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Original Article

Outcomes of Laparoscopic Gastric Resection for Submucosal Tumors at Difficult Locations: A Prospective Cohort Study

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Abstract

Background: The most common type of submucosal tumor in the stomach is gastrointestinal stromal tumors (GISTs). The standard treatment involves surgical removal with clear margins and without tumor rupture. Current treatment increasingly supports laparoscopic surgery, particularly for tumors located in difficult-to-access locations. This study compares laparoscopic surgery (LapS) and open surgery (OpenS) for gastric submucosal tumors located in such areas.

Objective: This study aimed to evaluate survival analysis and assess the surgical outcomes associated with both techniques.

Materials and Methods: A prospective cohort study was conducted between August 2021 and August 2024 at Buri Ram Hospital. Patients diagnosed with gastric submucosal tumors were evaluated through esophagogastroduodenoscopy (EGD). The tumors were located in challenging stomach areas, including the esophagogastric junction (EGJ), cardia, lesser curvature, posterior wall of the stomach, and pyloric ring of the antrum. The data were analyzed, and a *p*-value of less than 0.05 was considered statistically significant.

Results: Thirty-seven patients were included in the study, with 19 patients assigned to the LapS group and 18 patients assigned to the OpenS group. There were no statistically significant differences in age, sex, or BMI between the two groups. However, the tumors located at the lesser curvature of the stomach were significantly more prevalent in the OpenS group compared to the LapS group ($p = 0.044$). Partial gastric resection was performed more frequently in the LapS group compared to the OpenS group ($p = 0.004$). The LapS group demonstrated better postoperative outcomes, including reduced blood loss, earlier initiation of feeding, earlier passage of flatus, and a shorter duration of hospital stay. The median follow-up time was 19 months. The survival rate in the LapS group was 89.5%, compared to 77.8% in the OpenS group. No significant difference in survival analysis was observed between the two groups (HR 0.54, 95% CI: 0.09-2.98, $p = 0.482$).

Conclusion: For submucosal tumors located in challenging areas of the stomach, laparoscopic surgery offers advantages in terms of minimally invasive approaches and oncologic outcomes compared to open surgery.

Keywords: Gastric submucosal tumors, Gastrointestinal stromal tumors, GIST, Laparoscopic, Difficult

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Introduction

The most common group of submucosal tumors in the stomach is gastrointestinal stromal tumors (GISTs).[1] The standard treatment is the surgical removal of the entire tumor, aiming for curative resection with free margins and without tumor rupture. These factors significantly impact treatment outcomes; complete resection without rupture is associated with lower recurrence rates and improved overall survival.[2,3] In the past, most treatments were performed through open surgery. Lukaszczyk et al. performed the first successful laparoscopic surgical resection of gastric GISTs. This marked the introduction of laparoscopic surgery as a minimally invasive approach to treating GISTs.[4] Liangying Ye et al. conducted a meta-analysis comparing gastric GIST patients undergoing open surgery versus laparoscopic surgery. The results indicated no statistically significant differences between the two surgical methods in terms of survival rates, recurrence, or complications.[5] Current treatment guidelines increasingly endorse laparoscopic surgery, particularly for tumors located in regions amenable to this technique, such as the greater curvature or the anterior portion of the stomach.[6-8] Liao GQ et al. performed a retrospective comparative study of patients undergoing laparoscopic surgery for gastric GISTs. They compared patients with tumors located in easily accessible areas to those with tumors in more challenging positions. The study found that both surgical approaches can be performed safely for patients.[9] Chang-Ming Huang et al. compared patients undergoing laparoscopic and open surgery for gastric GISTs in easily accessible and difficult surgical locations. The results indicated no significant differences between the laparoscopic and open surgery groups, regardless of the tumor's location. Both approaches were found to be safe for patients.[10] Laparoscopic surgery offers the advantage of a minimally invasive approach, leading to reduced postoperative recovery times. In contrast, open surgery provides the benefit of superior palpation and tactile sensation, which can enhance intraoperative decision-making. However, when tumors are located in difficult-to-access areas of the stomach, assessment can be challenging. Current trends increasingly favor laparoscopic surgery, particularly for tumors in such locations.

