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Laparo-endoscopic transgastric resection of gastric submucosal tumors

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Abstract

Background—Laparoscopic and endoluminal surgical techniques have evolved and allowed improvements in the methods for treating benign and malignant gastrointestinal diseases. To date, only case reports have been reported on the application of a laparo-endoscopic approach for resecting gastric submucosal tumors (SMT). In this study, we aimed to evaluate the efficacy, safety, and oncologic outcomes of a laparo-endoscopic transgastric approach to resect tumors that would traditionally require either a laparoscopic or open surgical approach. Herein, we present the largest single institution series utilizing this technique for the resection of gastric SMT in North America.

Methods—We performed a retrospective review of a prospectively collected patient database. Patients who presented for evaluation of gastric SMT were offered this surgical procedure and informed consents were obtained for participation in the study.

Results—Fourteen patients were included in this study between August/2010 and January/2013. Eight (8) patients (57.1 %) were female and the median age was 56 years (range 29–78). Of the 14 cases, 8 patients (57.1 %) underwent laparo-endoscopic resection of SMTs with transgastric extraction, 5 patients (35.7 %) had conversions to traditional laparoscopic surgery, and 1 patient (7.2 %) was abandoned intraoperatively. The median operative time for this cohort was 80 min (range 35–167). Ten patients (71.4 %) had GISTs, 3 (21.4 %) had leiomyomas, and 1 (7.1 %) had schwannoma. There were no intraoperative complications. Two patients had postoperative staple line bleeding that required repeat endoscopy. The median hospital stay was 1 day (range 1–6) and there were no postoperative mortalities. At 12-month follow-up visit, only one GIST patient (10 %) had tumor recurrence.

Conclusion—Our experience suggests that this surgical approach is safe and efficient in the resection of gastric SMT with transgastric extraction. This study found no intraoperative complications and optimal oncologic outcomes during the follow-up period. Minimally invasive surgical approaches are emerging as a valid and potentially better approach for resecting malignancies; however, continued investigation is underway to further validate this data.

Keywords

Laparo-endoscopic surgery; NOTES; Tumor resection; Minimally invasive surgery; GIST; Leiomyoma

In recent years, the pathological concept of submucosal tumors (SMT) of the gastrointestinal (GI) tract has changed considerably [1]. The term SMT comprises GI tumors in the submucosa, including pancreatic rests, schwannomas, leiomyomas, leiomyosarcomas, and gastrointestinal stromal tumors (GIST), all of which are evaluated and defined with immunohistochemistry markers [2].

The incidence of these lesions is approximately 0.4 % and can arise along the GI tract, but is most commonly found in the stomach (40–60 %), followed by small intestine (30–35 %) and colorectum (5–16 %). SMT therefore is a relatively new entity of tumors and represents non-epithelial mesenchymal neoplasms of GI tract tumors. SMTs often present with GI bleeding and anemia, secondary to the ulceration of the tumor, however, small size tumors commonly present asymptotically [3].

Generally, the malignant potential is assessed by tumor size and number of mitoses, even though the biological behavior is unpredictable. With the advent of CD34 and c-Kit as discriminating marker antigens, formerly diagnosed leiomyoma or leiomyosarcoma are now frequently reclassified more precisely as GIST [4].

Previously published studies have showed that surgery is the only cure for the treatment of SMT, allowing minimally invasive surgery (MIS) to play an important role in the development of new approaches in the treatment of these tumors [5].

Laparo-endoscopic surgical procedures have been developed and well established as a part of the rapid evolution of the MIS field in recent years [6–8]. This approach allows surgeons extra advantages in comparison with the either traditional laparoscopic surgery or endoscopic surgery: (a) extra working port via the endoscope in order to minimize instrument changes, while decreasing the clutter/clashing of additional trocars/instruments, (b) hand-activated, auto-cleaning capability for the camera lens, (c) improved ability to visualize remote locations in the abdomen given the endoscope's flexibility, and (d) superior ergonomics when compared to single-access laparoscopic surgery [9, 10].

