortality in 2020, while for the small bowel gangrene operation, the mortality was the highest in 2018, closely followed by the year 2020. For adhesive ileus, ischemic colitis, and cholecystectomy, the mortality peaked in 2019. The highest mortality for the operation of perforated colon cancer and the perforated peptic ulcer was in 2017. Interestingly, complicated peptic ulcer operations had the lowest mortality during 2020.

DISCUSSION

In the present paper, we studied the epidemiological impact of the COVID-19 pandemic on the incidence and mortality of surgical emergency operations.

Our results showed that the incidence of most surgical operations fell during the COVID-19 years. This is in line with the reports of other authors [1, 2, 5]. Surek et al. observed a fall in the incidence of hernia operations, appendectomies, and cholecystectomies [2]. Rosa et al. reported a decrease in appendectomies, intestinal obstruction, diverticulitis, and gastrointestinal bleeding [5]. In addition to decreased incidence of cholecystectomies, hernia with incarcerated bowel operation, obstructive colon cancer, and perforated diverticulitis noted by other authors, we also observed a decrease in the number of the perforated colon, perforated colon cancer, ischemic colon resections and small bowel gangrene in our study. Surek et al. proposed that the decline in the incidence of these pathologies was observed because of the difficulties with gaining access to a primary care physician [2].

We agree with this conclusion. Primary care physician access was heavily restricted between 2019 and 2020 in Slovenia. Surek et al. additionally observed that due to the suboptimal primary care, the number of pathologies that could be treated conservatively increased [2]. The present study was performed in a tertiary referral center, and the number of conservatively managed pathologies was unknown. However, we observed a decline in cholecystectomies, hernia operations, and

diverticulitis. All the mentioned pathologies can be initially treated conservatively. We believe the decline of operative treatment of these pathologies during the pandemic might be due to a higher proportion of conservative approaches.

Another consequence of restricted primary care access might be reflected by the reduced incidence of perforated and obstructive colon cancer observed in our study. Many authors have reported a significant decrease in the number of colonoscopies during the pandemic [7, 8]. During the pandemic, fewer colonoscopies were performed, and less colon cancer was detected, leading eventually to an increase in advanced cases once the pandemic was over. This aligns with the results of Meyer et al., who reported an increase in advanced stages and cancer mortality [8]. We also noted an increase in operations for obstructing and perforated colon cancer after the lockdown in 2019 and 2020. The increase was most probably of the advanced tumor findings immediately after the reintroduction of elective colonoscopies after the COVID-19 pandemic.

An interesting finding is an increase in perforated ulcus incidence. An increase in peptic ulcer incidence was also noted in other studies [9, 10]. Jian et al. reported that complicated peptic ulcer disease increased in 2020, as observed in our study [9]. Jian et al. proposed that poorer access to primary care, upper gastrointestinal endoscopy, and medications in conjunction with higher social stress during the pandemic led to this increase in the incidence [9, 10]. Although it is impossible to confirm this based on our study, our results confirm the observations made by other authors and point out that the higher psychological stress in the general population under quarantine during the COVID-19 years must have caused the increase in the peptic ulcer incidence.

A key observation made by Surek et al. was that the reduced access to hospital care during the pandemic led to an increase in complicated surgical pathology that needed surgical care within the first hours of presentation [2]. Rosa et al. also concluded that general practitioners inappropriately managed most surgical emergencies at home [5]. We have made a similar observation in our study. While the incidence of cholecystectomies remained stable over the years with only a slight fall in the pandemic, there is a disproportional increase in the number of choledochal-jejunostomies because of bile duct injuries. This might be explained by the fact that fewer elective cholecystectomies were performed during the pandemic, leading to a more late and complex presentation of cholecystitis and more inadvertent bile duct injuries. The number of inadvertent bile duct injuries might be the most evident marker of the systematic reorganization results.

The late presentation and more complex pathology could be the culprit of the increase in surgical mortality during COVID-19. All the epidemiological data we have gathered from our morbidity and mortality reports point to a conclusion that the COVID-19 pandemic caused an indirect increase in the complexity of surgical emergencies and the mortality of the latter because the reorganization of the medical resources inevitably led to poorer primary care and diagnostics. If the COVID-19 virus-related infection had been itself the reason for higher mortality, we would have expected a cumulative increase in mortality regardless of the pathology. However, the highest mortality of perforated colon cancer operations was in 2017. Cancer patients are especially susceptible to COVID-19 infection due to lower immunity. Meanwhile, the mortality for these patients during 2019 and 2020 was the lowest since 2015.

Kolaric et al. [11] analyzed the mortality of COVID-19-positive patients operated during the pandemic on a tertiary reference center and observed 8.1% overall mortality. Additionally, they noted that

respiratory failure caused only 2.7% mortality in COVID-19-positive patients [11]. In our analysis, mortality peaked in the year 2020 at 4.3%. Assuming that the COVID-19 infection was responsible for 2% to 3% of deaths after surgery, it is evident that for most of the mortality after emergency surgical operations, different factors must have been responsible. Our results are in line with the conclusions of Seretis et al. [12]. They observed a 1% mortality rate in the COVID-19-positive patients undergoing emergency surgical procedures and concluded that emergency surgical procedures should not be deferred by a positive COVID-19 test [12]. The results of the present study are in line with the recommendations made by Seretis et al. [12]. We believe that emergency surgery should not be postponed due to COVID-19 status and that hospital reorganizations were responsible for increased mortality during the pandemic.

This study has some limitations. Because we did not have access to epidemiological data of all regional hospitals, the actual proportion of conservative treatment was unknown. The data in the present study were collected only from one referral center where most of the surgery was performed during the pandemic. We did not compare the causes of death over the years. If the reorganization of medical resources had caused the COVID-19 increase in mortality, the causes of death would not have been different in the COVID-19 and pre-COVID-19 periods. This will be the subject of future analysis.

Based on our results, we can conclude that the COVID-19 pandemic-related reorganizations of the medical system at our center had a disastrous impact on the incidence of most surgical emergencies. It not only led to poorer access to medical care but also resulted in later and more complex presentations of the pathology, leading to a higher mortality that was far greater than what we would expect to form COVID-19-related pneumonia.

STATEMENTS AND DECLARATIONS

Competing Interests: Not applicable.

Funding: Not applicable.

Acknowledgments: Not applicable.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper.

Ethics approval: The study was approved by the local ethics committee.

Conflicts of Interest: None declared.

Consent for publication: Not applicable.

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Surgery and Surgical Endoscopy

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Original article

Laparoscopic versus robotic-assisted colorectal operations at the General and Teaching Hospital Celje

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Key Words: colorectal cancer, robotic surgery, laparoscopic surgery

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Abstract

Aim: In this paper, we present the technique and the results of robotic colorectal surgery at the Department of General Surgery, Teaching Hospital Celje, and compare the results with a laparoscopic approach.

Methods: We included eighty-five patients operated on with the robotic-assisted approach and compared the results with those operated on laparoscopically.

Results: The average age of operated patients was similar in both groups (63 years), while the patients in the laparoscopic group tended to have more accompanying diseases. Most of the patients were operated on for adenocarcinoma in both groups. The most prevalent operation in the laparoscopic group was the right hemicolectomy, while significantly more anterior resections were performed in the robotic group (54% vs. 14%). The number of low anterior resections was comparable in both groups (7% in the robotic vs. 5% in the laparoscopic group). In both groups, the most prevalent UICC stage was stage III.

Conclusions: Robotic platforms have a decisive advantage as surgery is more accessible in small operative fields like the pelvis. This was possibly the reason for minor blood loss and lower conversion rate, faster postoperative regaining of digestive functions, and shorter hospital stay in the robotic group. Our results firmly support the further use of the robotic platform in colorectal cancer patients.

INTRODUCTION

Due to a relatively high incidence, colorectal cancer comprises almost two-thirds of general surgical procedures in Slovenia [1], whereby low anterior resection is performed in 39% of these patients [1]. Most colorectal operations are performed laparoscopically today. Surgeons are nowadays facing not only increasing numbers of patients but also more demanding ones. These are older, have additional commodities, and are more obese. All these characteristics make the low anterior resection a most challenging procedure in colorectal surgery. Obese and male patients with a narrow pelvis are perhaps the most challenging due to difficult dissection in the male pelvis. When operating in a small surgical field, the robotic surgical platforms have a decisive advantage compared to the laparoscopic approach. The angulated instruments, superior camera positioning, and a three-dimensional view allow better dissection in the most challenging areas [2]. In 2001 Ballantyne and Weber performed the first robotic colectomy [3]. Since then, robotic colorectal surgery has made tremendous progress. Today robotic surgery presents 32% of operations in the USA, 20% in Korea, 15% in Italy, 5% in Canada and Germany, and 2% in the Netherlands [2-4]. The first totally robotic-assisted low anterior resection at the department for abdominal and general surgery in the Teaching hospital Celje was performed in 2014. Since then, 85 robotic colorectal operations have been performed in our center. In this paper, we present the technique and the results of our robotic colorectal procedure and compare the results with the laparoscopic approach.

METHODS

Patients

Hundred laparoscopically and 85 patients operated with robotic surgery for colorectal cancer in the Teaching Hospital Celje were included in our analysis. We collected data regarding patients' age, sex, general condition (ASA score), histological results, procedural details, postoperative course, and TNM stage. The procedural information included the operation time, conversion rate, and blood loss. The operation time in robotic surgery was defined as the console time. In the postoperative period, we recorded the time to oral diet, the first passage of stool, the morbidity, and the hospital stay. The results were prospectively stored in the department's database. Patients gave their informed consent to participate in the analysis.

Surgery

Robotic surgery was performed according to the standards described elsewhere [2-4]. For surgery, we used the Da Vinci Si platform. The patient was positioned in the lithotomy anti-Trendelenburg position. The ports were positioned as depicted in Figure 1.

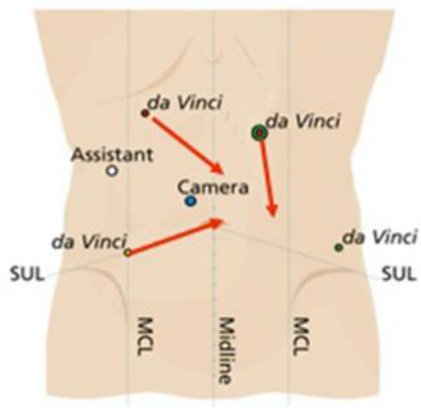

Figure 1. Port positioning for the Da Vinci Si platform

Figure 2. The positioning of the DaVinci Si platform

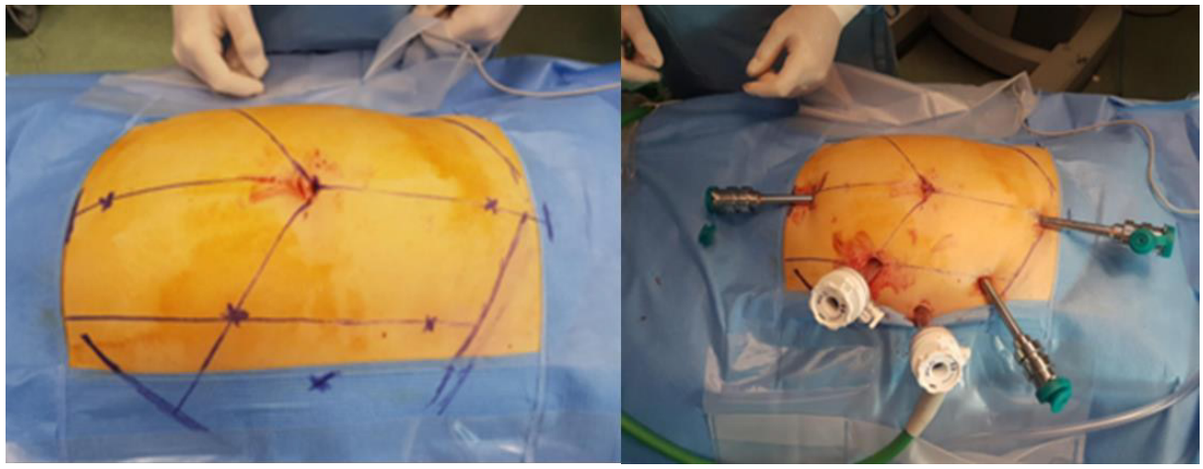

Figure 3. Port placement for robotic right hemicolectomy.

Figure 4. Postoperative view of the patient after robotic surgery.

The surgery was performed by a specially trained dedicated team under the leadership of the head surgeon IC. The positioning of the DaVinci Si system and the operating team is presented in Figure 2.