This study aims to compare laparoscopic surgery and open surgery for gastric GISTs located in difficult-to-access areas. The research employs a prospective data collection methodology to ensure a comprehensive analysis. The objectives of this study are to assess survival analysis and surgical outcomes associated with both surgical techniques.

Materials and Methods

A prospective cohort study was performed between August 2021 and August 2024 at Buri Ram Hospital, Buri Ram, Thailand.

Patients

All patients were 18 years or older at the time of diagnosis. Patients diagnosed with gastric submucosal of the stomach can be evaluated through esophagogastroduodenoscopy (EGD), which may reveal submucosal lesions or allow for tissue biopsy. Additionally, imaging techniques such as computed tomography (CT) scans and magnetic resonance imaging (MRI) can be utilized for assessment. The inclusion criteria were the patients who had American Society of Anesthesiologists (ASA) classification I-II and received neoadjuvant treatment before surgery. Surgical intervention is required, and treatment options include either open surgery or laparoscopic surgery. Postoperative complications were assessed using the Clavien-Dindo classification system. The exclusion criteria for this study included patients with a second primary cancer or those with metastasis at the time of diagnosis. Patients with contraindications for laparoscopic surgery were also excluded from the study. Additionally, all patients were required to sign an informed consent form before being included in the study. The tumor location was identified from EGD, CT scan, or MRI to locate the difficult area of the stomach to approach for surgery, including esophagogastric junction (EGJ), cardia, lesser curvature, posterior wall of the stomach, a pyloric ring of the antrum. For the other location were excluded from the study. The patients included in the study were divided into two groups: the laparoscopic surgery (LapS) group and the open surgery (OpenS) group. The sample size for this study consisted of 16 patients in each group. A dropout rate of 10% was anticipated, with an alpha level of 0.05 and a statistical power of 80%. The study utilized a 1:1 ratio, resulting in a total of 36 patients participating in the study.[10] Patient allocation will follow a 1:1 alternating pattern, as the study is prospective and non-randomized, with participants being assigned after they have been thoroughly informed of the relevant details.

Surgery

The surgical approaches were categorized into LapS and OpenS. The surgical procedure selection was based on the surgeon's judgment and the patient's condition. The technique for gastric resection was determined by the tumor's location and included partial gastric resection, proximal gastrectomy, distal gastrectomy, or total gastrectomy. For the LapS procedure, patients were positioned in reverse Trendelenburg. A trocar was inserted to create 3-4 ports in the anterior abdominal wall. The surgeon positioned themselves on the right side or between the patient's legs, depending on the tumor's location. The assistant or camera operator was positioned either between the patient's legs or on the right side. For the open surgery procedure, patients were positioned in a supine orientation. An upper midline incision was made, followed by the performance of the intra-abdominal procedure. In cases of challenging tumor localization, EGD was utilized. Gastric resection may be performed using gastrointestinal anastomosis (GIA) staplers or hand-sewn techniques. For tumors located near the EGJ or pyloric ring, EGD was conducted to identify potential issues and prevent suture compromise of the gastric lumen. The gastrotomy technique was utilized for tumor resection, ensuring clear margins while preserving the gastric lumen in lesions adjacent to it. In patients who performed distal or total gastrectomy, reconstruction was achieved using the Roux-en-Y gastrojejunostomy or Roux-en-Y esophagojejunostomy techniques. For patients who underwent proximal gastrectomy, esophagogastrostomy was performed for reconstruction. After the completion of the operation, a surgical suction drain was placed near the suture line of the stomach. The data on operative time, blood loss, and intraoperative complications were recorded. The tumors were sent for pathological evaluation, confirming a diagnosis of GISTs in all patients.

Post-operative care

After the patients fully recovered from general anesthesia, a liquid diet was permitted. Pain management was achieved with intravenous morphine injection. Patients without immediate complications were allowed to transition to a soft diet or continue with liquids as tolerated. A surgical suction drain was removed when serous output was observed or prior to patient discharge. The day feeding was initiated, the flatus's first passage and the duration of hospitalization were recorded.