Specifically, the role for laparo-endoscopic procedures in cancer surgery is clear and limited to specific circumstances in which the tumor resection does not include lymph node dissection, involves upper GI tract tumors, no anastomoses are required, or when the location is remote and otherwise difficult to access [11, 12].

In this study, we aimed to evaluate the efficacy, safety, and oncologic outcomes of this laparo-endoscopic approach with transgastric and transoral extraction in patients with such tumors that would traditionally require either laparoscopic or open surgical approaches. Herein, we present the largest single institution series utilizing this technique for the resection of gastric SMT in North America.

Materials and methods

Study design

This was a retrospective review of a prospectively collected patient database between August 2010 and January 2013. The study was conducted with approval from the Institutional Review Board at University of California San Diego. Patients who presented for the evaluation of gastric SMT were offered this surgical procedure and informed consents were obtained for participation in the study.

Patients

Eligible patients met the following criteria: ages between 18 and 75, ASA classification 2 or below, diagnosis of gastric SMT, and who desired surgical treatment. Patients with the following conditions were excluded: those taking immunosuppressive medications or were immunocompromised, evidence of abdominal abscess or mass, clinical diagnosis of sepsis, diffuse peritonitis on clinical examination, history of open abdominal surgery, and patients on blood thinners or platelets inhibitors or abnormal blood coagulation test. Informed consent was obtained by a physician, and an authorization for the use of protected health information for research purposes was signed to comply with HIPAA.

Preoperative evaluation

All patients preoperative work-up include esophagogastroduodenoscopy (EGD), endoscopic ultrasound (EUS), abdominal CT scan, and/or PET scan. The submucosal nature of the tumors and the absence of distant disease were confirmed. FDG-avid tumors were identified with PET scan.

Surgical technique

Preoperative antibiotics per Surgical Care Improvement Project (SCIP) guidelines were administered 30 min before incision. Under general anesthesia, the patient was placed in supine lithotomy position, the surgeon was positioned between the patient's legs, and the assistant was positioned to the patient's right. The assistant endoscopist was at the patient's head. The first 5-mm trocar was inserted 10 cm below the xiphoid, left of the midline using a visualizing trocar insertion technique (Fig. 1). CO₂ was utilized to create pneumoperitoneum to a pressure of 15 mm Hg. A 5-mm laparoscope was inserted into the abdominal cavity. After exploration of the abdominal cavity, an assistant performed endoscopy and insufflated the stomach with CO₂. Utilizing both laparoscopic and endoscopic views, two balloon-tipped trocars (5- and 12-mm in diameter) were placed transabdominally and into the stomach (Fig. 2). The balloons on the trocars were inflated and the pneumoperitoneum was partially released to a pressure of 10 mm Hg, allowing the stomach to be retracted against the anterior abdominal wall. Once this was achieved, using the endoscopic view and

intra-gastric insufflation, we were able to identify and manipulate the tumor using conventional laparoscopic instruments. The tumor was grasped and resection was achieved using a linear cutting stapler with either 60 or 45 mm loads (blue and gold) depending on the thickness of tissue (Echelon Surgical Stapling Reloads, Ethicon EndoSurgery®), loads that were placed through the 12-mm transgastric trocar (Fig. 3). Care was taken to ensure a negative margin. Once resected, the tumor was placed in an endoscopic retrieval bag (Fig. 4) and an endoscopic grasper was then used to retrieve the specimen through the mouth (Fig. 5). Lastly, a linear cutting stapler was then used from within the peritoneal cavity to close the gastrotomies.

Postoperative care and follow-up

Postoperatively, patients were admitted to the hospital and treated under the same standard of care as a laparoscopic tumor resection. Postoperative complications such as intra-abdominal bleeding were planned to be handled in the same fashion as any postoperative complication in laparoscopic surgery. Patients were evaluated in clinic at one week postoperatively, at 6 months, and 1 year postoperatively. On visit 2 and 3, EGD and CT Scans were planned to be performed.