Data sources

All data were prospectively stored in the department's database. In addition, we used the hospital's data registry to collect additional demographic data like comorbidity, previous medical history, and histology results. The data acquisition was made under strict central supervision. Only the permanent employees of the Department for abdominal and general surgery in the Teaching Hospital Celje had access to these databases. The quality of data acquisition and surgical quality control was assessed externally. The acquired procedural data was sent to ABA Medica (Gragnano, Italy). ABA Medica analyzed the data, and only certified robotic surgeons were allowed to send and request the data. For this study, all data has been blinded. The study was approved by a local ethics committee.

Data processing

The retrieved data is coded and analyzed by designated surgeons for robotic surgery (IC and OS). The patients were grouped by pathology and performed the surgery. The continuous data were presented as mean±SD, while the discrete variables were presented as %. All graphs were plotted with Microsoft Excel for Windows version 2022 (Microsoft, Washington, USA)

RESULTS

Patients

The average age of operated patients was similar in both groups (63 years), however; more patients in the laparoscopic group were male compared to the robotic group (64% vs. 51%). Seven patients in the robotic group received preoperative radio-chemotherapy for rectal cancer. Patients in the laparoscopic group tended to have more accompanying diseases. The most prevalent pathology was adenocarcinoma in both groups. The most common operation in the laparoscopic

group was the right hemicolectomy, compared to sigmoid resection in the robotic group. More patients had an anterior resection in the robotic group (54% vs. 14%). The proportion of low anterior resection was similar in both groups (7% in the robotic vs. 5% in the laparoscopic group). The TNM stage was similarly distributed in both groups. Stage pT3N0M0 was the most prevalent. In both groups, the UICC stage III was the most prevalent. The clinicopathological characteristics are presented in Table 1.

Perioperative results

The average console time in robotic surgery was 186.6 minutes, comparable to the operation time in laparoscopic surgery. The range of intraoperative blood loss in the robotic group was 50–150 ml, which was lower than in laparoscopic surgery (100–300 ml). The average number of extracted lymph nodes was comparable in both groups (18 in the robotic vs. 16 in the laparoscopic group). Patients in the robotic group resumed the oral diet faster (3.7 days vs. 4.6 days) and had a significantly shorter hospital stay than the laparoscopic group (7.5 days vs. 10.3 days). Morbidity was comparable in both groups, while the conversion rate was lower in the robotic group (4.5% vs. 7%).

DISCUSSION

Robotic surgery for colorectal cancer has been widely accepted and embraced in recent years [2, 13, 14]. It offers many decisive advantages to laparoscopic surgery and makes complex cases safer. The Department of Abdominal and General Surgery at the Teaching Hospital Celje introduced robotic colorectal surgery in Slovenia in 2014. At that time, this was a novel surgical procedure in Slovenia and opened the region for a wider acceptance of robotic surgery in other centers. In the paper, we present the initial experience of robotic colorectal surgery at the Department for abdominal and general surgery in Celje and compare the results to laparoscopic colorectal operations.

Although of comparable age to the laparoscopic group, patients in the robotic group were in better general shape. This might be due to the initial period of the robotic surgery introduction, where the patient selection might have been present. Even so, the distribution of presenting pathology and the stage distribution of tumors were similar. We could therefore argue that, although patients might have been in a better general condition in the robotic group, we did not select less complex patients with early cancer for robotic surgery. Therefore, we consider both groups comparable. This is also true for the patients who received anterior and low anterior resections. In both groups, these operations were similarly distributed and hence comparable.

Regarding the perioperative results, we could confirm that the morbidity of the robotic surgery was comparable to the laparoscopic procedures. Although these results present an initial introduction period of the robotic platform for colorectal patients, we could show that this method is safe and feasible and takes a comparable time to perform. Similar results were obtained in other pioneer studies [2-4]. Spinoglio et al. showed that robotic surgery is comparable to laparoscopy regarding safety [5]. We agree with Yasir et al., who stated that using the robotic platform is intuitive and has a short learning curve for an experienced laparoscopist [6]. Our results align with these observations since we could reduce the perioperative morbidity rates despite this being the initial period.

Robotic platforms not only have articulated instruments allowing better surgical dexterity, but

Table 1. Patients' characteristics, pathology, and operative results.

	Robotic surgery	Laparoscopic surgery
ASA		
I	37%	7%
II	62%	51%
III	1%	40%
IV	0%	2%
Sex		
M	51%	36%
F	64%	64%
Indication for surgery		
Adenocarcinoma	76.6%	74.1%
Adenoma	11.6%	15.2%
Polypectomy	10%	7.1%
Diverticulitis	1.7%	3.5%
Tumor location		
Right colon	21%	45%
Left colon	4%	7%
Sigmoid colon	13%	24%
Rectosigmoid junction	40%	15%
Rectum	22%	9%
Types of operations		
Right hemicolectomy	22%	46%
Left hemicolectomy	5%	9%

Sigmoid resections	12%	26%
Anterior rectal resection	54%	14%
Low anterior resection	7%	5%
T stage		
1	9%	17%
2	39%	35%
3	46%	44%
4	6%	4%
N stage		
0	40%	54%
1	36%	37%
2	24%	9%
UICC stage		
I	51%	30%
II	15%	33%
III	34%	37%
IV	0%	0%
Tumor Grade		
I	15.8%	7.8%
I-II	11.5%	17.9%
II	67.6%	67.2%
III	5%	6.2%
Operation time	186.6 min	187.6 min
Blood loss (range)	50-150 ml	100-300 ml

Number of extracted LNs	18.5	16.5
Oral diet	3.7 days	4.6 days
First stool	4.5 days	4.6 days
Morbidity	9%	10.3%
Conversion	4.5%	7%
Hospital stay	7.5 days	10.3 days

the decisive advantage is also that surgery is more manageable in small operative fields like the pelvis. As the male pelvis can be narrow, visibility, especially in obese patients, can be difficult. These are even more so challenging to overcome in laparoscopic surgery. Robotic surgery has decisive advantages with superior 3D visibility, motion scaling, and angulation. This was possibly the reason for minor blood loss and lower conversion rates in the robotic group. Other studies observed similar results [5, 7-12].

We believe less intraoperative bleeding and a more precise dissection in the robotic group were the main factors influencing the faster postoperative regaining of digestive functions. Patients in the robotic group passed stool and restarted oral intake earlier, leading to shorter hospital stays than the laparoscopic group. Similarly, Spinoglio et al. observed significantly shorter hospital stays in the robotic group compared to laparoscopic surgery [5].

This study presents only the initial experience of robotic surgery. Therefore, there might be some bias concerning patient selection. We still believe that our results firmly support the further use of robotic surgery in colorectal cancer patients. Robotic surgery allows surgeons to perform complex surgical tasks in confined surgical fields, which brings decisive advantages to demanding patients, reducing the need for conversions, blood loss, and other intraoperative complications. Additionally, shorter hospital stays could reduce treatment costs, justifying the robotic platforms' higher expenses compared to laparoscopy. Perhaps it is essential to recognize the limitations and benefits of both laparoscopic and robotic surgery, determine a suitable minimally invasive surgical approach and ultimately choose the ideal surgical technique most appropriate for the specific surgical indication.

DECLARATIONS

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Case report

Use of progressive preoperative pneumoperitoneum in a patient with a complex incisional hernia: Case report

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Abstract

The incidence of complex incisional hernias is increasing due to the increasing number of major abdominal surgeries, damage control surgeries with open abdomen, and delayed abdominal wall closure. In addition, advances in intensive care, an aging population, and the obesity epidemic are influencing the number of complex incisional hernias. Incisional hernia repair has evolved steadily, from open onlay mesh techniques or open IPOM to gold-standard Rives-Stoppa hernioplasty and minimally invasive laparoscopic procedures to component separation techniques recently for massive hernias. At the same time, due to the unsatisfactory results of modified surgical techniques and mesh placement methods in complex incisional hernias, new methods of extending the length of the abdominal wall emerged. These extension methods are progressive preoperative pneumoperitoneum (PPP), tissue expanders, and botulinum toxin A (BTA).This article reports our experience using BTA, PPP, and the transversus abdominis release separation technique (TAR) on a patient with a complex incisional hernia with loss of domain. In our opinion, PPP should be considered with BTA for incisional hernias with loss of domain. It may facilitate primary

closure, reintroduction of hernia sac contents into the abdomen, and reduction of complications after surgery.

INTRODUCTION

The incidence of complex incisional hernias (CIH) is increasing in most settings due to the increasing number of major abdominal surgeries, damage control surgeries with open abdomen, and delayed abdominal wall closure. In addition, advances in intensive care, an aging population, and the obesity epidemic influence the number of CIH [1]. In most cases, these hernias contain a significant amount of abdominal viscera outside the abdominopelvic compartment, which is commonly described in the hernia literature as "loss of domain " (LOD) [2]. According to the International Delphi Consensus of Expert Surgeons, LOD is a ventral hernia large enough that simple reduction and primary fascial closure are not possible without additional reconstructive techniques and without a significant risk of complications due to increased intra-abdominal pressure [2]. To objectively define LOD, Tanaka suggested calculating hernia sac volume (HSV) and abdominal cavity volume (ACV) based on computer tomography (CT) findings. If the ratio is more than 25%, LOD should be suggested [3].

Herniated intra-abdominal viscera cause a decrease in intra-abdominal pressure, resulting in a descent of the diaphragm and respiratory dysfunction. Portal vein stasis is common, leading to intestinal congestion, ischemic bowel, diarrhea, and abdominal pain. Abdominal muscle displacement, atrophy, and decreased intra-abdominal pressure led to an unsupported spine and chronic back pain [4].

The main challenge in CIH repair is to ensure tension-free closure of the fascial defect and to prevent abdominal compartment syndrome (ACS), which can occur after herniated contents are reduced into the abdominal cavity. ACS can lead to respiratory or multiple organ failure with severe morbidity and mortality [5,6].

Over the years, various methods of treating CIH have been described. In general, they can be divided into surgical techniques and techniques for abdominal wall extension. In 1990, Ramirez et al. introduced the anterior component separation technique. This technique is based on releasing the external oblique muscle aponeurosis, which allows the muscle/fascia layers to slide towards the midline and ensures a gain of 8–10 cm of the abdominal fascia surface [7]. Later, improved component separation techniques were introduced, such as the posterior component separation technique and the posterior component separation with transversus abdominis release, which have fewer wound infections and lower recurrence rates [8]. In parallel with new surgical methods, extension methods of the abdominal wall have been developed, such as preoperative pneumoperitoneum (PPP), tissue expanders, and Botulinum toxin A application (BTA) [9]. PPP was first described in 1947 by Argentine surgeon Goni Moreno, who used intra-peritoneal oxygen injections to treat a patient with an epigastric hernia [10]. The idea behind PPP is to gradually dilate the abdominal cavity preoperatively to minimize the postoperative risk of surgically induced respiratory problems [11]. Another well-documented and frequently used method of tissue extension is the preoperative use of BTA, which causes flaccid muscle paralysis with thinning and lengthening of the abdominal muscles. Clinically, the maximum effect of this method is achieved after two weeks and decreases after 12 weeks. This paper presents our experience with PPP and BTA before CIH surgery.

CASE REPORT

A 70-year-old man with a BMI of 30, non-smoker and without concomitant diseases, presented to our clinic because of CIH after laparotomy, midline, and transverse incision, for colon and hepatic resection because of cancer (Figure 1A).

The initial CT of the abdominal organs described a transverse hernia defect of 23 cm, a Tanaka index of 47%, and muscle thickness of 24 mm on the left and 34 mm on the right side at the level of lumbar vertebra 3 (L3). Due to the high Tanaka index and to avoid respiratory complications after hernia repair, both BTA and PPP were used for abdominal wall extension. In sterile conditions, BTA was applied under local anesthesia and was ultrasound (US) guided. The patient received a total of 400 IU of Botox or Xeomin. The application was performed as already described (12). The subsequent CT was performed three weeks after the BTA injection to assess the effects on abdominal wall extension. We measured a hernia transverse diameter of 21 cm, a Tanaka index of 40%, and muscle thickness of 20 mm on the left and 30 mm on the right side at the level of L3. To achieve pneumoperitoneum, a pigtail-peritoneal dialysis catheter was inserted laparoscopically four weeks after BTA injection under general anesthesia (Figure 2A). We used epidural filters (Perifix Catheter Connection System®) for sterile ambient air insufflation (Figure 2B). Air insufflation was performed daily for six days before surgery. The epidural filters were changed daily. A total of 6250 ml of air was insufflated (2000 ml on the first day, then between 500 ml and 1000 ml). During PPP, the patient did not report any pain. After each insufflation, we checked intra-abdominal pressure ranging from 12 mmHg on the first day to 18.5 mmHg on the fifth day. The circumference of the abdomen increased from the initial 120 cm to 130 cm.

