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DISSERTATION

Endoskopische Sleeve Gastroplastie (ESG) zur Therapie von Krankhaft Adipösen Patienten mit Klinisch Herausfordernden Situationen

Endoscopic Sleeve Gastroplasty (ESG) for the Therapy of Morbidly Obese Patients with Clinical Challenging Situations

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II. Abstract German

Morbid fettleibige Patienten mit klinisch schwierigen Situationen wie schweren, sogar tödlichen präoperativen Komorbiditäten oder mit Superfettleibigkeit, die sich als klinisches Problem für die bestehenden Adipositaschirurgieverfahren erwiesen und bereits zu unbefriedigenden bariatrischen Ergebnissen nach der herkömmlichen Adipositaschirurgie geführt hatten. In jüngster Zeit wurden neuartige bariatrische Therapien, die auf endoskopischen Techniken basieren, entwickelt und als potenzielle alternative und brauchbare Behandlungen für die oben genannten klinischen Situationen angesehen. Dies gilt insbesondere für die endoskopische Sleeve-Gastroplastie (ESG), die bei Patienten mit morbider Adipositas erfolgreich durchgeführt wurde und zufriedenstellende bariatrische Ergebnisse und ein günstiges Sicherheitsprofil aufweist. Daher könnte die klinische Anwendung des ESG-Verfahrens der endgültigen Lösung der oben genannten schwierigen Bedingungen möglicherweise einen großen Schub verleihen.

Ziel unserer Studie war es, das Sicherheitsprofil und die potenzielle Wirksamkeit von ESG bei der Behandlung von krankhaft fettleibigen Patienten mit schwierigen klinischen Situationen zu bewerten. Die demografischen und klinischen Daten der Patienten wurden prospektiv erfasst, die Follow-up-Daten wurden durch regelmäßige ambulante Nachuntersuchungen oder telefonische Befragungen erhoben. Die Hauptergebnisse waren die Erfolgsrate der ESG, die Morbidität nach dem Eingriff und die ESG-bedingte Mortalität sowie die Veränderung von BMI und Gewicht. Das sekundäre Ergebnis war die Remission von mit Adipositas verbundenen Begleiterkrankungen. Alle ESG-Verfahren wurden mit dem Apollo OverStitch-Gerät (Apollo Endosurgery, Austin, Texas, USA) durchgeführt.

Alle in Frage kommenden vierundzwanzig Fälle wurden als Hochrisikofälle eingestuft. Das ESG-Verfahren wurde bei allen eingeschlossenen Fällen erfolgreich durchgeführt, ohne dass es während des ESG-Verfahrens zu unerwünschten Ereignissen kam. Es

wurde nur ein Zwischenereignis nach dem ESG-Verfahren (Magenblutung) gemeldet, während eine verfahrensbedingte Sterblichkeit nicht beobachtet worden war. Im Durchschnitt betrugen der prozentuale Gesamtgewichtsverlust (%TBWL) und der prozentuale Übergewichtsverlust (%EWL) 11,3 % (± 4,7 %) und 25,0 % (± 9,1 %) bzw. 12,2 % (± 8,9 %) und 29,1 % (± 17,9 %) 6 Monate und 1 Jahr nach der ESG. Die mit Adipositas verbundenen Begleiterkrankungen wie gastroösophagealer Reflux, Dyslipidämie, Typ-2-Diabetes und arterielle Hypertonie wurden nach dem ESG-Verfahren verbessert.

Das ESG-Verfahren kann als neuartige bariatrische Therapie für fettleibige Hochrisikopatienten betrachtet werden, da es ein günstiges Sicherheitsprofil und zufriedenstellende bariatrische Ergebnisse aufweist. Die klinischen Anwendungen der ESG könnten auf der Grundlage dieser Studie möglicherweise erweitert werden.

III. Abstract English

Morbidly obese patients with clinical challenging situations like with serious even fatal preoperative comorbidities or with super-obesity, which had emerged as the clinical tough problem for the existing obesity surgeries and had already led to unsatisfactory bariatric outcomes after the conventional obesity surgery. Recently, novel bariatric therapies based on the endoscopic techniques were emerging and considered as potential alternative and useable treatments for the above-mentioned clinical situations. Especially for the endoscopic sleeve gastroplasty (ESG) procedure, which had been successfully performed for patients with morbid obesity and achieved satisfactory bariatric outcomes and favorable safety profile. Hence the clinical application of ESG procedure might potentially provide mighty boosts for the final solution of the above-mentioned challenging conditions.

The purpose of our study was to assess the safety profile and potential efficacy of ESG for the treatment of morbidly obese patients with clinical challenging situations. Demographic and clinical data of patients were prospectively recorded, the follow-up data was acquired through the periodical returning visit in outpatient or the telephone interview. The main outcome measures were the success rate of ESG, post-procedure morbidity and ESG-related mortality, and the alteration of BMI and weight. The secondary outcome was remission of obesity associated comorbid diseases. All ESG procedures were performed based on the Apollo OverStitch device (Apollo Endosurgery, Austin, Texas, USA).

All eligible twenty-four cases were classified as high-risk cases. The ESG procedure had been performed for all included cases successfully, without any adverse event (AE) during the ESG procedure. Only 1 intermediate post-ESG AE (hemorrhage of the stomach) was reported, while procedure-related mortality had not been observed. On average, percent of total body weight loss (%TBWL) and percent of excess weight loss (%EWL) were 11.3% (± 4.7%) and 25.0% (± 9.1%), and 12.2% (± 8.9%) and 29.1%

(± 17.9%) at 6-month and 1-year after ESG, respectively. The obesity associated comorbidities like gastroesophageal reflux, dyslipidemia, type 2 diabetes, and arterial hypertension were improved after the ESG procedure.

The ESG procedure can be considered as a novel bariatric therapy for high-risk obese patients with the favorable safety profile and satisfactory bariatric outcomes. The clinical applications of the ESG could potentially be expanded based on this study.

1. Introduction

In recent decades, obesity has become an increasing epidemic in the population worldwide, which has placed enormous pressure and burdens on our medical system and society[1, 2]. Obesity has very critical effect on the occurrence and development of numerous obesity-associated comorbidities, including serious and even fatal diseases, for instance, hypertension, type-2 diabetes (T2D), obstructive sleep apnea syndrome (OSAS), gastroesophageal reflux disease (GERD), cardio-cerebrovascular diseases and even malignant tumors, ultimately shortening life expectancy and resulting in untimely death[2, 3]. Fortunately, obesity surgeries like adjustable gastric banding (AGB), Roux-en-Y gastric bypass (RYGB), and sleeve gastrectomy (SG) have already been proven and performed as safe, viable and effective therapies for morbid obese patients, the abovementioned surgeries can sustain adequate weight reduction and satisfactory obesity-associated comorbidity remission for patients in the long-term follow-up[4-6] and further lengthen the expected lifespan and mitigate the risk of postoperative mortality of morbidly obese patients compared to conservative obesity therapy[3].

However, except for the satisfactory outcomes of conventional bariatric surgeries for patients with morbid obesity, which had been reported in previous studies, in some clinically challenging situations, for instance, in patients suffered from a high body mass index (BMI= more than 50 kg/m^2) which is including super-obesity and super-super-obesity, in patients with severe comorbid diseases such as cardiovascular risk, or in patients with impenetrable abdomen caused by numerous previous open surgeries or large incisional hernias of the abdominal wall, the existing bariatric surgeries might not be the most appropriate clinical solutions[7-14]. Fortunately, in the last few years, following the rapid development of endoscopic instruments and skills, several kinds of endoscopic bariatric treatments (EBTs) have been successively introduced and successfully performed for patients with morbid obesity and have achieved satisfactory preliminary outcomes, for instance, intragastric balloon (IGB)

insertion, aspiration therapy with the Aspire-Assist device, and endoscopic insertion of the duodenojejunal bypass (DJBS) sleeve (Endobarrier technology)[15]. In view of this, encouragingly, EBT procedures may latently provide novel and alternative solutions for patients with the abovementioned challenging situations.