Data collection and statistical analysis

Data were analyzed using Stata 11.0 (StataCorp. 4905 Lakeway Dr. College Station, TX 77845, USA). Continuous variables were presented as medians and range. Categorical data were presented as numbers and percentages. Data were collected prospectively, including but not limited by patient demographics, operative timings and postoperative recovery parameters such as length of hospitalization, ICU admission, operative complications, tumor location, tumor size, immunohistochemistry, mitotic index, tumor recurrence, adjuvant imatinib therapy, and mortality were also reviewed.

Results

From August 2010 to January 2013, a total of 14 patients were included in this study and 8 patients (57.1 %) underwent laparo-endoscopic removal of SMTs with transgastric extraction in our institution. Eight (8) patients (57.1 %) were female and the median age was 56 years (range 29–78). Ten (10) patients (71.4 %) were white, 3 (21.4 %) were Hispanic, and 1 patient (7.1 %) was unknown. The median body mass index (BMI) was 27.6 (range 18–38). All patients had an American Society of Anesthesiology (ASA) classification of 2 or below. One case planned for tumor resection using this technique was abandoned intraoperatively secondary to the tumor location and the patient had not signed the consent form for conversion to laparoscopic surgery. The tumor location and distribution is described in (Table 1).

The median operative time in this cohort was 80 min (range 35–167) and median of the length of hospital stay was 1 day (range 1–6). There were five conversions to traditional laparoscopic surgery and no conversions to an open operation. The conversions to traditional laparoscopic surgery were due to the tumor location (limited access) and serosa involvement of the tumor (exophytic growth pattern). There were no intraoperative complications. Two

patients had postoperative bleeding that required repeat endoscopy during the first 24 h; in both cases, the bleeding was controlled with endoscopic clips. Postoperative bleedings occurred in cases number 2 and 4 of this series, with diagnosis of leiomyoma and schwannoma, after these initial cases no more bleeding complications were seen postoperatively. The median estimated blood loss was 20 ml (range 5–50).

Other minor postoperative complications in this group of patients included nausea (3 patients), abdominal pain (2 patients), and urinary retention (1 patient) and all these complications were managed with conservative treatments. No patients required admission to an intensive care unit and no blood transfusions were needed in this cohort. The mortality rate was 0 % at 30 days postoperative (Table 2). Patients were followed for a median of 5.4 months (range 1–15). Ten (10) patients (71.4 %) had GISTs, 3 (21.4 %) had leiomyomas, and 1 patient (7.1 %) had schwannoma (Table 3).

In the GIST subgroup, the median largest tumor size was 3.4 cm (range 2–5) and the median mitosis index (N/50 HPF) was 4 (range 1–20). The margin status reported in all cases was R0 with no tumor ruptures. All GISTs were defined KIT-positive and DOG-1-positive. Two cases had adjuvant therapy with imatinib after the surgical procedure due to the high-risk behavior of the tumor, and at 12-month follow-up visit only one case of these patients with adjuvant therapy with imatinib had tumor recurrences (Table 4).

Discussion

In 1997, Wolfsohn et al. reported a case in which a combined approach including a gastrointestinal endoscopy, laparoscopy, and laparoscopic ultrasound was used to resect a gastric leiomyoma [13]. In this report, a safe procedure was found providing new surgical alternatives for gastric tumors. Two years later, in 1999, three additional reports were published [14–16]. Cheng et al. showed their experience with 9 patients with benign gastric tumors treated with a laparoscopic wedge resection of the stomach [14]. In this study, 7 patients had GISTs and there were no relevant intraoperative complications, and they found shorter hospital stays, earlier postoperative oral intake and lower analgesic usage rate. They concluded that this approach was recommended as a MIS procedure.