Definitions

The risk of recurrence is determined by the National Institutes of Health (NIH) consensus classification system, which includes tumor size and mitotic count. Tumor size is defined as the maximum diameter of the tumor. The mitotic rate is assessed by counting the number of mitoses per 50 high-power fields (HPF) and is classified into very low, low, intermediate, and high-risk categories.[11]

Adjuvant treatment and follow-up

Adjuvant treatment for gastric GISTs depends on the risk classification. Patients identified as having a high risk of recurrence may receive adjuvant imatinib; however, this is not universally applicable to all high-risk patients, as it depends on the individual patient's financial capacity to support the cost of imatinib. The date of the last follow-up was recorded. The local recurrence and metastasis were observed.

Ethics consideration

This study was reviewed and approved by the Buri Ram Hospital Ethics Committee under reference number BR0032.102.1/37.

Statistical analysis

The baseline characteristics of patients, tumors, and outcome of surgery were compared using the Chi-square or Fisher's exact test for categorical variables and the t-test for continuous variables. The survival and recurrence were analyzed using the Kaplan-Meier curve and logistic regression. A p-value < 0.05 was considered statistically significant.

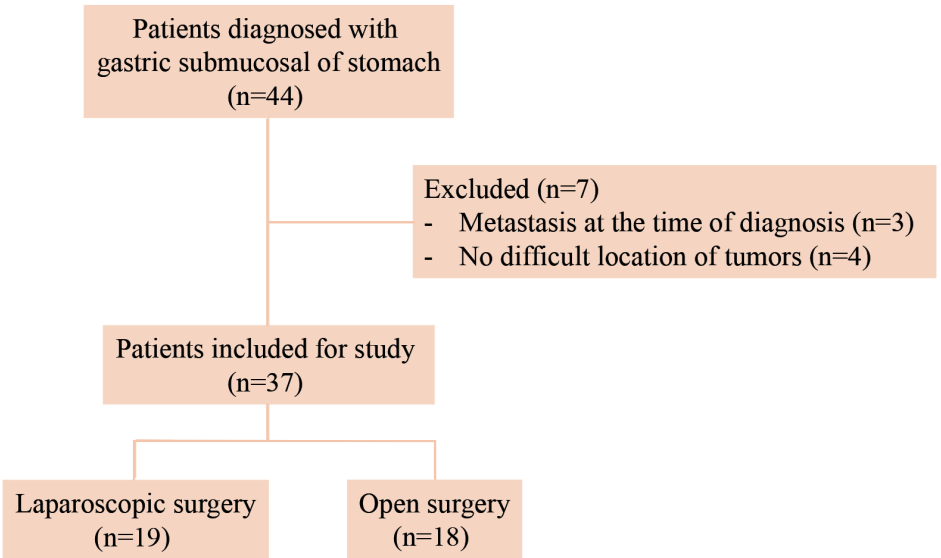


Figure 1 Flow chart diagram of patients

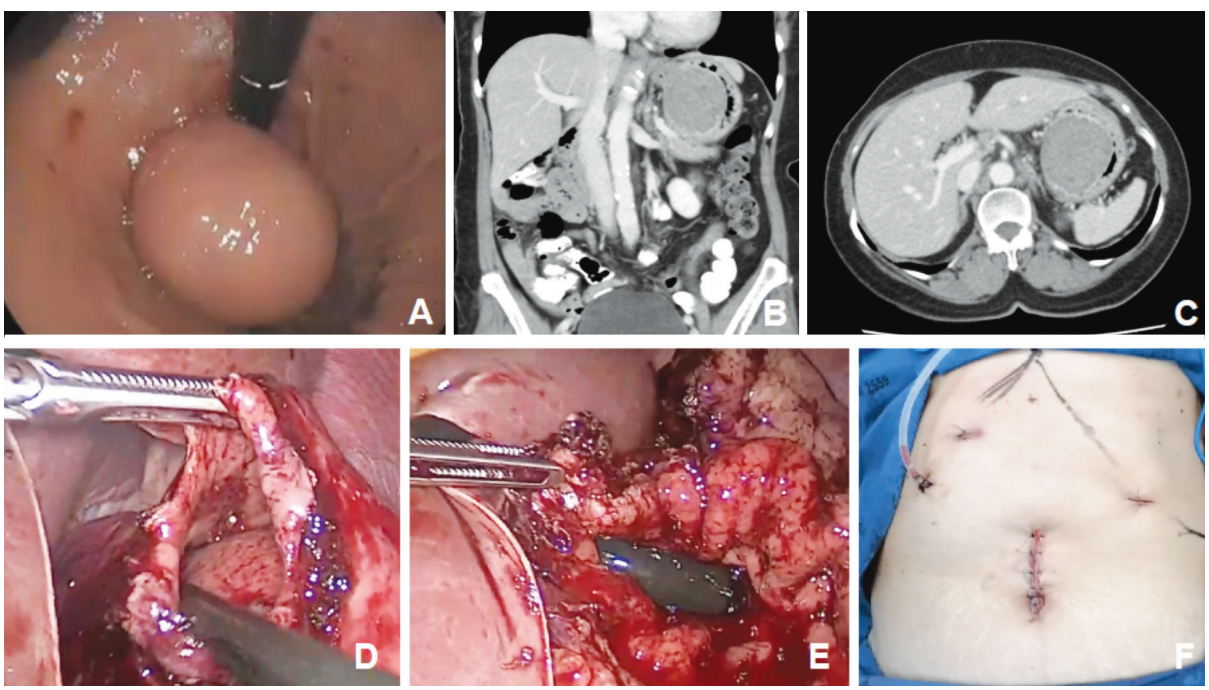


Figure 2 Shows a patient presenting with a gastric GIST at the EGJ.

A: Shows the endoscopic findings of a submucosal lesion at the EGJ.

B, C: The CT scan shows a gastric mass at the EGJ.

D, E: Laparoscopic surgery was performed via gastrotomy, and the gastric defect was closed using an intracorporeal manual running suture.

F: Surgical incision following laparoscopic surgery.