Among the existing EBT procedures, endoscopic sleeve gastroplasty (ESG) has been considered as an innovative and efficient bariatric procedure for the therapy of patients with morbid obesity that can help patients sustain satisfactory long-term weight reduction. The average percent of total weight loss (%TWL) and the average percent of excess weight loss (%EWL) at 5 years post-ESG can reach 15.9% and 45.3%, respectively[16], while ESG can improve obesity-associated comorbid diseases[17, 18] and provide satisfactory safety profile results[16, 19]. In addition, compared to traditional bariatric surgery, a lower risk of postoperative complications and de novo GERD symptoms and a faster postoperative recovery were observed in patients underwent ESG[20, 21]. Therefore, our research team performed the ESG for treatment of patients with the abovementioned clinically challenging situations, and its safety, viability, and efficacy in these situations has been evaluated and introduced in the published study[22] for the first time.

2. Methodology

2.1 Conception and design of the study

The published study[22] was a pilot clinical study that was approved by the local Institutional Review Board (EA1/193/16) and was performed based on the Helsinki Declaration (1964) and the later amendments of it. Before endoscopic sleeve gastroplasty (ESG) was performed, detailed information on the procedure, such as the clinical indications, the specific operation process, all latent operation risks, and the possible therapeutic effects, was provided to the patients and their families, and informed consents for the ESG procedure were signed by all patients preoperatively.

2.1.1 Participants

In our research group, all admitted patients with morbid obesity were first fully evaluated by the multidisciplinary team and their data were prospectively documented. Among the admitted patients, when traditional bariatric surgeries were contraindicated or inappropriate, which resulted from a high BMI (> 50 kg/m^2), severe or fatal pre-ESG comorbid diseases, or impenetrable abdomen because of a huge incisional hernia of the abdominal wall or a history of numerous previous open surgeries, patients with these conditions were scheduled to receive the ESG procedure. These eligible patients were enrolled in the published study[22], and all included patients were defined as high-risk cases. Meanwhile, if the patients who were morbidly obese refused to undergo ESG, they were excluded from the study. Between 2016 and 2019, twenty-four eligible patients were consecutively enrolled, and none of them were included in other homochronous clinical studies.

The diagnosis of obesity was dependent on the BMI (kg/m^2) value of patients, and the computational formula for BMI value was the weight (kilograms) divided by the height (meters) squared. If the BMI ranged from 18.5 to 24.9 kg/m^2, it was categorized as being in the healthy weight range; if the BMI ranged from 25.0 to <30.0 kg/m^2, it was categorized as overweight; if the BMI ranged from 30.0 to 34.9 kg/m^2, ranged from 35.0 to 39.9 kg/m^2, and ≥ 40.0 kg/m^2, it was categorized as obesity grade I, II, and III,

respectively.

2.1.2 Technique

The clinical consensus of the ESG applied for therapy of high-risk patients with morbid obesity still has not been reached. Therefore, the viability, advantages, and latent risks of performing ESG for each eligible patient who was considered to undergo the ESG procedure was fully and meticulously assessed by our multidisciplinary team before the procedure. However, the final decision for undergoing ESG therapy was made by the patients and their families.

The preliminary experiences and skills of performing ESG for high-risk obese patients were introduced by our research group previously[23]. Furthermore, in this published study[22], all ESG procedures were carried out under general anesthesia and based on the OverStitch™ apparatus of Apollo Endosurgery Inc. And with patients in the supine position and with tracheal intubation. Preventive anti-infectious therapies and deep vein thrombosis (DVT) precautions were routinely provided for all patients. During the procedure, the surgeon and the assistant were both on the left side of the operating table, screen was placed in front of them. Transoral insertion of an overtube device of Apollo Endosurgery Inc. was to protect the esophageal mucosa and maintain good airtightness of the stomach after insufflation with CO_2. Then, after being combined with the OverStitch™ suturing apparatus, a GIF-2TH180 type double-channel gastroscope of Olympus Medical Systems Corp. was inserted into the cavity of stomach and finally reached the gastric antrum.

Multiple endoluminal transmural sutures including five to eight “U”-shaped sutures along with the gastric greater curvature were performed from the level of incisura angularis of the stomach to the esophagogastric junction to finally establish a stricture sleeved stomach while avoiding closure of the upper gastric fundus. For each “U”-shaped mode suture, which was a 2-row mode and included six to eight stitches, the initial row began at anterior gastric wall, with the next stitch on gastric greater curvature

as well as the final stitch positioned on posterior gastric wall. Then, the mode of initial row was repeated contrariwise (posterior gastric wall – gastric greater curvature – anterior gastric wall) in the second row of sutures. Tissue helix device of Apollo Endosurgery Inc. was applied to ensure that continuous transmural stitches were achieved, which was essential for the durability and therapeutic effect of the ESG procedure. The “U” pattern suture was tightened by using the cinching device to bring the gastric wall together. In the procedure’s denouement, an endoscopic examination without the suture device was performed to confirm the optimal shape of the sleeved stomach and ensure that intraprocedural adverse events, such as perforation and hemorrhage, had not occurred. Upper gastrointestinal (UGI) contrast studies were performed for all eligible patients postoperatively. After discharge from the hospital, our multidisciplinary team, which included endocrinologists, pulmonologists, psychiatrists, nutritionists, and rehabilitation therapists, provided health consultations, the specialist treatment, and the professional guidance for all patients when required and finally helped them develop healthy dietary, exercise and living habits.

2.1.3 Data collection

In the published study[22], demographic characteristics and clinical variables of all patients who were enrolled in the study were documented prospectively, including the following: age, sex, history of previous surgeries, pre-ESG height (meters), pre-ESG weight (kilograms) and pre-ESG BMI (kg/m^2), obesity-associated comorbidity (diabetes, hypertension, dyslipidemia, etc.), other comorbidity (heart, renal or respiratory failure, etc.), American Society of Anesthesiologists (ASA) classification, pre-ESG pharmacotherapy, diagnoses, preprocedural Edmonton Obesity Staging System (EOSS) score[24, 25], intraprocedural adverse events (hemorrhage, perforation, etc.), operation time (minutes), time to liquid diet, duration of postprocedural hospital stay (days), postprocedural adverse events and mortality (within 30 days after undergoing ESG).

Our research team routinely obtained the follow-up data of eligible patients via

telephone interviews or periodic return visits in outpatient facilities, which included BMI reduction (△BMI, kg/m^2), changes in weight (△weight, kg), percent of excess weight loss (%EWL), percent of total body weight loss (%TBWL), post-ESG pharmacotherapy, remission of obesity-associated comorbid diseases, and mortality at 1-month, 6-month, and 12-month after ESG. According to the standard lexicon of the American Society for Gastrointestinal Endoscopy (ASGE)[26], postprocedural adverse events (AEs) were normally divided into 4 grades, which were mild, intermediate, serious and fatal, respectively. Ideal weight corresponded to a BMI value of 25.0 kg/m^2, and the difference between preprocedural body weight and ideal weight was the excess weight. The computational formula for %EWL was percent of weight loss compared with excess weight. The calculating formula for %TBWL was percent of weight loss compared with preprocedural body weight.