Followed by this, Cueto et al. published in their report a 29-year-old male patient with an ileal GIST and a severe lower gastrointestinal hemorrhage with successful laparoscopic-assisted diagnosis and resection [15]. Months later, Ohgami et al. reported the use of laparoscopic surgery in wedge resections of the stomach for GIST. Developing a lesion-lifting partial gastrectomy, they concluded that this approach was safe and feasible as a surgical treatment in the hands of an experienced laparoscopic surgeon [16]. In 2000, Otani et al. presented their experience in 34 patients with SMTs in the stomach treated with a laparoscopic wedge resection. In this cohort, all surgical margins were clear for malignancies, no intraoperative complications were seen, and no recurrences were observed over the 5-year follow-up period [17]. In this study, they confirmed that solid SMT of the stomach larger than 20 mm in diameter could be treated safely with this approach.

Then with the rapid evolution of diagnostic and surgical instruments, in 2005, Gotoda et al. described the implementation of endoscopic submucosal dissections (ESD) as a new alternative for the endoscopic treatment of early gastric cancer. The ESD technique resulted in high rates of complications due to perforation of the stomach and massive bleeding; at the end of this study, they suggested that this procedure was suitable for the resection of mucosal and submucosal layers, but not for the muscle layer [18].

Based on the previous experience, in 2008 Hiki et al. published the first report describing the combination of laparoscopic and endoscopic surgery procedures (laparoscopic and endoscopic cooperative surgery) for gastric wedge resection of SMT independent of tumor location and size. This approach applies the surgical principles for the treatment of these lesions: low risk of tumor rupture, no need of lymphadenectomy due to the rare involvement of lymph nodes, and achievement of negative margins [3]. This initial experience showed the safety of this approach and showed acceptable clinical outcomes including reasonable operation times, low rate of complications, and no relation between success of the procedure and tumor location [19–23].

Although several authors have described this technique [24–26], important modifications were made to this procedure in our institution to reduce the numbers of trocars and remove the specimen through the mouth (transoral).

The principles for the surgical treatment of SMTs have been previously described by different authors and are available in the current guidelines: achievement of negative margins both macroscopically and microscopically, a complete resection of the tumor with low risk of tumor rupture and potential peritoneal seeding, and no lymphadenectomy due to the rare involvement of lymph nodes [27, 28]. On the other hand, it is also affirmed that the survival of patients with these tumors is related with tumor size and histological composition and not associated with microscopic margins of resection, allowing an expanded role for MIS procedures [29].

We first published our experience with the initial technique used for laparo-endoscopic approaches in 1997 describing a case report of a 38-year-old woman with chief complain of dyspepsia and a mass at the gastroesophageal junction. In this report, a combined approach that included gastrointestinal endoscopy, laparoscopy, and laparoscopic ultrasound was used to resect a gastric leiomyoma. We found that this procedure was a feasible, safe, and successful alternative for submucosal gastric tumors in well-evaluated cases [13].

The modified technique that was used in this series of patients has several advantages that are not reported with similar laparo-endoscopic and traditional laparoscopic techniques.

First of all, this technique allows surgeons the resection of tumors located at the proximal stomach without major gastric resections, and while simultaneously using the stapler for tumor resection and gastric wall closure. In some tumors located at the anterior wall of the stomach, the laparoscopic approach with wedge resection with endoscopic guidance is recommended based on the difficulties to resect the mass with other techniques. Tumors near to the pylorus usually require distal gastrectomies and anastomosis to avoid strictures related with wedge resection in this area [30]. Tumors located either at the GE junction or the

antrum (3 cm from pylorus) are considered to be difficult to access, as previous studies have reported technical limitations using the traditional laparoscopic approach [24–26, 31].

