Review Article

Open versus laparoscopic treatment for small bowel gastrointestinal stromal tumors

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Abstract: Gastrointestinal stromal tumors (GISTs) are the most common soft-tissue sarcoma of the gastrointestinal tract. Those found in the small bowel behave more aggressively than tumors originating in the stomach and confer a higher risk of metastases. Minimally invasive resection, including laparoscopic and robotic approaches, has been established as a safe and feasible alternative to conventional open resection for gastric GISTs, with improved perioperative morbidity and non-inferior oncologic outcomes. Data, however, are less established for small bowel tumors. Currently, there are emerging data suggesting that minimally invasive resection is a safe and feasible surgical option with similarly favorable outcomes for small bowel GISTs. Duodenal GISTs, rarer still, are a subset that offer unique anatomic challenges to minimally invasive resection. While minimally invasive approach for duodenal tumors has been described, data remains insufficient to draw clear conclusions on laparoscopic or robotic resection for GISTs located in the duodenum. Caution is merited to avoid overinterpretation of the current limited data. Future research to validate minimally invasive techniques for duodenal lesions is necessary. Regardless of minimally invasive approach, oncologic principles of resection apply. Surgical approach and oncologic planning are dependent on location and size of the tumor, with a range of surgical techniques illustrated in the literature. These techniques and surgical pearls are reviewed to guide technical decision making for these lesions. This narrative review aims to present the latest data on minimally invasive resection for small bowel and duodenal GISTs and discuss surgical considerations.

Keywords: Gastrointestinal stromal tumors (GIST); small bowel GIST; duodenal GIST; laparoscopy; minimally invasive surgery

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Introduction

Gastrointestinal stromal tumors (GISTs) are the most common soft-tissue sarcomas of the gastrointestinal tract and arise from interstitial cells of Cajal (1,2). GISTs are most commonly discovered in the stomach (50–70%), followed by small intestine (30–45%), esophagus and colon (5–15%) (1-4). Tumor size and mitotic rate are traditional predictors of recurrence and metastatic disease; however, tumor origin now is an additional prognostic factor used for risk stratification due to differences in biologic behavior (2,3,5). Gastric GISTs behave more indolently, while small bowel GISTs behave more aggressively, conferring a higher

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rate of metastatic potential for tumors with mitotic rate >5 mitoses/50 high-power field (2,5). Colon and rectal GISTs are even less common and thought to behave just as, if not more aggressively than small bowel GISTs (6-9).

Surgical resection remains the mainstay of therapy for primary GISTs, with the goal of complete resection and histologically negative margins (1,5,10). Lymphadenectomy is typically not required due to low incidence of lymphatic spread, unless enlarged lymph nodes are present on preoperative imaging or found unexpectedly at surgery (2,5,11). Historically, while a minimally invasive (MIS) approach was recommended for small tumors, caution was deemed to be warranted for large lesions due to the friable nature of the capsule making them susceptible to rupture and risk of subsequent tumor dissemination (2,10,12). While the present literature has established the safety profile and feasibility of performing MIS resections of gastric GISTs (13-20), the role for MIS surgery has yet to be clearly defined for small bowel GISTs.

The aim of this narrative review is to present the latest data on perioperative and oncologic outcomes of MIS resection compared to conventional open resection of small bowel and duodenal GISTs, as well as discuss technical considerations at surgery. We present the following article in accordance with the Narrative Review reporting checklist (available at http://dx. doi. org/10. 21037/ls–20–90).

Methods

The PubMed database was queried for all articles relevant to minimally invasive resection of small bowel GISTs published prior to May 2020. Keywords used for search queries include 'small bowel gastrointestinal stromal tumor/GIST', 'intestinal gastrointestinal stromal tumor/GIST', 'duodenal gastrointestinal stromal tumor/GIST', 'gastrointestinal stromal tumor/GIST of duodenum', 'small bowel gastrointestinal stromal tumor resection', 'laparoscopic resection', 'robotic resection', 'robot-assisted resection'. All English published articles, including cohort studies, case series, meta-analyses, and reviews were selected. Select case reports were included in the review and discussion of robot-assisted resection of duodenal GISTs due to the rarity of this procedure and indication.