The therapeutic effect of the ESG procedure on obesity-associated comorbidities was assessed according to the change in pharmacotherapy and the improvement of relevant symptoms after undergoing ESG. Without any change or improvement, the comorbidity was defined as maintained. If the dosage of medicines used was decreased or symptoms were improved, the comorbidity was classified as improved. If drug discontinuance or total remission of symptoms was reported, the comorbidity was defined as resolved.

2.1.4 Outcome measures

In the published study[22], the evaluation of the viability, safety, and effect of the ESG therapy for high-risk patients was the research purpose. Therefore, the success rate (%) of technology, postprocedural AEs and ESG-related mortalities, and alteration of BMI and weight, which were evaluated by △weight (kg), △BMI (kg/m^2), the %TBWL as well as the %EWL, were considered as the primary outcome measures. The improvement of obesity-associated comorbid diseases after undergoing ESG was defined as the secondary outcome measure.

2.2 Analysis of data

The collection and recording of clinical data and the final creation of the informatics database were all performed based on the Microsoft Excel (Microsoft, Redmond, WA) platform. All collected data were imported and statistically analyzed using statistics software SPSS version 22 (IBM) in the published study[22]. In outcomes of descriptive statistics, continuous variables were expressed in the form of median (interquartile range, IQR) and/or mean (± standard deviation, ± SD), while classification variables were reported in the manner of frequency and/or proportion.

3. Results

In the published study[22], the success rate of the endoscopic sleeve gastroplasty (ESG) procedure reached 100% for all high-risk cases, and twenty-four patients consisted of 75.0% men (18 cases) and 25.0% women (6 cases). Among them, the mean age was 55.6 (± 9.2) years old (median: 55.5 (48.0, 59.0) years old). According to the baseline BMI of the patients, 1 (4.2%), 3 (12.5%), and 20 (83.3%) patients were classified as having obesity grade I, grade II, and grade III, respectively. In cases of obesity grade III, 9 patients with BMI > 50 kg/m^2, which was defined as a high BMI. The most prevalent obesity-associated comorbidities were hypertension, OSAS, and T2D, which were reported in 21 (87.5%), 17 (70.8%), and 15 (62.5%) patients, respectively. These were followed by dyslipidemia (n= 8, 33.3%), osteoarthritis (n= 7, 29.2%), obesity hypoventilation syndrome (OHS) (n= 4, 16.7%), depression (n= 4, 16.7%), gastroesophageal reflux disease (GERD) (n= 3, 12.5%), hypothyroidism (n= 2, 8.3%), and hyperuricemia (n= 1, 4.2%) (Figure 1A). For other comorbid diseases, giant abdominal incisional hernia (n= 6, 25.0%), anticoagulation (n= 5, 20.8%) and heart failure (n= 5, 20.8%) were the most common (Figure 1B), and the remaining comorbidities are shown in Figure 1B. The mean number of comorbidities (including obesity-associated comorbidities and other comorbidities) per patient was 5.2 (± 2.1) (median: 5.0 (4.0, 7.0)). Nineteen patients (79.2%) had a history of previous surgeries. Based on the clinical situations of the patients before undergoing ESG procedures, 8 cases (33.3%) were classified as having an EOSS-score of 2, 14 cases (58.3%) were defined as having an EOSS-score of 3, and the remaining 2 cases (8.3%) were defined as having an EOSS-score of 4.

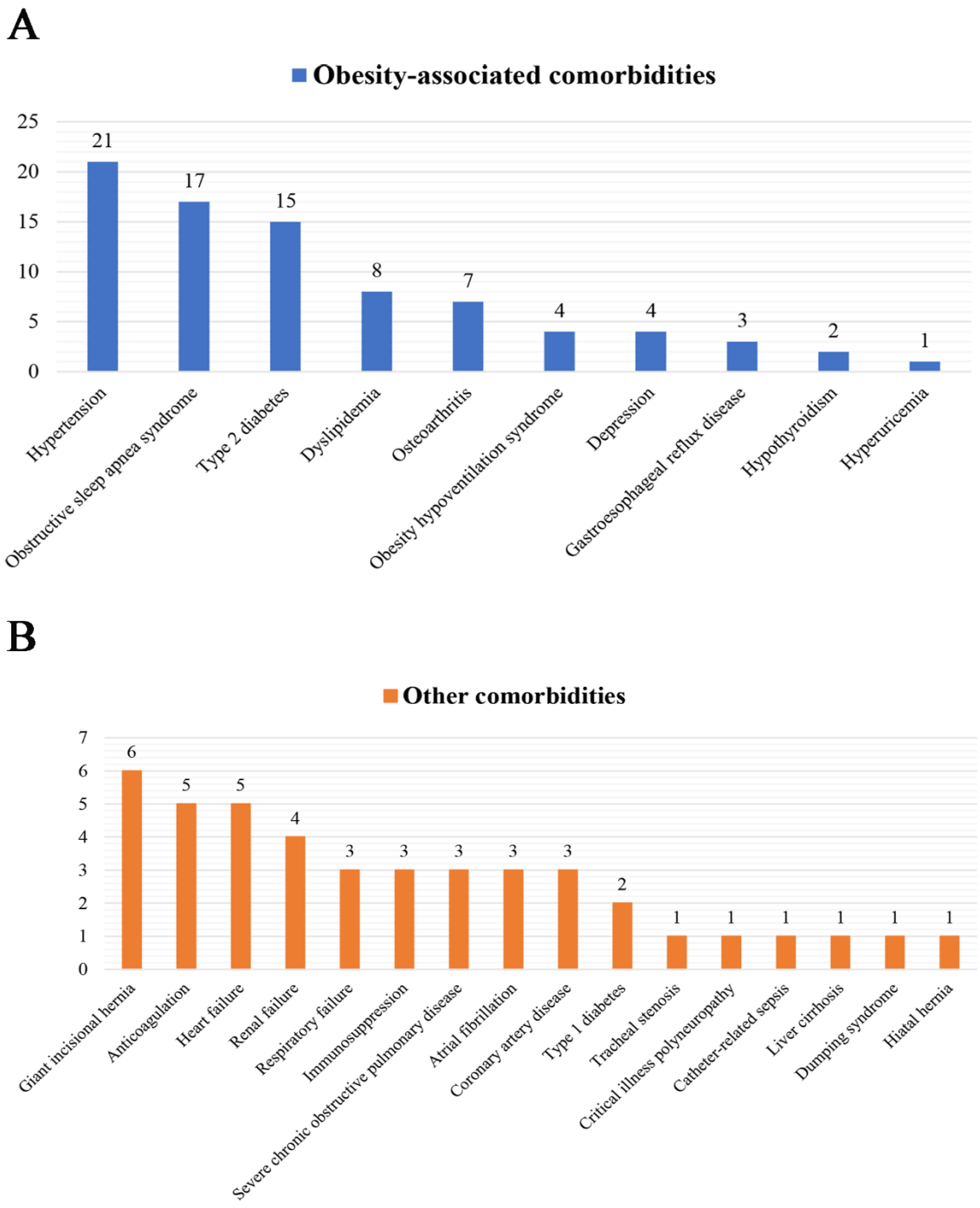

Figure 1. Preprocedural comorbid diseases included obesity-associated comorbid diseases (A) and other comorbid diseases (B).

The high-risk factors for patients who were included in the published study[22] are fully described in Figure 2, which involved having a high BMI (kg/m^2), a severe or fatal pre-ESG comorbidity, an EOSS score ≥ 3 as well as an impenetrable abdomen.

