Mini-Review

Minimally invasive surgery for gastric gastrointestinal stromal tumors

Ye-Xin Koh[1], Brian K. P. Goh[1,2]

[1]Department of Hepatopancreatobiliary and Transplant Surgery, Singapore General Hospital, Singapore, Singapore; [2]Duke NUS Medical School, Singapore, Singapore

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Correspondence to: Brian K. P. Goh, MBBS, MMed, MSc, FRCSEd. Department of Hepatopancreatobiliary and Transplant Surgery, Singapore General Hospital, Singapore 169856, Singapore. Email: bsgkp@hotmail.com.

Abstract: Minimally invasive surgery has been increasingly performed for gastric gastrointestinal stromal tumors (GIST). In this review we discuss and summarize the current evidence on minimally invasive surgery for gastric GISTs. Laparoscopic resection for gastric GIST has been consistently shown to be associated with superior perioperative outcomes with no compromise in oncological outcomes when compared to open resection in numerous retrospective case-control studies. It has also been shown to be safe and feasible for large tumors or tumors located in unfavorable sites. However, to date, there remains a lack of level 1 evidence from prospective randomized control trials in support of laparoscopic resection.

Keywords: Laparoscopic; robotic; minimally invasive surgery; gastric; gastrointestinal stromal tumor (GIST)

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Introduction

Over the past 2 decades, minimally invasive surgery has emerged as the standard of care for surgical procedures of the appendix, gallbladder, spleen, and colon. Laparoscopic procedures confer perioperative benefits of shortened hospitalization, faster recovery, earlier oral intake as compared to the traditional open procedures (1-6). Similarly, these benefits have been observed when laparoscopic resection is performed for gastric gastrointestinal stromal tumors (GIST). Numerous retrospective case control studies have confirmed the benefits of faster recovery, lower perioperative morbidity and overall superior short-term outcomes of laparoscopic versus open resection for gastric GISTs (7,8). However, studies reporting on long term oncological outcomes of minimally invasive surgery for gastric GIST remains limited (7) and no randomized trials have been reported to date. Nonetheless, level 1 evidence from randomized trials have reported equivalent oncological outcomes of laparoscopic surgery for gastric and colorectal cancers (9,10). Laparoscopic lymphadenectomy and adequate resection margins have also been shown to be technically reproducible and feasible (4-6,9,10). These promising results can be extrapolated to laparoscopic resection of gastric GISTs because of a similar, if not lower, level of complexity of oncological resection. More recently, propensity matched analysis and matched case control studies have been reported similarly supporting the oncological safety for laparoscopic resection for gastric GISTs (11).

The surgical approach for gastric GISTs is usually straightforward in expert hands because local resection is adequate and formal gastrectomy with regional lymphadenectomy is not usually required (12,13). Even though ideally tumor-free resection margins should be obtained, wide resection margins are not mandatory unlike gastric adenocarcinomas as submucosal lymphatic spread does not occur. Furthermore, it has been observed

that microscopically involved margins have no apparent detrimental effect on overall survival after complete surgical resection for GIST (14). The favorable disease biology of GIST, allows laparoscopic organ sparing surgery in the majority of cases with excellent long term functional outcomes. In a prospective single institution study, the average Gastrointestinal Quality of Life Index (GIQLI) of the patients who underwent laparoscopic gastric wedge resection was similar to otherwise healthy participants. With the exception of a minority of the patients (~10%) having worse regurgitation symptoms, the majority had a GIQLI within normal range, correlating with an excellent quality of life (15).

Resection for tumors in difficult locations

As shown in many studies, organ sparing surgery in the form of wedge resections can be carried out expeditiously for most gastric GISTs in favorable locations such as the anterior wall and greater curve of the stomach (6-8). However, this approach is sometimes challenging in difficult anatomic locations, such as the gastric cardia or distal antrum. A recent study presented the feasibility of laparoscopic wedge resections for GIST at these difficult locations under the guidance of intraoperative endoscopy. In that study, over 40% of the cases presented were located in the lesser curve, antrum or cardiac. Wedge resection guided by intraoperative endoscopy resulted in a 100% R0 resection with similarly favorable perioperative and long term oncological outcomes, where over 95% 5-year overall survival was achieved (16). More complex approaches such as the intragastric or "endoluminal" surgery through the use of intra-gastric working ports have also been described for challenging locations such as posterior wall gastric GISTs (17,18). Tumors in the abovementioned locations require more advanced laparoscopic skills such as suture manipulation of the tumour, intra-gastric dissection and intra-corporeal suturing to achieve safe resection and reconstruction.

