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Clinical outcomes and cost-effectiveness analysis of robotic and endoscopic cooperative surgery for treating gastric submucosal tumors: a longitudinal nested cohort study

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Abstract

Background Robotic and endoscopic cooperative surgery (RECS) is an emerging and promising therapeutic approach for treating gastric submucosal tumors (GSMTs). However, the efficacy of RECS has not been well established, and its high medical costs significantly limit its application.

Methods This nested cohort study examined patients with GSMTs managed with different surgical techniques. A total of 314 consecutive patients were enrolled in this study, including 61 patients treated with RECS, 196 patients treated laparoscopically, and 57 patients treated with open surgery. To mitigate confounding bias, 1:1:1 propensity score matching (PSM) was utilized. The perioperative outcomes, postoperative gastrointestinal symptoms, long-term outcomes, and cost-effectiveness among the three groups were compared.

Results After PSM, 51 patients were included in each group. Compared with the laparoscopic and open surgical groups, the RECS group presented significantly lower intraoperative bleeding volumes, times to first flatus, times to liquid intake, and postoperative hospital stay. The severity of gastrointestinal symptoms in the RECS group was notably better than that in the laparoscopic and open groups 3, 6, and 12 months postsurgery. Regarding long-term outcomes, there were no differences in overall or relapse-free survival among the three groups. The total hospitalization cost was significantly greater in the RECS group, primarily due to surgical cost differences. The incremental cost-effectiveness ratios per quality-adjusted life year for the RECS group relative to the laparoscopic and open groups were 18,244 and 56,914 Chinese yuan (CNY), respectively. Analysis of the cost-effectiveness acceptability curves indicated that across all willingness-to-pay thresholds, the probability that RECS was cost-effective exceeded 90%.

Conclusions RECS is a safe and effective method for treating GSMTs, offering faster postoperative recovery and fewer gastrointestinal symptoms than laparoscopic and open surgeries. Despite the increased costs associated with the introduction of RECS technology, it remains a cost-effective option.

Keywords Gastric submucosal tumors · Robotic and endoscopic cooperative surgery · Laparoscopic surgery · Open surgery · Clinical outcomes · Cost-effectiveness analysis

Gastric submucosal tumors (GSMTs) are neoplasms that originate from the submucosal or muscularis propria layers of the gastric wall and account for approximately 3% of all gastric tumors [1]. With the widespread adoption of endoscopic technologies for cancer screening, including esophagogastroduodenoscopy and endoscopic ultrasonography, the detection rates for GSMTs have significantly increased in recent years. Given the rarity of lymph node metastasis in patients with GSMTs, local excision with negative surgical margins has become the standard surgical procedure for managing these tumors [2, 3].

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Advances in surgical techniques have also led to improvements in the treatment of GSMTs. Numerous studies have confirmed that both laparoscopic and open surgery can achieve complete surgical GSMT resection [4–6]. The National Comprehensive Cancer Network and the European Society for Medical Oncology support the safety and technical feasibility of both laparoscopic and open surgical approaches for treating patients with GSMTs [7, 8]. However, existing mainstream surgical methods are hindered by some limitations. For GSMTs located in specific locations, such as the gastroesophageal junction or pylorus, traditional surgical resection presents challenges, including an increased risk of stenosis or excess damage to the gastric tissue. The two-dimensional views inherent in laparoscopic surgery, combined with the use of linear staplers, often leads to excessive resection of the gastric wall, which in turn is associated with an increased incidence of postoperative complications and an increased prevalence of gastrointestinal dysfunction. Furthermore, the communication between the gastric cavity and the abdominal cavity increases the risk of tumor dissemination and intra-abdominal infection.

To address these challenges, we present a novel technique termed robotic and endoscopic cooperative surgery (RECS) [9]. During the operation, both intraluminal and abdominal approaches are used to accurately locate the tumor location and extent of resection. While ensuring the integrity of the gastric mucosal layer, the tumor is subsequently completely excised via the high-definition, three-dimensional visualization provided by the surgical robot and the flexible robotic arm. Aside from this surgical technique, several pilot studies have reported preliminary findings regarding the use of robotic wedge resection for the treatment of GSMTs [10, 11]. To our knowledge, there is a lack of research focusing on the postoperative functional outcomes and long-term results of the treatment of GSMTs with robotic surgery. Furthermore, the adoption of robotic surgery has been contentious, primarily due to the significant medical costs involved. However, studies assessing the costs and economic benefits of the use of robotic surgery for GSMTs are similarly lacking. Therefore, the objective of this study was to provide additional clinical evidence and recommendations to facilitate the promotion and implementation of RECS in clinical practice. This was accomplished by comparing the perioperative and long-term clinical outcomes, as well as the cost-effectiveness, of patients treated with RECS with those of patients treated with conventional laparoscopic and open surgical techniques.