Specifically, a high BMI was classified as super-obesity corresponded to a BMI > 50 kg/m^2 and super-super-obesity corresponded to a BMI > 60 kg/m^2. The EOSS-3 and EOSS-4 scores were both defined as high-risk factors for weight loss surgery because of their higher risk of complications after surgery than the EOSS-0, EOSS-1, and EOSS-2 scores[14]. Furthermore, a giant incisional hernia of the abdominal wall (6 patients) and a history of multiple previous open surgeries (8 patients) separately or collectively contributed to an impenetrable abdomen in 10 patients. Among patients with giant incisional hernias, epigastric and middle abdominal incisional hernias were reported in 4 patients, while hypogastric incisional hernias were reported in 2 patients; one of them had a history of numerous previous open surgeries, and the other had undergone left epigastric and middle abdominal colostomy. Therefore, the implementation of conventional bariatric surgery would be significantly hindered for the abovementioned 10 patients with impenetrable abdomens.

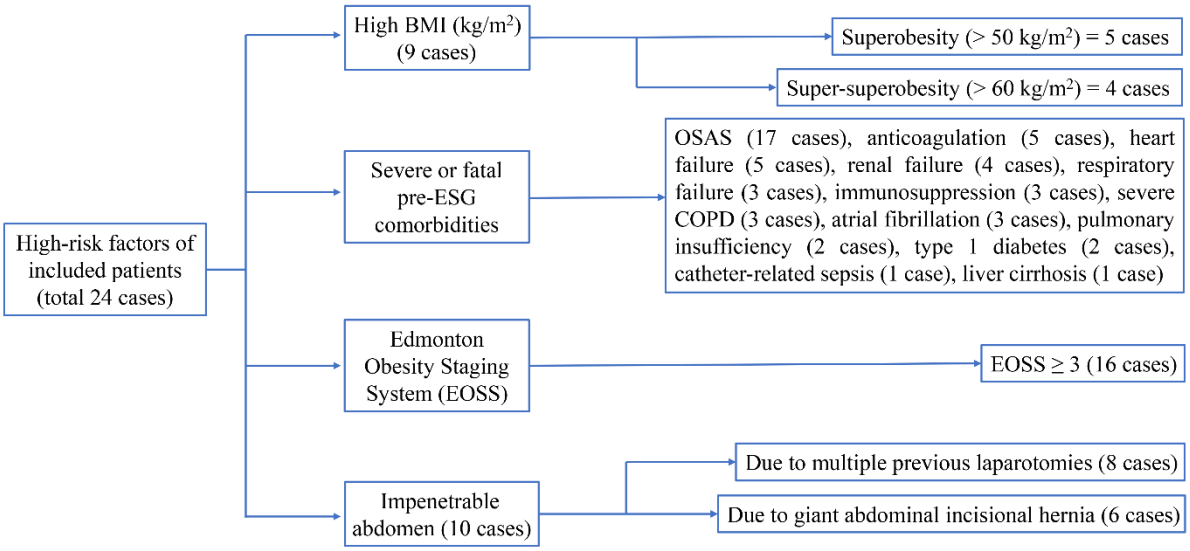

Figure 2. All clinical high-risk factors for included patients.

Adverse events were not observed during the ESG procedure. On average, the duration of the operation was 114.7 (± 26.0) minutes (median: 110.0 (98.0, 129.5) minutes). A fluid diet was provided to patients on the day of the ESG procedure. The average duration of stay after the procedure was 5.5 (± 7.8) days (median: 4.0 (2.0,

5.8) days). After undergoing ESG, mild adverse events (AEs), such as vomiting or queasiness, which did not require further pharmacotherapy, were not systematically documented. One (4.2%) moderate AE was observed: a patient experienced hemorrhage of the stomach 72 hours after the ESG procedure, blood transfusions and endoscopic therapy were performed, and the symptoms were finally completely resolved. After discharge from the hospital, the patient did not experience rebleeding or 30-day readmission. Severe or fatal AEs were not observed, and without ESG procedure associated mortality.

The change trends of weight (kg) and BMI (kg/m^2) are shown in Figure 3A-B. On average, the weights of patients in the pre-ESG period and post-ESG at 1-month, 6-month, and 12-month were 157.9 (± 49.1), 153.5 (± 35.5), 134.1 (± 30.6), and 123.9 (± 37.1) kg, respectively. The mean BMI was 49.9 (± 14.4), 46.4 (± 9.6), 42.3 (± 8.6), and 39.0 (± 6.8) kg/m^2 in the pre-ESG period and post-ESG at 1-month, 6-month, and 12-month, respectively. Meanwhile, the average △ weight (kg), △ BMI (kg/m^2), %TBWL, and %EWL were 16.8 (± 8.2) kg, 5.0 (± 2.3) kg/m^2, 9.3 (± 2.8)%, and 19.1 (± 3.9)% at 1 month postprocedure, 17.9 (± 11.3) kg, 5.6 (± 3.4) kg/m^2, 11.3 (± 4.7)%, and 25.0 (± 9.1)% at 6 months postprocedure, and 17.5 (± 14.6) kg, 5.6 (± 4.6) kg/m^2, 12.2 (± 8.9)%, and 29.1 (± 17.9)% at 12 months postprocedure. The follow-up rates were respectively 45.8% (11 patients), 50.0% (12 patients), and 29.2% (7 patients) at 1-month, 6-month, and 12-month postprocedure.

