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Laparoscopic organ-preserving gastric resection improves the quality of life in stromal tumor patients. An Observational Study with 23 Patients

AIM*: The aim of this study is to investigate whether organ preserving gastrectomy (OPG) would yield a greater ability to save more tissue and functions of the stomach and eventually provide better quality of postoperative life (QoPL) for patients with primary gastric gastroinstestinal stromal tumor (PG-GIST).*
MATERIAL AND METHODS: *A retrospective analysis of 23 consecutive patients with PG-GIST who underwent laparoscopic conventional surgery and OPG from June 2008 to December 2016 was performed. Gastrointestinal quality of life index (GIQLI), the area of tumor-free tissue (TFT), body mass index, and postoperative complications were recorded.*
RESULTS: *Both first- and sixth-month GIQLI scores (mean = 105.4 ± 9.5 and 117.0 ± 11.1, respectively) were significantly higher than baseline scores (mean = 100.9 ± 10.2) of the study population (z = –3.32 and –3.86, p = 0.001 and 0.0001, respectively). GIQLI scores were inversely related to TFT area (r = –0.635, p = 0.001). Linear regression analysis revealed 0.130 decrease in GIQLI scores at 6 months each cm2 of removed TFT area.*
Conclusion: Laparoscopic OPG seems to be useful in terms of oncologic safety, minimizing the excessive resection of TFT and maximizing the gastric remnant, thereby improving the QoPL of the patients.

KEY WORDS: Function-preserving surgery, Gastric stromal tumor, GIST, GIQLI, Laparoscopic gastrectomy

Introduction

Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumor of the gastrointestinal tract [1,2], and the stomach is the most commonly affected organ in up to 55.6% [3,4] of patients. Complete surgical resection with adequate safety margins is still the only potentially curative treatment for primary gastric GIST (PG-GIST) [5], and lymph node dissection is usually unnecessary because lymph node involvement is very rare [2,6]. These features make the PG-GIST very favorable for laparoscopic surgery. Although tearing of the pseudocapsule during surgery may result in increased risk for recurrence and decreased survival [4,5,7], the feasibility and safety of minimally invasive surgery have been well established [2,8-10]. Laparoscopic surgical treatment of GISTs has experienced a rapid and major evolutionary process and, currently, it is being advocated as a standard approach for gastric GISTs irrespective of size or location [9-14]. Furthermore, estimated 5-year and 10-year recurrence-free survival rates were found to be 70.5% and 62.9%, respectively [4].
Consequently, considering the oncologic properties of the tumor, an ideal laparoscopic PG-GIST surgery should

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follow oncologic principles and achieve a function and organ-preserving gastrectomy (OPG) with the aim of better quality of postoperative life (QoPL) at the same time [2,7-9,15]. Although there is no single accepted definition, the concept of OPG can be defined as a tailoring gastric resection to avoid post-gastrectomy syndrome, gastric stasis, reflux disease, or a narrowness of the lumen due to excessive gastric resection, or injury to pyloric or lower esophageal sphincter complex or the vagus nerve and its branches [16]. OPG was originally prescribed for the treatment of peptic ulcers with satisfactory results [17], it has since been further elaborated to preserve gastric function and maintain a better QoPL in patients with early gastric cancer [16,18-21].

Because we believed that this concept can be applied in laparoscopic PG-GIST surgery, we conducted a study to investigate the effect of laparoscopic OPG on the QoPL of the patients with PG-GIST. We hypothesized that OPG would yield a greater ability to save more tissue and functions of the stomach and eventually better the QoPL of patients. Therefore, as the more gastric tissue protected during laparoscopic OPG, the QoPL of the patients with PG-GIST would be better, conversely resection of more gastric tissue would worsen the QoPL.

Materials and Methods

Study Design and Setting

A retrospective, single-center and single-arm observational analytic study was conducted to investigate whether the amount of removed gastric tissue during OPG would associate to the postoperative quality of life of the patients with primary gastric GIST (PG-GIST). Between June 2008 and December 2016, twenty and three consecutive patients with PG-GIST who were admitted or referred to the center and underwent laparoscopic resection by the author experienced in advanced laparoscopic surgery (MK) were included in the study. To test the hypothesis, the gastrointestinal quality of life index (GIQLI) scores, the area of tumor-free tissue (TFT, cm^2), BMI, and early and late complications of the patients were analyzed. In this ongoing study, the patients were targeted for follow-up exams at 1, 3, 6, and 12 months for the first year, followed by every 6 months for a 5-year period, then annually.

The study was conducted in the General Surgery Department of Medical Park Gaziantep Hospital in Turkey. More than 200 advanced laparoscopic surgeries have been performing per year since 2008 at this center, including total laparoscopic pancreaticoduodenectomy [22], bariatric surgeries, Nissen fundoplication, colorectal resections, and solid organ surgeries. The study was reviewed and approved by the review board of the institution and was registered at *ClinicalTrials.gov with number NCT02662478.*

Data Collection

Using the Turkish national procedural classification code number for laparoscopic stomach surgeries, a search was made in the patient database, which identified 64 patients who underwent laparoscopic gastric resection for a tumor between the designated time periods. Then a second search was performed to obtain a PG-GIST subgroup according to the histopathological results. Following the exclusion of patients who did not meet the inclusion criteria, a total of 23 consecutive patients were identified. The flowchart of the study population with the details of recruited and excluded patients is shown in Fig. 1.

Specifically, inclusion criteria were defined as all patients who underwent laparoscopic gastric resection for PG-GIST and whose diagnosis was subsequently confirmed with immunohistochemical evaluation. Patients were excluded if they underwent concurrent surgeries, had metastatic disease, were diagnosed with other than PG-GIST, received or converted to open surgery, and refused to give informed consent for laparoscopic surgery.