We performed a third CT scan before surgery to evaluate the effect of BTA and PPP. It showed a transverse hernia defect of 21 cm, a Tanaka index of 65%, and muscle thickness of 15 mm on the left and 25 mm on the right side at the level of L3. Surgery was performed seven days after the onset of PPP. Preoperatively, the patient received thromboprophylaxis and antibiotics (first-generation cephalosporines) for seven days. After medial laparotomy, bilateral TAR was performed using two 30 cm x 30 cm, medium-weight (30–60 g/m2), wide-pore (pore> 1 mm), self-adhesive meshes and two 30 cm x 30 cm large, medium-weight, and wide-pore meshes. All the meshes were placed in a sublay position (Figure 2C). Because of the insufficient length of the anterior sheet of the rectus muscle, bridging was required over an area of 5 cm x 5 cm, although some additional incisions were made. Four suction drains were placed, two on each side of the abdominal wall and two in the groin area. The patient received an abdominal restrain belt. For safety reasons, the patient was transferred to the intensive care unit for one day. During the postoperative course, the patient required blood transfusions due to anemia. Large suffusions were noted in the lower abdomen. US examination of the abdominal organs revealed no free fluid. A 120 ml fluid collection was described on the right side of the abdominal wall, and a 150 ml fluid collection in the pubic area. We decided to treat these collections conservatively and to perform regular check-ups. The patient was discharged home nine days after surgery. At the second follow-up (23 days after discharge), the patient reported dysuria, and the laboratory testing revealed elevated inflammatory parameters. A CT scan was performed, which described already known fluid collections without

Figure 1. A) Patient with complex incisional hernia with loss of domain before surgery. B) Patient after surgery.

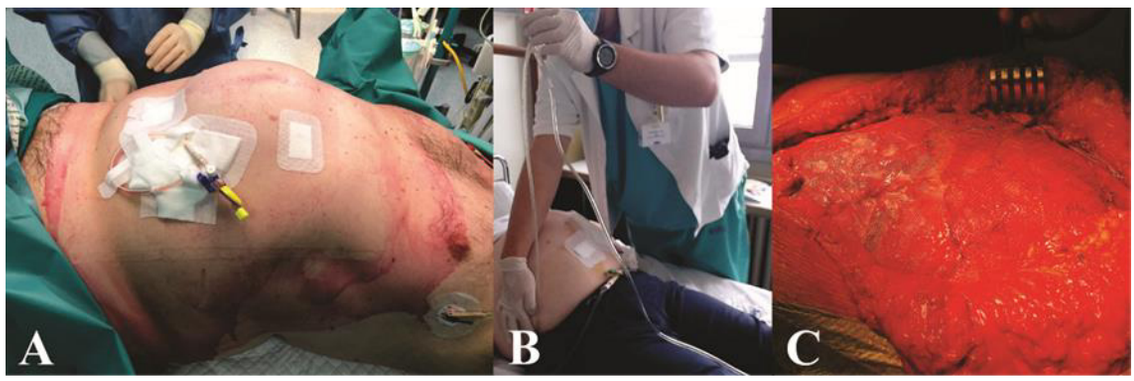

Figure 2. A) Patient after laparoscopic placement of pigtail peritoneal dialysis catheter. B) Air insufflation was performed with epidural filters (Perifix Catheter Connection System®) for sterile ambient air insufflation. C) Abdominal wall reconstruction with TAR, the mesh was placed in a sublay position.

evidence of inflammation. We decided to initiate antibiotic therapy and performed US-guided drainage of collections. The patient was readmitted to our department for six days. After discharge, the patient had no significant problems, and no hernia recurrence was observed during follow-up (Figure 1B).

DISCUSSION

Nowadays, the treatment of CIH consists of surgical repair and wall extension methods. One of the techniques for wall extension is PPP, a procedure introduced more than 70 years ago and has become more prevalent in recent years. The proper indication for PPP remains controversial. Mainly, the procedure is used for clinically observed giant hernias, more often in the upper abdomen, hernias with a transverse diameter of more than 10 cm, and when the CT volumetric ratio of HSV/ACV or HSV/total peritoneal volume (ACV+HSV) is more than 25% or more than 20% [3,11,13]. The rationale of PPP is to allow a more gradual and physiological adjustment of the abdominal wall, to allow a reduction of abdominal contents, and to prevent ACS [6].

The PPP procedure is not standardized, so several options are described regarding the puncture site, insufflation device, gas type, gas volume, insufflation frequency, and criteria for termination of PPP. To achieve PPP, most punctures are still performed using anatomical marks such as Palmer's point, but there are also reports about image-guided punctures or surgical accesses [14]. We used a laparoscopic approach to achieve PPP for safety reasons since severe adhesions were expected. We inserted a pigtail-curved peritoneal dialysis catheter in most (16%) of the reviewed studies [14]. Other possible devices to achieve PPP

were a spinal needle, implantable subcutaneous reservoir ports, a vascular catheter, a central venous catheter, a long straight needle, a Veress needle, and different combinations of devices. In most studies (62.4%), ambient air without filters was used, and no intra-abdominal pressure monitoring was performed [14]. We decided to filter air and monitor intra-abdominal pressure for safety reasons.

In contrast to most reviewed studies, we did not insufflate air until the patient experienced symptoms, but we chose to use a target volume per session. On the first day, we insufflated 2000 ml of air [15] from 500 ml to 1000 ml the following days. Our target volume per session, total insufflated volume, and maintenance of PPP before incisional hernia surgery were comparable to most other studies [14].

The effect of BTA and PPP on hernia transverse diameter and ACV were evaluated based on performed CT scans. The hernia transverse diameter shrank by 2 cm (5%), which is comparable to the results of Bueno-Lledó et al. [16]. Since they did not observe a significant reduction in hernia diameter, they concluded that the modification in muscle length and width after BTA application helped achieve a tension free hernia closure. However, using BTA before hernia surgery results in abdominal cavity enlargement due to stretching and flattening of the lateral abdominal wall [17]. We observed thinning of the lateral abdominal muscles for an average of 9 mm (46%) and measured a lower Tanaka index (40% vs. 47%), favoring ACV enlargement. A further rise in ACV was expected after PPP [14–16]. However, Tashkandi et al. found no extra increase in ACV when comparing groups of patients who received BTA alone or BTA+PPP [18]. Interestingly, we observed an increase in the Tanaka index after PPP (65% vs. 40%) due to the enlargement of HSV for 46%. We placed the dialysis catheter so that adhesions prevented a proportional enlargement of ACV, which increased by only 12%. We must consider that our patient was operated on twice for malignant disease and received chemotherapy. This is why the abdominal adhesions were massive, and the optimal position of the PPP catheter was difficult to achieve even with a laparoscopic approach [19]. Nevertheless, we reintroduced the entire hernia sac into the abdomen during the hernia surgery, and no resection was necessary. The patient had no respiratory distress during or after the surgery. Although we used BTA, PPP, and a component separation technique (TAR), bridging was necessary. In the study of Yurtkap et al., patients with similar transverse hernia diameters treated with BTA, PPP, and anterior component separation techniques needed bridging in 37.5% of cases. Still, the reported average Tanaka index was lower than in our case (31%) [20]. However, to date, no relevant study has combined all three extension methods (PPP, BTA, and tissue expanders). Our patient had no side effects after the BTA application and PPP. According to the review by Alam et al., the rate of complications associated with PPP was around 12%. The most frequently reported complication was subcutaneous emphysema, followed by wound infection [9]. After surgery, we observed large suffusions in the lower abdomen due to blood collections in the abdominal wall. Correction of anemia was necessary with later US-guided drainage of the collections. Bueno-Lledó et al. reported surgical complications in 27% of cases, most of them grade I according to Clavien-Dindo Classification, but in 7% of cases, the complications were severe (grade IV) [16]. Tashkandi et al. concluded that adding PPP to BTA resulted in a lower surgical complication rate (18). Recent studies described hernia recurrence rate at 2.2–8% [16,21].

In our opinion, PPP associated with BTA should be considered for incisional hernias with loss of domain since it may facilitate primary closure, reintroduction of the hernia sac contents into the

abdomen, and lower the complication rate after surgery.

STATEMENTS AND DECLARATIONS

Competing Interests: Not applicable.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper.

Ethics approval: The study was approved by the local ethics committee.

Conflicts of Interest: None declared.

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January 2023

Case report

Minimally invasive Ivor-Lewis procedure with linear stapled anastomosis for esophagogastric Siewert II carcinoma: Case report

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Keywords: minimally invasive Ivor Lewis esophagectomy; prone position; linear stapled anastomosis

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Abstract

In the present article, we present a technique using the intrathoracic linear stapled in the prone-positioned patient.

Case: A minimally invasive thoraco-laparoscopic Ivor Lewis procedure with the patient in the prone position was performed in a patient with a histologically verified adenocarcinoma of the esophagogastric junction. Preoperative staging revealed a moderately differentiated adenocarcinoma, and patients received four cycles of the FLOT regimen. The patient's postoperative course had been uneventful despite the COVID-19 infection. The water-soluble passage on days 3 and 5 excluded potential anastomotic leaks and revealed a good pulmonary image. The histology revealed complete tumor regression with the final stage ypT0N0M0. All of the 43 extracted lymph nodes had been negative.

Conclusion: Our results conclude that the presented surgical technique should be implemented in highly specialized centers.

INTRODUCTION

In recent years there has been an increase in the incidence of esophagogastric junction carcinoma in Slovenia [1]. Currently, the treatment of choice for patients with locoregional disease is neoadjuvant therapy with FLOT regiment, restaging, followed by operation and adjuvant FLOT chemotherapy [2]. Surgery is the cornerstone of treatment. For patients with distal third esophageal adenocarcinoma or esophagogastric junction carcinoma, the Ivor-

Lewis procedure should be performed. This procedure includes the right thoracotomy and intrathoracic anastomosis. Because of the complications associated with the right thoracotomy, the minimally invasive Ivor Lewis procedure has been gaining popularity. The procedure starts with the laparoscopic proximal gastric resection and the lymphadenectomy of the coeliac trunk. A gastric tube is fashioned during this step, which is pulled into the thoracic cavity in the second part of the procedure. This stage is performed thoracoscopically and has the benefit of sparing the patients a thoracotomy. A minimally invasive procedure has been shown to have fewer perioperative pulmonary complications [3, 4]. The main cause of morbidity after the minimally invasive procedure are anastomotic complications occurring in 15% to 23% [5-7]. Anastomotic leaks can result in significant morbidity and mortality. In addition, preoperative radiochemotherapy treatment has been said to increase the rates of these complications [12, 13]. To decrease these complications, many strategies have been used. Most centers use intraoperative indocyanine green control of the gastric tube perfusion. Meanwhile, not all anastomotic leakages are caused by ischemia of the anastomosis. Many leaks are caused by insufficient gastric tube length with tension on the anastomosis or even technical failure of the stapling device. The latter has been addressed by using different anastomotic techniques. In the present article, we present a technique using the intrathoracic linear stapled in the prone-positioned patient.

PATIENT

A 77-year-old patient had been previously diagnosed with esophagogastric junction carcinoma because of anemia. A complete endoscopic workup was performed. The upper gastrointestinal endoscopy revealed an exophytic growth 45 cm distal from the incisors. The histological exam confirmed a moderately differentiated adenocarcinoma. A preoperative staging was performed with computer tomography of the thorax and the abdomen. A PET/CT scan excluded distant metastases. The preoperative clinical stage was T3N0M0. The patient was scheduled for perioperative chemotherapy with the FLOT regiment. The patient tolerated the chemotherapy well. Because of the COVID-19 infection, he had to be rescheduled for the surgery for ten days.