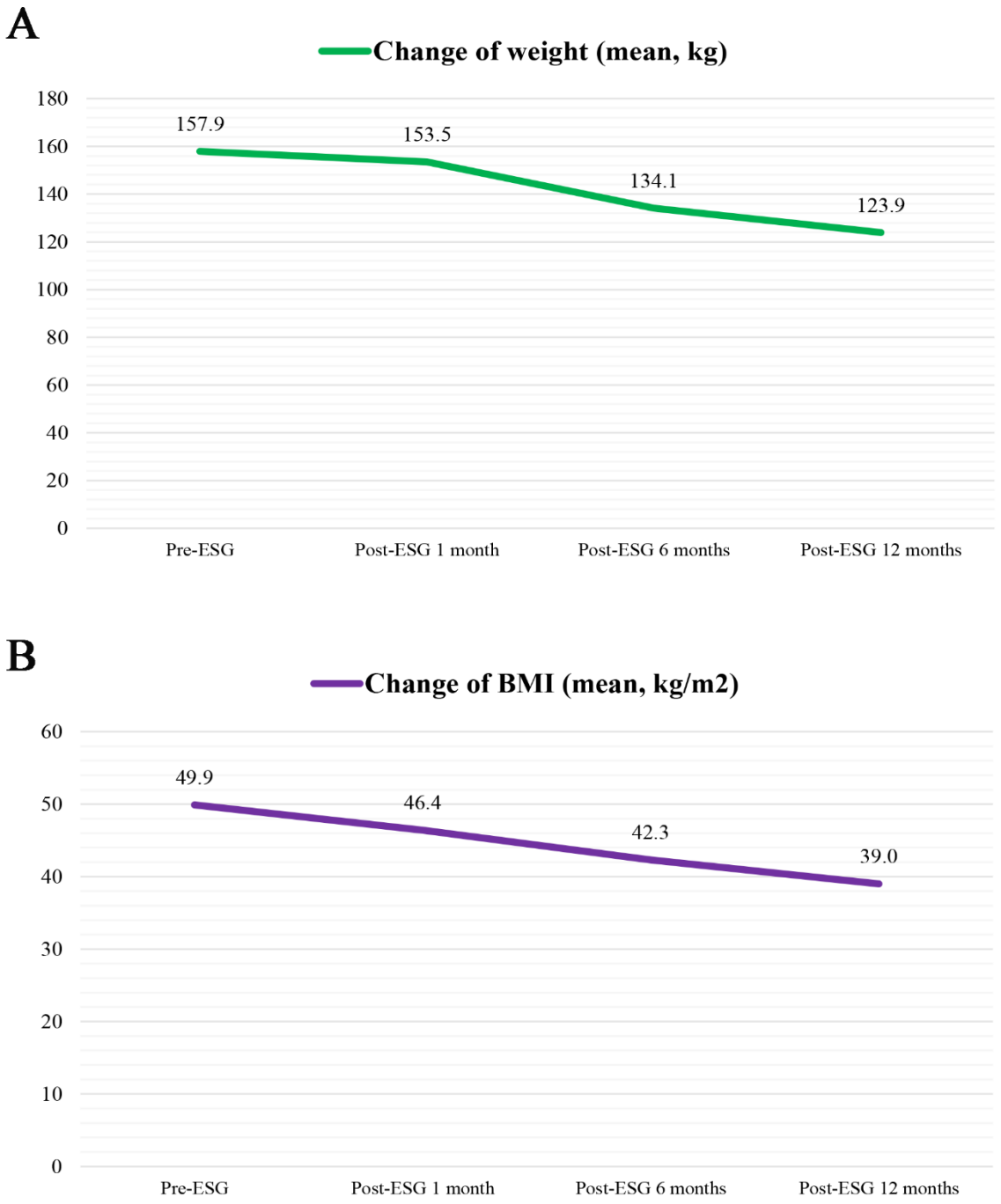

Figure 3. The change trends of weight (kg) (A) and BMI (kg/m^2) (B) after the endoscopic sleeve gastroplasty (ESG) procedure.

Fourteen patients (58%) reported post-ESG remission of obesity-associated comorbidities in the published study[22], half (7 patients) reported post-ESG remission at 6 months after ESG, and the rest (7 patients) reported post-ESG remission at 1 year

after the procedures. Among the comorbidities, obesity was accompanied by hypertension in thirteen cases; 69.2% of the patients (9 patients) reported improvement after the ESG procedure, and the remaining four patients (30.8%) were maintained. Obesity was accompanied by T2D in eight cases, and 1 (12.5%) and 7 (87.5%) patients were reported as having complete resolution and improvements after the ESG procedure, respectively. Obesity was accompanied by dyslipidemia in four patients: 1 (25.0%) patient reported improvement after the procedure, and the remaining three patients (75.0%) were reported as maintained. Obesity was accompanied by GERD in one patient and it was resolved completely after ESG treatment (100%).

4. Discussion

4.1 Bariatric therapies for high-risk obese patients: the long-term predicament

To date, bariatric surgeries are still the only proven therapy that can maintain long-period favorable bariatric outcomes such as sufficient weight reduction and satisfactory resolution of obesity-associated comorbid diseases for patients with morbid obesity. Meanwhile, due to rapid development of surgical equipment and techniques, increasingly normalized and perfect clinical training for surgeons, and comprehensive improvement of perioperative therapeutic and care strategies, have significantly increased the safety profile of bariatric surgeries for therapy of morbidly obese patients, and mortalities of bariatric and metabolic surgeries have decreased to lower than 0.5% in recent years[12]. However, despite the abovementioned superior outcomes of bariatric surgeries, it is worth noting that inferior or unsatisfactory outcomes of weight loss surgeries had been reported in some special clinical situations, such as patients suffered from high BMI (corresponded to a BMI > 50 kg/m^2), patients suffered from risks of pulmonary embolus, or patients with severe or even fatal comorbid diseases such as hypertension, severe venous stasis disease, hepatic diseases, cardiac failure, and pulmonary dysfunction[7, 9, 11-13, 27, 28].

For patients with high BMI, a study with more than ten years follow-up demonstrated that patients suffered super-obesity (≥ 50.0 kg/m^2) lost weight more quickly after bariatric surgery and regained weight faster after achieving nadir weight than morbidly obese patients (corresponded to a BMI < 50.0 kg/m^2). Therapeutic failure was determined when the ultimate BMI was ≥ 35.0 kg/m^2 and ≥ 40.0 kg/m^2 for patients suffered morbid obesity and patients suffered super-obesity, respectively. Failure rate of patients suffered super-obesity (34.9%) was higher than that of patients suffered morbid obesity (20.4%) at least 10 years after the gastric bypass procedure[7]. In another study with a large sample size (n= 28,634, including 20,797 patients suffered morbid obesity and 7837 patients suffered super-obesity), compared with morbidly obese patients, super-obese patients with longer operation times and longer durations of hospital stay, and had a heightened risk of postoperative adverse events (e.g.,

wound complications and septic shock) and thirty-day mortality[9]. Similar results have also been reported in patients suffered super-super-obesity (corresponded to a BMI > 60.0 kg/m^2) when compared to morbidly obese and/or superobese patients[8, 10, 11].

For patients with severe or fatal comorbid diseases. Mosko et al.[29] reported that the mortality rates of patients suffered from compensated cirrhosis (0.9%) and decompensated cirrhosis (16.3%) were higher than those of noncirrhotic patients (0.3%) after bariatric surgeries (P< 0.05). In detail, compared to the noncirrhotic group, larger than twofold and more than 20-fold greater rates of mortality were observed in the compensated and decompensated cirrhotic groups, respectively, and the differences were both statistically significant. A longer mean duration of hospital stay was also reported in the compensated and decompensated cirrhotic groups. In a case control study that included 16 cirrhotic patients (Child A) and forty-eight noncirrhotic patients (match group), the results demonstrated that compared with the noncirrhotic group, the cirrhotic patients had a heightened risk of postoperative complications, especially for complications which were classified as the Clavien-Dindo ≥III[30]. Meanwhile, a systematic review was performed by Lazzati et al.[31] to assess safety and efficacy of bariatric surgery for therapy of candidates for liver transplantation (LT) and patients after LT. Higher mortality, morbidity and rate of reoperation were observed in patients with these conditions, which were 10.7%, 23.2%, and 12.2%, respectively. In addition, Benotti et al.[12] demonstrated that obese patients with cardiac failure, hepatic diseases, and pulmonary insufficiency had a significantly increased risk of post-RYGB thirty-day mortality.

In view of these findings, first, several risk prediction models have been previously established and performed to grade the surgical risk of obese patients perioperatively, especially before bariatric surgery. For example, DeMaria and colleagues established and validated a mortality risk score for the gastric bypass procedure, which included five parameters (age older than forty-five years, male sex, and risks of pulmonary embolus, arterial hypertension, and super-obesity (≥ 50 kg/m^2)), and one point was

given to each parameter. The mortality risk was classified as low, moderate, and high risk grade based on the final score for each patient, which corresponded to Class A, B, and C, respectively[13, 32]. Moreover, the EOSS score was proposed according to the evaluation of the severity of obesity-associated diseases and functional conditions, which included a score of 0-4 and could be used to predict complications and mortalities after bariatric surgery[14, 25]. The aim was to optimize surgical selection, guide the implementation of individualized therapy for patients with different degrees of risk, and improve perioperative care strategies.

Second, some experienced surgeons have already tried to perform traditional bariatric surgeries such as SG procedure for therapy of high-risk patients with morbid obesity and have achieved satisfactory preliminary outcomes. Hawkins et al.[33] demonstrated that laparoscopic SG was a safe as well as effective weight-loss therapy for candidates for cardiac transplantation who had left ventricular assist devices, which could maintain adequate weight loss, improve cardiac function, and subsequently enhance patients' opportunities to undergo heart transplantation. Meanwhile, Rebibo et al.[34] reported that compared with patients without cirrhosis, patients with cirrhosis who were classified as Child A did not have increased postoperative mortalities and morbidities and achieved comparable weight reduction after sleeve gastrectomy. However, the existing relevant studies are still limited to small sample sizes and methodologies, so the safety and therapeutic effect of traditional weight-loss surgeries for high-risk patients with morbid obesity are still controversial. Subsequently, relevant randomized controlled trials (RCTs) and/or large sample prospective studies are needed to provide more reliable clinical evidence.