When treating gastric GISTs, the surgeon should be aware of the rare and challenging situation of an extra-intestinal GISTs. These lesions when located posterior to the stomach, have a tendency to invade the surrounding structures such as the pancreas and spleen necessitating a more complex and extensive surgical procedure which might be challenging if attempted laparoscopically (19). The open approach remains the preferred surgical approach for GISTs that require complex multivisceral resection or large lesions that require delicate tissue handling (to prevent tumor rupture) or necessitating a large incision for specimen retrieval (20).

Resection for large GISTs

Despite the advances and increasingly widespread adoption of minimally invasive surgery for gastric GISTs, intraoperative rupture of GISTs remains a significant challenge especially for large cystic GISTs. Should tumor rupture and spillage occur, the prognosis of the patient will be significantly compromised and this should be weighed against the perioperative benefits of the laparoscopic approach (11,21). However, with favorable case selection and expertise in minimally invasive surgery, several authors have reported that selected cases of large gastric GISTs can safely undergo laparoscopic resection (22-24) with minimal risk of rupture. In two recent studies which compared the outcomes of laparoscopic versus open resection of gastric GISTs larger than 5 cm, the laparoscopic approach continued to yield superior perioperative outcomes with no significant differences in complication rates (overall morbidity ~10%, major morbidity <5%, perioperative mortality 1% or less), 5-year disease free survival rates at around 92% or overall survival rates over 93% (24,25). Similarly, results from expert centers have also demonstrated that laparoscopic resection is safe and feasible even for tumors located in unfavorable locations (26).

Comparison between laparoscopic versus open resection for GISTs

To date, several large case-control studies have reported on the outcomes of laparoscopic resection of gastric GIST in comparison with conventional open resection. *Tables 1-3* summarizes the results from several of these large (n>50) case-control studies demonstrating that laparoscopic resection can be performed with a low conversion rate and was associated with superior perioperative outcomes such as shorter hospital stay, earlier oral intake, lower morbidity with similar oncological outcomes compared to the open approach (27-32). Similarly, several systematic reviews and meta-analyses have demonstrated that laparoscopic resection was superior in perioperative outcomes compared to open surgery (33-35). In the latest systematic review of 24 studies involving 2,140 patients demonstrated that laparoscopy was associated with superior outcomes including decreased operative time [weighted mean

Table 1 Summary of studies of laparoscopic resection of gastric GISTs (n>50) showing conversion rates

Author	Country	Year	Study period	LAP	Open	Conversion (%)	LAP, follow up duration (months)	Open, follow up duration (months)
Lee *et al.* (27)	Korea	2011	2001–2008	50	50	2	21.1 [0–64]	22.3 [0–93]
Wan *et al.* (28)	China	2012	2004–2011	68	88	NR	29 [4–89]	36 [4–90]
Kim *et al.* (29)	Korea	2014	1998–2012	156	250	NR	42.9 [2–166]	NR
Cai *et al.* (30)	China	2015	2006–2013	90	66	NR	21 [1–90]	44.5 [1–96]
Goh *et al.* (8)	Singapore	2015	1988–2013	50	50	10	27 [1–140]	60 [6–170]
Chen *et al.* (31)	China	2016	2006–2012	71	71	0	36 [1–111]	NR
Hu *et al.* (32)	China	2016	2009–2014	91	85	0	32±16.3	34.2±14.5

NR, not reported; GIST, gastric gastrointestinal stromal tumor; LAP, laparoscopic.