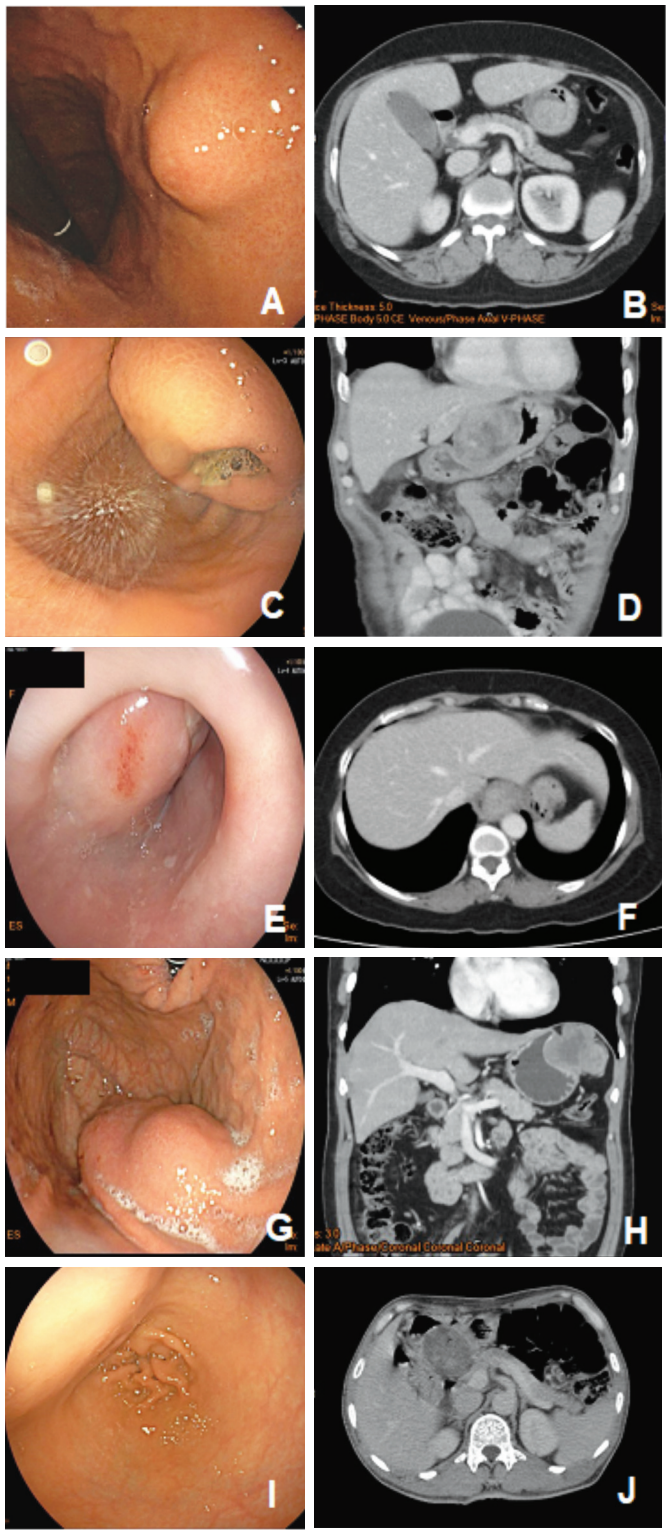


Figure 3 Shows the endoscopic findings and computed tomography (CT) scans of submucosal lesions on the posterior wall of the stomach, lesser curvature, esophagogastric junction (EGJ), cardia, and pyloric ring of the antrum.

A and B: show the submucosal lesion at the posterior wall of the stomach

C and D: show the submucosal lesion at the lesser curvature of the stomach

E and F: show the submucosal lesion at EGJ

G and H: show the submucosal lesion at the gastric cardia

I and J: show the submucosal lesion at the pyloric ring of the antrum

Results

A total of 44 patients were diagnosed with submucosal tumors of the stomach. Seven patients were excluded from the study: three presented with metastasis at the time of diagnosis, and four did not have tumors located in difficult positions within the stomach. Ultimately, 37 patients were included in the study, with 19 patients assigned to the LapS group and 18 patients assigned to the OpenS group. Patient baseline characteristics, including tumor locations, types of surgery, and postoperative outcomes, are presented in Table 1. There were no statistically significant differences in age, sex, or BMI between the two groups. However, the tumors located at the lesser curvature of the stomach were significantly more prevalent in the OpenS group compared to the LapS group ($p = 0.044$). Partial gastric resection was performed more frequently in the LapS group compared to the OpenS group ($p = 0.004$), while no differences were noted for other procedures. The LapS group demonstrated