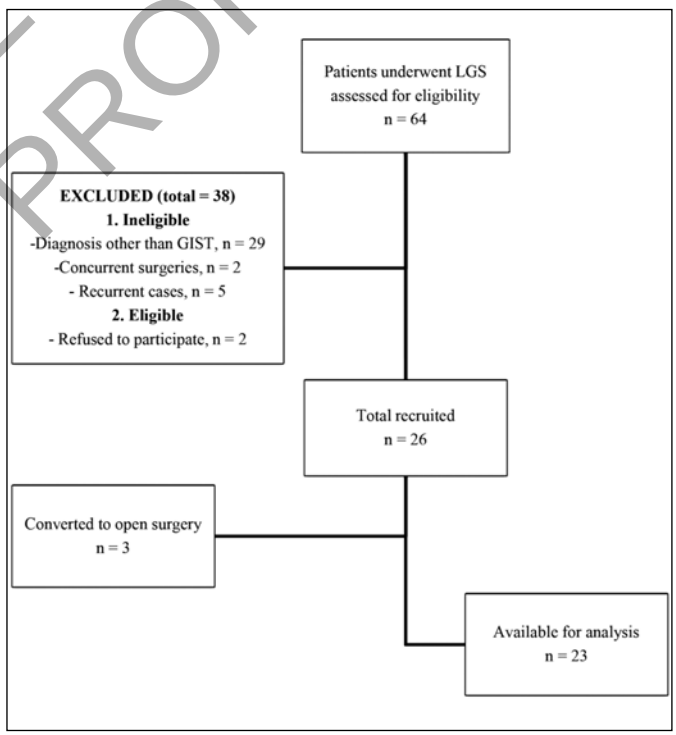

Fig. 1: Flowchart of the study. A search in the database identified 64 patients who underwent laparoscopic gastric surgery. Because 29 patients were diagnosed with other than GIST, 5 patients were operated on for recurrent disease, 2 patients had concurrent surgeries, and 2 patients had been living in another city and could not recommit to follow-up examinations, a total of 38 patients were excluded from the study. Another 3 patients who were eligible but converted from laparoscopic to open surgery were also not included in the analysis; therefore, 23 patients overall were analyzed.

Patients were evaluated prior to the surgery by a multidisciplinary team according to routine standard surgical care in the institution until March 2012 and those patients were treated mostly with laparoscopic anatomic gastric resection (historical group). After this point in time, the operative strategy was generated by the guidance of morpho-anatomical properties of the tumor in addition to the standard preoperative evaluation. Those 13 patients were tried to treat with laparoscopic OPG. Assessment was based on clinical examinations, blood tests, abdominal ultrasonography (US), and/or computerized tomography (CT) scan, upper gastrointestinal endoscopy, and endosonography with fine-needle biopsy when available. Patient demographics, clinical and pathologic details, preoperative, intraoperative, and postoperative data, as well as diagnostic investigations, details of performed procedures, and outcomes of surgeries for all patients who underwent laparoscopic PG-GIST resection were collected from the institutional database that was routinely maintained in the department.

Records were also reviewed to classify laparoscopic procedures performed as well as the size, anatomic location, originating surface, growing direction, and base diameter of the tumor.

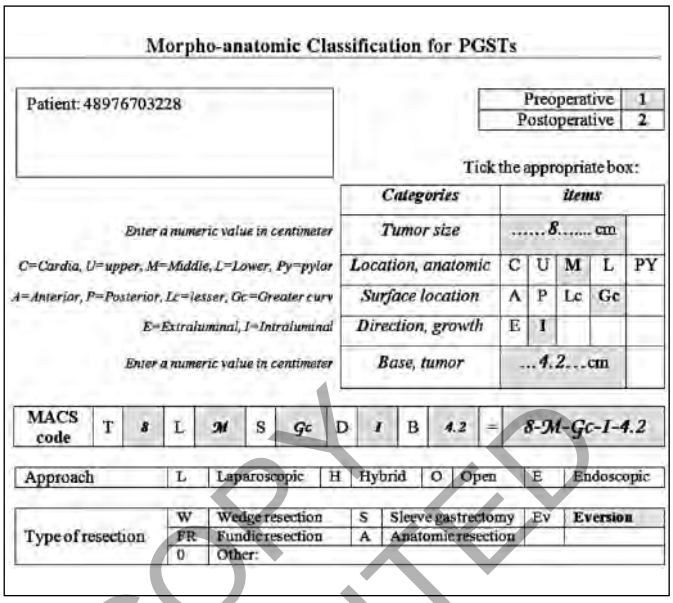

Fig. 2: Morpho-anatomic classification form. An example of the MACS form is illustrated. The filled boxes are grey. The form was completed by the multidisciplinary team according to the morpho-anatomic properties of the tumor, and the obtained MACS code (8MGcI4.2) was used for choosing the most appropriate surgical option (for instance, eversion technique in this case).

Morpho-Anatomic Features of the Tumor

Morpho-anatomical features of the tumor used to determine the strategy for laparoscopic OPG were tumor size, anatomic location, surface location, growing direction, and the diameter of the area the tumor involved. Subdivision and details of the categorization of each item are shown in Table I.

After the tumor characteristics were evaluated by the pretreatment multidisciplinary team, including the laparoscopic surgeon, oncologists, radiologist, and pathologist, the possible operational scenarios were discussed preoperatively. The best surgical option was selected among the possible alternatives according to the result of the consensus and recorded on a form (Fig. 2). This systematic evaluation was an essential guide to treatment selection and enables the assessment of therapeutic options.