Table 2 Summary of studies of laparoscopic resection of gastric GISTs (n>50) showing oral intake and hospital stay

Author	Country	Year	Study period	LAP, mean time to oral intake (days)	Open, mean time to oral intake (days)	LAP, mean hospital stay (days)	Open, mean hospital stay (days)
Lee *et al.* (27)	Korea	2011	2001–2008	2.3	3.5	5.7	7.8
Wan *et al.* (28)	China	2012	2004–2011	NR	NR	NR	NR
Kim *et al.* (29)	Korea	2014	1998–2012	NR	NR	NR	NR
Cai *et al.* (30)	China	2015	2006–2013	3.2	4.1	6	8
Goh *et al.* (8)	Singapore	2015	1988–2013	3	5	4	6
Chen *et al.* (31)	China	2016	2006–2012	3.9	5.1	8.8	13.3
Hu *et al.* (32)	China	2016	2009–2014	7.6	8.2	8.8	15.3

NR, not reported; GIST, gastric gastrointestinal stromal tumor; LAP, laparoscopic.

Table 3 Summary of studies of laparoscopic resection of gastric GISTs (n>50) showing complications and recurrence rates

Author	Country	Year	Study period	LAP recurrence	Open recurrence	LAP complications	Open complications
Lee *et al.* (27)	Korea	2011	2001–2008	NR	NR	2/50 (4%)	1/50 (2%)
Wan *et al.* (28)	China	2012	2004–2011	3/68 (4.4%)	4/88 (4.5%)	4/68 (5.9%)	20/88 (2.3%)
Kim *et al.* (29)	Korea	2014	1998–2012	0/156 (0%)	11/250 (4.4%)	NR	NR
Cai *et al.* (30)	China	2015	2006–2013	2/90 (2.2%)	2/66 (3%)	4/90 (4.4%)	8/66 (12.1%)
Goh *et al.* (8)	Singapore	2015	1988–2013	0/50 (0%)	4/50 (8%)	3/50 (6%)	5/50 (10%)
Chen *et al.* (31)	China	2016	2006–2012	6/71 (8.5%)	5/71 (7%)	4/71 (5.6%)	16/71 (22.5%)
Hu *et al.* (32)	China	2016	2009–2014	12/91 (13.2%)	17/85 (2%)	9/91 (9.9%)	16/85 (18.8%)

NR, not reported; GIST, gastric gastrointestinal stromal tumor; LAP, laparoscopic.

difference (WMD), –30.71 min; 95% CI, –58.48 to –2.95]; decreased intraoperative blood loss (WMD, –60.90 mL; 95% CI, –91.53 to –30.28); decreased time to flatus (WMD, –1.10 days; 95% CI, –1.41 to –0.79); decreased time to oral intake (WMD, –1.25 days; 95% CI, –1.64 to –0.86); decreased length of hospital stay (WMD, –3.42 days; 95% CI, –4.37 to –2.46); decreased morbidity (OR, 0.38; 95% CI, 0.27–0.54); and lower recurrence (OR, 0.45; 95% CI, 0.30–0.66) (35). Nonetheless, it is important to emphasize that current evidence in support of the minimally invasive approach is presently limited to retrospective case control studies with an inherent potential for selection bias. However, although ideal, the rarity of GIST and the lack of obvious therapeutic equipoise makes prospect of conducting a prospective randomized control trial difficult today.

Robotic resection for GISTs

Robotic surgery was first introduced to overcome the limitations of conventional laparoscopy especially with the high definition 3D monitor and the increased dexterity of the robotic arms. With regards to resection for gastric GISTs, the robotic approach potentially expands the indications of minimally invasive surgery by enabling minimally invasive procedures for tumors located in places that are more difficult to access via conventional laparoscopic surgery such as in the cardioesophageal and duodenogastric junctions. It also simplifies complex tasks such as intracorporeal suturing in difficult locations (36). Presently, experience with robotic resection for gastric GISTs remains limited. However, several small case series have demonstrated the oncological safety, low complication and low conversion rates associated with robotic assisted excision of large GISTs (>5 cm) in difficult locations (37-41). However, robotic assistance has been reported to be associated with an increase in operating time and its cost-effectiveness remain a major obstacle to the widespread adoption of this technology.

Conclusions

In summary, minimally surgery for gastric GISTs has been widely adopted today and is an excellent procedure especially for tumors in favorable locations within the stomach allowing patients to enjoy superior perioperative outcomes over the open approach without compromising oncological outcomes. In expert hands, the surgical indications can potentially be safely expanded to large tumors or tumors in difficult locations.

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Footnote

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