Laparoscopic management of gastrointestinal stromal tumours: review at a Canadian centre

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Background: Laparoscopic wedge resection has been widely accepted for small benign gastric tumours. Large gastrointestinal stromal tumours (GISTs), however, can be difficult to manipulate laparoscopically and are at risk for capsule disruption, which can then result in peritoneal seeding. Some authors have suggested that large GISTs (> 8 cm) are best approached using an open technique. However, there has been no consensus as to what the cut-off size should be. We conducted one of the largest Canadian series to date to assess outcomes and follow-up of the laparoscopic management of GISTs.

Methods: All patients with gastric GISTs presenting to Vancouver General Hospital and University of British Columbia Hospital between 2000 and 2008 were reviewed. Most lesions were resected using a wedge technique with closure of the stomach facilitated by an endoscopic linear stapling device.

Results: In all, 23 patients presented with GISTs; 19 patients underwent laparoscopic resection and, of these, 15 had a purely laparoscopic operation and 4 had a hand-assisted laparoscopic resection. Mean tumour size was 3.2 cm, with the largest tumour measuring 6.8 cm. There were no episodes of tumour rupture or spillage and no major intraoperative complications. All margins were negative. Mean follow-up was 13.3 (range 1–78) months. There was no evidence of recurrence or metastasis.

Conclusion: The laparoscopic management of gastric GISTs is safe and effective with short hospital stays and good results over a mean follow-up of 13.3 months. We believe that it should be the preferred technique offered to patients.

Contexte : La résection cunéiforme par laparoscopie est généralement acceptée pour les petites tumeurs gastriques bénignes. Les grosses tumeurs du stroma gastro-intestinal (TSGI) peuvent toutefois être difficiles à manipuler par laparoscopie et une rupture possible de la capsule peut entraîner une atteinte du péritoine. Certains auteurs ont laissé entendre que la technique ouverte constitue la meilleure façon d'aborder une TSGI de grande taille (> 8 cm). Il n'y a toutefois pas de consensus sur la dimension limite. Nous avons effectué l'une des plus importantes séries canadiennes réalisées jusqu'à maintenant pour évaluer les résultats et le suivi du traitement de la TSGI par laparoscopie.

Méthodes : Nous avons étudié les dossiers de tous les patients qui avaient une TSGI gastrique et qui se sont présentés à l'Hôpital General de Vancouver et à l'Hôpital de l'Université de la Colombie-Britannique entre 2000 et 2008. La plupart des lésions ont été retirées par résection cunéiforme et une agrafeuse linéaire endoscopique a facilité la fermeture de l'estomac.

Résultats : Au total, 23 patients se sont présentés avec une TSGI et 19 ont subi une résection laparoscopique. Sur ce total, 15 ont subi une laparoscopie pure et 4, une laparoscopie avec assistance manuelle. La taille moyenne de la tumeur s'établissait à 3,2 cm et la plus grosse mesurait 6,8 cm. Il n'y a eu aucun cas de rupture ni de fuite, ni aucune complication majeure au cours de l'intervention. Toutes les marges se sont révélées négatives. Le suivi moyen s'est établi à 13,3 (écart 1–78) mois. Il n'y avait aucun signe de récidive ni de présence de métastases.

Conclusion : Le traitement par laparoscopie de la TSGI gastrique est sécuritaire et efficace, les séjours à l'hôpital sont courts et les résultats sont bons au cours d'un suivi moyen de 13,3 mois. Nous sommes d'avis qu'il devrait s'agir de la technique privilégiée à offrir aux patients.

Gastrointestinal stromal tumours (GISTs) are rare gastrointestinal cancers (0.1%–3%).[1–3] They most commonly affect the upper gastrointestinal tract with involvement of the stomach in more than 50% of cases.[1–4] Although patients can present with abdominal pain or bleeding, they are often asymptomatic. The increased number of upper gastrointestinal endoscopies and endoscopic ultrasounds being performed has likely contributed to the increased incidence of GISTs.[5]

Recent research has brought new understanding to the pathophysiology and management of GISTs. They tend to remain localized as opposed to diffusely infiltrating the primary organ.[3] It is also known that they do not typically metastasize to lymph nodes.[5] As a result, a localized wedge resection of the lesion is an acceptable treatment option when anatomically feasible.[6]

Laparoscopic wedge resection has been widely accepted for benign gastric tumours.[7] For GISTs, the technique was applied in 1999 by Ohgami and colleagues.[8] Since then, many centres around the world have published the results of their own series, showing the laparoscopic approach to be safe and oncologically equivalent to open techniques. Large tumours, however, can be difficult to manipulate laparoscopically and are at risk for capsule disruption, which can then result in peritoneal seeding. As a result, some authors have suggested that large GISTs are best approached using an open technique. However, there has been no consensus as to what the cut-off size should be.[2]

We conducted one of the largest Canadian series to date to assess outcomes and follow-up of the laparoscopic management of GISTs.