Current outcomes for MIS vs. open resection

Most data published on MIS resection for GISTs focus on gastric GISTs. The great bulk of the literature reflects laparoscopic resection, with few recent series and case reports describing robot-assisted resection (21-26). It has previously been established that laparoscopic resection for gastric GISTs is associated with reduced intraoperative blood loss, shorter operative time, faster recovery of bowel function and resumption of oral diet, and shorter hospital length of stay as compared to conventional open surgery (13,14,16-19). Long-term oncologic outcomes were previously found to be non-inferior (27,28), and perhaps even better (observed, but may be selection bias) (15,17,20,29,30) for laparoscopic approach compared to open resection in meta-analyses, even for large tumors >5 cm. As such, MIS resection is a safe and feasible technique with non-inferior oncologic outcomes for gastric GISTs.

In contrast, outcomes after minimally invasive resection of GISTs from other sites are less established (3). There are a small number of retrospective case series describing single-institution laparoscopic experience (without a comparison open cohort) which combine gastric and small bowel GISTs (*Table 1*, #1–#4). These studies describe short hospital stays with minimal complications (31-34). The largest of these series describes the ten-year laparoscopic experience for 89 gastric and 26 small bowel GISTs (31). The authors found that length of hospital stay and perioperative morbidity were similar between laparoscopic gastric and small bowel resections. Mean tumor size was approximately 4 cm for both gastric and small bowel lesions. The authors noted that small bowel GISTs were more likely to present acutely, requiring emergent intervention. Notably, patients with small bowel GISTs had similar recurrence rates, disease-free survival and overall survival compared to those with gastric GISTs after laparoscopic resection.

There are also a growing number of retrospective cohort studies that sought to compare open versus laparoscopic techniques. Again, a number of these investigators combined gastric and small bowel GISTs, and generally did not stratify results based on tumor location (*Table 1*, #5–#7). These studies demonstrated similarly favorable short-term outcomes, including faster postoperative recovery with shorter time to resumption of oral diet, shorter hospital length of stay, and fewer complications associated with laparoscopic resection (35-37). A recently published analysis using the National Cancer Database (NCDB) sought to determine survival outcomes for laparoscopic versus open resection of gastric and small bowel GISTs, stratified by pathologic stage (*Table 1*, #8) (38). The authors demonstrated improved overall survival for patients who

Table 1 Review of published studies on laparoscopic versus open resection of small bowel gastrointestinal stromal tumors