SURGICAL PROCEDURE

The first part of the procedure was performed with the patient in the supine position with abducted legs. Five ports were inserted. The umbilical 11 mm optical port, two 11 mm ports in the left and right middle clavicular line, and two 5 mm ports in the left and right anterior axillary line. The first step was the dissection of the hepatogastric ligament. The patient had a strong replacing left hepatic artery. This artery was preserved during the first step. In addition, the lymphadenectomy was performed. The next step was the mobilization f the pharyngoesophageal ligament and the esophagus. The esophagus was completely mobilized during this step. Then the adhesion between the omentum and spleen was removed, the splenogastric ligament was incised, and the lymphadenectomy of the number 10 lymph nodes was performed. The complete great curvature of the stomach was mobilized, taking special care not to injure the epiploic arcade. The lymphadenectomy of the number 8 lymph node station was performed in the final steps. We identified the coeliac trunk and finished with the complete number 9 lymph node station clearance preserving the replacing left hepatic artery. A gastric tube was fashioned and sutured to the specimen in the next phase. Drains were placed. (Figure 1)

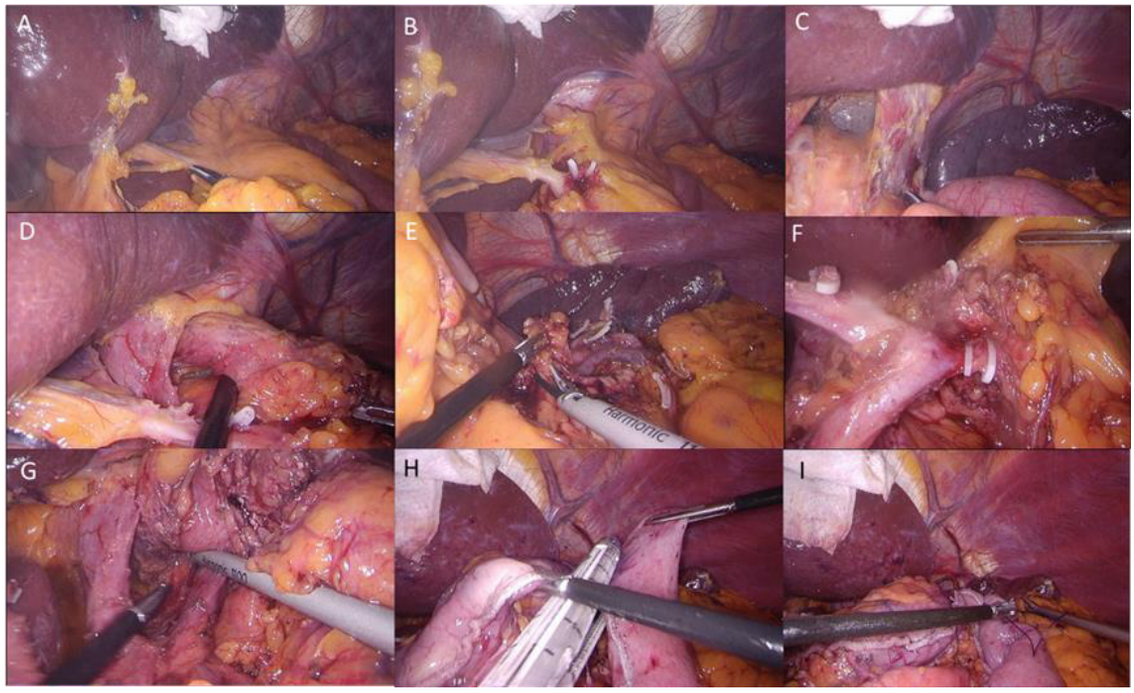

Figure 1. The abdominal phase of the minimally invasive Ivor Lewis procedure

A: Incision of the hepatoduodenal ligament; B: Dissection of the aberrant left hepatic artery; C: Incision of the phrenicoesophageal membrane; D: Mobilization of the esophagus; E: Lymphadenectomy of LN station 10; F: Dissection of the LN stations 7 and 9; G: Transhiatal mobilization of the esophagus; H and I: Creation of the gastric tube.

Figure 2. Positioning of the patient in the prone position.

The patient was reintubated with a double lumen endotracheal tube and placed in the prone position with the right arm abducted to 90 degrees and the forearm flexed. This positioning helped to rotate the scapula, making it easier for the surgeon to access the area of interest. The head was well supported to prevent any displacement of the endotracheal tube (Figure 2).

The surgeon and the assistant stood on the patient's right side, with the video monitor directly opposite on the left. This positioning allowed for optimal visualization of the surgical field and efficient communication between surgical team members. We applied the three-port technique, as a port for lung retraction is not required. A 10mm 30-degree scope was inserted through a port in the 7th intercostal space between the middle and posterior axillary line. A 10mm port inserted in the 5th intercostal space in the posterior axillary line was used for an ultrasonic scalpel, scissors, needle holder, and clip applicator. A third, 5mm port was inserted in the 9th intercostal space in the posterior axillary line and was used as a grasper. Capnothorax with pressures between 8–10mmHg depressed the diaphragm caudally and the right

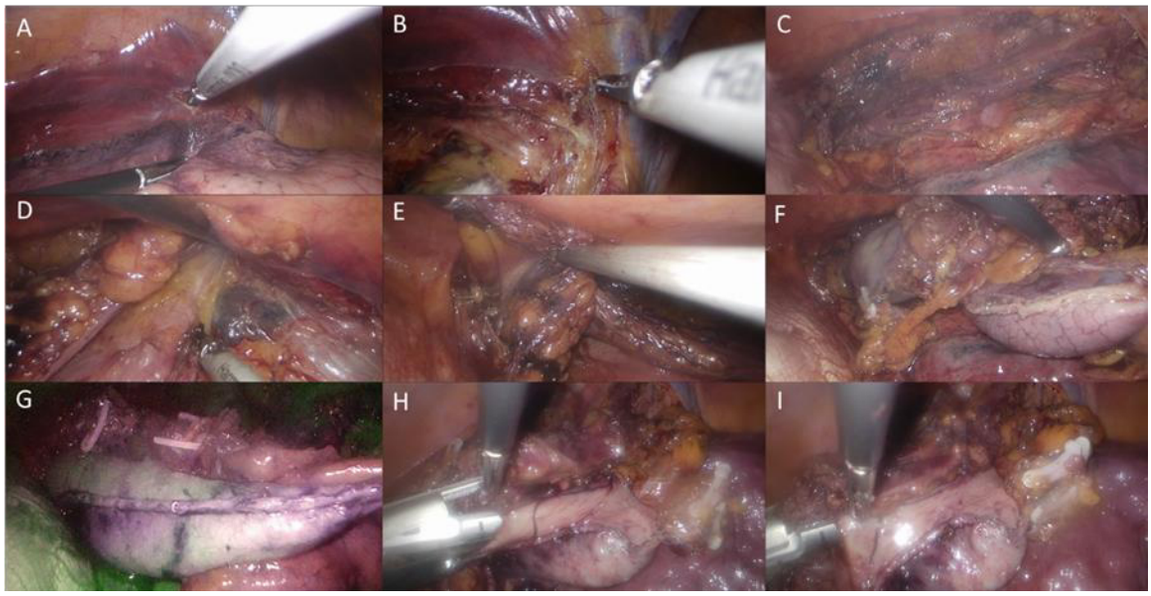

Figure 3. The thoracal phase of the minimally invasive Ivor Lewis procedure.

A: Opening of the parietal pleura; B: Dissection around the azygos vein; C: Pleura incision posterior to the esophagus; D: Mediastinal LN dissection; E: Mediastinal pleura incision and LN dissection; F: Pulling of the gastric tube into the thoracic cavity; G: ICG control of the gastric tube perfusion; H and I: Linear stapled anastomosis.

lung anteriorly, significantly improving exposure and visibility during the procedure and facilitating the extraction of coagulation smoke. The general operative technique following port insertion was similar to traditional two-stage procedures. The grasper was held in the left hand, and the ultrasonic scalpel was in the right. The mediastinal pleura overlying the anterior part of the esophagus was incised up to the azygos vein, which was preserved. The parietal pleura posterior to the esophagus was opened from the azygos vein to the crus, and blunt dissection was used to identify the thoracic duct and arterial branches originating from the aorta, which are clipped and transacted using a harmonic scalpel. The esophagus was mobilized from the azygos vein superiorly to the hiatus inferiorly, and paraesophageal, subcarinal, paratracheal, and bilateral tracheobronchial nodes were dissected to remain en-bloc with the specimen. Due to sufficient previous mediastinal dissection and complete mobilization of the esophagus, there was no need to tape the esophagus with a Penrose drain for tension during mobilization.

Once the esophagus was mobilized entirely, the specimen and the gastric tube were pulled into the thoracic cavity. The gastric tube was checked for perfusion with the ICG camera. A transaction above the tumor with sufficient margin and below the azygos vein was performed, and a linear stapled anastomosis was performed. The air leak test was performed to exclude the misfiring of the stapler. The specimen was extracted through a mini-thoracotomy, and a thoracic drain was placed next to the anastomosis. (Figure 3)

POSTOPERATIVE COURSE

The fast antigen test for COVID-19 infection was negative at admission, and the patient underwent surgery. During the operation, no complications were noted. At the end of the surgery, the patient was extubated and admitted to the intensive care

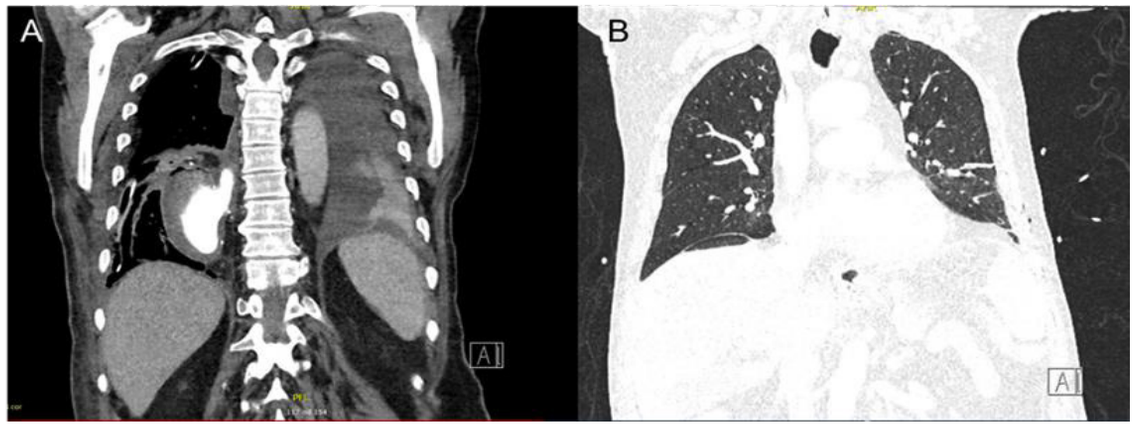

Figure 4. CT thorax with triple contrast on day five.

A: Portal phase with intraluminal contrast excluded an anastomotic leak; B: Pulmonary window revealed well-expanded lungs with no infiltrates.

Figure 5. Patient at discharge.

A: front view; B: dorsal view.

unit. After surgery, we repeated the COVID-19 testing, and the PCR results showed that the patient was borderline positive. He was put under isolation. Despite the COVID-19 infection, no pulmonary complications were noted. The patient's postoperative course had been uneventful. We noted clear drain discharges. On postoperative days three and five, a CT scan with water-soluble contrast was routinely performed, excluding any eventual leakages. On postoperative day five, the patient was transferred to the surgical ward. The PCR for COVID-19 was negative. He was put on an oral diet and was discharged on

postoperative day 11. Figure 5 shows the patient at discharge.

HISTOLOGY

The histological analysis of the surgical specimen revealed an ulcer on the esophagogastric junction. The tumor had shown complete regression and was staged as ypT0N0(0/43)M0. All extracted lymph nodes were negative for cancer.

The histological analysis revealed an ulcer in the region of the gastric cardia. There was a complete tumor regression. The length of the proximal resection margin was 2 cm, and the length of the distal resection margin was 6m. None of the 43 extracted lymph nodes were positive. The final stage was ypT0N0(0/43)M0 R0 TRG Dworak 4.

DISCUSSION

Minimally invasive Ivor Lewis procedure has been quickly gaining popularity in recent years. The lower pulmonary complications and faster postoperative recovery have made it the therapy of choice in many centers [4, 11]. Despite many advantages, the main concern is still the anastomotic leakage rate after the minimally invasive Ivor Lewis operations. The paper presents a patient after a minimally invasive Ivor Lewis procedure with linear stapled anastomosis.

Hypoperfusion of the gastric tube has been said to be the most prevalent cause of anastomotic leakage after minimally invasive surgery for esophagogastric junction carcinoma [7]. This complication carries high mortality rates and is still the cause of many concerns. The leading cause of hypoperfusion is believed to be the iatrogenic damage of the epiploic arcade during surgery [7]. Therefore, particular care should be taken during the surgery when handling the gastric conduit. We agree with Urshel et al. that iatrogenic epiploic arcade damage is a significant cause of gastric conduit hypoperfusion [7]. We believe minimally invasive surgery offers a decisive advantage in preventing epiploic arcade damage.