Methods

We reviewed the cases of all patients with gastric GISTs who presented to Vancouver General Hospital and University of British Columbia Hospital between 2000 and 2008. Surgical resection using a laparoscopic approach, either purely laparoscopic or with a hand-assisted technique was the preferred procedure.

The data recorded included patient age, sex, body mass index, location of the tumour (from preoperative imaging studies), final size of the tumour (resected specimen), symptoms at presentation, diagnostic workup, type of operation, conversion rate, length of stay in hospital, and early and late complications.[6] Pathologic classification of the tumour as well as outpatient follow-up data were also recorded. All patients had preoperative computed tomography (CT) scans for surgical planning and staging.

Most lesions were resected using a wedge technique with closure of the stomach facilitated by an endoscopic linear stapling device. Specimens were routinely removed using a specimen retrieval bag or a wound protector. The same technique was applied to posterior gastric wall tumours, after entrance to the lesser sac and division of the short gastric vessels. In our patients, only 1 transgastric approach (the Ohashi method) was needed and performed through a hand-port, and no combined endoscopic–laparoscopic technique was judged necessary. Endoscopy was performed selectively at the end of the procedure to confirm the absence of narrowing of the gastroesophageal (GE) junction. Bougies were used selectively in this study to prevent narrowing when patients had tumours in the gastric fundus that were near the GE junction. Nasogastric tubes were not used routinely and were placed at the discretion of the surgeon. They tended to be used in cases of large resections and when there was a lot of manipulation of the stomach.

Pathologically, tumours were classified has having low, intermediate or high malignant potential based on the number of mitoses and tumour size (Fletcher risk classification).[6,9]

Results

Between 2000 and 2008, specialists in minimally invasive surgery at the Vancouver General Hospital and UBC Hospital surgically managed the cases of 23 patients (10 men and 13 women with a mean age of 62 years) with gastric GISTs. The outcomes from these procedures are reported along with follow-up data. Demographic and clinical characteristics of patients are reported in Table 1. All GISTs were located in the stomach: 12 in the fundus, 8 in the body and 3 in the antrum. Abdominal pain (35%) and gastrointestinal bleeding (43%) were the most common presenting symptoms, and the remaining patients were asymptomatic (22%).

Table 1. Demographic and clinical characteristics of patients treated for gastrointestinal stromal tumours

Characteristic	No. (%)*
Male	10 (43.5)
Female	13 (56.5)
Mean age, yr	62
Mean body mass index	26.13
Symptoms	
Asymptomatic	5 (21.7)
Abdominal pain	8 (34.8)
GI bleeding	10 (43.5)
Diagnostic workup	
EGD without biopsy	1 (4.3)
EGD and biopsy	14† (60.8)
EUS without biopsy	1 (4.3)
EUS with FNA biopsy	4‡ (17.4)
CT scan	4 (17.4)
Incidental finding	1§ (4.3)

CT = computed tomography; EGD = upper gastrointestinal endoscopy; EUS = endoscopic ultrasound; FNA = fine-needle aspiration; GI = gastrointestinal.
*Unless otherwise indicated.
†All negative for gastrointestinal stromal tumours.
‡All positive for gastrointestinal stromal tumours.
§During splenectomy.

As part of the initial diagnostic workup, most patients underwent upper gastrointestinal endoscopy (EGD) with or without biopsies (65% and 3.8%, respectively). All biopsies taken during EGD were negative, likely because GISTs are submucosal, and standard biopsy forceps often do not sample deeper tissue layers. Since C-kit testing can be done on fine-needle aspirates (FNA), endoscopic ultrasound (EUS) with biopsy is much more sensitive (sensitivity 84.4%).[10] The 4 patients (15%) who had EUS with biopsy had the diagnosis of GIST confirmed before surgery. One case was diagnosed incidentally during splenectomy for massive splenomegaly. In 4 patients, the GIST was diagnosed using only the CT scan.