Author, year	Study design, n	Country/Region	Study period	Location of GIST			Surgical approach		LOS	Comp	Recur	DFS	OS
				Gastric	SB	Duo	Lap	Open					
#1. Tabrizian *et al.*, 2014 (31)	RCS, n=116	New York, USA	1999–2011	89	26	–	116	–	[=]	[=]	[=]	[=]	[=]
#2. Loureiro *et al.*, 2016 (32)	CS, n=15	PR, Brazil	2009–2013	13	2	–	15	–	–	–	–	–	–
#3. Matlok *et al.*, 2015 (33)	CS, n=27*	Krakow, Poland	2009–2013	21	4	–	27	–	–	–	–	–	–
#4. Nguyen *et al.*, 2006 (34)	CS, n=43	New York, USA	2000–2005	28	15	–	43	–	–	–	–	–	–
#5. Chen *et al.*, 2012 (35)	RCS, n=58	Taipei, Taiwan	2005–2010	40	18	–	16	42	[-]	[=]	[=]	[X]	[X]**
#6. Fisher *et al.*, 2013 (36)	RCS, n=156*	Georgia, USA	2002–2011	118	14	19	47	109	[-]	[-]	[=]	[X]***	[X]
#7. Schwameis *et al.*, 2013 (37)	RCS, n=159*	Vienna, Austria	1994–2011	106	29	6	40	113	[X]	[-] (no P value)	[X]	[X]	[X]
#8. Inaba *et al.*, 2019 (38)	NCDB RCS, n=5,096	California, USA	2010–2014	3,533	1,563	–	1,895	3,201	[-]	[X]	[X]	[X]	[+] (stage I, II), [=] (stage III)
#9. Zhou *et al.*, 2018 (39)	CS, n=32	Wuhan, China	2013–2017	–	28	4	7	25	–	–	–	–	–
#10. Wan *et al.*, 2012 (40)	RCS, n=81	Shanghai, China	2004–2010	–	81	–	43	38	[-]	[-]	[X]	[=]	[X]
#11. Cai *et al.*, 2011 (41)	RCS, n=85	Shanghai, China	2002–2007	–	85	–	38	47	[-]	[=]	[X]	[=]	[X]
#12. Liao *et al.*, 2015 (42)	RCS, n=85	Taoyuan, Taiwan	2005–2013	–	85	–	26	59	[-]	[=]	[=]	[=]	[=]
#13. Ihn *et al.*, 2012 (43)	RCS, n=95	Seoul, South Korea	1993–2011	–	95	–	41	54	[-]	[=]	[-]	[=]	[=]
#14. Chen *et al.*, 2017 (44)	Meta-analysis (6), n=391	Hangzhou, China	2008–2015	–	391	–	170	221	[-]	[-]	[=]	[=]	[X]
#15. Hoeppner *et al.*, 2013 (45)	CS, n=9	Freiburg, Germany	2002–2011	–	–	9	1	8	–	–	–	–	–
#16. Chung *et al.*, 2010 (46)	CS, n=9	Gyeonggi-do, South Korea	2001–2009	–	–	9	2	7	–	–	–	–	–
#17. Abe *et al.*, 2017 (47)	CS, n=3	Tokyo, Japan	2016	–	–	3	3	–	–	–	–	–	–
#18. Tanaka *et al.*, 2015 (48)	RCS, n=19	Seoul, South Korea	2003–2013	–	–	19	8	11	[-]	[=]	[=]	[X]	[X]

*, these cohorts included patients with GISTs located elsewhere in the extra- or intra-gastrointestinal tract; **, no mortality within the study period; ***, all 47 patients who underwent laparoscopic resection were alive at 25.4 months, without evidence of disease. [=], equivocal results (e.g., similar recurrence rate, no difference in survival); [-], shortened or fewer (e.g., shortened hospital length of stay, fewer complications); [+], longer or lengthened (e.g., longer or improved survival); [X], variable was not included in study results. GIST, gastrointestinal stromal tumor; SB, small bowel (jejunum/ileum); Duo, duodenum; Lap, laparoscopic approach; LOS, [hospital] length of hospital stay; Comp, complications; Recur, recurrence; RCS, retrospective cohort study; CS, case series; NCDB, National Cancer Database; DFS, disease-free survival; OS, overall survival.

underwent laparoscopic resection for Stage I and II disease, but no difference in Stage III disease. It is not intuitive why this would be the case, but perhaps this is related to selection bias of patients deemed appropriate for each surgical approach.

There is a paucity of studies that solely examine MIS resection for small bowel GISTs. Currently, there are a handful of retrospective cohort studies evaluating laparoscopic versus open resection of small bowel GISTs alone (excluding gastric GISTs) (*Table 1*, #9–#13). These authors found that laparoscopic resection of small bowel GISTs resulted in shorter operative time, earlier return of bowel function, and shortened hospital length of stay (39-43). The median tumor size was approximately 4–5 cm and conversion rate was between 1.1–4.9% among these studies. These data reinforce the findings from the mixed gastric/small bowel cohorts—there was no difference in recurrence and survival, suggesting that laparoscopy is an acceptable alternative approach from a safety and oncologic perspective. These findings were supported by a recently published meta-analysis (*Table 1*, #14) (44), but the authors caution interpretation of the data due to limitations of the selected studies and analysis.