Third, because of the rapid advancement of endoscopic skills and instruments, clinical cooperation between bariatric surgeons and endoscopists is becoming increasingly close. Different kinds of endoscopic techniques have been successively applied for therapy of high-risk patients with morbid obesity. Younus et al.[35] reported that high-risk obese patients attained satisfying weight reduction and obesity-associated

comorbidity remission 12 months after the placement of an endobarrier (duodenal-jejunal bypass sleeve was inserted via endoscopy). Meanwhile, endobarrier placement combined with subsequent bariatric surgery had a shorter operation time of the bariatric surgery, shorter duration of stay in the intensive therapy unit, and fewer serious complications for high-risk patients than bariatric surgery alone. Intragastric balloon (IGB) insertion was also performed for treatment of high-risk super-obese patients. Satisfactory bariatric outcomes (including changes in BMI and body weight, and remission of obesity-associated comorbidities) were observed in previous studies, especially when IGB insertion was combined with subsequent bariatric surgery[36-38]. Therefore, endoscopic bariatric treatment can be the latent solution for high-risk obese patients, but higher-level and more reliable research evidence should be provided in subsequent prospective studies or randomized controlled trials with large sample sizes.

Given the above information, despite the satisfactory preliminary outcomes of some clinical studies of high-risk obese patients, the most appropriate bariatric treatment for high-risk obese patients is still debatable and under exploration to date.

4.2 Endoscopic sleeve gastroplasty for high-risk patients: An evidence-based and effective procedure?

The endoscopic sleeve gastroplasty (ESG) procedure with multiple transmural sutures, based on the Apollo OverStitch suturing system that was initially introduced in 2013 can significantly decrease the gastric volume by creating a sleeved stomach[39]. Moreover, after the ESG procedure, the sensitivity of insulin was obviously improved, the satiation of obese patients was obviously enhanced, and the emptying of the stomach was obviously postponed for solid food but not for liquid meals. Meanwhile, ESG could obviously reduce fasting ghrelin and ghrelin levels after a meal[40]. The abovementioned significant changes in physiology and endocrine function are now known causes of satisfactory weight reduction and resolution of obesity-associated comorbid diseases after ESG therapy.

ESG was idealized as a method aiming to be similar to the SG procedure. According

to previous studies comparing ESG and SG, it is noteworthy that first, although SG procedure led to superior weight reduction compared to ESG for all obese patients, statistically meaningful differences of weight reduction were not discovered between SG and ESG procedures for patients whose BMI were lower than 40 kg/m^2[20, 41]. Second, patients who underwent ESG procedures had an obviously lower risk of postoperative adverse events and de novo GERD symptoms and a shorter duration of hospital stay than patients who underwent the SG approach[20, 41]. After SG, the incidences of the Barrett's esophagus, the esophagitis, and the symptomatic gastroesophageal reflux increased to 18.8%, 41.0%, and 76.0%, respectively, ≥ 5 years after the SG procedure[42], which has not been observed in existing studies of ESG. Finally, the ESG procedure has other advantages compared to the SG procedure. For example, ESG is a scarless procedure, and the complete anatomical structure and nerve and blood vessels of the stomach can all be preserved after ESG, which can not merely decrease the risk of postoperative adverse events, but retain the possibility for the restoration or reoperation of the stomach[39]. Meanwhile, intragastric balloon (IGB) insertion has been one of the most commonly used endoscopic weight-loss treatments all over the world, the safety and efficacy of which has been well proven for patients with morbid obesity[43]. Compared with IGB treatment, patients who underwent the ESG procedure achieved longer sustained and obviously superior weight reduction and had a lower risk of postprocedural complications[43, 44].

In view of these findings, the ESG procedure can be the latently suitable bariatric therapy for the high-risk obese patient population. Previously, relevant studies have reported that the prevalence of adverse events (AEs), which were classified as intermediate and serious after the ESG procedure, was < 3%, including pulmonary embolism, pneumothorax, leakage, perigastric fluid collection, and hemorrhage of the upper digestive tract; the latter two were the most frequent post-ESG intermediate and serious AEs, and ESG-associated mortalities had not yet been observed. The safety profile and viability of the ESG procedure for morbidly obese patients have already been well proven in previous relevant studies[16, 19, 45-47]. Similar results have been

observed in our published study[22]. In the present study[22], all high-risk patients had successfully undergone ESG procedures, and intraoperative adverse events were not observed in all cases. Meanwhile, only one (4.2%) moderate post-ESG adverse event, hemorrhage of the upper digestive tract, was reported; specifically, the patient was required to have and was waiting for a cardiac transplant, had atrial fibrillation and received periodic anticoagulant therapies before undergoing ESG. After receiving clinical therapies, the hemorrhage was completely resolved and without relapse. Possibly, the anticoagulation situation of this patient increased the risk of bleeding after the ESG procedure. In view of this, the safety profile of the implementation of ESG procedures in the published study was favorable and acceptable[48].

Normally, patients are discharged from the hospital on the same day as their ESG procedures, according to previous studies[45-47, 49]. However, a longer duration of hospital stay was observed in the present study[22] because all included cases were high-risk obese patients, with obesity accompanied by several kinds of and serious pre-ESG comorbid diseases, most of whom should be given clinical therapies in the intensive care unit (ICU) postoperatively. Meanwhile, some included patients had already been treated in the ICU with hemodynamic and/or cardiopulmonary support before ESG procedure.

Satisfactory and optimal bariatric outcomes, such as reduction in weight and BMI after undergoing ESG, have already been previously reported. For short-term bariatric outcomes, Barrichello et al.[47] showed that after the ESG procedure, the average %TBWL and %EWL were 14.25% ± 5.26% and 56.15% ± 22.93% at six months and were 15.06% ± 5.22% and 59.41% ± 25.69% at twelve months. In another multicenter study, on average, weight loss, BMI reduction, %TWL, and %EWL at six months postprocedure were 16.4 ± 10.7 kg, 5.6 ± 3.2 kg/m^2, 14.9% ± 6.1%, and 50.3% ± 22.4%, respectively[46]. A meta-analysis study of ESG came up with similar results, the average amalgamative %TWL and %EWL were 14.86% and 55.75% at six months postprocedure and 16.43% and 61.84% at 1 year postprocedure[19]. For long period

bariatric outcomes, according to a meta-analysis research by Singh et al.[19], mean %TWL and %EWL were 20.01% and 60.40% at two years after the ESG procedure, respectively. In addition, after the five-year follow-up, Sharaiha and colleagues observed that the mean %TBWL and mean %EWL were 14.9% and 45.1% at three years post-ESG and 15.9% and 45.3% at five years after the ESG procedure[16].