The optimal PG-GIST treatment strategy during laparoscopic OPG largely depends on the tumor and patient characteristics obtained from the preoperative systematic assessment of morpho-anatomic features of the tumor;

Table I - *Morpho-anatomic classification system for primary gastric GISTs*

Category	Items	Explanations
Tumor size	Numeral	Centimeter
Location, anatomic	C/U/M/L/Py	Cardia, Upper, Middle, Lower, Pylor
Surface, stomach	A/P/Gc/Lc	Anterior, Posterior, Greater curve, Lesser curve
Growing direction	E/I	Extraluminal, Intraluminal
Base diameter	Numeral	Centimeter

Each category is subdivided as follows. The first item, tumor size (T), was used simply to identify the greater diameter of the tumor in centimeters. The second item, location (L), is determined by the anatomic location of the tumor in the stomach, which is divided into five parts: cardiac (c), upper (u), middle (m), lower (l), and pylorus (py). The third item, surface (S), is specified by the cross-sectional parts of the gastric wall on which the tumor originates. The cross-sectional circumference of the stomach is divided into four equal parts: the anterior (a) and posterior (p) surfaces, and lesser (lc) and greater (gc) curvatures. The fourth item, direction (D), is categorized as either extraluminal (e) or intraluminal (i), which describes the outward or inward direction of the growth of the tumor in the stomach, respectively. The fifth item, base (B), describes the diameter of the area where the tumor involves the stomach. It was expressed by numerical values in centimeters.

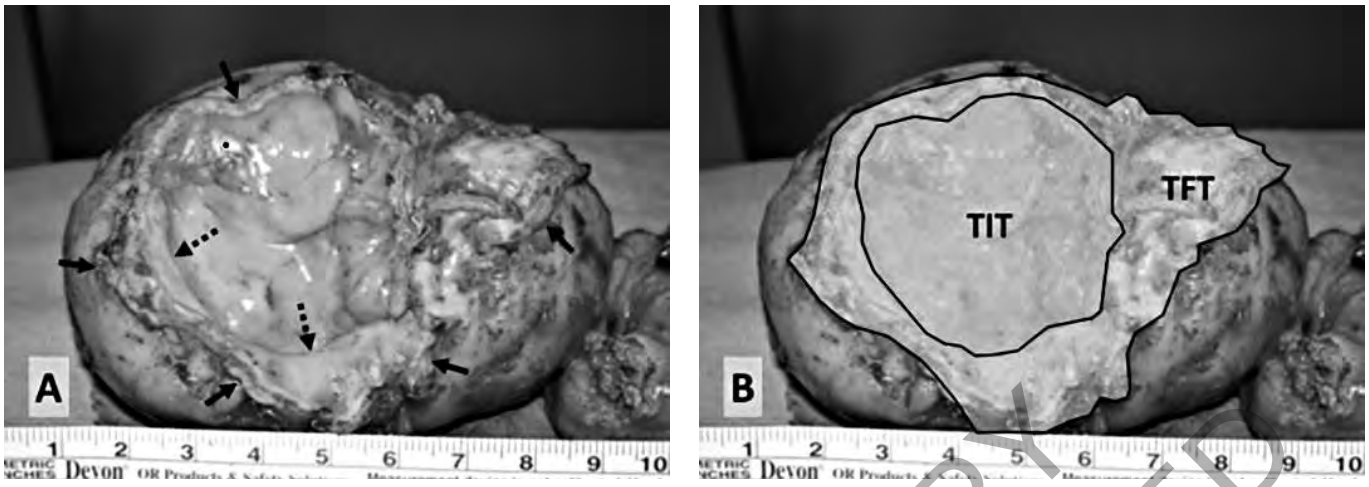

Fig. 3: The resection material of a tumor, 8 cm in diameter with classification code 8MGcI4.2, was located in the middle part of the stomach, originated from a greater curvature, and was growing intraluminally. A) The border of the tumor-involved area is indicated by dotted arrows, whereas the solid arrows show the edge of the tumor-free surgical margins. B) Total resected tissue (TRT) area is the sum of the tumor-free tissue (TFT) area and tumor-involved tissue (TIT) area. Therefore, in this example, the TFT area, which was calculated by software, is equal to subtracting the TRT area (21.68 cm^2) from the TIT area (9.65 cm^2), which gives the TFT area of 12.03 cm^2.

selecting a strategy also depends on the available options for primary tumor control, which in turn depend on the accuracy of the preoperative classification. Adequate preoperative evaluation and accurate assessment of the MACS status are therefore crucial in making the best therapeutic decision for each patient.

Outcome Variables

The instruments used for the evaluation of the outcomes of the surgeries were GIQLI questionnaires as a tool for assessment of the functional result of the surgery; the area of the tumor-free gastric tissue in the removed specimen as an indicator of OPG; BMI and the frequency of patients with more than 10% of body weight loss in three months after surgery (BWL ≥ 10%) as an indicator of nutritional status; the rate of disorders related to the gastric surgery in postoperative endoscopic examinations; and the rate of early and late surgical complications.

Because GIQLI was considered to be associated with gastric functions, it was measured as a primary outcome of the study. The remaining variables were considered secondary outcomes.

The GIQLI is a 36-item scale specifically designed to evaluate the quality of life in patients with gastrointestinal disorders. Because this variable was considered an objective tool for comparing the clinical outcome of the patient groups, it was used since 2008 as a routine patient evaluation tool in all surgical patients who underwent a gastrointestinal surgery in the institution where the study was conducted. This scale consists of five domains; each domain is scored on a five-response-level Likert scale of 0–4, ranging from worst to best. The GIQLI generates a maximum total score of 144 points, with a higher score implying a better QoPL [23].

An independent staff was trained to obtain baseline and follow-up measurements. The staff assigned to the survey asked patients to complete the questionnaire on-site in a self-reported manner within 30 min. All patients who completed the preoperative questionnaire were subsequently followed up by correspondence, using the GIQLI scale at 1 and 6 months after surgery.