While earlier recommendations reserve MIS resection for small lesions less than 2cm in size (2,12,36), there are reports of larger lesions resected by MIS means. Although the reported average (mean or median) size of resected tumors has ranged around 4–6 cm, in their NCDB study, Inaba et al found 286 stage III GISTs (118 small bowel origin) that were resected laparoscopically despite a mean size of 9.5 cm (38). Others reported successfully resecting small bowel lesions up to 11.5 cm in size (31). MIS approach has also been reported to successfully address acute presentations of small bowel GISTs (4,31,37,39,49). Symptomatic GISTs can present with gastrointestinal bleeding, obstruction, or rarely as incarcerated hernias. It is important during these urgent procedures to follow oncologic principles of resection. An important consideration is postoperative referral to medical oncology for evaluation of adjuvant therapy for high risk lesions or with those with rupture of the pseudocapsule during urgent resection (49,50).

Duodenal GISTs

Duodenal GISTs are a rarer still subset of GISTs, occurring in approximately 20% of small bowel GISTs (46,51), and accounting for only 3–5% of all GISTs (10,50,52). In prior studies, duodenal GISTs are found most commonly in the second portion (46), followed by the third portion, fourth portion and lastly the first portion of the duodenum (52,53). Generally, because GISTs rarely exhibit intramural spread, extended anatomic resections and complex multi-visceral resections can often be avoided. Published studies evaluating open resection have described a spectrum of techniques from enucleation to limited wedge or segmental resection, to pancreaticoduodenectomy (46,51).

Not surprisingly, pancreaticoduodenectomy was associated with longer hospital length of stay and perioperative complications (10,54,55). Recurrence and overall survival were similar between limited resection and pancreaticoduodenectomy (10,53,54,56,57), although Lee *et al.* noted lower 5-year relapse-free survival associated with limited resection compared to pancreaticoduodenectomy (55). Limited resection is recommended when anatomically feasible and extensive resections are reserved for duodenal tumors involving the ampulla of Vater. As such, it has also been recommended to consider a course of neoadjuvant therapy to potentially downsize the lesion prior to resection (10,46,53,58).

Due to the rarity and anatomic considerations of duodenal GISTs, data and literature on MIS resection of duodenal GIST lesions are scarce, limited to small series and case reports. Several series evaluated laparoscopic versus open resection for duodenal lesions (*Table 1*, #15–#16), describing limited laparoscopic wedge resections and primary closures (45,46). A smaller case series reviewed laparoscopic-assisted resection and extracorporeal closure for ulcerated duodenal GISTs (*Table 1*, #17) (47). Tanaka et al focused on resection for lesions found at the duodenojejunal junction (*Table 1*, #18) (48). In this cohort of 19 patients, 11 underwent open and 8 laparoscopic segmental resections with duodenojejunostomies. There was no difference in recurrence, though it is notable that the two recurrences were from the open cohort. Robot-assisted resections utilizing various techniques have also been reported as case reports and part of case series (25,59-65). These authors suggest that robot-assistance may have a role in duodenal GIST resection, given the advantages of the robotic platform, including specifically the increased surgical dexterity for suture closure of the duodenal wall or anastomosis. Nonetheless, data remains insufficient to draw clear conclusions on laparoscopic or robotic resection for duodenal GISTs.

This review is limited by the number of publications presently available on the relevant topics and the study

Figure 1 Axial computational tomography imaging of a small bowel gastrointestinal tumor (arrowhead) located in the wall of the jejunum. These small bowel (jejunal or ileal) lesions can be resected with segmental resection and extra- or intracorporeal anastomosis.

cohorts. At this time, all studies that involve a minimally invasive approach for small bowel GISTs are retrospective in nature. The majority of the studies are single institution retrospective cohort studies or smaller case series. The largest cohort study uses the NCDB as the cohort and is the only study utilizing a national database. In addition, there is only one meta-analysis published on laparoscopic versus open resection of small bowel GISTs, which closely examines six studies that met inclusion criteria. There are fewer studies focused on minimally invasive resection of duodenal GISTs, mainly case series and case reports that evaluate robot-assisted resection. Presently, there are no published prospective trials on these topics. Though these studies report favorable results, future research is needed to better characterize the outcomes (survival, oncologic, perioperative) after minimally invasive surgery for small bowel GISTs.