better postoperative outcomes, including reduced blood loss, earlier initiation of feeding, earlier passage of flatus, and a shorter duration of hospital stay. However, the operative time was shorter in the OpenS group compared to the LapS group. No complications were observed in either group.

Table 1 Baseline characteristics of patients, location of tumors, surgery types, and post-operative outcome

Factors	Total n = 37 (%)	LapS n = 19 (%)	OpenS n =18 (%)	*p*-value
Age (years), mean (± SD)	60.3 (12.3)	58.9 (13.1)	61.7 (11.6)	0.254
Sex				0.219
Male	14 (37.8)	9 (47.4)	5 (27.8)	
Female	23 (62.2)	10 (52.6)	13 (72.2)	
BMI, mean (± SD)	22.1 (3.2)	22.5 (3.3)	21.8 (3.1)	0.254
Locations of tumors				
Esophagogastric junction (EGJ)	5 (13.5)	3 (15.8)	2 (11.1)	0.677
Cardia	8 (21.6)	5 (26.3)	3 (16.7)	0.476
Lesser curvature	9 (24.4)	2 (10.5)	7 (38.9)	0.044
Posterior wall of stomach	7 (18.9)	5 (26.3)	2 (11.1)	0.238
Pyloric ring of the antrum	8 (21.6)	4 (21.1)	4 (22.2)	0.931
Surgery type				
Partial gastric resection	23 (62.2)	16 (84.2)	7 (38.9)	0.004
Proximal gastrectomy	3 (8.1)	0 (0)	3 (16.7)	0.063
Distal gastrectomy	9 (24.3)	3 (15.8)	6 (33.3)	0.214
Total gastrectomy	2 (5.4)	0 (0)	2 (11.1)	0.135
Operative outcomes				
Operative time (minutes, ± SD)	147.2 (54.8)	170.8 (56.4)	122.2 (41.5)	0.002
Blood loss (ml. ± SD)	154.6 (210.3)	50 (55.6)	265 (252.9)	< 0.001
Day feeding initiated (day ± SD)	1.9 (1.2)	1.1 (0.2)	2.7 (1.2)	< 0.001
First passage of flatus (day ± SD)	2.8 (0.9)	2.3 (0.6)	3.3 (0.8)	< 0.001
Duration of hospital stay (day ± SD)	7.4 (2.7)	5.6 (1.4)	9.4 (2.5)	< 0.001