Calculation of Unnecessarily Removed Tumor-Free Tissue Area

Unnecessarily removed tumor-free tissue (TFT) describes the remaining portion of the specimen following excision of the tumor-involved tissue (TIT) from the total resected tissue (TRT) with two or three millimeters' margin of normal tissue. It is calculated as an indicator for OPG. Because we believed that the gastric functions would be associated with the amount of removed gastric tissue, preserving gastric functions would depend on how minimal a resection could be achieved to obtain a negative surgical margin. Therefore, this variable was used to evaluate the technical success of the groups.

All specimens were sent to the pathology department and were processed immediately. Tumors were removed with a safe margin and photos of the remaining normal gastric tissue were taken. These photos were then coded and copied on a computer by an independent computing expert who was blind to the study, and image-processing software calculated the area of irregular shapes of uninvolved gastric tissue. An explanatory example of a case is illustrated in Fig. 3.

BMI, WEIGHT LOSS, AND COMPLICATIONS

Height and body weight measurements at baseline, 1 month, and 3 months after surgery were obtained from the patients' records. From these data, BMI, BMI change at 1 month and 3 months, and BWL ≥ 10% were calculated for all patients. In addition to intra- and postoperative complications, some of the gastrointestinal disorders associated with the surgery and BWL ≥ 10% that affect the GIQLI were also regarded as complications.

SURGICAL TECHNIQUES AND STEPS OF THE PROCEDURE

An endotracheal intubation with general anesthesia was used on all patients, and they were placed in the French position with reverse Trendelenburg; the table was tilted slightly to the right. A Veress needle established CO_2 insufflations. Entrance site of the telescope and the number, size, and entry points of the other trocars were tailored to the tumor location and size. Lymph node dissection was unnecessary.

In the earlier period, conventional laparoscopic resections were done according to the surgeon's knowledge and experience. In general, for upper/anterior/extraluminal, and small-based lesions, a fundic resection was done; middle/anterior or posterior/extra- or intra-luminal lesions were removed with a double-wall wedge resection or sleeve gastrectomy; for lower or pyloric lesions, antrectomy with gastroenterostomy were performed.

In the second period, organ- and function-preserving laparoscopic resections were performed according to the guidance of MACS. The main difference in this approach compared with the earlier was the special attempt to preserve the vagus nerve and its branches, including the hepatic, celiac, and pyloric plexus, and to protect the lower esophageal sphincter and pylorus as well as to save unexposed gastric tissue as much as possible. The morpho-anatomic classification of the tumor, its type, and number of operations performed in each group are shown in Table II.

As described earlier, the anatomic and surface location, base diameter, and growth pattern of the tumor, in addition to the tumor size, were the important factors in determining resectability through minimally invasive techniques. Accordingly, extraluminal masses located in the greater curvature (Gc), fundus (U) and anterior wall of the stomach (A) were easily amenable to partial resection, and several laparoscopic Endo-GIA™ (Ethicon Endo-surgery, Inc.) staplers were used to remove the tumor. Extraluminal tumors (E) located in the posterior gastric wall (P) were turned over toward the abdominal cavity after cutting the blood vessel around the greater curvature, then resected directly or by Endo-GIA stapler. Intraluminal (I) tumors were wedge resected using Endo-GIA staplers if they were small; eversion of the tumor through a gastrotomy opening and resection with minimal tissue loss were preferred if the tumor was large. An example of such a case is shown in Fig. 4. Distal third and masses near the pylorus (Py and L) were

TABLE II - *Distribution of surgeryreceived and MACS of the tumor according to the time periods*

Patient no.(n = 23)	Before March 2012	After March 2012	Surgery received
5	3UAE2.5 7.5UAE3	6UAE4 4UPI2.8 5UAE3.1	Fundic resection
7	10MAE3.5 6MAI3.6 4.8MPI3.4 5.5MPI2.5 8.8MGcI4.1	9.5MAE5 9MAE5 11MGcE5.3 5.5MGcE3	Sleeve gastrectomy or wedge resection
3	5LAE3 4.5LGcE4.2 4.5LLcE2.9	Antrectomy and gastroenterostomy	
3		7MAI3.6 8MGcI4.2	Eversion and wedge resection
1		2.5CLcE1.5	Wedge resection and fundoplication
3		6.5LAI3.4 4.5LLcE2.8	Pylorus preserving segmental gastrectomy
2		3PyAE1.5	Wedge resection and pyloroplasty