Surgical considerations for MIS resection

Oncologic principles of MIS resection include complete resection with histologically negative margins, preservation of tumor pseudocapsule to avoid tumor spillage and dissemination, and removal within a specimen bag to prevent seeding of port sites (5,12). Due to the fragile nature of the capsule, careful handling of the tumor and gentle dissection are paramount (1,2,66). If possible, direct manipulation of the tumor should be avoided, instead handling the adjacent bowel and mesentery (2,40,42).

Resection of small bowel GISTs can be achieved with segmental bowel resection with extra- or intracorporeal anastomosis (*Figure 1*) (3,11,43,66). Resection of duodenal GISTs, however, is dependent on location and size of the lesion (*Figure 2*). Small lesions are amenable to wedge resection with primary closure, as long as the lumen remains adequately patent and ampulla of Vater preserved (46). It can be beneficial to perform a concomitant cholecystectomy and pass a balloon catheter through the cystic duct and down the common bile duct into the duodenal lumen. This will facilitate localization and safe preservation of the ampulla when resecting periampullary lesions. Larger tumors in the third and/or fourth part of the duodenum may require segmental duodenectomy with duodenojejunostomy (*Figure 2C-2F*) (46,48,53). Tumors in the transverse portion of the duodenum can be approached from below the transverse mesocolon. Dissection is performed on either side of the root of the mesentery. The reconstruction is performed on the antimesenteric side of the duodenum, opposite the ampulla (behind the hepatic flexure). Duodenal GISTs located on the antimesenteric border of the second and/or third parts of the duodenum can be approached with partial duodenectomy and Roux-en-Y duodenojejunostomy (46,51,53,67).

Tumors located on the medial wall of the second and/or third portions of the duodenum involving the ampulla of Vater or pancreas will likely require pancreaticoduodenectomy (*Figure 2A,2B*) (10,58). These have been successfully performed in a minimally invasive fashion, both laparoscopically and with robot-assistance (61,65,68). Larger lesions or those in close proximity to the ampulla of Vater should be considered for a course of neoadjuvant therapy to potentially downsize the lesion prior to resection (*Figure 2E,2F*) (10,46,53,58). In addition, the wrist articulation and dexterity of the robotic platform may assist in intraoperative dissection and suturing of anastomoses/gastrointestinal reconstruction (60,61,64).

Summary

Though MIS resection was previously recommended for small GISTs, more data are demonstrating safety and potential for resecting larger lesions in a minimally invasive fashion. There is a clear application for laparoscopic and robotic approach in resecting gastric GISTs, with the current known safety profile and non-inferior perioperative and oncologic outcomes. While the current literature cannot similarly validate the outcomes and feasibility for MIS resection of small bowel GISTs, the early available data suggests favorable results and outcomes. Data

