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Treatment Results of Small Intestinal Gastrointestinal Stromal Tumors Less than 10 cm in Diameter: A Comparison between Laparoscopy and Open Surgery

Kyong Ihn[1], Woo Jin Hyung[1,2], Hyoung-Il Kim[1], Ji Yeong An[1], Jong Won Kim[1], Jae-Ho Cheong[1], Dong Sup Yoon[1], Seung Ho Choi[1], and Sung Hoon Noh[1]

[1]Department of Surgery, Yonsei University College of Medicine, [2]Robot and MIS Center, Severance Hospital, Yonsei University Health System, Seoul, Korea

Purpose: To evaluate the technical feasibility and oncologic safety, we assessed the short-term and long-term outcomes of laparoscopic resection of the small bowel gastrointestinal stromal tumors smaller than 5 cm by comparing those of open surgery by subgroup analysis based on tumor size.

Materials and Methods: From November 1993 to January 2011, 41 laparoscopic resections were performed among the 95 patients who underwent resection of small intestine ≤10 cm in diameter. The clinicopathologic features, perioperative outcomes, recurrences and survival of these patients were reviewed.

Results: The postoperative morbidity rates were comparable between the 2 groups. Laparoscopic surgery group showed significantly shorter operative time (P=0.004) and duration of postoperative hospital stay (P<0.001) than open surgery group and it was more apparent in the smaller tumor size group. There were no difference in 5-year survival for the laparoscopic surgery versus open surgery groups (P=0.163), and in 5-year recurrence-free survival (P=0.262). The subgroup analysis by 5 cm in tumor size also shows no remarkable differences in 5-year survival and recurrence-free survival.

Conclusions: Laparoscopic resection for small bowel gastrointestinal stromal tumors of size less than 10 cm has favorable short-term postoperative outcomes, while achieving comparable oncologic results compared with open surgery. Thus, laparoscopic approach can be recommended as a treatment modality for patients with small bowel gastrointestinal stromal tumors less than 10 cm in diameter.

Key Words: Gastrointestinal stromal tumors; Laparoscopy; Intestine, small

Introduction

Gastrointestinal stromal tumors (GISTs) are the most common type of subepithelial tumor of the gastrointestinal tract (GI) and account for only 0.1% to 0.3% of all GI tumors.(1) After finding out that GISTs originate from the interstitial cell of Cajal, an immunohistochemical marker CD 117 for the KIT protein enables in distinguishing GIST from other subepithelial tumor such as leiomyoma, leiomyosarcoma and leiomyoblastoma.(2,3) Understanding of these disease entities make it possible to apply targeted therapy using tyrosine kinase inhibitors for metastatic or inoperable tumors. However, surgical resection with a negative margin is the main treatment for primary GISTs.(4-6)

GIST most commonly arises in the stomach and secondarily in the small intestine along the digestive tract. There have been only a few studies of small intestinal GISTs unlike gastric GISTs and some study reports that small intestinal GISTs are more malignant than gastric tumors with similar size and mitosis parameters in almost all categories.(7,8) In the meantime, laparoscopic resection

Correspondence to: Woo Jin Hyung
Department of Surgery, Yonsei University College of Medicine, 50, Yonsei-ro, Seodaemun-gu, Seoul 120-752, Korea
Tel: +82-2-2228-2129, Fax: +82-2-313-8289
E-mail: wjhyung@gmail.com
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with a negative gross margin is oncologically justified for gastric GISTs smaller than 5 cm.(9-13) However, it still remains unknown whether minimally invasive resection of small intestinal GIST is technically and oncologically feasible. To the best of our knowledge, there have been no study evaluating both the technical safety and oncologic feasibility of laparoscopic resection of performed for GISTs of small intestine. The purpose of this study is to evaluate the surgical outcomes following laparoscopic resection of small bowel GIST by comparing those following open surgery in terms of early postoperative outcomes and long-term oncologic outcomes.