Operative and postoperative data are shown in Table 2. Most patients (n = 19) were treated with either a purely laparoscopic operation (n = 15) or with a hand-assisted laparoscopic operation (n = 4). There were several reasons why a hand-assisted technique was used. One was an incidental GIST found during a hand-assisted splenectomy. One tumour was very close to the GE junction, and the surgeon felt that it would be safer to perform the operation using a hand-port device. In 1 patient conversion to a hand-assisted technique was needed owing to the size of the tumour (6.8 cm) for easier manipulation and extraction. And in 1 patient a hand-port was inserted because the tumour was on the posterior wall of the stomach, and an anterior gastrotomy was performed (Ohashi method)[11] through the hand-port access site to resect the tumour. There were no conversions to a formal open technique. Among the 4 patients who underwent open techniques, 1 had a tumour that was too large (19.5 cm) to be approached laparoscopically. The other 3 patients underwent laparotomy because of the tumours' proximity to the GE junction and to prevent narrowing during the resection.

The mean duration of surgery was 88 minutes in the laparoscopic group (range 56–164 min) and 92 minutes in the open group (range 82–136 min). The duration was longer in the open group likely because the tumours were much larger and were in technically challenging locations. The mean follow-up time was 13.3 months (range 1–78 mo), with no evidence of metastasis or recurrence.

One patient had a high-grade tumour and peritoneal carcinomatosis. There were no episodes of tumour rupture or spillage and no major intraoperative complications. There was 1 early complication (wound infection), and there were 2 late complications (incisional hernias), all of which occurred in the open group. The average length of stay in hospital was 6 days (laparoscopic 5 d v. open 12.5 d).

Tumour characteristics are reported in Table 3. The mean tumour size in the laparoscopic group was 3.2 cm, with the largest tumour measuring 6.8 cm. The mean tumour size in the open group was 7.5 cm, with the largest tumour measuring 19.5 cm. All margins were negative. According to the GIST risk criteria, 20 patients (86.9%) had a low-grade tumour. Two patients (8.7%) had a moderate-grade tumour and were treated with adjuvant imatinib mesylate therapy. One patient (4.3%) had a high-grade tumour and peritoneal carcinomatosis and was lost to follow-up.

Table 2. Operative and postoperative characteristics of patients treated for gastrointestinal stromal tumours

Characteristic	No. (%)*
Purely laparoscopic	15 (65.2)
Converted to hand-assisted	4 (17.4)
Open	4 (17.4)
Early complications	1† (4.3)
Late complications	2† (8.6)
Resection margins	All negative
Average length of stay, d	6.0
Laparoscopic	5.0
Open	12.5
Follow-up time, mean (range), mo	13.3 (1–78)
Local recurrence	0

*Unless otherwise indicated.
†Open.

Discussion

Gastrointestinal stromal tumours, although rare, are the most common mesenchymal tumour of the gastrointestinal tract.[1] Lymph node metastases are very rare, and routine lymphadenectomy is not required. Although enucleation is associated with high rates of recurrence, wedge resection of gastric GISTs has been widely reported to be successful. The goal of surgical resection should be complete removal of the tumour with clear resection margins. Because these tumours do not usually diffusely infiltrate the wall of the stomach, resection margins of 1–2 cm are usually sufficient. Tumour rupture during laparoscopy should be avoided as peritoneal seeding can affect the disease-free period and overall patient survival.

Table 3. Tumour characteristics of patients treated for gastrointestinal stromal tumours

	Group; no. (%)*	
Characteristic	Laparoscopic	Open
Tumour size, mean (range) cm	3.2 (0.6–6.8)	7.5 (1.8–19.5)
Location of tumour		
Fundus	8 (34.7)	4 (17.4)
Body	8 (34.7)	0
Antrum	3 (13.0)	0
Pathology risk classification		
Low risk	18 (78.3)	2 (8.7)
Moderate risk	1 (4.3)	1 (4.3)
High risk	0	1 (4.3)

*Unless otherwise indicated.

Most patients presenting to our group were first offered a minimally invasive approach either laparoscopically or with a hand-assisted technique. It is possible, however, that patients presenting to our group, which performs most of the advanced laparoscopic surgeries in our hospital, may have been "preselected" for a laparoscopic resection by the referring physician. It is possible that patients with larger and more advanced gastric GISTs were not referred to our group.