Secondly, the technique minimizes the risk of potential port-site complications such as hernias, fistulas, bleeding, and better cosmetic results, complications previously reported with the traditional laparoscopic approach. In our cohort, the most frequent complication postoperatively was bleeding at the staple line of the tumor resection, seen in 2 patients (14.3 %). Patients showed a dropping in the hemoglobin levels during the first 24 h postoperatively and EGD revealed active gastric bleeding. The bleeding was controlled in both cases with endoscopic clips and there were no reoperations. Similar results in terms of postoperative complications were found by Qui et al. in 2012 [27]. In our experience, the cause of the bleeding was interpreted as a technical failure in the staple device. Based on the clinical experience of these 2 cases of postoperative bleeding, we decided that at the time of the terminal staple fire, a white load should be used instead of blue load to reduce the risk of postoperative hemorrhage. As a complementary strategy, we began using staple line reinforcement with a bioabsorbable matrix—Seamguard (W.L. Gore & Associates, Inc., Flagstaff AZ). Current scientific evidence shows that this reinforcement may reduce the rates of bleedings and leaks at the resection site [32].

Next, due to transgastric extraction capabilities, large abdominal incisions are not required to remove the tumors from the abdominal cavity. It is important to note, however, that transgastric extraction of SMTs is generally safe and feasible for only tumors <3–4 cm in size. Larger tumors will require anterior gastrotomy to extract the specimen. In this study, there was one conversion to traditional laparoscopic surgery due to the large size of the tumor (wide base and slightly elevated) and lack of space to manipulate surgical instruments [33]. Even still, there were no conversions to open surgery seen in this series. Comparable results were observed in previous studies published by Hiki et al., Qui et al., and Tsujimoto et al. [1, 3, 12].

In terms of costs, there are no current studies published comparing the cost of laparo-endoscopic techniques and traditional laparoscopic approaches, however in our experience, we have not seen increases in the cost of these procedures since we are using the same resources available (surgical instruments and supplies) for other laparoscopic and endoscopic procedures.

Finally, this technique creates an academic and professional environment for teamwork among gastrointestinal surgeons, gastroenterologists, pathologists, and radiologists, providing better care to our patients as recommended by current National Comprehensive Cancer Network (NCCN) and European Society of Medical Oncology (ESMO) guidelines [34, 35].

Similar surgical approaches and techniques have been developed and evaluated for the management of colon and rectum tumors. In 2010, Kuroki et al. reported 34 consecutive cases of residual and locally recurrent colorectal tumors treated with ESD [36]. The perforation rate was 14.7 %, reoperation was required in one case, and the rates of *en bloc* resection and complete resection were 93 and 82 %, respectively. This study concluded that

the use of ESD for residual/locally recurrent lesions was curative and efficacious, and this technique reduced surgical resection requirements.

Other MIS approaches in colorectal malignancies were evaluated by Kiriya et al. in the study entitled “Comparing endoscopic submucosal dissection with transanal resection (TAR) for non-invasive rectal tumor: a retrospective study” published in 2011 [37]. TAR and transanal endoscopic microsurgery (TEM) were proposed as well-developed surgical procedures for the local excision of rectal adenomas, intramucosal cancers, and superficial submucosal cancers of the rectum, including GIST. TEM provided better visualization than TAR, and the clinical results with TEM were superior. ESD was associated with a longer procedure time than TAR, but ESD was more effective than TAR for the treatment of non-invasive rectal tumors, with lower recurrence rates and shorter hospital stays.

In our study, GISTs were the most common type of SMTs (71.4 %) treated with this approach. The primary treatment for resectable GIST is surgery, but this approach is not always curative. Complete (R0) resection can be achieved in up to 85 % of patients with primary disease and approximately 50 % of patients develop metastasis or recurrences within 5 years of primary resection. Treatment response of GISTs depends on factors such as primary tumor location, tumor size, and mitotic index [22, 38].

GISTs patients are divided in three groups, low risk, intermediate risk, and high risk depending upon tumor size, mitotic index [MI, mitoses per 50 high-power fields (HPF) equals 5 mm²], and location. In high-risk patients, the combination with neoadjuvant/preoperative and adjuvant/postoperative with chemotherapy (imatinib) is recommended and can improve recurrence-free and overall survival [39]. Two cases in our study were classified as high-risk patients and were initiated combined therapy with imatinib. One case reported a recurrence during the first 12 months after the primary resection procedure and initiated combined therapy with imatinib, for a total recurrence rate of 10 % in the GIST group.