Materials and Methods

Between November 1993 and January 2011, 120 patients underwent surgery for small bowel GISTs at the Department of Surgery, Yonsei University Health System, Seoul, Korea. Among them, 8 patients had coexistence of other malignancies and 17 patients had a tumor greater than 10 cm. After excluding those 25 patients, we included 95 patients with small bowel GIST for the analyses. There were 54 patients who underwent open surgery (OPEN group) while the other 41 patients underwent laparoscopic surgery (LAP group). For LAP group, complete small bowel exploration and localization of tumors were performed laparoscopically, followed by resection of small bowel and either intracorporeal or extracorporeal anastomosis. Small bowel division was performed by linear stapler. The specimen was retrieved through the umbilical incision or minilaparotomy. Small bowel continuity was recovered by stapled side-to-side anastomosis or end-to-end hand sewn anastomosis performed extracorporeally, or intracorporeally.

The clinicopathological characteristics and data obtained for each patient included following: age, gender, tumor size, tumor location, abdominal operation history, operation type, operation time, postoperative complications, duration of postoperative hospital stay, recurrence and survival. Tumor risk category was defined by tumor size, mitotic index and tumor location, as suggested by Fletcher et al.(14) All the operations were performed by a various surgeons and surgical technique was selected according to individual surgeon's preference and patient's consent. Follow-up results were obtained from patient's medical records, and recurrences were detected by computed tomography, positron emission tomography, etc.

1. Statistical analysis

All the statistical analyses were performed using IBM SPSS ver. 20.0 for Windows (IBM Co., Armonk, NY, USA). Categorical variables were presented in proportions using the chi square tests. Continuous variables were presented as mean and standard deviation and Student t-test (parametric distribution) or Mann-Whitney test (nonparametric distribution) were used to analyze differences. Differences were considered statistically significant at a P-value of <0.05 at the conventional two-tailed alpha level of 0.5. The survival was calculated on the basis of the interval from surgery to patient's death or last time to follow-up. Recurrence-free and overall survival rate were estimated using a Kaplan-Meier method. A log-rank method was used to test the equality of survival distributions between the two groups.

Results

The clinical characteristics of the LAP and OPEN groups were described in Table 1. The two groups were similar in terms of age, gender, tumor location, previous abdominal operation history. The median tumor size of surgically resected specimens in OPEN group was larger than that in LAP group (P=0.006). The proportion

Table 1. Clinical characteristics of small bowel GISTs patients

Variable	Open (n=54)	Laparoscopy (n=41)	P-value
Age (yr)	58 (24~79)	57 (20~77)	0.651
Gender			0.634
Male	25 (46.3)	21 (51.2)	
Female	29 (53.7)	20 (48.8)	
Age (yr)	58 (24~79)	57 (20~77)	0.651
Tumor location			0.161
Duodenum	19 (35.2)	9 (22.0)	
Jejunum, Ileum	35 (64.8)	32 (78.0)	
Tumor size (cm)	5.4 (1.3~10.0)	4.0 (1.5~10.0)	0.006†
≤5	26 (48.1)	28 (51.9)	0.050‡
5<size≤10	28 (68.3)	13 (31.7)	
Previous abdominal operation history	15 (27.8)	9 (22.0)	0.517
Risk stratification*			0.045
Low	23 (42.6)	28 (68.3)	
Intermediate	16 (29.6)	7 (17.1)	
High	15 (27.8)	6 (14.6)	

Values are presented as median (range) or median (%). GIST = gastrointestinal stromal tumor. *Based on modification of the National Institutes of Health consensus classification system regarding tumor site and tumor rupture, †Student t-test, ‡chi-square test.

of intermediate and high risk tumors in OPEN group was higher than that in LAP (P=0.045).