Many authors routinely perform ICG control of perfusion to rule out ischemia of the gastric conduit [6]. Pather et al. have shown that anastomotic leakage occurred in 60% of patients with non-perfusion on ICG compared to 33% of patients with good perfusion on ICG [6]. We strongly agree with this conclusion and routinely perform intraoperative ICG perfusion control of the gastric tube. We completed the ICG test during the thoracic phase in the present case. Although some authors advocate ICG testing during the abdominal phase, early testing might mask ischaemic gastric remnant areas, eventually leading to late anastomotic leakage.

Laparoscopy offers better exposure without a significant displacement of the gastric tube. It allows for a complete lymphadenectomy in a more confined space compared to open surgery. Abdominal compartment lymphadenectomy is a major component of treating patients with esophagogastric cancer. Schurr et al. reported that more than 40% of Siewert II patients presented with upper abdominal compartment LNs metastases [8]. In the present case, we were able to dissect 43 lymph nodes. The superior lymph node yield from the abdominal lymph node stations corroborates the superiority in the exposition with laparoscopy. It was possible to perform even the complete clearance of the number 10 lymph node station, often neglected during the Ivor Lewis procedure. The No. 10 lymph node dissection in esophagogastric adenocarcinoma Siewert II and III remains controversial [9, 10].

Meanwhile, in SII and SIII, cardia cancer metastases can be found in up to 27% of the LN station 10 [9, 10]. Therefore, many authors insist on the No. 10

lymphadenectomy [9]. We agree with this opinion. Positive lymph nodes are a substantial negative prognostic marker common in Siewert II and III patients. We, therefore, insist on complete clearance of the No. 10 lymph node station. Minimally invasive surgery in experienced hands offers superior visibility of this region and total upper abdominal lymph node clearance.

Many types of reconstruction have been performed in the minimally invasive Ivor Lewis operation. We believe that the 25 mm Orvil circular stapled technique has some disadvantages. As the stapler's head is pulled through an esophagotomy, we believe that, in some cases, the esophageal wall has insufficient tensile strength to hold the head in place firmly. Some surgeons, therefore, put additional purse string sutures to reinforce the stapler's head position until stapling. Another method that was previously described is the thoracoscopic placing of the purse string suture. However, this is due to the confined space being very burdensome and having to be performed next to major vascular structures. We used the linear stapling technique [...]. The liner stapler produces a common tract using three rows of staples. This creates a secure stapling line superior to two rows of staples of the circular stapler. Another advantage of linear stapling is that the overlapping anastomosis functions as a pouch reservoir. The lumen of the anastomosis is wider compared to the fixed circumference of the circular stapled anastomosis.

In the present case, we performed a CT scan of the thorax. The images excluded an anastomotic leak and confirmed good pulmonary image. Even though the patient was recovering after the COVID-19 infection, the minimally invasive operation did not worsen his respiratory function.

The present case of the minimally invasive Ivor Lewis operation in the prone position with linear stapled anastomosis supports the technique's feasibility. From the oncological point of view, it allows complete tumor clearance, with sufficient clear tumor margins and the complete clearance of thoracic and abdominal lymph node fields. Despite the preoperative chemotherapy, we observed no difficulties during and after the operation. We conclude that the presented surgical technique should be implemented in highly specialized centers based on our results.

STATEMENTS AND DECLARATIONS

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Surgery and Surgical Endoscopy

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Review article

Covering of traumatic defects with dermal substitutes: A review of the literature

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Key Words: Trauma; soft tissue defect; dermal substitute; Matriderm; Integra

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Abstract

Dermal substitutes are heterogeneous biomaterials composed of substances like dermis and enable permanent tissue covering. Initially, they were used for treating acute burns; however, their use was expanded to traumatic wounds, venous and chronic ulcers, and other reconstructive surgeries. The purpose of this article was to present the possible surgical treatment option in covering traumatic wounds with dermal substitutes (Matriderm, Integra), which are a part of the reconstructive ladder. We compared dermal substitutes with each other and with other treatment options. While some are more expensive than others, all have produced better results regarding surgical cost, surgical and hospitalization time.

INTRODUCTION

Skin substitutes are heterogeneous biomaterials designed to enable temporary or permanent wound covering and to replace some of the skin functions [1, 2, 3]. Permanent substitutes can be divided into epidermal, dermal, and composite substitutes, regarding replacing a specific component of human skin [2, 3, 4].

Dermal substitutes are composed of substances like dermis and can be of human origin (allograft), animal origin (xenograft), or synthetic origin [2, 3, 4, 5]. They are biodegradable materials composed of a bilayer of collagen and glycosaminoglycan or elastin, sometimes covered by a temporary epidermal substitute [1, 2, 3, 5]. They act through four phases, described by Moiemen et al., imbibition, fibroblast migration, neovascularization, and remodeling and maturation, creating a neodermis [1].

The first dermal substitute was developed in 1981 by Yannas and Burke to treat extensive acute burns [1]. Since then, dermal substitutes have spread their use across traumatic wounds, venous and chronic ulcers, reconstructive scar surgery, aesthetic reconstructions, abdominal wall repair, dermal excision surgeries, and breast implants [1, 4].

The purpose of this article is to present the possible surgical treatment option for covering traumatic wounds with a dermal substitute when local or free flaps are not possible, and skin grafts are not the best choice. We performed electronic searches in PubMed and Ovid's databases based on covering traumatic wounds with a dermal substitute. We included review articles, research articles, and case reports. Only English literature was reviewed.

DERMAL SUBSTITUTES

When searching through the literature, we acknowledge that the most used dermal substitutes for covering traumatic wounds are Matriderm and Integra.

Matriderm is a neodermis composed of bovine collagen type I, III, and V, supplemented by elastin, obtained from the bovine nuchal ligament [2, 3, 5, 6, 7, 8, 9, 10, 11]. It allows the ingrowth of host fibroblast and other cells to regenerate the dermis, so it has similar properties to intact skin [5]. While Integra is a bilayer dermal regenerate template comprised of a porous matrix of bovine collagen and glycosaminoglycans that acts as a neodermis. It has an artificial epidermal layer, which can be removed, is composed of silicone, controls moisture loss, and provides protection [2, 5, 12, 13, 14].

All traumatic wounds must be covered to reduce tissue infection and desiccation and allow for earlier mobilization [1]. The approach to all traumatic wounds is by reconstructive ladder, to which, in 2011, dermal substitutes were added [1, 11]. Flap coverage is usually indicated based on the reconstructive ladder for full-thickness wounds, with exposed tendons without paratenon, bones without periosteum, and joints without articular capsules. In avulsion injuries without exposure to underlying structures, split thickness skin grafts (STSG) are sufficient [7, 8, 12, 15]. However, the problem with STSG for large wounds is considerable donor site morbidity, poor skin quality, and possible scar contracture [6, 7, 8, 13]. Complex large wounds are also not eligible for flap surgery, which is not risk-free [6, 11].

The major contraindication for applying dermal substitute is gross infection [16], while common complications are hematoma formation, infection graft failure, and the need for multiple procedures [17].

When approaching traumatic wounds, we must first debride the devitalized tissue until reaching a viable and aseptic bed [1, 4]. Negative pressure wound therapy (NPWT) can be added to clear the infection, reduce fluid accumulation, and encourage granulation tissue formation [6, 16]. After that, we can use a dermal substitute to cover the defect [6, 7, 8]. Wounds must be free of infection before placing a dermal substitute [6].

NPWT can also be used after dermal substitute application. It has gained popularity by placing it over dermal substitute or STSG to reduce shearing

forces and fluid accumulation while supporting vascular ingrowth [16].

Matriderm can be used in a one-stage procedure, while Integra requires a two-stage procedure [9]. Matriderm must be positioned and fixed on the defect, without any bubbles underneath, and covered by a meshed split thickness skin graft [6, 7, 8, 9]. Before using it, it must be rehydrated in saline solution [7]. We can also use more layers of Matriderm if the defect is deep [6]. After suturing the skin graft onto a dermal substitute, NPWT can be applied for the first 5 to 7 days for protection and to enhance neovascularization [10, 16].

Integra is cut in to fit the wound without any wrinkles or bubbles. After 2–3 weeks, a second stage operation is performed at which the silicone layer is removed, and meshed split thickness skin graft is applied [5, 14, 15, 16]. In some cases, Integra can also be used without silicone as a single-stage reconstruction [5]. Before applying STSG, we can also use NPWT to reduce shearing forces, hematoma, and seroma formation. Hematoma formation is one of the most common complications of Integra placement [13].

Scheider and collages found no differences between Matriderm and Integra regarding vascularization, graft take, and neodermis formation [6]. Also, Philandrianos et al. compared five acellular dermal substitutes, including Matriderm and Integra, in covering full thickness wounds and found no differences in long-term healing [3]. While both substitutes can cover traumatic wounds with exposed tendons [9], Integra even exposed bones [12], Matriderm is a less expensive substitute and can be used in a single-stage operation [9].

DISCUSSION

The coverage of traumatic soft tissue defects still presents an issue, especially in hospitals without a plastic surgeon.

When covering soft tissue defects, we must consider a reconstructive ladder. Split thickness skin grafts are a reliable technique for large defects but can produce undesirable functional and cosmetic results with tremendous donor site morbidity [8, 18]. Free flaps might be possible but bring various potential side effects and donor site morbidity, while pedicle flaps are not amenable for all body parts or defect sizes [6]. Full thickness skin defects with exposed tendons/bones/joints can be covered with pedicles or free flaps, while full thickness or split thickness skin grafts are not recommended [10, 11, 18]. Despite STSG being the gold standard in covering skin defects, for more mobile and requiring areas, full thickness skin grafts (FTSG) are preferred [15]. However, in large extremity full thickness wounds, FTSGs have limited availability, while flap coverage is difficult because of the large zone of injury [15, 16]. In all such cases, dermal substitutes present an alternative for covering. In a retrospective case study of complex combat soft tissue wounds with exposed tendons, Helgeson et al. advocated the use of a dermal substitute [18].

Demiri et al. stated that indications for dermal substitute application are size and location of skin defect not amenable for split thickness or full thickness skin grafts, extended skin losses over joints, and a small area of exposed tendons [15].

Full-thickness skin defects of the hand and wrist can be covered by STSG, except if there are exposed tendons or bones. In that case, we use flap coverage. Because flaps are usually too bulky and aesthetically unpleasant, a dermal substitute may come in place [10]. Especially Integra is a unique substitute that can cover tissue stripped of nutritive structures, such as paratenon and

periosteum [19]. For Helgeson et al. primary indication for Integra placement are wounds not amendable for skin grafts [16]. The only problem with Integra application on hand defects with exposed structures, as described by Weigert et al., is an inability to revascularize minor defects. They stated that the ratio between the exposed and the to-be-vascularized structure and vascularized environment should be greater than one to allow the revascularization process [14]. On the other hand, Matriderm is a valid treatment option for fingertip injuries, whether used alone or combined with skin grafts [11].

There are many comparisons between dermal substitutes and skin grafts or flaps when covering dermal defects. Regarding skin elasticity, Min et al. found that grafted skin with Matriderm had the same elasticity as normal skin [8, 9]. The same was proven by Nguyen et al. [13].

Also, when comparing dermal substitutes with standard treatment, the advantages are reduced overall hospitalization time, a less invasive procedure, considerably lower operation time, and fewer complications [4]. One of the main drawbacks of dermal substitutes is cost [6, 13]. Despite higher costs of materials, Inhoff et al., in their research comparing reconstruction of scalp defects with flaps or substitutes, concluded that dermal substitutes are economically more feasible. It was due to the shorter treatment period, fewer dressing changes, and patient comfort [6].

It seems to be that the only disadvantages of dermal substitutes are lacking essential components of normal skin as sweet glands and hair follicles and suboptimal restoration of sensitivity. All is rather vital in treating defects of the palm and fingers. Even so, Graham et al. and Taras et al. presented excellent results in treating soft tissue defects with exposed structures on the hand and fingers [1]. Also, Nguyen et al. showed that regenerated skin was equivalent to normal skin regarding sensitivity to touch, heat, and cold [13].

CONCLUSION

Dermal substitutes represent an alternative to flaps and grafts in traumatic defect covering and are part of the reconstructive ladder. The most used are Integra and Matriderm. Based on the review of the English literature for traumatic defect covering, we concluded that surgical cost, surgical time, and hospitalization time are lower using a dermal substitute.

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Surgery and Surgical Endoscopy

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Review article

Degenerative Disc Disease: Morphological Substrate, Pathophysiological Changes and Etiology: A review of the literature.