Because GISTs are submucosal, regular endoscopic biopsies rarely provide pathologic confirmation. But now that C-kit testing can be performed on FNA specimens, and because FNA is associated with a very low risk of seeding, many GISTs can be diagnosed preoperatively using EUS and FNA.[10] This method was used in 4 patients in our series.

Most patients in this study underwent a purely laparoscopic technique to remove their tumours. Four procedures (17%) were converted to a hand-assisted technique, a bridge between a purely laparoscopic and an open technique. The hand-assisted approach was useful in managing larger tumours or tumours that were in difficult locations, since these tumours are at a higher risk of rupture during manipulation in a purely laparoscopic operation. The hand-assisted technique was not associated with increased morbidity, and it did not compromise oncologic outcomes.

Reports from the 2004 National Comprehensive Cancer Network GIST Task Force and the GIST Consensus Conference under the auspices of the European Society of Medical Oncology recommend that laparoscopic or laparoscopic-assisted resection may be used for small (< 2 cm) GISTs.[7] In our series, we demonstrated that GISTs larger than 2 cm can be safely removed laparoscopically (mean tumour size 3.2 cm in the laparoscopic group) with oncologic results similar to those obtained using an open technique. Other studies have also confirmed the feasibility and safety of laparoscopic resection of tumours measuring up to 5 cm.[12–16] The largest GISTs removed laparoscopically in our study measured 6.2–6.8 cm.

Laparoscopic stapling of the stomach for GIST resection may sometimes result in an excessive amount of normal gastric mucosa being removed. This in turn may cause stomach deformity and narrowing, particularly in areas such as the esophagogastric junction. The "new-shaped" stomach may also result in dysmotility problems. A cut and sew technique might be superior to the use of staplers in these difficult areas to avoid the sacrifice of an excessive amount of normal gastric mucosa.[16] Esophageal bougies can also be used before applying a stapler when the tumour is close to the GE junction.[17] Bougies were used selectively in this series when patients had tumours in the gastric fundus. We selectively used the hand-port and performed endoscopy during surgery to prevent narrowing of the GE junction after stapling of the stomach.

Gastrointesinal stromal tumours are resistant to conventional chemotherapy and radiotherapy. Imatinib mesylate has proven useful in the treatment of recurrent or metastatic GISTs and is now accepted as an adjuvant therapy after surgical resection. However, resistance to imatinib is a growing problem, and other targeted agents, such as sunitinib, are available.[18,19] Until proven otherwise, complete excision with clear resection margins and without tumour rupture remains the mainstay of treatment for primary GISTs. In our series, the 2 patients with moderate-risk GISTs were offered imatinib mesylate as adjuvant therapy. The patient with peritoneal carcinomatosis was lost to follow-up.

Many of the tumours in this series were considered low-risk based on size and mitotic index. There is some controversy about whether these low-risk tumours measuring less than 2 cm can be followed without resection. Some authors recommend that all GISTs be resected because of the potential for malignant transformation. Most guidelines, however, suggest that surveillance is probably a safe approach for the management of asymptomatic patients with an incidentally discovered small GIST (< 2 cm) that does not display suspicious endosonographic features (e.g., irregular border, presence of cystic spaces, echogenic foci,)[20] Of course, some patients with small GISTs, such as young patients with small GISTs that would require years of surveillance and patients who are noncompliant with regular follow-up testing, may still benefit from surgical resection.

Conclusion

This report summarized the experience at a single institution and is one of the largest Canadian studies to report on the laparoscopic management of GISTs. We conclude that the laparoscopic management of GISTs of the stomach is safe and effective, with short stays in hospital and good results over a mean follow-up of 13.3 months. We believe that it should be the preferred technique offered to patients. The use of the laparoscopic approach should be based on a variety of factors, including patient characteristics, tumour size, presence of invasion, location and the surgeon's experience and laparoscopic expertise.

A laparoscopic approach may be the preferred resection technique in most patients with small- and medium-sized gastric GISTs. Larger GISTs in difficult anatomic locations may still require an open technique, as a formal gastric resection may be required. If the expertise is available, a combined laparoscopic–endoscopic "rendezvous" approach may be considered. We also advocate a hand-assisted technique, when needed, to facilitate tumour manipulation and resection. This technique allows for gentle tumour handling, tactile feedback and precise placement of endoscopic staplers.