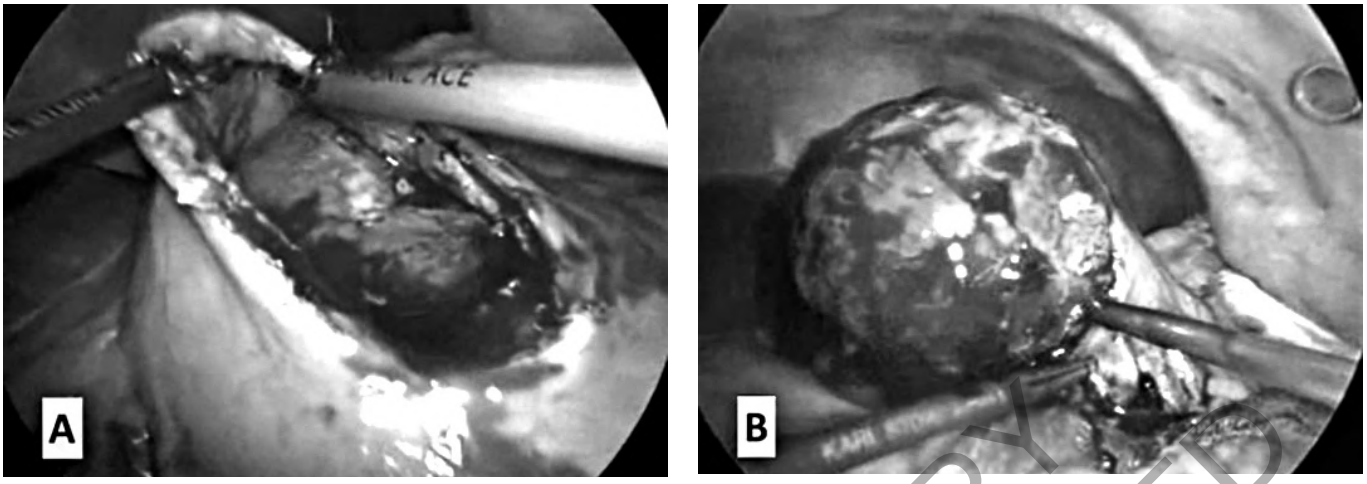

Fig. 4. Illustration of laparoscopic OPG, using eversion technique in a patient with MACS classification code 8MGcI4.2 PS-GIST in SG (i.e., a tumor 8 cm in diameter, middle located, greater curvature originated, intraluminally growing, and 4.2 cm in base diameter). A) Performing a gastrotomy on the anterior surface of the stomach close to the mass. B) Eversion of the tumor through the gastrotomy incision. C) Closing the defect with intracorporeal, hand-sewn sutures following resection of the tumor.

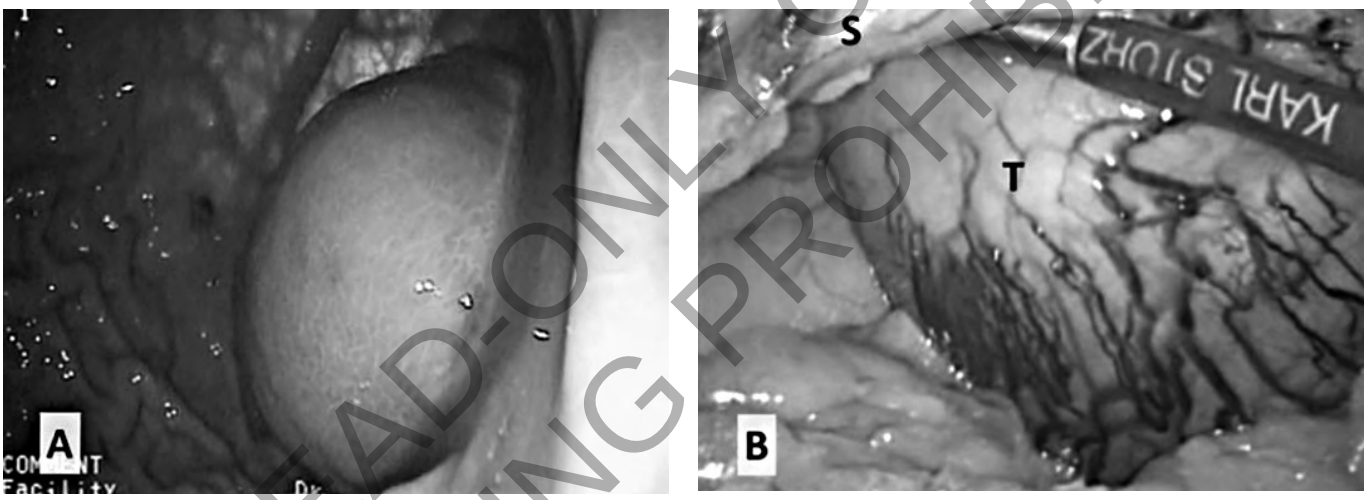

Fig. 5. Endoscopic aid during resection of a large tumor with the classification code 11MGcE5.3, located middle portion and greater curvature of the stomach. A) Intraluminal and B) laparoscopic view of the tumor (S: stomach, T: tumor). C) Endoscopic control of the staple line integrity (arrows) following excision of the tumor.

removed by laparoscopic pylorus-preserving surgery or wedge resection with pyloroplasty. Intraoperative endoscopy was used to determine the exact location of the tumor and to avoid narrowing of the gastric lumen, especially for tumors of the cardia and pylorus and around the incisura angularis, as shown in Fig. 5.

An intra-abdominal drain was placed around the surgical site when necessary. All specimens were retrieved in a plastic bag through a transverse, muscle-splitting incision in the suprapubic area. Post-operatively, nasogastric tubes were used routinely and removed at 12 or 24 h post-surgery. On the first postoperative day, the patients were encouraged to walk around the bed and drink water if there were no complaints associated with postoperative complications. Patients were discharged when they were able to tolerate a regular diet.

Statistics

Continuous data were expressed as mean ± SD or median with minimum – maximum range, and categorical data were expressed as *n* (%).

The Wilcoxon signed-rank test was used to ascertain whether laparoscopic surgery improved the total GIQLI scores at baseline as well as at the follow-up time points. Pearson correlation analysis was performed to identify the relationship between the GIQLI scores and TFT area. Then a simple linear regression was calculated to predict postoperative sixth-month GIQLI scores based on the area of the TFT. A p value of < 0.05 was accepted as the threshold for statistical significance. All data were processed and analyzed using SPSS version 16.0 statistical software (SPSS Inc.).

Results

Three patients with BMI over 35 were converted from laparoscopic to open surgery due to the technical difficulties associated with the obesity, and they were excluded from the study; therefore, 23 patients overall were included in the analyses in which immunohistochemical analysis confirmed the diagnosis of GIST with a positive staining for c-kit or platelet-derived growth factor receptor.