SD: standard deviation; BMI: body mass index

Table 2 presents tumor characteristics and systemic treatments. Tumor size and the incidence of tumor rupture were significantly higher in the OpenS group compared to the LapS group ($p = 0.012$ and $p = 0.030$, respectively). However, large tumors, specifically those measuring approximately 10 cm (greater than 9 cm), were analyzed to evaluate the clinical outcomes and the challenges associated with both surgical procedures. No statistically significant difference was observed between the two procedures ($p = 0.310$).

Table 2 Tumor characteristics and systemic treatment

Factors	Total n = 37 (%)	LapS n = 19 (%)	OpenS n = 18 (%)	*p*-value
Size of tumor (cm., ± SD)	6.9 (4.1)	5.5 (1.8)	8.5 (5.3)	0.012
Mitotic count (HPF, ± SD)	8.7 (12.4)	6.9 (10.9)	10.6 (13.8)	0.191
Tumor rupture	4 (10.8)	0 (0)	4 (22.2)	0.030
LVI	1 (2.7)	1 (5.3)	0 (0)	0.324
Metastasis	6 (16.2)	2 (10.5)	4 (22.2)	0.335
Lung	2 (5.4)	0 (0)	2 (11.1)	0.135
Liver	4 (10.8)	2 (11.5)	2 (11.1)	0.954
Neoadjuvant imatinib	3 (8.1)	1 (5.3)	2 (11.1)	0.515
Adjuvant imatinib	11 (29.7)	6 (31.6)	5 (27.8)	0.800

SD: standard deviation; HPF: high-power fields; LVI: lymphovascular invasion

Table 3 The risk of recurrence is determined by the NIH consensus classification system

Factors	Total n = 37 (%)	LapS n = 19 (%)	OpenS n = 18 (%)	*p*-value
Risk category				
Low	15 (40.5)	10 (52.7)	5 (27.8)	0.124
Intermediate	8 (21.6)	5 (26.3)	3 (16.7)	0.476
High	14 (37.9)	4 (21.1)	10 (55.5)	0.031

The risk of recurrence was determined using the NIH consensus classification, as presented in Table 3. A higher proportion of patients in the OpenS group were categorized as high risk for recurrence compared to the LapS group, while no differences were observed in the low and intermediate risk categories between the two groups.

The median follow-up time was 19 months. The median survival analysis was not reached in either group. The survival rate in the LapS group was 89.5%, compared to 77.8% in the OpenS group. No significant difference in survival analysis was observed between the two groups, with a hazard ratio (HR) of 0.54, 95% CI: 0.09-2.98, $p = 0.482$. No local recurrences were detected in either group (Figure 4).