In view of the results in previous relevant studies, the bariatric outcomes of the present research[22] may latently be thought to be suboptimal. It is worth noting that first, the present study included patients suffered high body mass index (corresponded to a BMI > 50 kg/m^2), and patients suffered from several kinds of severe and even fatal comorbid diseases; therefore, clinical success and efficacy of ESG therapy should not be assessed based on previous evaluation criteria[45, 46, 48]. Second, the purpose of reducing the weight and BMI of patients with large incisional hernias of the abdominal wall and patients who were required to have and waiting for cardiac and renal transplant operations was to decrease the latent risk of follow-on herniorrhaphy and organ transplant surgery. Third, for most high-risk obese patients in this study[22], the ESG procedure was the only viable and latent effective bariatric therapy under their circumstances. Finally, the ESG procedure could be performed as the first-step bariatric therapy for some high-risk obese patients and provide them with opportunities to receive subsequent surgical bariatric treatments when their clinical situations have been improved after ESG procedure[23]. Hence, in the published study[22], after ESG therapy, the included patients could benefit from any extent of reduction in BMI and weight, which could not be realized or obtained via conventional noninvasive bariatric treatments alone. Thus, clinical success after ESG in our study was defined as obtaining any extent of reduction in BMI and weight. Meanwhile, the average BMI and weight significantly decreased to 42.3 kg/m^2 and 134.1 kg, respectively, half a year after ESG and to 39.0 kg/m^2 and 123.9 kg, respectively, one year post-ESG in the published study[22].

In addition to alterations in BMI and body weight, remission of obesity-associated comorbid diseases was another important evaluation index of therapeutic effect of ESG therapy for morbidly obese patients in short- and long-period of time. The satisfactory improvement and resolution of obesity related comorbidities after ESG for morbidly obese patients have been observed in previous studies[17, 18]. Similar outcomes were observed in the present study, which showed that ESG therapy could still provide satisfying improvement of metabolic comorbid diseases such as gastroesophageal reflux, T2D, arterial hypertension and dyslipidemia for high-risk obese patients[22].

Last but not the least, inspiringly, new bariatric therapies, such as the hypodermic injection of semaglutide, have been introduced and successfully applied for the therapy of patients with obesity, and satisfactory preliminary bariatric outcomes and favorable safety profiles have been observed and reported previously[50]. In view of these findings, pharmacotherapy using semaglutide might latently provide a novel and noninvasive clinical solution for obese patients with high-risk clinical factors included in our published study[22]. However, some existing barriers still need to be solved. First, the clinical application of semaglutide for obesity in German medical centers has not yet been approved. Moreover, the viability, safety profile, and therapeutic effect of clinical application of semaglutide for the therapy of obese patients with high-risk clinical factors still haven't been comprehensively assessed, which should be performed in subsequent relevant studies. In addition, our research group will subsequently continue to explore novel, viable and effective bariatric therapies for high-risk obese patients in an attempt to finally solve the abovementioned long-term clinical predicament.

Limitations were inevitable for the published study[22]. Primarily, the sample size of the study was small; hence, more cooperating medical centers and eligible patients could be included in the subsequent studies. Second, this was a pilot clinical study, and the comparison between the ESG procedure and novel pharmacotherapy or other

endoscopic bariatric therapies or surgical bariatric operations for the therapy of high-risk obese patients should be performed in subsequent studies. Finally, the follow-up time in our study only lasted for 1 year. Bariatric outcomes such as changes in weight and BMI and obesity-associated comorbidity remission, and safety profiles such as postprocedural adverse events and mortality of the ESG treatment for high-risk obese patients, should be observed and assessed for a longer follow-up time in future studies.

In conclusion, the most appropriate bariatric therapy for morbidly obese patients with clinically challenging situations, such as patients with high BMI, those with numerous and serious or even life-threatening preoperative comorbid diseases, those with large incisional hernias of the abdominal wall, or those with a history of numerous previous abdominal open surgeries, is still under exploration. The ESG procedure, as a new endoscopic bariatric therapy, has provided a viable and safe clinical solution with favorable therapeutic effect for patients in abovementioned conditions.

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6. Affidavit

Statutory Declaration

“I, [Renjie, Li], by personally signing this document in lieu of an oath, hereby affirm that I prepared the submitted dissertation on the topic [Endoskopische Sleeve Gastroplastie (ESG) zur Therapie von Krankhaft Adipösen Patienten mit Klinisch Herausfordernden Situationen; Endoscopic Sleeve Gastroplasty (ESG) for the Therapy of Morbidly Obese Patients with Clinical Challenging Situations], independently and without the support of third parties, and that I used no other sources and aids than those stated.
All parts which are based on the publications or presentations of other authors, either in letter or in spirit, are specified as such in accordance with the citing guidelines. The sections on methodology (in particular regarding practical work, laboratory regulations, statistical processing) and results (in particular regarding figures, charts and tables) are exclusively my responsibility.

[In the case of having conducted your doctoral research project completely or in part within a working group:] Furthermore, I declare that I have correctly marked all of the data, the analyses, and the conclusions generated from data obtained in collaboration with other persons, and that I have correctly marked my own contribution and the contributions of other persons (cf. declaration of contribution). I have correctly marked all texts or parts of texts that were generated in collaboration with other persons.

My contributions to any publications to this dissertation correspond to those stated in the below joint declaration made together with the supervisor. All publications created within the scope of the dissertation comply with the guidelines of the ICMJE (International Committee of Medical Journal Editors; www.icmje.org) on authorship. In addition, I declare that I shall comply with the regulations of Charité – Universitätsmedizin Berlin on ensuring good scientific practice.

I declare that I have not yet submitted this dissertation in identical or similar form to another Faculty.

The significance of this statutory declaration and the consequences of a false statutory declaration under criminal law (Sections 156, 161 of the German Criminal Code) are known to me.”

Date Signature

Declaration of your own contribution to the publication

[Renjie Li] contributed the following to the below listed publications:

Publication: Endoscopic Sleeve Gastroplasty (ESG) for High-Risk Patients, High Body Mass Index (> 50 kg/m^2) Patients, and Contraindication to Abdominal Surgery.
Renjie Li, Wilfried Veltzke-Schlieker, Andreas Adler, Maximilian Specht, Wael Eskander, Mahmoud Ismail, Harun Badakhshi, Manoel Passos Galvao, Ricardo Zorron
Obesity Surgery (the official journal of the International Federation for the Surgery of Obesity and metabolic disorders (IFSO))
Submitted and accepted year: 2021

Contribution (please set out in detail):
In the published study, Renjie Li was responsible for study conception and design under the supervision of Ricardo Zorron. Renjie Li systematically searched and reviewed all relevant literatures and combined with conditions of clinical practices, finally proposed research idea and developed the study protocol and research plan, which were all approved by Harun Badakhshi, Ricardo Zorron and Mahmoud Ismail. Renjie Li prospectively collected and documented the demographic and clinical data of all eligible patients. After that, Renjie Li asked some colleagues, Maximilian Specht and Wael Eskander, to call the patients for the last follow-up. Meanwhile, Renjie Li achieved the follow-up information via the regular outpatient visit of some included patients in the medical center with the help of Ricardo Zorron. Renjie Li prepared the plan of statistical analysis and discussed it with Wilfried Veltzke-Schlieker, Andreas Adler, and Ricardo Zorron. Renjie Li performed all statistical analyses by using the SPSS version 22.0 statistical software (IBM Corporation, Armonk, NY, USA) and prepared the description of the statistical method. Renjie Li formulated tables 1, 2, and 3 in the Microsoft Office Word based on the demographic and clinical characteristics and the follow-up outcomes of all included patients. Meanwhile, Renjie Li created figures 1, 2, 3, and 4 by using the Microsoft Office PowerPoint and the Photoshop software (CS6 version, Adobe). The process and results of statistical analyses and all tables and figures which were involved in this study were carefully checked by Wilfried Veltzke-Schlieker, Andreas Adler, and Ricardo Zorron. Renjie Li modified all tables and figures based on advices and comments from co-authors. Finally, Renjie Li wrote the original draft of the manuscript and made the critical revision of the manuscript based on comments from Manoel Passos Galvao and Ricardo Zorron. The final approval of the manuscript and submission to the "*Obesity Surgery*" were made by all authors.