As in any retrospective review of a prospectively collected patient database, this study has limitations. A case series is uncontrolled, authors were subject to selection bias since they self-select the cases and we depended on the accuracy and the availability of medical records. Herein, we present the largest single institution series utilizing this technique for the resection of gastric SMT in the US.

Conclusion

We present the largest single institution series utilizing this technique for the resection of SMTs in North America. Our experience suggests that this surgical approach is safe and effective at a consistent level. This study in particular showed no intraoperative or postoperative complications and optimal oncologic outcomes during the follow-up period.

In general, MIS approaches are emerging as a valid and potentially superior approach for resecting malignancies since they limit surgical trauma and maintain oncologic standards. However, continued investigation is underway to further validate this data.

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Fig. 1.
Port placement

Fig. 2.
Trocar placement: **A** laparoscopic and endoscopic view **B** endoscopic view

Fig. 3.
Tumor resection and stapling (endoscopic view)

Fig. 4.
Tumor extraction using an endobag (endoscopic view)

Fig. 5.
Transoral tumor extraction: **A, B** laparoscopic and endoscopic view **C** external view

Table 1

Demographic information and tumor location

	Number	Percent (%)
Age		
Mean	56.8 ± 13.0	
Median	56	
Range	29–78	
Gender		
Male	6	42.9
Female	8	57.1
Race		
White	10	71.4
Hispanic	3	21.4
Unknown	1	7.1
Type of operation		
Laparo-endoscopic	8	57.1
Traditional laparoscopic surgery	5	35.7
Cases abandoned	1	7.2
Location of tumor		
Antrum	6	40
Duodenum*	1	6.7
Fundus	2	13.3
GE junction	4	26.7
Lesser curvature	2	13.3

Table 2

Post-operative outcomes

	Number	Percent (%)
Operative time (min)		
Mean	84.1 ± 33.9	
Median	80	
Range	35–167	
Estimated blood loss (ml)		
Mean	20 ± 12.8	
Median	20	
Range	5–50	
Length of postoperative hospital stay (days)		
Mean	1.8 ± 1.5	
Median	1	
Range	1–6	
Patients with intra-operation complication		
Yes	0	0
No	14	100
Reoperation		
Yes	0	0
No	14	100
Patients with post-operation complication		
Bleed at resection site/hematemesis	2	14.3
Nausea	3	21.4
Abdominal pain	2	14.3
Other (urinary retention)	1	7.1
30-day mortality		
Yes	0	0
No	14	100

Table 3

Pathology results

	Number	Percent (%)
GIST	10	71.4
Leiomyoma	3	21.4
Schwannoma	1	7.1

Table 4

GIST tumors characteristics and follow-up

Patient	Size path report (cm)	Mitosis index (N/50 HPF)	Margin status (R0, R1, R2)	Tumor capsule intact (Y/N)	Tumor rupture	KIT-positivity (Y/N)	DOG-1-positivity (Y/N)	Adjuvant imatinib (Y/N)	Follow-up 12 m recurrence (Y/N)
1	3.9	2	R0	Y	N	Y	Y	N	N
2	3.6	20	R0	N	N	Y	Y	Y	N
3	2.0	1	R0	Y	N	Y	Y	N	N
4	3.3	3	R0	Y	N	Y	Y	N	N
5	2.1	8	R0	Y	N	Y	Y	Y	Y
6	4.2	4	R0	Y	N	Y	Y	N	N
7	3.8	1	R0	Y	N	Y	Y	N	N
8	4.5	4	R0	Y	N	Y	Y	N	N
9	2.8	NA	R0	Y	N	Y	Y	N	N
10	3.2	4	R0	Y	N	Y	Y	N	N

NA not available