Competing interests: None declared.

Contributors: All authors designed the study, reviewed the article and approved its publication. C. Daigle and J. Lam acquired the data, which C. Daigle and O.N.M. Panton analyzed. C. Daigle and A.T. Meneghetti wrote the article.

References

1. Basu S, Balaji S, Bennett DH, et al. Gastrointestinal stromal tumors (GIST) and laparoscopic resection. *Surg Endosc* 2007;21:1685-9.
2. Bédard EL, Mamazza J, Schlachta CM, et al. Laparoscopic resection of gastrointestinal stromal tumors: Not all tumors are created equal. *Surg Endosc* 2006;20:500-3.
3. Nguyen SQ, Divino CM, Wang JL, et al. Laparoscopic management of gastrointestinal stromal tumors. *Surg Endosc* 2006;20:713-6.
4. Catena F, Di Battista M, Fusaroli P, et al. Laparoscopic treatment of gastric GIST: report of 21 cases and literature's review. *J Gastrointest Surg* 2008;12:561-8.
5. Lai IR, Lee WJ, Yu SC. Minimally invasive surgery for gastric stromal cell tumors: intermediate follow-up results. *J Gastrointest Surg* 2006;10:563-6.
6. Blay JY, Landi B, Bonvalot S, et al. [Recommendations for the management of GIST patients] [Article in French]. *Bull Cancer* 2005;92: 907-18.
7. Demetri GD, Benjamin RS, Blanke CD, et al.; NCCN Task Force. NCCN Task Force report: management of patients with gastrointestinal stromal tumor (GIST)–update of the NCCN clinical practice guidelines. *J Natl Compr Canc Netw* 2007;5 Suppl 2:S1-29; quiz S30.
8. Ohgami M, Otani Y, Kumai K, et al. Curative laparoscopic surgery for early gastric cancer: five years experience. *World J Surg* 1999;23: 187-92; discussion 192.
9. Hindmarsh A, Koo B, Lewis MP, et al. Laparoscopic resection of gastric gastrointestinal stromal tumors. *Surg Endosc* 2005;19:1109-12.
10. Sepe PS, Moparty B, Pitman MB, et al. EUS-guided FNA for the diagnosis of GI stromal cell tumors: sensitivity and cytologic yield. *Gastrointest Endosc* 2009;70:254-61.
11. Novitsky YW, Kercher KW, Sing RF, et al. Long-term outcomes of laparoscopic resection of gastric gastrointestinal stromal tumors. *Ann Surg* 2006;243:738-45, discussion 745-7.
12. Fletcher CD, Berman JJ, Corless C, et al. Diagnosis of gastrointestinal stromal tumors: a consensus approach. *Hum Pathol* 2002;33:459-65.
13. Nishimura J, Nakajima K, Omori T, et al. Surgical strategy for gastric gastrointestinal stromal tumors: laparoscopic vs. open resection. *Surg Endosc* 2007;21:875-8.
14. Otani Y, Kitajima M. Laparoscopic surgery for GIST: too soon to decide. *Gastric Cancer* 2005;8:135-6.
15. Hiki N, Yamamoto Y, Fukunaga T, et al. Laparoscopic and endoscopic cooperative surgery for gastrointestinal stromal tumor dissection. *Surg Endosc* 2008;22:1729-35.
16. Huguet KL, Rush RMJ, Tessier DJ, et al. Laparoscopic gastric gastrointestinal stromal tumor resection: the Mayo Clinic experience. *Arch Surg* 2008;143:587-90; discussion 591.
17. Taniguchi E, Kamiike W, Yamanishi H, et al. Laparoscopic intragastric surgery for gastric leiomyoma. *Surg Endosc* 1997;11:287-9.
18. Quek R, George S. Update on the treatment of gastrointestinal stromal tumors (GISTs): role of imatinib. *Biologics* 2010;4:19-31.
19. Law C, Swallow C, Blackstein M, et al. *Current multidisciplinary strategies and future trends in the management of primary and advanced GIST*. Montréal (QC): SNELL Medical Communication Inc.; 2010.
20. Sepe PS, Brugge William R. A guide for the diagnosis and management of gastrointestinal stromal cell tumors. *Nat Rev Gastroenterol Hepatol* 2009;6:363-71.

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