TABLE III - *Demographics and clinical features of the patients and morpho-anatomic features of the tumors*

Features	Values
Demographic/clinic	
Age, years, med (range)	58 (41 – 71)
Sex (M/F), n	13/10
Overall symptoms, yes/no	11/12
Nausea/vomiting, n (%)	11 (47.8)
Melena, n (%)	9 (39.1)
Abdominal pain, n (%)	4 (17.4)
Hematemesis, n (%)	2 (8.7)
Tumor size, > 5 cm, n (%)	13 (56.5)
Tumor size, ≥ 10 cm, n (%)	2 (8.7)
Mitotic index	
≤5/50 HPF, n (%)	14 (60.9)
>5/50 HPF, n (%)	9 (39.1)
MAC system	
Tumor size, cm, med (range)	5.5 (2.5 – 11)
Location (C/U/M/L/Py), n	1/5/11/4/2
Cardia (C), n (%)	1 (4.3)
Upper (U), n (%)	5 (21.7)
Middle (M), n (%)	11 (47.8)
Lower (L), n (%)	4 (17.4)
Pylorus (Py), n (%)	1 (4.3)
Surface (A/P/Gc/Lc), n	11/4/5/3
Anterior (A), n (%)	11 (47.8)
Posterior (Py), n (%)	4 (17.4)
Greater curvature (Gc), n (%)	5 (21.7)
Lesser curvature (Lc), n (%)	3 (13)
Growing pattern (E/I), n	15/8
Extraluminal (E), n (%)	15 (65.2)
Intraluminal (I), n (%)	8 (34.8)
Tumor base, cm, med (range)	3.4 (1.5 – 5.3)
Operative features	
R0 resection, yes/no	23/0
Lymph node dissection, yes/no	0/23
Operation time, min, med (range)	95 (50 – 155)
Hospital stay, day, med (range)	5 (3 – 11)
Follow-up, month, med (range)	36 (6 – 75)

extraluminal/INTRALUMINAL

ABBREVIATIONS: med: median; range: minimum – maximum values; M/F: male/female; n: number; C/UM/L/Py: cardia/upper/middle/lower/pylor; A/P/Gc/Lc: anterior/posterior/ greater curvature/lesser curvature; E/I:

Demographic features of the patients and morpho-anatomic characteristics of the tumors are shown in Table III. The median age of the study population was 58 years (range, 41–71); male to female ratio was 13:10. More than half of the patients were asymptomatic (52.2%). The most frequent symptoms were nausea and vomiting (47.8%), melena (39.1%), abdominal pain (17.4%), and hematemesis (8.7%). The ratio of the tumors larger than 5 and 10 cm were 56.5% and 8.7%, respectively. The diagnosis was confirmed in all patients with histopathologic and immunochemistry evaluation, and the mitotic index of the tumors was predominantly ≤ 5 / 50 high-power field (60.9%). The median tumor size and base diameter were 5.5 (range, 2.5-11) cm and 3.4 (range, 1.5-5.3) cm, respectively. The tumors were located most frequently in the middle part and on the anterior surface of the stomach (47.8%) with extraluminal growth (65.2%). In all patients, an R0 resection was achieved without a need for lymph node dissection. The overall median operation time was 95 (50-155) minutes, and the median hospital stay was 5 (range, 3-11) days. The median follow-up time was 36 (range, 6-75) months.

TABLE IV - *Primary and secondary outcomes*

Features	Total
Primary outcomes	score, mean ± SD
Total GIQLI, baseline	100.9 ± 10.2
Total GIQLI, 1 month	105.4 ± 9.5
Total GIQLI, 6 months	117.0 ± 11.1
Secondary outcomes	cm2, med (range)
TRT area	56.8 (8.2 – 203.7)
TIT area	9.1 (3.0 – 21.5)
TFT area	48.1 (4.4 – 192.8)
BMI	kg/m2, med (range)
Baseline	28.0 (21 – 38)
6 month	27 (19 – 36)
COMPLICATIONS	number (%)
Overall	11 (47.8)
BWL ≥ 10%	6 (26.1)
Gastroparesis	4 (17.4)
Reflux disease	4 (17.4)
Bile gastritis	4 (17.4)
Intraabdominal infection	3 (13.0)
Narrowness	1 (4.3)
Marginal ulcer	1 (4.3)
Pneumonia	1 (4.3)
Tumor rupture	0
Recurrence	1 (4.3)
Perioperative mortality	0
Late mortality	2 (8.6)

ABBREVIATIONS: med: median; range: minimum – maximum values; SD: standard deviation; GIQLI: gastrointestinal quality of life index; TRT: total-resected area, TIT; tumor-involved area; TFT: tumor-free area; BMI: body mass index; BWL ≥ 10%: body weight loss equal to or more than 10% in last three months