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Abstract

The intervertebral disc is a complex structure that, under multifactorial influences, can lead to a process known as degenerative disc disease. Otherwise, the intervertebral disc is a complex structure that serves the body in an upright position and provides mobility while being architecturally solid. The softcore, connective tissue ring, and terminal surface allow the disc to maintain homeostasis and physiological function of the functional segment of the spine, of which the intervertebral disc is an integral part.

A positive feedback loop of degenerative processes occurs in degenerative disc disease, damaging the entire disc and adjacent structures. Thus, there is degeneration of the microarchitecture of the extracellular matrix of the softcore, destruction of the lamellar structure of the connective tissue ring, damage to the subchondral bone at the endplate, and loss of permeability of the same. These changes lead to structural instability, damage to the surrounding tissues, and other pathological processes expressed in the clinical picture of degenerative disc disease.

Despite the excellent research attention, the background of these processes has not yet been fully elucidated. The multifactorial genesis of the disease itself is indicated, and numerous studies reveal the role of individual risk factors, such as environmental, metabolic,

genetic, and mechanical factors. However, their role has not yet been fully elucidated.
Therefore, according to the current literature findings, this paper aims to present the anatomy of the intervertebral disc and the pathological changes with the onset of degenerative disc disease.

INTRODUCTION

The intervertebral disc (IVD) is a complex soft tissue structure in the human spine that, together with two adjacent vertebrae, forms a functional spinal unit called a motion segment. The IVD can structurally degenerate under multifactorial pathogenesis, resulting in a condition known as degenerative disc disease (DDD) [1,2]. DDD is one of the leading causes of low back pain and, as such, is a significant public health problem, leading to more disability than any other condition. It often affects younger working-class people, a significant socio-economic burden even in developed countries [1-5]. Despite its widespread prevalence and high morbidity, many questions remain unanswered regarding its etiology, pathophysiology, and possible causal therapeutic interventions [1, 2, 6, 7].

Our work aims to present the current state of knowledge about anatomical structure, histology, biomechanics, and pathological processes that affect them in the process of DDD based on a literature review.

THE INTERVERTEBRAL DISC EMBRYONIC ORIGIN AND ITS STRUCTURAL AND FUNCTIONAL ANATOMY

In the motion segment, the IVDs are surrounded by two vertebrae. In this situation, the IVDs act as the largest joint in the human body, allowing the vertebral column to flex, rotate and distribute the vertical pressure loads of the spine while maintaining an upright posture [4, 7, 8]. The IVD consists of three main components, namely the soft core called the nucleus pulposus (NP), the surrounding lamellar annulus fibrosus (AF), and the cartilaginous endplate (CEP), which is intertwined with the adjacent overlying surface of the vertebra above and below it, the bony endplate (BEP) [2, 4, 9].

From an embryological point of view, the IVD is of both notochordal and sclerotomal origin – NP originating from the axial notochord, whereas AF and CEP originate from the paraxial mesoderm (PM). The IVD is the largest avascular and aneural structure in the body, as it begins to lose disc vasculature and lymphatic drainage soon after birth, so in its physiological state, the IVD is predominantly an avascular and aneural structure in adulthood, except its most outer AF lamellae's (oAF) [2, 4, 8, 10-13].

Nucleus pulposus

The central structure of the IVD, which accounts for up to 50% of the IVD volume, is NP. It contains a high proportion of water, proteoglycans, and an irregular network of type II collagen fibers and elastin, that extends throughout the NP and allows it to retain its structure. The high percentage of water that NP binds in youth, up to 90%, decreases with age. Water binding to the matrix creates hydrostatic pressure, enabling circumferential tension in AF and pressure distribution during load [4, 8, 9, 13, 14].

In embryogenesis, NP forms from a temporary notochord, a rod-like structure that serves as a preliminary axial skeleton. The interaction of the

notochord and sclerotome, a transient embryonic tissue composed of pluripotent mesenchymal stem cells and a precursor of the vertebrae and AF, allows for the segmentation and formation of mature IVD and vertebral bodies. Mechanical forces and the ECM environment with growth factors (EGF, VEGF, FGF, and GF-1) are thought to play a crucial role in further differentiation into NP and its notochordal-like cell differentiation, which continue to populate healthy NP also in adulthood and are capable of synthesizing ECM aggrecan and collagen type II [13, 15, 16].

The binding of water itself is made possible by a high proportion of proteoglycans, which amounts to 35-65% of the dry weight of NP. In particular, the central proteoglycan of NP represents aggrecan, which generates osmotic pressure due to its relatively high content of anionic glycosaminoglycans. The latter is required to maintain compressive force – IVD damping, which allows flexibility and resistance to deformation, and obtain the structural tension of AF [4, 8, 9, 14].

The cellular architecture of NP is predominantly of notochondral origin, but with age, the proportion of notochondral-like cells decreases. The original notochondral cells are morphologically large vacuolated cells that enable synthesis of the NP ECM and thus provide mechanical support. During the maturation process of the skeletal system, under the influence of mechanical forces and the avascular milieu, the proportion of these cells decreases significantly, and they are replaced by smaller round cells, morphologically similar to chondrocytes [4, 10, 14, 17-19].

Annulus fibrosus

In axial projection, the NP is surrounded by a circumferential connective tissue structure called AF. AF is a highly organized lamellar structure with an average of 15-25 layers with a lamellar thickness of 50-500 μm; the thickness of the lamellae themselves increases as they approach the centrally located NP [4, 8]. At the same time, some lamellae are circumferentially incomplete, their proportion is up to 48% and increases with age, and they are oriented at an angle of 25-45% with respect to the axial plane, with a tendency to increase the angle in inner layers Annulus Fibrosus (iAF) [8]. The lamellae are interconnected by elastin fibers that allow the AF to return to its original position after flexion and extension movements. Also crucial in maintaining the shape and tension of the AF fibers is the direct radial force from the NP and the tensile force from the CEP side, where the AF also attaches at its extreme craniocaudal edges [2, 4, 8].

Like NP, AF is also relatively rich in water, but its proportion is much less in comparison with the former; namely, the proportion of water is up to 65–70% in youth and, as in NP, decreases with age. AF is also rich in collagen fibers; this proportion makes up 50–70% of its dry weight, proteoglycans 20%, and elastin up to 2%. The distribution of each component also differs between the AF lamellae themselves. The more centrally located ones generally have a higher proportion of water and a higher proportion of type II collagen fibers than the lamellae on the outer circumference. In contrast to NP, AF is dominated by type I collagen fibers, which provide tensile strength with their structural makeup. The collagen fibers of type II form fine fibers that join together to form networks, which enables the binding of proteoglycans and, thus, a higher water content, according to the principle as in NP [2, 4, 8, 14].

From a cellular point of view, AF consists of spindle cells, which are morphologically related to fibroblasts and align parallel to the extracellular matrix to form the fibrous structure. Compared to NP cells, which are of notochondral origin, AF cells originate from the PM, more specifically from the sclerotome - a transient structure with mesodermal properties – that, after organization in a somitocoel, migrates to the notochord during

embryogenesis. After migration, AF precursor fibroblast-like cells are arranged in an array oriented along the embryonic NP caused by a network of actin stress fibers that provide a template for collagen deposition. This then allows the formation of the characteristic lamellar AF structures with a collagen network [2, 10, 13, 20].

Cartilaginous endplate

Both cranially and caudally, above and below the NP, there is a predominantly homogeneous structure of hyaline cartilage called CEP, which is fused to the adjacent roof surface of the vertebral body, bony endplate, and marginally to AF. The CEP, approximately 0.6 mm thick, combined with AF, thus surrounds NP and isolates it within the IVD. Structurally CEP is spindle-shaped and thickens in the very center. At the circumferential outer edge, it is attached with an AF lamella. Moreover, they surround the entire circumference of the CEP and connect with the bone of the vertebral body. According to the size in the axial plane, the CEPs differ according to the adjacent vertebrae, with the diameter of which the covering surface also coincides and thus gradually increases from the cervical spine region to the sacrum. Thus, CEP sizes increase from the cervical spine, where dimensions are 16-19 mm in the anteroposterior plane and 17–29 mm in lateral width, to averages of 30–36 mm anteroposteriorly and 43–54 mm in the lumbar spine. Due to its cartilaginous morphology and adhesion to the adjacent end surface of the vertebral body, CEP is structurally strong, preventing significant water leakage from the NP during spinal motion [4, 8, 20].

As with NP and AF, a significant amount of bound water is found in CEP, approximately 60%. Otherwise, CEP is morphologically similar to cartilage elsewhere in the body and consists of type II collagen fibers with proteoglycan inclusions. Their ratio varies topographically within the TP, such that the proportion of collagen decreases relative to the center and, conversely, the proportion of proteoglycan is highest in the center. Regarding cell structure, CEP also resembles cartilaginous tissues elsewhere in the body, predominantly homogeneous in the form of round cells of mesodermal origin – chondrocytes [4, 8, 20-23].

NUTRIENT SUPPLY AND INTERVERTEBRAL DISC METABOLISM

The IVD is an avascular structure except for the extreme oAF. Therefore, the supply of nutrients to the cells of the IVD, especially NP, is limited and depends on diffusion processes and the movement of fluid currents according to the convection principle [8, 22, 23].

Diffusion, which proceeds according to the principle of selectively permeable membrane mainly through CEP and, to a lesser extent, through AF, represents the supply path of smaller molecules over shorter distances and in the direction of the diffusion gradient. In this way, NP is supplied with oxygen, which, despite the method mentioned above, reaches the deep NP only in limited quantities. In the v NP is following this mainly an anaerobic metabolism that leads to an acidic environment and high lactate concentrations. In addition to diffusion, in which single molecules move, the principle of convection also plays a role in IVD nutrition, in which the migration of fluid currents allows larger molecules to enter and leave that could not otherwise enter the IVD by diffusion via CEP or AF [22-26].

Because of this, the homeostasis of the IVD, especially NP cells, is in a fragile equilibrium in which the processes of catabolism and anabolism, tightly regulated by growth factors, constantly alternate to maintain structural integrity. Due to the absence of direct blood flow and nutrition by diffusion or convection, the IVD milieu is more susceptible to imbalances. Even short-term

metabolic disturbances, changes in CEP, or chronic hypoxemia can have irreversible consequences for IVD and lead to cell death. The cartilaginous structure of CEP itself is thought to play a significant role in this pathogenesis, providing a more pronounced specific permeability sieve for nutrients compared to the adjacent subchondral bone of the vertebral body [20-22, 24-27].

STRUCTURAL CHANGES IN THE PROCESS OF DEGENERATIVE DISC DISEASE

The DDD process is associated with changes in all components of the IVD as well as some paradisiacal structures – ligaments, muscles, and joints [8, 9, 14]. Changes in the NP itself can be detected early in the DDD process. Physiologically, the extremely water-rich structure gradually loses its structural architecture and water content, followed by a decrease and fragmentation of the proteoglycans that allow the maintenance of a high hydration level. This leads to another cascade of events, followed by a reduction in the osmotic gradient and a decrease in the ability to retain water. Consequently, this leads to an imbalance of metabolic processes and cell death. In response to the changes in milieu, the cell composition of the NP also changes, from large vacuolated cells to small round chondrocyte-like cells. These events form a positive loop that causes further degeneration, provokes an inflammatory response, and degenerates adjacent structures [8, 9, 25, 26].

Changes can also be detected in AF due to the loss of intradiscal pressure, AF bulges and IVD protrusions, lesions in the area of the AF ring itself, delamelization, and in advanced stages, loss of the ability to maintain continuity and disk herniation. Pre-arranged fibers in individual lamellae gradually become more and more disordered in the process of degeneration. At the same time, they additionally lose their primary role, and the proportion of elastin and water also decreases. There is also de novo innervation of the inner lamellae of AF; under physiological conditions, thin nerve fibers – type C are present only in the outermost lamellae, and de novo veins develop, which grow independently to the inner lamellae. The aforementioned pathological innervation and inflammatory changes are believed to be essential factors in developing lumbar pain with DDD [8, 9, 12].

In addition to the abovementioned changes, the DDD process also affects CEP leading to other events due to its physiological role in IVD nutrition, further reinforcing the positive loop. Indeed, during DDD, sclerosis of the adjacent subchondral bone of the vertebral body can be detected in the endplate area, as well as changes in the CEP itself that are consistent with the degenerative changes of articular cartilage elsewhere in the body - water loss, calcification, decreased diffusion capacity and gradual cell death [3, 8, 9, 28].

ETIOLOGY FOR DEGENERATIVE DISC DISEASE

To date, the etiology of IDD has not been fully elucidated despite many studies. Numerous studies have shown the influence of genetic, environmental, and enzymatic changes, metabolic disorders, microtrauma, inflammatory processes, age-related changes, and structural changes. The etiology of DDD is therefore considered to be multifactorial [3, 8, 9, 14, 28].