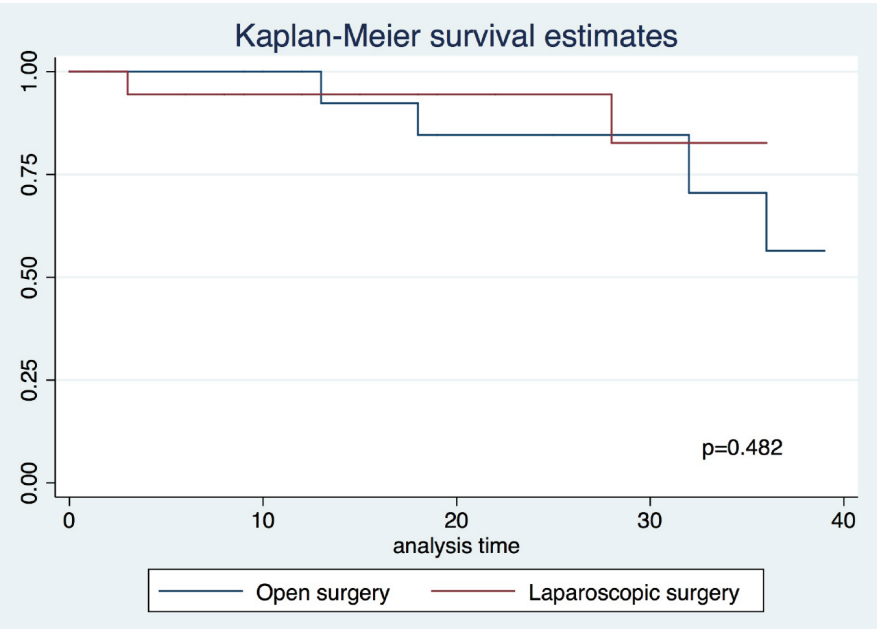


Figure 4 Kaplan-Meier graph shows survival analysis between open and laparoscopic surgery.

Subgroup analysis was performed by risk category based on the surgery type. Median survival was not reached in the LapS group, including the low, intermediate, and high-risk groups, as well as in the OpenS group with the low-risk category. In the OpenS group, the median survival for the intermediate and high-risk categories was 36 and 32 months, respectively. The Log-Rank test for subgroup analysis of survival between Open and laparoscopic surgery by risk category (low, intermediate, and high) showed no statistically significant results, with *p*-values of 0.119, 0.294, and 0.406, respectively (Figure 5).

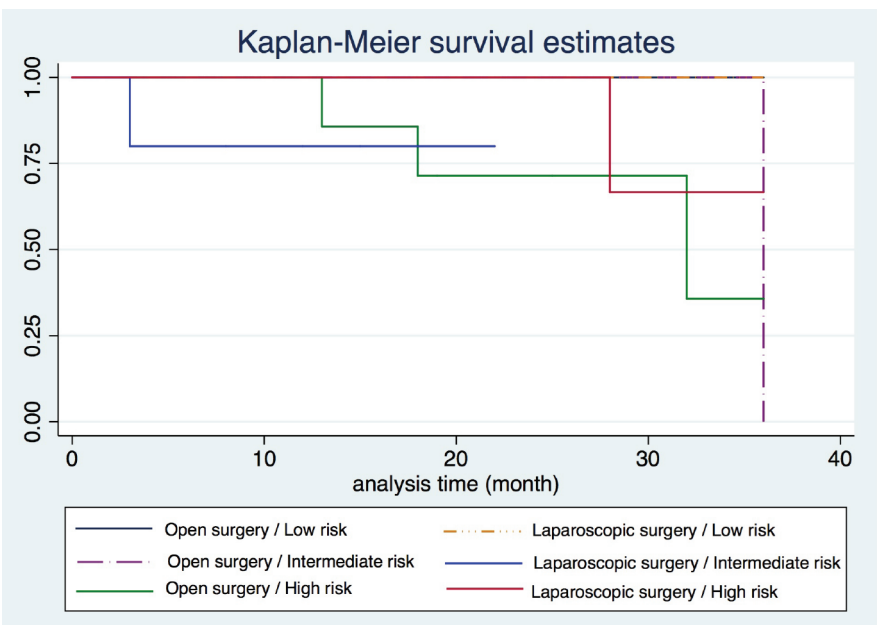


Figure 5 A Kaplan-Meier graph showing subgroup survival analysis between open and laparoscopic surgery, stratified by the risk of recurrence as determined by the NIH consensus classification system.