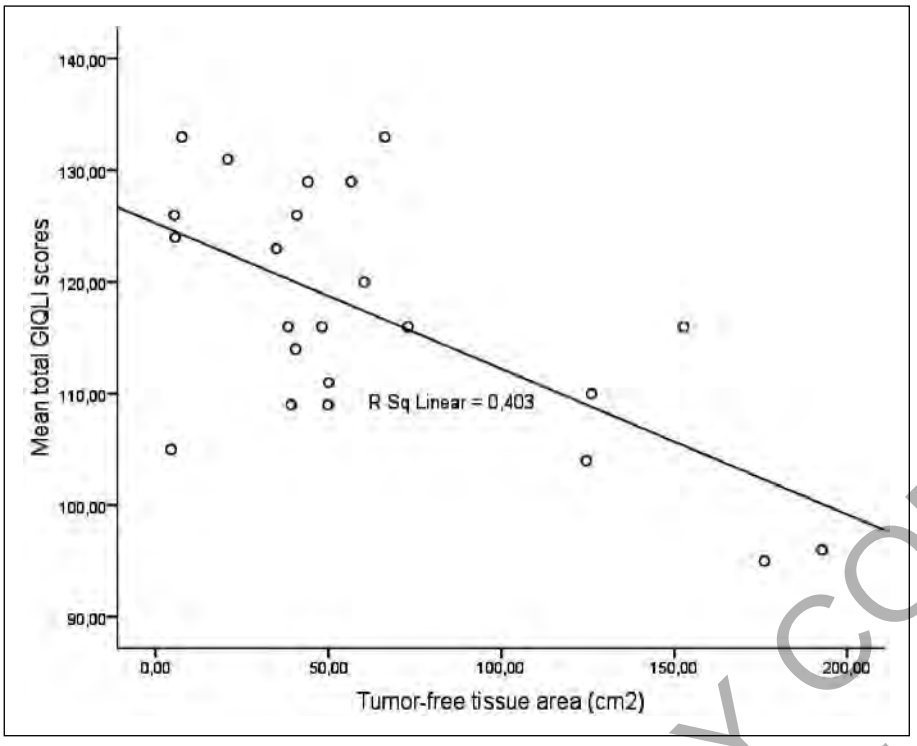

Fig. 6. Mean total GIQLI scores as a function of the TFT area in patients who underwent laparoscopic gastric resection for PG-GIST (n = 23). A negative correlation was identified between GIQLI scores and TFT (r = -0.635, p = 0.001). A significant regression equation in in the simple linear regression analysis [F (1, 21) = 14.18, p = 0.001], with an R2 of 0.40. Participants' GIQLI scores at 6 months decreased 0.130 for each cm2 of TFT area excised.

TABLE V - *Results of the Wilcoxon signed-rank test to compare the total GIQLI scores at different time points*

Time points	GIQLI scoremed (range)	GIQLI scoremed (range)	Z - value	P value
Baseline/1 month	99 (84 – 119)	107 (87 – 119)	-3.32	0.001
Baseline/6 month	99 (84 – 119)	116 (95 – 133)	-3.86	0.0001
1 month/6 month	107 (87 – 119)	116 (95 – 133)	-3.71	0.0002

The results of the primary and secondary outcomes of the patients are shown in Table IV. The mean total GIQLI scores of the patients were 100.9 ± 10.2, 105.4 ± 9.5 and 117.0 ± 11.1 at baseline, 1 month and 6 month respectively. The Wilcoxon signed-rank test was used to ascertain whether laparoscopic surgery improved the total GIQLI scores of the patients, and it indicated that both first- and sixth-month GIQLI scores (mean = 105.4 ± 9.5 and 117.0 ± 11.1, respectively) were significantly higher than baseline scores (mean ± SD = 100.9 ± 10.2) in the study population (z = –3.32 and –3.86, p = 0.001 and 0.0001, respectively; Table V).

The median TRT, TIT and TFT area of the study population were calculated to be 56.8 (8.2 – 203.7), 9.1 (3.0 – 21.5) and 48.1 (4.4 – 192.8 cm^2), respectively (Table IV). Pearson correlation analysis was performed to identify the relationship between the total GIQLI scores and TFT. Based on the results of the test, GIQLI scores were inversely related to TFT area (r = –0.635, p = 0.001). Then a simple linear regression was calculated to predict postoperative sixth-month GIQLI scores based on the area of the TFT. A significant regression equation was found [F (1, 21) = 14.18, p = 0.001], with an R^2 of 0.40. Participants' predicted GIQLI at the sixth month was equal to 125.3 – 0.130 (TFT) scores when the TFT area was measured in cm^2. Participants' GIQLI scores at 6 months decreased 0.130 for each cm^2 of TFT area (Fig. 6).

Although statistically insignificant, there was a reduction in BMI after 6 months of surgery (27, 19-36) from the baseline (28.0, 21-38). There was no perioperative mortality, although overall complications were seen in 11 patients (47.8%). There were no serious intraoperative complications such as tumor rupture, massive bleeding, leakage, or injury to the other organs. The most frequent complication was BWL ≥ 10% of baseline body weight within 3 months after surgery (n=6, 26.1%). Other complications, according to the order of frequency, were gastroparesis (17.4%), intra-abdominal infection (13.0%), bile gastritis (17.4%), and reflux disease (17.4%). Inflammatory intra-abdominal collection developed in three patients who managed successfully with conservative treatment. However, in one patient, a narrowness of the gastric lumen arose at the incisura angularis, which subsequently needed reoperation and management with stricturoplasty. Although there was no

tumor rupture in all, one patient in the CG developed metastasis in the liver 5 years after surgery. Despite appropriate therapy, he died because of the disease progression; one patient died in SG for a reason unrelated to the tumor in the follow-up period.

Discussion

The first conclusion that could be drawn from the results was that laparoscopic surgery was safe and feasible for PG-GIST even larger than 5 cm in diameter, as previously demonstrated by others (9-12). Seeing that the size and technical limitations for laparoscopic PG-GIST resection have apparently changed, every effort should focus on increasing the functional capacity of the stomach, as we aimed to do in this study. We hypothesized that OPG would help reduce the amount of unnecessarily removed TFT, which subsequently would ensure better GIQLI scores in patients with PG-GIST. The results of the study have confirmed this hypothesis. According to the analysis of primary outcome, a significant improvement in the GIQLI scores was observed. Furthermore, we found a substantial reduction in the area of the TFT requiring removal, following the use of MACS oriented OPG, and, more important, patients' sixth-month GIQLI scores were calculated to have decreased 0.130 for each cm^2 of removed TFT area. These results clearly demonstrated that, although achieving negative surgical margins is mandatory for oncological reasons, it is also important to preserve gastric tissue as much as possible for better QoPL; that is, the greater the organ preservation, the better the QoPL.