The surgical outcomes of the two groups are presented in Table 2. Mean operation time of the LAP group was significantly shorter than that of the OPEN group (LAP 111.6 minutes versus OPEN 169.0 minutes, P=0.005). The statistical difference was noted only in the subgroup below 5 cm in diameter (LAP 109.6 minutes versus OPEN 180.7 minutes, P=0.005). Although operation time of LAP group (116.3 minutes) was shorter than that of OPEN (158.2 minutes) in the subgroup larger than 5 cm, the difference was not statistically significant (P=0.241). The median duration of postoperative hospital stay for LAP group was shorter than OPEN group (LAP 7.1 days versus OPEN 12.4 days, P<0.001). Operation-related morbidities were not significantly different between the two groups; 8 patients in OPEN group (14.8%) and 5 in the LAP group (13.7%). There was one perioperative death in the LAP group, related to bleeding secondary to recurrent anastomosis leakages. There was one conversion of laparoscopy to open. However, there was no episode of tumor rupture or spillage, and no major intraoperative complications in both groups. Sixteen patients in the OPEN group and three in the LAP group received imatinib treatment, respectively. The number of patients with GIST received adjuvant

Table 2. Operative characteristics and perioperative outcomes

Variable	Open (n=54)	Laparoscopy (n=41)	P-value
Operation type			0.033
Wedge resection	11 (20.4)	18 (43.9)	
Segmental resection	38 (70.4)	23 (56.1)	
Pancreaticoduodenectomy	4 (7.4)	0 (0)	
Distal gastrectomy	1 (1.9)	0 (0)	
Operation time (min)	169.0±106.3	111.6±75.6	0.005
≤5 in tumor size	180.7±105.7	109.6±72.1	0.005
5<minutes≤10 in tumor size	158.2±107.8	116.3±86.3	0.241
Postoperative hospital stay (d)	12.4±6.2	7.1±7.8	<0.001
≤5	12.0±4.9	7.3±9.1	0.022
5<day≤10	12.8±7.2	6.9±4.2	0.009
Postoperative mortality	0 (0.0)	1 (2.3)	
Postoperative complications	8 (14.8)	5 (13.7)	0.713
Curability			0.045
R0	49 (90.7)	41 (100.0)	
R1	0 (0.0)	0 (0.0)	
R2	5 (9.3)	0 (0.0)	

Values are presented as overall mean (%) or overall mean±standard deviation.

Table 3. Adjuvant treatment and oncologic outcomes for laparoscopic versus open small bowel GIST resections

Variable	Open (n=54)	Laparoscopy (n=41)	P-value
Adjuvant treatment			0.043
None	38 (70.4)	36 (87.8)	
Imatinib	16 (29.6)	5 (12.2)	
Recurrences, metastatis	13 (24.1)	3 (7.3)	0.031

Values are presented as number (%). GIST = gastrointestinal stromal tumor.

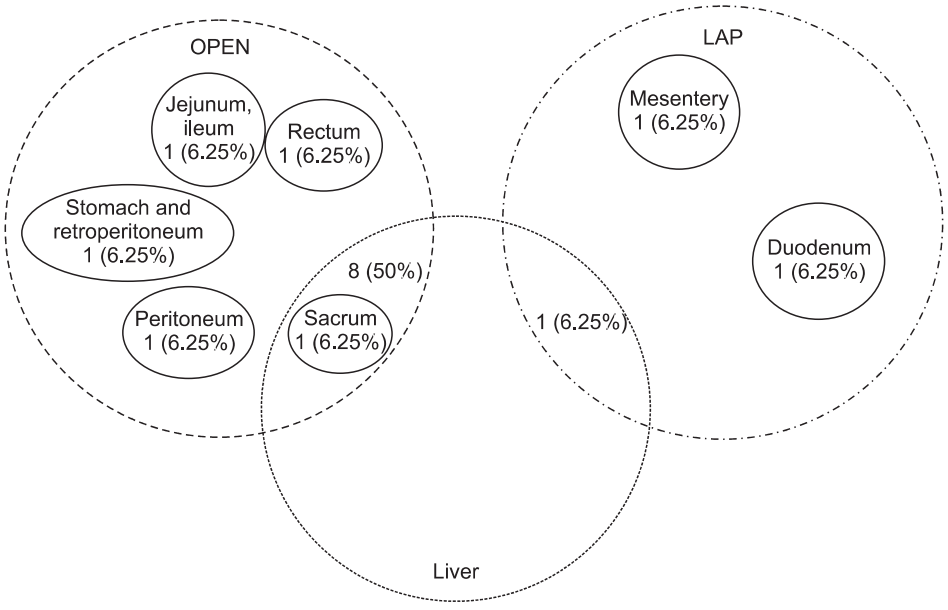

Fig. 1. Venn diagram depicting recurrence patterns, with number (percent) of patients with each category of recurrence pattern. OPEN = open surgery; LAP = laparoscopic surgery.