Materials and methods

Study population

Between January 2014 and June 2023, a total of 396 patients with GSMTs underwent surgical treatment at The First Affiliated Hospital of Xi'an Jiao Tong University. Of these, 314 patients were ultimately enrolled in this study, all of whom provided consent for their data to be utilized. The exclusion criteria were as follows: (1) tumors combined with mucosal ulceration or bleeding, (2) metastasis or invasion of adjacent organs, (3) treatment with robotic gastrectomy (total or subtotal), (4) R1 or R2 resection, and (5) missing clinicopathological data or follow-up data. All patients were categorized into three groups: those who underwent RECS, those who underwent laparoscopic surgery (LAP group), and those who underwent open surgery (OPEN group). The screening flowchart is depicted in Supplementary Fig. 1. This study was approved by the Ethics Committee of The First Affiliated Hospital of Xi'an Jiao Tong University (XJTU1AF2018LSK-168) and was registered on ClinicalTrials.gov (number NCT03804762).

Surgical procedures

GSMTs were resected via open, laparoscopic, or robotic techniques, depending on the location and size of the tumor and the patient's preference. All patients were placed in a supine position and received conventional endotracheal intubation anesthesia.

Open resections were typically conducted through a 10–15 cm midline incision. For laparoscopic procedures, following routine establishment of artificial pneumoperitoneum, the laparoscopic instruments were introduced, and the abdominal cavity was explored. Once the tumor was adequately exposed, wedge resection of the gastric wall or gastrectomy (total, distal, or proximal) was performed, depending on the size and location of the tumor. For both laparoscopic and open resections, the entire tumor was removed via an extraction bag, and all the incisions were covered with a protective sleeve.

At our institution, robotic GSMT resection is often performed via a combined surgical and endoscopic approach. The detailed surgical procedure for RECS has been thoroughly described in our previous studies [9, 12]. Following the setting up of the da Vinci surgical system, the location of the tumor was identified, and any necessary adhesiolysis was performed. Endoscopic submucosal injections were then administered to establish the "third space," the definition of which is further explained in the Supplementary Materials. Subsequently, robotic submucosal dissection of the tumor was performed, and the seromuscular incision was closed.

Gastrointestinal function evaluation and follow-up

The Gastrointestinal Symptom Rating Scale (GSRS) was used to assess postoperative gastrointestinal function [13]. The GSRS consists of 15 items, each rated on a scale from 0 to 3 according to the severity of the symptoms. A score of 0 indicates the absence of symptoms or a normal condition, whereas a score of three reflects the most severe symptoms. Patients were instructed to complete the GSRS 3, 6, and 12 months postoperatively.

The same follow-up strategy was applied to patients who underwent any of the three surgical procedures. Patients classified as intermediate or high risk were monitored every 3 to 6 months for the first three years, followed by biannual assessments thereafter. Conversely, patients identified as very low risk or low risk were followed up every six months for five years. The follow-up assessment regimen included a combination of laboratory tests, radiographic imaging (including computed tomography or magnetic resonance imaging), and gastrointestinal endoscopy when clinically indicated. Relapse-free survival (RFS) was defined as the interval from surgery to the date of the first documented recurrence, which was established through imaging studies or pathological findings. Overall survival (OS) was calculated as the time from surgery to death from any cause. The final date of follow-up was August 31, 2024.

Cost-effectiveness analysis

Patient hospitalization expenses included laboratory fees, imaging examination fees, surgical fees, medication costs, nursing fees, and additional expenses. Each of these costs is calculated in Renminbi (RMB, the currency of China, reported in yuan, ¥). All costs were adjusted for inflation via China's consumer price index and standardized to the 2023 RMB. Medical expenses and GSRS outcomes were utilized to evaluate both costs and effectiveness at the individual patient level. During the follow-up period, patients completed the GSRS questionnaire to estimate the quality-adjusted life years (QALYs) [14]. The average differential cost and average differential QALY were computed and represented on a cost–utility plane. Furthermore, the incremental cost-effectiveness ratio (ICER), incremental net monetary benefit (INMB), and cost-effectiveness acceptability curve (CEAC) were employed to summarize and present the cost-effectiveness results [15]. The ICER was determined as the incremental cost (measured in RMB) divided by the incremental effectiveness (measured in QALYs), with a higher ICER indicating greater costs for each additional QALY gained. Confidence intervals derived from the INMB were used to construct the CEAC, providing a probabilistic analysis for a range of cost-effectiveness thresholds for surgeons. A tornado diagram was performed to show the results of univariate sensitivity analyses. The Chinese gross domestic product (GDP) per capita in 2023 (89,360 yuan) was considered a reference value, assuming an ICER of 1xGDP, to define an intervention as cost-effective. Additionally, the threshold of willingness to pay (WTP) was established as the GDP per capita of China in 2023.