Genetic factors in degenerative disc disease

Several genes have been identified whose expression increases the possibility of IDD. Studies describe an increased incidence of gene expression of CLIP, THBS2, ASPN, CHTS, and PARK2, as well as single nucleotide polymorphisms (SNP), namely COL1A1, COL9A3, COL11A2, COL11, and CHST3 [29,30]. They also play a role in increasing the incidence of IDD mutations in genes

otherwise involved in matrix synthesis. Thus, the mentioned genes cause increased susceptibility to the occurrence of DDD in 75% of all cases, but with the simultaneous influence of other factors, especially environmental factors [9, 29, 30].

Mechanical load

Numerous animal models of DDD have shown the causality of structural damage with the onset of a degenerative process. Injuries in the endplate area were particularly susceptible. Thus, it is assumed that IVD microtraumas represent one of the reasons for faster degeneration and thus lead to the multifactorial cascade to the formation of DDD. The main risk factors include strenuous physical work, smoking, obesity, and poor posture [2, 9].

Metabolic factors

IVD cells, especially NP cells, live in adulthood in a fragile balance of anabolic-catabolic processes characterized by an anaerobic acidic environment with a high lactate content. This equilibrium is maintained by diffusion and convection from the surrounding structures in the event of a disturbance that would jeopardize the delivery of nutrients to the IVD. This would endanger the vital population of IVD cells, which, due to their structure, have extremely limited reparation possibilities. Thus, metabolic disturbances can lead to apoptosis and consequent structural disturbance of IVD itself, thus triggering a positive feedback loop [2, 9, 14, 28].

CONCLUSION

DDD represents a multifactorial process that leads to a progressive cellular response to structural damage. Despite its frequency and morbidity, the pathophysiology of DDD is still not fully elucidated. The latter would allow for the potential design of targeted therapeutic interventions and thus have a significant public health impact.

ABBREVIATIONS

AF - Annulus Fibrosus

BEP - Bony Endplate

CEP - Cartilaginous Endplate

DDD - Degenerative Disc Disease

ECM - Extracellular Matrix

iAF - inner Annulus Fibrosus

IVD - Intervertebral Disc

NP - Nucleus Pulposus

oAF - outer Annulus Fibrosus

PM - Paraxial Mesoderm

SNP - Single Nucleotide Polymorphisms

STATEMENTS AND DECLARATIONS

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Review article

Medical and surgical aspects of weight recurrence after bariatric surgery: A review of the literature

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Keywords: Definitions; Mechanisms of weight regain; Insufficient weight loss; Bariatric surgery; Predictors; Management; anti-obesity medications; Bariatric surgery; Behavior therapy; Obesity; Weight recurrence.

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Abstract

Obesity is a chronic, progressive disease with a tendency to recidivism regardless of the type of excessive weight loss, which has been presented through clinical studies. Bariatric and metabolic surgery (MBS) is the most efficacious and durable intervention for morbid obesity and metabolic syndrome, with unique perspectives on T2DM treatment. Prevalence and predictors for insufficient weight loss and recurrence after bariatric surgery (MBS) are complex. Risk factors related to weight recurrence (WR) fall into five categories: anatomical, genetic, dietary, psychiatric, and temporal.

Energy restriction initiates powerful compensatory mechanisms to resist weight loss and defend the higher body weight. MBS alters the secretion profile of hormones involved in regulating hunger and satiety. At the same time, it influences long-term weight maintenance through caloric and content restriction after surgery related to weight maintenance and weight recurrence. The gap between observed and predicted energy expenditure after massive weight loss represents metabolic adaptation; a greater metabolic adaptation could be partly responsible for a lower weight loss after surgery. Prevention and treatment strategies should be implemented in clinical management MDT protocols, including protocols for medical preoperative metabolic improvement to reduce perioperative and late postoperative complications, including weight recurrence.

Many patients experience significant WR during long-term follow-up attributed to anatomic and surgical causes. Adjuvant pharmacotherapy can help treat weight recurrence after bariatric surgery. As an adjunct to lifestyle modification might induce clinically meaningful weight loss related to metabolic improvement

and reduction of de-novo presentation of obesity-related comorbidities. Technical complications of the surgery or failure of the surgical method can cause WR after BMS. Identifying the cause is the basis for selecting the treatment algorithm with revision surgical and endoscopic interventions and pharmacotherapy.

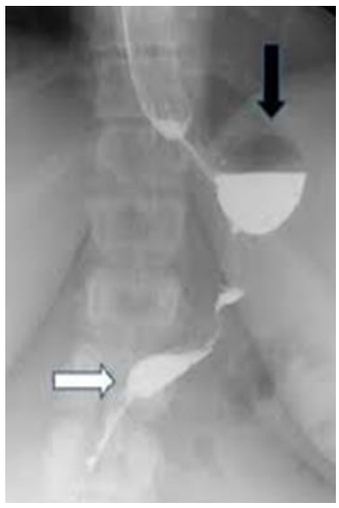
INTRODUCTION

A lack of consensus on WR (weight recurrence) after MBS is an important limiting factor for standardizing clinical practice and interventions [1, 2]. In general, the causes of weight recurrence after MBS could be divided into the failure of the surgical technique, technical complications of the surgical technique, and causes related to dysregulated/maladaptive eating behaviors, lifestyle factors, and physiological compensatory mechanisms [1, 2, 3, 4]. Studies based on clinical data have presented insufficient results based on isolated dietary, supportive, behavioral, and exercise interventions on weight reduction in the case of WR, and there are essential and evidence-based interventions for pharmacotherapy, targeted to preoperative excessive weight loss and WR.

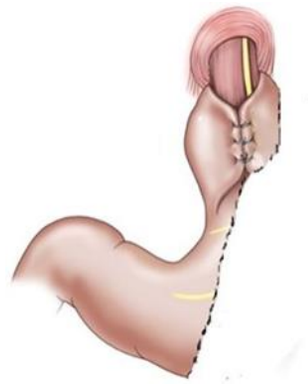
From a general point of view, the risk factors for WR might be divided into enlarged gastrojejunal stoma diameter, larger gastric volume following SG and inappropriate technical resection with remnant fundus, longer post-operative follow-up, incomplete resolution of T2DM, persistent pathological feeding disorders: loss of control eating (LOCE), increased food urges, nocturnal eating; other factors related to WR: lower physical activity, lower social support, life stresses, problematic alcohol use, and depressive symptoms [1, 2, 5, 6]. Among laboratory factors, WR is associated with hormonal factors, most studies have been conducted on higher pre-prandial ghrelin and lower post-prandial GLP-1 levels, but more studies are needed to provide solid evidence.

Technical complications of BMS and weight recurrence

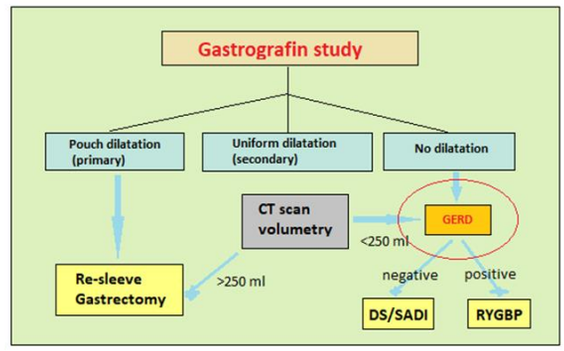
Among the technical complications of surgical techniques, it is essential to note that complications from a technical point of view occur in the case of non-adherence to specific techniques or in the case of non-adherence to existing recommendations in terms of nutritional treatment and lifestyle [5, 6, 7]. Among the anatomical failures of surgical technique, the following are important and related to technical aspects; band migration in adjustable gastric banding, dilated gastric fundus after sleeve gastrectomy, and pouch dilatation or oversizing at primary intervention in case of primary sleeve gastrectomy. In bypass surgeries, pouch oversizing at primary intervention, pouch dilatation, and band migration in banded bypass are important from the weight regain perspective. Among the mechanisms that could influence WR, the length of the alimentary and biliary limbs and the adaptive mechanisms involved in limiting the effects of malabsorption are also technically relevant. Still, the latter is mainly engaged later after the MBS intervention. Important technical aspects are related to a presentation of gastro-gastric fistula after Roux-en-Y and one-anastomosis gastric bypass surgery, sleeve-leak with fistula formation leading to WR, and concomitant disease progression [8, 9, 10].



Picture 1 and 2. Remnant gastric fundus after sleeve gastrectomy. Gastrografin study and endoscopy are basic diagnostic tools, followed by CT scan volumetry.

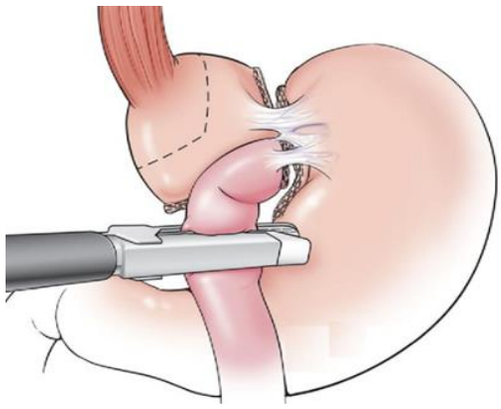


Picture 3. Nissen-sleeve with remnant fundus for re-operation or as the primary operation. Crural repair is mandatory in hiatal hernia with optional fixation to crura in case of revisional surgery.

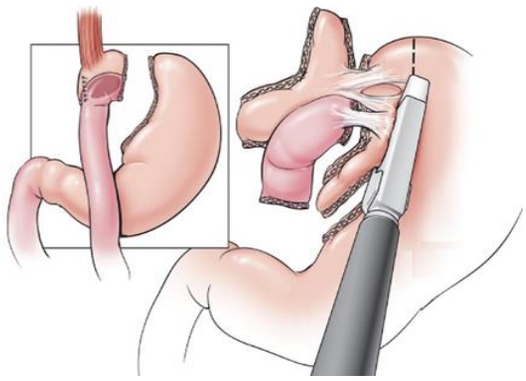


Picture 4. Algorithm for surgical treatment of sleeve failure. When defining sleeve gastrectomy complications, we follow the recommendations for post-operative follow-up, excluding GERD and all clinical entities associated with esophageal pressure abnormalities. The technique of choice is HRM (high-resolution manometry).

The technical aspects of the approach to gastro-gastric fistula care include complete excision of the fistula and re-formation of the RYGBP if the clinical circumstances allow; the latter consists of a nutritional assessment and an endocrinological assessment due to the possibility of metabolic complications in case of significant clinical abnormalities [8, 9].



Picture 5. Gastro-gastric fistula after Roux-en-Y gastro-By-pass surgery for morbid obesity.



Picture 6. Surgical management of gastric fistula.

Clinically relevant complications that could influence the decision on the type of reconstruction in both SG and RYGBP include the presence of resistant dumping syndrome; in addition, with the increased risk of GERD, both the algorithms for postoperative endoscopic follow-up and the preferential conversion of SG should be considered in the presence of a pronounced clinical picture of reflux, which is evaluated by histopathological assessment. Preoperative diagnostic methods should focus on the search for a preexisting or de novo hiatal hernia, which requires both a reconstructive procedure on the hiatus (cruroplasty) and an antireflux part of the procedure; from a technical point of view for the antireflux part of the procedure, the residual fundus (Dor fundoplication) is used for SG, whereas for RYGBP, the fundus of the native stomach can be used for the antireflux part of the procedure [9, 10, 11, 12].

Picture 7: CT verification of gastro-gastric fistula after bypass surgery

Picture 8. Oral enema for verification of gastro-gastric fistula.

Data from the bariatric registry presented that > 600,000 surgeries are performed annually worldwide, of which SG's share over 60%, RYGBP 18%, and an increasing number of other procedures, particularly from the view of revisional surgery. WR is common after patients reach their nadir weight; approximately 20–25% suffer from considerable WR after MBS.

BMS vs. pharmacotherapy

The superiority of MBS to non-surgical weight loss interventions has been proven in clinical studies. A significant proportion of patients achieve less-than-expected benefits due to suboptimal weight loss (SWL) or weight regain (WR). In clinical settings, WR is defined as initially achieving expected weight loss after surgery and recurrence of excessive weight/sub-optimal weight loss [1, 2, 3]. To make it clear, this represents not achieving a

weight loss of 40% to 60% of baseline excess body weight (EWL%) over 1–2 years and represents an essential point in the clinical decision-making process for either surgical revision or non-surgical methods, especially medical interventions with the incidence of occurrence of 11% to 22% of patients following bariatric surgery.