Discussion

The most common location for submucosal tumors was the stomach, with GISTs being the most prevalent submucosal lesions in this area.[12-14] Surgical resection with clear margins and avoidance of tumor rupture is the recommended treatment for curative intent. Meticulous dissection to prevent tearing of the pseudocapsule is critical in reducing the risk of recurrence and preventing peritoneal seeding.[14-16] In this study, all submucosal tumors of the stomach were diagnosed as gastric GISTs. Laparoscopic surgery is increasingly being utilized for the resection of gastric GIST following the same principles as open surgery. Prior studies comparing laparoscopic surgery with open surgery have shown comparable outcomes, with no significant differences in survival rates, local recurrence, or complications.[4,5] Several treatment guidelines recommend laparoscopic surgery, particularly for tumors located in areas amenable to this technique, such as the greater curvature or the anterior portion of the stomach.[6-8] Karakousis GC et al. reported that laparoscopic surgery for gastric gastrointestinal stromal tumors (GISTs) is appropriate for tumors smaller than 8 cm.[17] Piessen G et al. compared laparoscopic surgery with open surgery for gastric gastrointestinal stromal tumors (GISTs) and found that the outcomes in terms of survival and complications were similar.[18] Some studies suggest that laparoscopic surgery should be performed in favorable tumor locations, such as the anterior gastric wall or lesser curvature of the stomach. Tumors larger than 10 cm are generally not recommended for this approach due to the increased risk of tumor rupture.[15] In this study, tumor size was found to be significantly larger in the OpenS group compared to the LapS group; however, the tumors in both groups were smaller than 10 cm. This suggests that both laparoscopic and open-surgical approaches are suitable for managing these tumors. Tumor locations were classified as follows: esophagogastric junction (EGJ), cardia, lesser curvature, posterior wall of the stomach, and pyloric ring of the antrum. Although the study was prospective, tumors located in the lesser curvature were more frequently managed with open surgery than with laparoscopic surgery. Conversely, partial gastric resection was significantly more common in the laparoscopic surgery group. The risk of recurrence was higher in the OpenS group compared to the LapS group, encompassing factors such as tumor size, incidents of tumor rupture, and high-risk classification, according to the NIH consensus. These data suggest that patients at risk of tumor recurrence, particularly those with larger tumors or unfavorable tumor locations, should undergo open surgery to minimize the risk of recurrence. However, surgery outcomes were more favorable in the LapS group, including reduced blood loss, earlier initiation of feeding, earlier passage of flatus, and a shorter duration of hospital stay, all of which were statistically significant. Huang CM et al.[10] compared patients undergoing laparoscopic and open surgery for gastric GISTs in easily accessible and challenging surgical locations. The findings revealed no significant differences between the laparoscopic and open surgery, irrespective of the tumor's location. Laparoscopic surgery significantly reduced the duration of the operation, minimized intraoperative bleeding, and decreased the time to the first passage of flatus as well as the time to initiate a fluid diet. Additionally, it lowered the rate of postoperative complications, indicating that laparoscopic procedures can offer patients superior short-term outcomes compared to open surgery.

The survival rate in this study was slightly lower than that reported in previous studies, most of which included patients with both favorable and unfavorable tumor locations, as well as those who received adjuvant imatinib according to the NIH consensus classification system.[10,19,20] In contrast, this study focused exclusively on tumors located in challenging areas of the stomach, and the majority of patients did not receive adjuvant imatinib treatment. Nonetheless, there was no significant difference in survival between the LapS and the OpenS groups.

Conclusion

For submucosal tumors located in challenging areas of the stomach, laparoscopic surgery offers advantages in terms of minimally invasive techniques and surgical outcomes compared to open surgery. Ultimately, the choice between laparoscopic and open surgery depends on the surgeon's experience, the risk of tumor recurrence associated with specific tumor locations, and the need to avoid tumor rupture during surgery. Nonetheless, both techniques result in similar short-term oncologic outcomes.

Limitation of study

Although gastric submucosal tumors are rare, the sample size in this study is limited but adequate for statistical analysis. This investigation was conducted at a single center; however, future research could be expanded to a multicenter framework involving a larger patient cohort and designed as a randomized controlled trial with long-term follow-up to detect oncologic outcomes.

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