The minimalization of therapeutic invasiveness with the aim of preserving QoPL, known as the organ- and function-preserving gastrectomy, has recently been a major topic in the management of early gastric cancers [16,18,19,21]. Although it is a relatively new concept, and there are very few reports regarding its long-term results, we believe that this concept might also successfully be applied to PG-GIST, which have oncologically less aggressive features than gastric cancer. However, due to the complexity of stomach functions, scientific assessment of the outcome following OPG is not easy. The stomach has complicated motor and secretory functions as well as extrinsic and intrinsic innervations [25]. Therefore, there are many methods in the literature attempting to evaluate each of these functions after OPG[16,19,21].

The GIQLI, one of these methods, is an instrument validated to evaluate quality-of-life changes after surgery [23]. Literature review revealed only one study that specifically analyzed GIQLI outcomes in patients operated on for gastric stromal tumor [15]. In their study, the long-term outcome of GIQLI scores was found to be quite satisfactory compared with healthy subjects. Although little is known about the GIQLI of patients following laparoscopic PG-GIST resection, we used this scale to compare short-term results in the groups. In this sense, we found that both first and sixth-month GIQLI scores were significantly improved from the baseline in patients who underwent laparoscopic surgery for PG-GIST. Using MACS might contribute to this improvement by individualization of OPG for each patient; it was designed to preserve important anatomic structures and main extrinsic innervations and protect the stomach from excessive tissue resection by which pacemakers, important motor regulators of the stomach, could be[16,18-21].

As a result of this individualization, six patients could receive MACS-guided OPG compared to patients with similar characteristics in the historical group (Table II). Instead of traditional anatomical double-wall distal gastrectomy, two patients underwent eversion and wedge resection for middle and intraluminal tumor (7MAI3.6 and 8MGcI4.2), which saved a considerable amount of gastric tissue with the preservation of the pylorus (Figs. 3, 4). For lesions located in the lower part of the stomach in two patients (6.5LAI3.4 and 4.5LLcE2.8), a pylorus-preserving segmental gastrectomy was performed, which has recently become a popular method for treating early gastric cancer in Japan [20]. The other different surgeries were wedge resection and pyloroplasty in one patient (3PyAE1.5) and wedge resection with fundoplication for a tumor located on the right side of the cardia (2.5CLcE1.5), for which an attempt was made to keep pyloric and lower esophageal sphincter functions, respectively.

We believe that all these organ- and function-preserving surgeries had a positive effect on the QoPL; however, difficulties relating to these procedures must be taken into account. It has been shown that surgical inexperience is an independent risk factor for postoperative complications after laparoscopic distal gastrectomy [26-28]. It is a demanding procedure; therefore, it requires a significant accumulation of surgical experience; the ability for intracorporeal hand-sewn suturing and anastomosis; and a well-equipped, high-volume institution with an endoscopist available for intraoperative endoscopy on demand. Kunisaki et al. [28] demonstrated that high BMI independently predicted conversion to open surgery and postoperative complications for laparoscopic-assisted distal gastrectomy. In three patients who were excluded from this study, the reason for conversion to open surgery was technical difficulties associated with obesity (BMI > 35); otherwise, we did not experience any difficulties requiring conversion to open surgery in 23 patients.

However, early and late overall complications developed in 47.8% of patients, of which most consisted of minor complications. Because the study focused on the functional outcomes of the patients, we included some relatively minor illnesses in the analysis as a complication. That could be because of the small number of cases, which was one of the weaknesses of the study.

BWL ≥ 10% in the last 3 months which was detected

in 26% of patients was the most common complication. This might be the result of having a smaller residual stomach capacity and less preservation of functionally important structures, thereby causing more digestive problems. To minimize complications, all patients who underwent OPG also underwent flexible endoscopy to guide the resection line and checks for narrowing or lost integrity of the closed areas (Fig. 5). Therefore, except for one patient, we did not experience a narrowness or leakage in any of the patients.

Some limitations did affect the results of the study. The main limitation was the small sample size due to the rarity of the disease, which remained quite unsatisfactory for subgroup or intergroup analysis, that is, the impact of surgical techniques or anatomic and surface location or size of the tumor on functional outcomes. Thus, no definitive conclusion may be drawn in this respect. In addition to that, in spite of prospectively maintained and well-documented data, this was a retrospectively designed study with inherent selection bias, which constituted the second major limitation for the study. Further prospective studies with larger study size are needed to discern the utility of MACS oriented OPG patients with gastric stromal tumors. Furthermore, multicenter studies may help provide a sufficient study population.

Despite these limitations, we believe that the results of the study clearly demonstrated that using MACS might provide many advantages for tailoring an OPG in patients with PG-GIST. In addition, it helped reduce the amount of unnecessarily removed TFT, thereby improving the QoPL of the patients; it also may facilitate oncologic principles and reduce the limitations of laparoscopic surgery. Moreover, MACS may provide clearer information during consultation with a colleague about the resectability of a tumor and the selection of surgical options. Finally clinical trials, using MACS, can be compared more easily. For instance, a patient with a MACS code of 4.8MPI3.4 explains in a succinct manner "a patient with a tumor 4.8 cm in diameter located in the middle portion and posterior surface of the stomach, growing intraluminally with a base diameter of 3.4 cm." With this concise expression reported in a study, for instance, one can easily understand the tumor characteristics and compare the results of studies properly or collect cases with the same characteristics for a meta-analysis or a systematic review.

Conclusions

Laparoscopic OPG seemed to be useful in terms of oncologic safety and minimizing the excessive resection of TFT and maximizing the gastric remnant, thereby improving the QoPL of the patients. We recommend laparoscopic OPG customized to the disease characteristics derived from MACS in appropriate patients in advanced laparoscopy centers to maintain patients' QoPL while treating the tumor definitively. Further prospective, multicenter, randomized-controlled trials are necessary to evaluate survival and postoperative QoPL associated with MACS-oriented OPG.

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