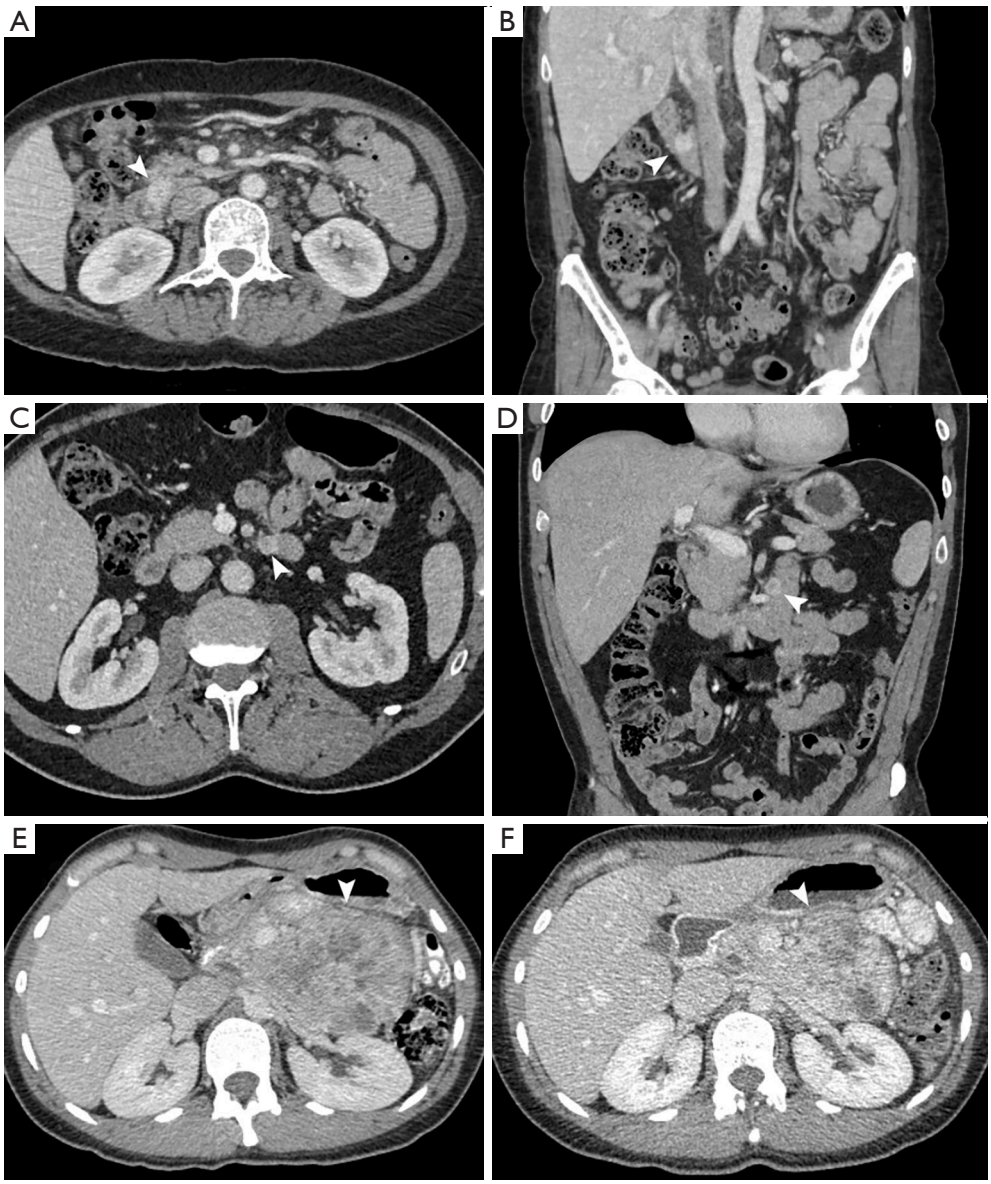

Figure 2 Computational tomography axial and coronal imaging of a duodenal gastrointestinal stromal tumors (GISTs) (arrowhead) in the (A,B) second portion of the duodenum and (C-F) the fourth portion of the duodenum. (A,B) Periampullary GISTs require pancreaticoduodenectomy, which can be performed with laparoscopic and robotic approach. (C,D) GISTs located in the fourth portion of the duodenum can be resected segmentally with duodenectomy and duodenojejunostomy anastomosis. Segmental duodenectomy with duodenojejunostomy was completed for resection of this lesion and the anastomosis was performed under the transverse mesocolon. (E,F) A large 10 cm duodenal GIST involving the third and fourth portions of the duodenum demonstrates good response and shrinkage of tumor (E) before and (F) after completing a preoperative course of imatinib, then was resected through MIS means with duodenectomy and duodenojejunostomy.

on MIS resection for duodenal GISTs are even more limited, and more complex given anatomic considerations needed for duodenal lesions. Caution is merited to avoid overinterpretation of the current limited data. Future research is needed to better characterize MIS resection for small bowel and duodenal GISTs. Nevertheless, at this time, MIS resection appears to be a safe and promising surgical option with careful patient selection.

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Footnote

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Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at http://dx. doi. org/10. 21037/ls–20–90). The series "Minimally invasive approach in Gastrointestinal Stromal Tumors (GISTs)" was commissioned by the editorial office without any funding or sponsorship. The authors have no other conflicts of interest to declare.

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