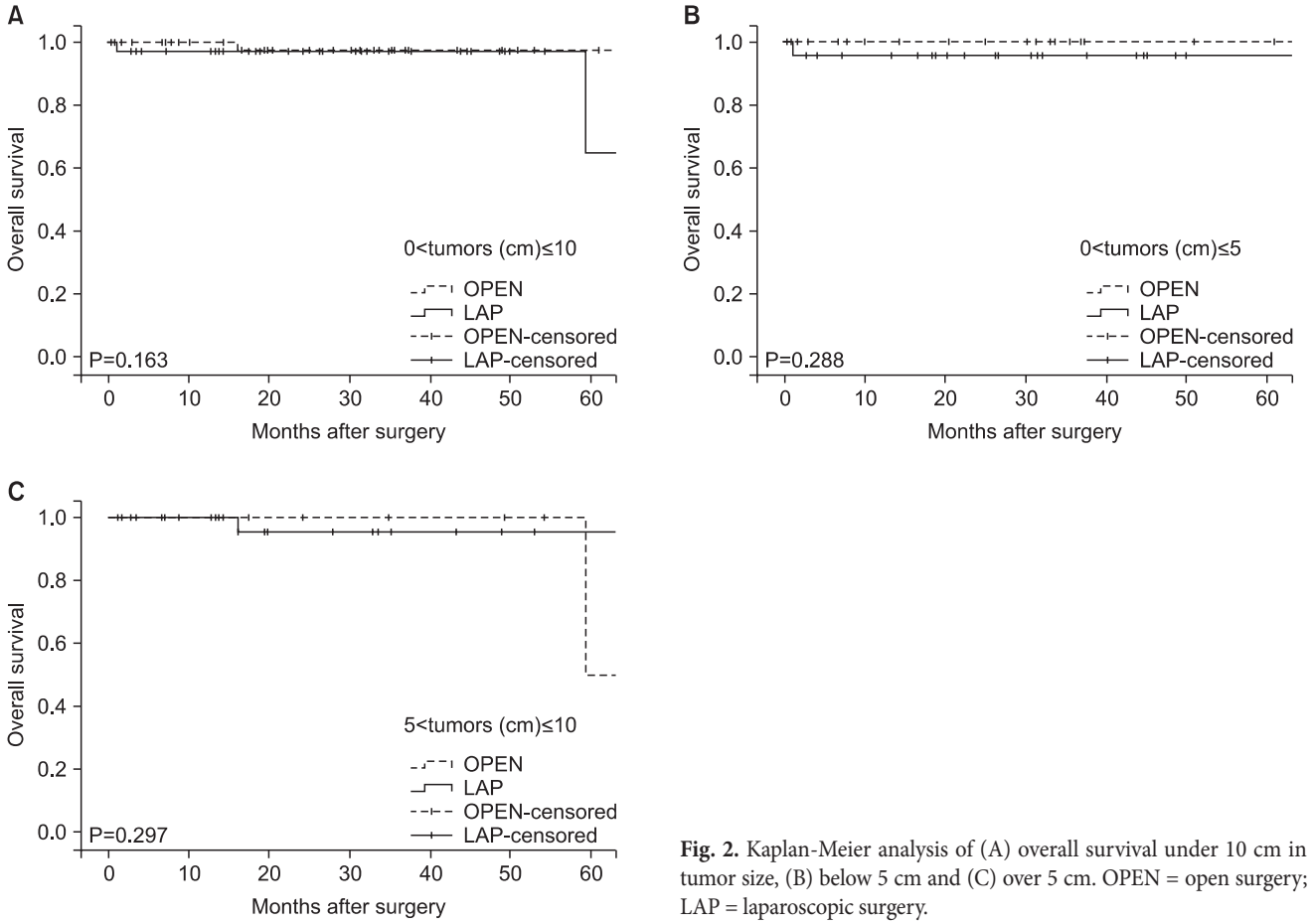

Fig. 2. Kaplan-Meier analysis of (A) overall survival under 10 cm in tumor size, (B) below 5 cm and (C) over 5 cm. OPEN = open surgery; LAP = laparoscopic surgery.

treatment and oncologic outcomes between the two groups are shown in Table 3.