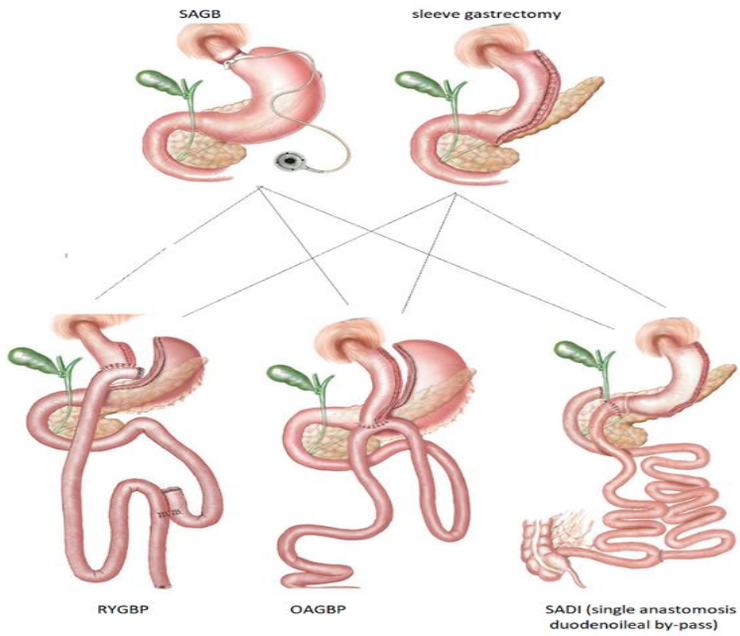
Three maladaptive eating behaviors, such as grazing, loss-of-control eating, and binge eating, have been commonly reported among bariatric surgery patients and related to WR. De-novo recurrence of obesity-related comorbidities, including T2D, hypertension, and dyslipidemia, significantly increases healthcare costs and has a negative effect on the overall risk of obesity-related cancer incidence, life expectancy, quality of life, and emotional health. Importantly, WR is related to disability and absenteeism.

Therapies with proven efficacy have been introduced for improved and optimized management of weight recurrence and to maximize the long-term benefits of surgery. Retrospective studies have proven that dietary, behavioral, and exercise interventions have not demonstrated efficacy in reversing WR after bariatric surgery.

Revisional BMS is oriented to certain anatomical causes of weight regain after primary Roux-en-Y gastric bypass (i.e., pouch/stoma dilation or gastrogastric fistula), sleeve gastrectomy (i.e., antrum or fundus dilation) or gastric band. In retrospective studies, the authors have shown that reversal of weight recurrence represented as percent excess body mass index loss (%EBMIL) after RYGBP ranged from 43.3–63.7% at one year and 14–76% at three years post-revision and was related to the type of revisional surgery. Compared to SG, in converting to RYGB for WR, a 40% excess body weight loss (%EBWL) has been achieved at 12 months, but results are related to single studies. Conversion from gastric band to SG or RYGBP ranged from 23 to 74 %EBWL, with limited follow-up data in this group of patients. Importantly, revisional surgical procedures are related to higher morbidity than primary procedures. They should be performed in selected patients after intensive pre-operative preparation and exclusion of complication risk factors [10, 11, 12, 13].

Surgical interventions for WR and pharmacotherapy for WR and preoperative weight loss

Identifying the problem of WR is vital from a practical point of view; the increasing number of operated patients and the introduction of non-standardized surgical techniques whose effects are not proven in metabolic studies, including poor adherence to the management of patients after BMS, dictate the design of effective interventions for the prevention and early limitation of weight gain after MBS. In addition to proven effective interventions related to dietary treatment, LS interventions, and changes in the social environment, drug therapy, and re-do BMK interventions are the intervention methods of choice. It should be borne in mind that the effectiveness of MBS re-interventions is related to other, not just technical aspects of BMS. The most performing revisional procedures after the failure of restrictive surgery due to satisfying short and mid-term weight loss and low early and late morbidity are single-anastomosis duodeno-ileal bypass and one-anastomosis gastric bypass. It has been presented in retrospective studies that both surgical interventions have acceptable risk, and besides, the single-anastomosis duodeno-ileal bypass has a low risk of weight recidivism [11, 12, 13].



Picture 9. Revisional BMS for failed restrictive procedures.

%TWL one- and three-years post-surgery by single-anastomosis duodeno-ileal bypass (9.24 and 19.13), one-anastomosis gastric bypass (7.16 and 13.1), and Roux-en-Y gastric bypass (4.68 and 7.3) compared to re-sleeve gastrectomy represent an acceptable risk and efficient weight loss. RYGBP is related to a significantly higher late complication rate and significant morbidity. Compared to re-sleeve gastrectomy frequently performed due to a likely misassessment of efficacy and the level of risk of complications, single anastomosis duodeno-ileal by-pass has a significantly lower incidence of complications and notably better long-term effects and lower risk for WR (OR: 0.07). ELEGANCE RE-DO trial (14) presented results of revisional BMS in the case of gastric band surgery. It demonstrated the efficacy of a long biliary limb with a shorter alimentary limb of RYGBP. Still, it is essential to be aware of the adverse metabolic effects and the risk of bacterial overgrowth with a negative impact on the incidence of metabolic complications. A growing number of retrospective and prospective studies demonstrate the safety and efficacy of one-anastomosis gastric bypass (OAGBP) with low risk of complications and very good short- and medium-term outcomes, the same range as RYGBP [12, 13, 14].

Pharmacotherapy and weight loss after BMS

The efficiency of pharmacotherapy for reversing weight recurrence after bariatric surgery has been presented and discussed in retrospective studies and open-label trials. Topiramate (TPM) and phentermine (PHEN) were the most prescribed drugs, and there is limited evidence for the effectiveness of topiramate and liraglutide. Also, there was a limited approach to their retrospective data collection and a lack of predetermined censoring of the beginning and end of data collection. Constructive discussion cannot, therefore, be the subject of these studies, nor can the applicability of the results to clinical practice [15, 16, 17, 18].

Bupropion reduces appetite and increases energy expenditure through increased dopamine activity and proopiomelanocortin (POMC) neuronal activation, modest dose-dependent weight-lowering efficacy has been shown in several clinical studies. Literature reports on the limited efficiency of bupropion in WR after BMS; the fixed-dose combination bupropion/naltrexone may be helpful in selected patients after BMS and WR, but the lack of long-term and cardiovascular safety data limits the use of this drug in patients with increased cardiovascular risk. Long-term use reported an average of 5.4% weight loss in one year [16, 17, 18, 19].

The study of Zilberstein et al. assessed the use of topiramate 12.5–50 mg nightly a mean % excess weight loss of 20.9% (4.6–40%) at 5–13 months after surgery was observed. They also reported an increase in mean percent excess weight loss (EWL) from 20.9 to 34.1% at three months of follow-up [1, 16, 17].

Ard et al. reported [18] the use of preoperative phentermine and topiramate extended-release (Phen/Top) combination therapy in patients with severe obesity (BMI ≥ 50 kg/m2) undergoing laparoscopic sleeve gastrectomy (LSG); dosing /top 7.5/46–15/92 mg daily for at least three months preoperatively and 24 months postoperatively induced significantly higher %EWL matched to control group, preoperatively 28.1 ± 12.8 kg versus 12.3 ±12.5 kg. Weight loss postoperatively was considerably more remarkable in the treatment group at 12 (− 39.3% versus − 31.4%, p = .018) and 24 months (− 38.2% versus − 27%, p = .007). Data presented strongly suggest that adjunct pharmacotherapy can enhance and maintain weight loss in patients with severe obesity. There is a lively discussion in the literature targeting preoperative medical weight loss; the principles of preoperative preparation are based on specific interventions that remain the cornerstone of eating disorder management and are aimed at reducing the risk of complications; from this point of view, there is a justifiable reluctance to prescribe drug therapy in the preoperative period widely.

There is an increasing body of postoperative liraglutide treatment in the literature [19, 20, 21]. The overall conclusion of these studies is that liraglutide has similar efficacy in post-bariatric and nonsurgical patients. More weight loss has been observed with pharmacotherapy after RYGB than SG. This last observation dictates further studies.

There is a leak of the standard definition of WR after BMS; the percent of maximum weight lost is a parameter that most strongly correlates with several clinically relevant outcomes. To standardize the reporting practice, it is suggested to use this as a standard measure of weight recidivism after surgery. Clinically speaking, it is strongly recommended that the decision to begin anti-obesity pharmacotherapy should be individualized. Factors behind the decision to prescribe pharmacotherapy are the patient's weight history, presence or recurrence of comorbid conditions, and symptoms (e.g., appetite, binging). A threshold at which medications should be initiated has not yet been established [1, 2, 3, 22, 23]. Before any prescription, risk factors for WR should be discussed and excluded. From the clinical point of view, it would be reasonable to consider metformin and/or a GLP-1 agonist as first-line therapy for individuals with insulin resistance or diabetes. For patients suffering from depressed mood, bupropion or bupropion/naltrexone might be preferable. It is to consider pharmacotherapy for concomitant disease treatment.

A growing body of evidence in the literature supports the beneficial effects of incretin therapy, including the currently popular GLP-1 agonist [15, 19, 20] (GLP-1) is physiologically released from gut enteroendocrine cells and controls meal-related glycemic excursions through insulin augmentation

and glucagon secretion inhibition. Other physiologic effects are related to delayed gastric emptying and reduced food intake. The benefits of GLP-1 agonists and side effects associated with bariatric surgery are controlling islet function, appetite, inflammation, and cardiovascular pathophysiology. Glucagon-like peptide-1 receptor agonists (GLP1-RAs) are the most efficacious weight-lowering drugs with acceptable efficacy and safety profile. Data from the literature report an average body weight loss of up to 15%, usually transient mild to moderate gastrointestinal side effects, and cardiorenal benefits.

Comparing the efficiency of subcutaneous semaglutide (2.4 mg) vs. daily subcutaneous liraglutide (3.0 mg) in patients with overweight or obesity without T2D demonstrated a total body weight loss of 15.8% with semaglutide vs. 6.4% with liraglutide after 68 weeks of therapy, as reported by Jensen et al.

Our unpublished results can contribute to this finding; both in patients with metabolic syndrome treated with semaglutide and in patients with WR after bariatric surgery at a dose of 1.2 mg weekly subcutaneously, we achieved an average absolute weight loss of 8-12 kg over a 12-week interval, representing an average weight loss of 10-15%. Combined with LS intervention, we observed significant improvements in metabolic parameters, physical well-being, exercise capacity, and mental status. However, caution and careful selection of patients for prescribing incretin therapy should be emphasized; with limited prescription duration and favorable efficacy, the likelihood of a rebound phenomenon is relatively high, associated with both metabolic and technical complications of BMS.

Finally, the effectiveness of pharmacotherapy after BMS is related to the type of surgery. Different surgical technics for weight loss are joined to anatomical changes in the gastrointestinal tract. Linked to the drastic weight loss and altered body composition, unpredictable changes in the pharmacokinetics of drugs should be expected with the limited efficiency of anti-obesity medicines and their combinations.

In conclusion, adjuvant pharmacotherapy can help treat weight recurrence after bariatric surgery and might induce clinically significant weight loss as an adjunct to lifestyle modification. The next suggestion would be that further prospective studies are needed to assess the best medication or combination of medications for different patient populations and the optimal timing of initiating medications after bariatric surgery. As the pharmacologic armamentarium continues to expand, we can expect further reports on the efficiency of dual GLP-1-GIP agonists and leptin sensitizers. This further increases the range of pharmacotherapy options after BMS. Still, it is vital to be aware of the basic principles of treatment and careful patient selection for the type of BMS and pharmacotherapy introduction.

BMS is the most effective obesity treatment for weight loss and ameliorating most weight-related comorbidities, especially T2D. Many patients experience significant WR during long-term follow-up attributed to anatomic and surgical causes. The highest proportion of WR is due to post-operative increased caloric intake. The most studied factors contributing to WR are increased appetite, maladaptive or dysregulated eating, inadequate physical activity, and psychosocial stress. WR is associated with the recurrence of previously controlled T2D, hypertension, and other weight-related comorbidities, with lowered quality of life and emotional health. For reversal of WR, revisional surgery can be effective in some cases but is generally associated with a higher rate of complications than primary bariatric surgery. Isolated dietary, behavioral, and exercise interventions have demonstrated limited efficacy; combined pharmacotherapy and LS intervention have been proven efficient in reducing WR and

improving metabolic dysregulation, reducing the overall risk for complications related to WR and obesity.

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