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Signature, date and stamp of first supervising university professor / lecturer

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Signature of doctoral candidate

7. Excerpt of the Journal Summary List

Journal Data Filtered By: **Selected JCR Year: 2019** Selected Editions: SCIE,SSCI
Selected Categories: **"SURGERY"** Selected Category Scheme: WoS
Gesamtanzahl: 210 Journale

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
1	JAMA Surgery	8,471	13.625	0.038280
2	ANNALS OF SURGERY	50,639	10.130	0.061400
3	JOURNAL OF NEUROLOGY NEUROSURGERY AND PSYCHIATRY	30,621	8.234	0.028510
4	JOURNAL OF HEART AND LUNG TRANSPLANTATION	12,465	7.865	0.028140
5	ENDOSCOPY	10,838	7.341	0.015620
6	AMERICAN JOURNAL OF TRANSPLANTATION	25,598	7.338	0.046240
7	BRITISH JOURNAL OF SURGERY	23,036	5.676	0.027310
8	EUROPEAN JOURNAL OF VASCULAR AND ENDOVASCULAR SURGERY	9,932	5.328	0.013510
9	Hepatobiliary Surgery and Nutrition	939	5.296	0.002520
10	AMERICAN JOURNAL OF SURGICAL PATHOLOGY	19,940	4.958	0.020820
11	NEUROSURGERY	29,977	4.853	0.021690
12	Digestive Endoscopy	2,867	4.774	0.006000
13	JOURNAL OF THE AMERICAN COLLEGE OF SURGEONS	16,886	4.590	0.026130
14	JOURNAL OF BONE AND JOINT SURGERY-AMERICAN VOLUME	45,256	4.578	0.038360
15	LIVER TRANSPLANTATION	9,816	4.570	0.012610
16	Journal of NeuroInterventional Surgery	5,583	4.460	0.015900
17	JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY	28,491	4.451	0.034300

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
18	CLINICAL ORTHOPAEDICS AND RELATED RESEARCH	38,340	4.329	0.030260
19	ARTHROSCOPY-THE JOURNAL OF ARTHROSCOPIC AND RELATED SURGERY	16,791	4.325	0.020530
20	Bone & Joint Journal	6,764	4.306	0.021970
21	TRANSPLANTATION	24,561	4.264	0.029910
22	PLASTIC AND RECONSTRUCTIVE SURGERY	39,008	4.209	0.029680
23	Journal of Hepato-Biliary-Pancreatic Sciences	3,686	4.160	0.005640
24	World Journal of Emergency Surgery	1,483	4.100	0.002940
25	ANNALS OF SURGICAL ONCOLOGY	29,538	4.061	0.044180
26	DISEASES OF THE COLON & RECTUM	14,061	3.991	0.012380
27	JOURNAL OF NEUROSURGERY	36,589	3.968	0.027880
28	EJSO	9,499	3.959	0.016680
29	JAMA Otolaryngology-Head & Neck Surgery	3,492	3.848	0.012300
30	Surgery for Obesity and Related Diseases	6,756	3.812	0.013780
31	Aesthetic Surgery Journal	4,118	3.799	0.006000
32	JAMA Facial Plastic Surgery	1,216	3.787	0.003300
33	Neurosurgical Focus	7,703	3.642	0.011260
34	ANNALS OF THORACIC SURGERY	35,221	3.639	0.040380
35	EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY	16,682	3.486	0.025820
36	OBESITY SURGERY	13,608	3.412	0.019160

2

Selected JCR Year: 2019; Selected Categories: "SURGERY"

8. Appendix

Publication: Endoscopic Sleeve Gastroplasty (ESG) for High-Risk Patients, High Body Mass Index (> 50 kg/m^2) Patients, and Contraindication to Abdominal Surgery.

Li R, Veltzke-Schlieker W, Adler A, Specht M, Eskander W, Ismail M, Badakhshi H, Galvao MP, Zorron R. Obes Surg. 2021 Aug;31(8):3400-3409.

doi: 10.1007/s11695-021-05446-2. Epub 2021 Apr 27.

Publication: Endoscopic Sleeve Gastroplasty (ESG) for High-Risk Patients, High Body Mass Index (> 50 kg/m^2) Patients, and Contraindication to Abdominal Surgery.

Li R, Veltzke-Schlieker W, Adler A, Specht M, Eskander W, Ismail M, Badakhshi H, Galvao MP, Zorron R. Obes Surg. 2021 Aug;31(8):3400-3409.

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https://doi.org/10.1007/s11695-021-05446-2

9. Curriculum Vitae

My curriculum vitae does not appear in the electronic version of my paper for reasons of data protection.

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10. Publications

1. Feng X, **Li R**, Zhang P, Chen T, Qiu H, Zhou Y, Du C, Yin X, Pan F, Zheng G, Sun X, Yu J, Chen Z, Zhao Y, Liu X, Li J, Zhang B, Zhou Y, Huang C, Zhou Z, Li G, Tao K, Li Y. Current status of surgical treatment of gastric gastrointestinal tumors: a national multi-center retrospective study. Zhonghua Wei Chang Wai Ke Za Zhi. 2016 Nov 25;19(11):1258-1264. Impact Factor: 0 (2016)

2. Zheng J, **Li R**, Qiu H, Chen T, Zhou Y, Huang C, Li G, Zhou Z, Li Y. Tumor necrosis and >20 mitoses per 50 high-power fields can distinguish 'very high-risk' and 'highest-risk' within 'high-risk' gastric gastrointestinal stromal tumor. Future Oncol. 2018 Mar;14(7):621-629. Impact Factor: 2.279 (2018)

3. Hu W, Zheng C, **Li R**, Feng X, Zheng G, Zheng Z, Xiong W, Lin G, Zhou Y, Wang W, Zhao Y, Li Y. Retroperitoneal Extragastrointestinal Stromal Tumors Have a Poor Survival Outcome: A Multicenter Observational Study. Cancer Manag Res. 2020 Oct 23;12:10491-10504. Impact Factor: 3.983 (2020)

4. **Li R**, Ismail M, Badakhshi H, Zorron R. Intragastric single-port surgery (IGS) for gastric endophytic gastrointestinal stromal tumor (GIST): A novel surgical treatment. Surg Oncol. 2020 Dec;35:12-13. Impact Factor: 3.270 (2020)

5. Badakhshi H, Wang ZM, **Li RJ**, Ismail M, Kaul D. Survival and Prognostic Nomogram for Primary Gastrointestinal Melanoma (PGIM): A Population-based Study. Anticancer Res. 2021 Feb;41(2):967-974. Impact Factor: 2.482 (2020)

6. **Li R**, Veltzke-Schlieker W, Adler A, Ismail M, Badakhshi H, Zorron R. Intragastric Single-Port Surgery: An Innovative and Multipurpose Technique for the Therapy of Upper Digestive Tract Lesions. Surg Innov. 2021 Apr 29:15533506211015386. Impact Factor: 2.058 (2020)

7. **Li R**, Veltzke-Schlieker W, Adler A, Specht M, Eskander W, Ismail M, Badakhshi H, Galvao MP, Zorron R. Endoscopic Sleeve Gastroplasty (ESG) for High-Risk

Patients, High Body Mass Index (> 50 kg/m^2) Patients, and Contraindication to Abdominal Surgery. Obes Surg. 2021 Aug;31(8):3400-3409. Impact Factor: 4.129 (2020)

11. Acknowledgements

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