With a mean follow-up of 24.7 months in the LAP group and 51.6 months in the OPEN group, tumor recurrence was detected in 13 cases in the OPEN group and 3 in the LAP group. The sites of recurrences are shown in Fig. 1. Hepatic metastasis was the most common site of recurrence. As for LAP group, one case was found at liver, 1 at mesentery/omentum, and 1 at duodenum. No lymph node recurrence was noted in both subgroups.

There were no significant difference in overall survival for the LAP versus OPEN groups (P=0.163), and in recurrence-free survival (P=0.262). The subgroup analysis by 5 cm in tumor size (≤5 and 5<size≤10) also shows no significant differences in overall and recurrence-free survival between two groups (Fig. 2, 3).

Discussion

We found that laparoscopic resection can be safely performed for small intestinal GIST with less than 10 cm in diameter compared with open surgery. Laparoscopic approach showed better early postoperative outcomes than open approach in terms of operation time, estimated blood loss, and postoperative hospital stay, especially for small intestinal GIST. Besides, laparoscopic resection was oncologically comparable to open surgery when it was compared with respect to not only margin status and tumor spillage during operation but also recurrence and survival after surgery.

It has been suggested that large size gastric GIST is not recommended for laparoscopic surgery because of difficulties in manipulating tumor without tumor cell spillage.(15) Unlike to gastric GIST, laparoscopic operative techniques for small intestinal GIST are diverse and depending on the location of the small bowel.(16) If there is no adjacent organ invasion, small intestinal GIST can be manipulated without any direct contact to the mass by grabbing the mesentery or nearby normal small bowel segment. With this mobility, most small bowel GIST can be treated by simple segmental resection either by intracorporeal or by extracorporeal anastomosis, except for duodenal and proximal jejunal GISTs. In most of the cases, GISTs are oval shape thus specimen can be delivered through a bit smaller incision size than shortest diameter of the mass. Thus, even with the mass size in 10 cm in diameter, it can be delivered

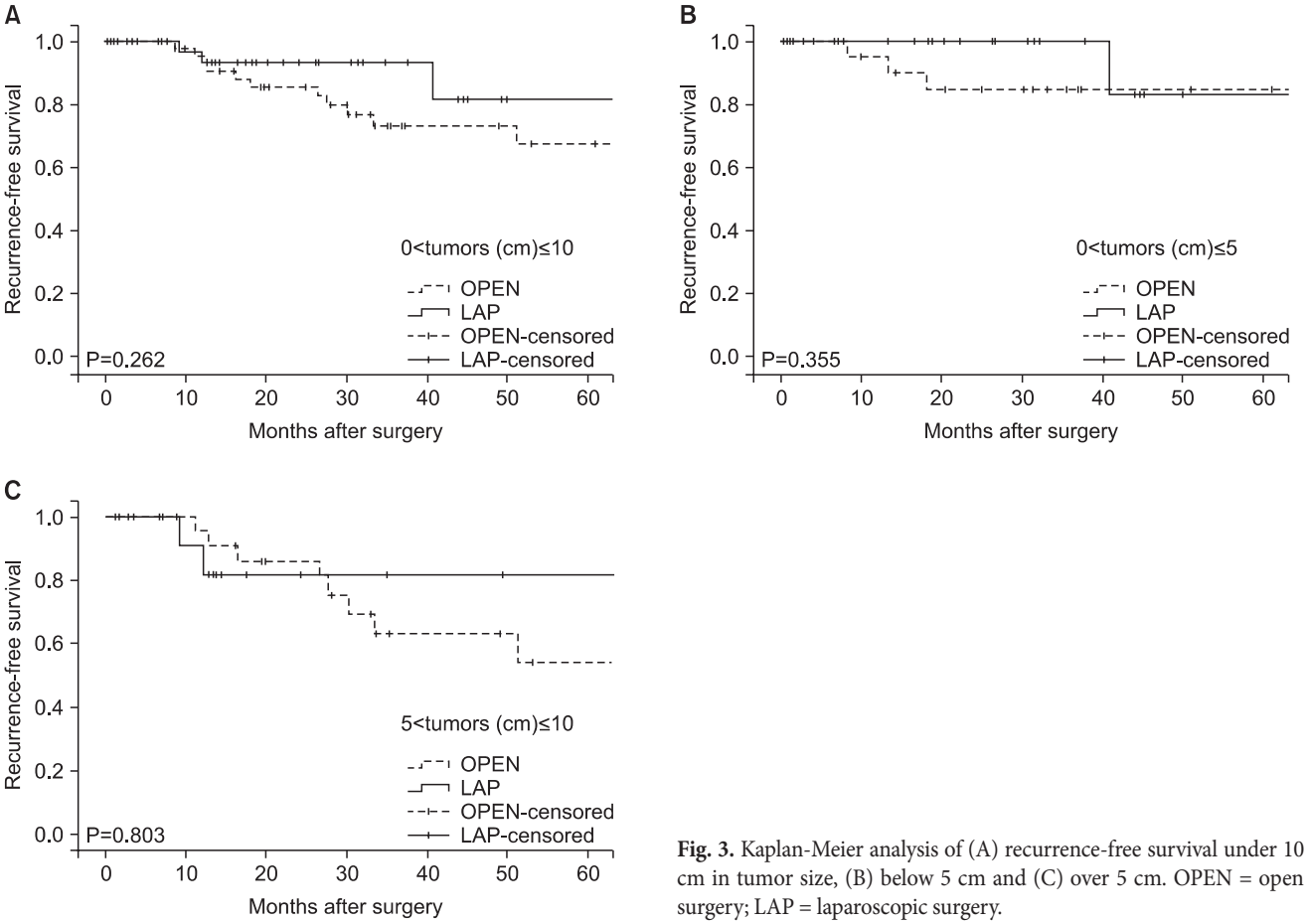

Fig. 3. Kaplan-Meier analysis of (A) recurrence-free survival under 10 cm in tumor size, (B) below 5 cm and (C) over 5 cm. OPEN = open surgery; LAP = laparoscopic surgery.

through a much small incision. Thus, small intestinal GISTs have several appealing characteristics for laparoscopic approach.

When we are trying to apply laparoscopic approach for small intestinal GIST, we have to consider long-term outcomes as well as early postoperative results. As small intestinal GIST is regarded as having a more aggressive malignant potential than gastric GIST has, evaluation of long-term oncological outcomes is essential, especially when size of the tumor is large.(17,18) While there have been many studies for the oncological safety of LAP group for gastric GIST of larger tumors, studies dealt with long-term outcomes after LAP group for small intestinal GIST compared with open surgery are rare. Our study adds evidence that laparoscopic application for small intestinal GIST can be safely applied.

However, our study has limitations mainly coming from its retrospective nature. Although most baseline characteristics were comparable, patients treated by laparoscopy had smaller tumors. Thus, we analyzed outcomes after size stratification. There were selection bias in selecting operative approaches by the surgeons' preference. Some surgeons have little experience of advanced laparoscopic procedure and some surgeons were expert in LAP group. In addition, patients were also biased based on their information for the types of surgery, thus the selection of the operation type was decided based on their limited knowledge. Other limitation was rather long study duration makes it difficult to evaluate the LAP group. Relatively more patients of the OPEN group was skewed towards early period of study compared to those of the LAP group. This may have introduced biases because of the differences in mastering operational skills and by rapid development and improvement of instruments.

In conclusion, our study demonstrated that laparoscopic approach can be safely adopted for small intestinal GIST. Laparoscopic resection for small bowel GISTs could get favorable short-term postoperative outcomes while achieving comparable oncologic results compared with open surgery. Thus, laparoscopic approach can be regarded as an recommendable treatment modality for patients with small bowel GISTs less than 10 cm in diameter.

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