Statistical analysis

Statistical analysis was conducted in R version 4.1.5 (R Foundation for Statistical Computing, Vienna, Austria). A two-tailed P value of less than 0.05 was considered to indicate statistical significance. The chi-square test or Fisher's exact test was used to compare categorical variables among the three groups, whereas one-way analysis of variance (for normally distributed data) or the Kruskal–Wallis test (for nonnormally distributed data) was used to compare continuous variables among the groups. Survival data were analyzed via the log-rank test. To mitigate confounding biases, propensity score matching (PSM) was performed to adjust for baseline covariates across the three groups. The covariates included in the PSM were age, sex, American Society of Anesthesiologists (ASA) score, body mass index (BMI), history of previous abdominal surgery, disease course, tumor location, pathological diagnosis, tumor size, risk stratification, and the mitotic index. Matching was conducted at a 1:1:1 ratio via greedy matching with a caliper width of 0.2. The absolute standardized mean difference (SMD) was calculated to assess the balance in baseline characteristics among the three groups before and after PSM; a lower SMD indicated a better match of clinicopathological characteristics.

Results

Patient characteristics

The demographics and clinical characteristics of the three groups are summarized in Table 1. Prior to PSM, no significant differences were observed among the groups in terms of sex distribution, ASA score, BMI, previous abdominal surgery, disease course, tumor location, pathological diagnosis, risk stratification, or mitotic index. However, the mean age of the patients in the RECS group was younger than that of the patients in the other two groups (56.8 ± 11.1 vs. 59.6 ± 10.2 vs. 64.4 ± 9.8 years, $P < 0.001$). Additionally, significant differences in tumor size were noted among the three groups (4.4 ± 1.6 vs. 4.7 ± 1.7 vs. 5.4 ± 2.1 cm, $P = 0.007$). Following PSM, all matched covariates were found to be comparable among the groups; the changes in SMD values for clinicopathological features further indicated increased homogeneity among the groups after matching.

Table 1 Baseline characteristics of enrolled patients before and after propensity score matching

Characteristics	Before matching			SMD	*p*-value	After matching			SMD	*p*-value
	RECS (*n* = 61)	LAP (*n* = 196)	OPEN (*n* = 57)			RECS (*n* = 51)	LAP (*n* = 51)	OPEN (*n* = 51)		
Age (year, mean ± SD)	56.8 ± 11.1	59.6 ± 10.2	64.4 ± 9.8	0.486	< 0.001	60.2 ± 7.7	61.6 ± 8.9	62.4 ± 8.2	0.178	0.404
Sex, n (%)				0.119	0.459				0.079	0.789
Male	35 (57.4)	95 (48.5)	30 (52.6)			27 (52.9)	30 (58.8)	27 (52.9)		
Female	26 (42.6)	101 (51.5)	27 (47.4)			24 (47.1)	21 (41.2)	24 (47.1)		
ASA score, n (%)				0.175	0.261				0.106	0.723
I, II	54 (88.5)	170 (86.7)	45 (78.9)			44 (86.3)	42 (82.4)	41 (80.4)		
III, IV	7 (11.5)	26 (13.3)	12 (21.1)			7 (13.7)	9 (17.6)	10 (19.6)		
BMI (kg/m^2, mean ± SD)	23.0 ± 2.1	22.6 ± 1.9	22.0 ± 2.2	0.332	0.019	22.9 ± 2.1	22.1 ± 1.4	22.1 ± 2.2	0.276	0.061
Previous abdominal surgery, n (%)	6 (9.8)	17 (8.7)	7 (12.3)	0.079	0.715	3 (5.9)	5 (9.8)	6 (11.8)	0.139	0.577
Disease course (month), median (IQR)	24 (13–38)	19 (11–31)	24 (12–36)	0.643	0.214	24 (12–33)	18 (9–24)	24 (12–36)	0.423	0.427
Tumour location, n (%)				0.261	0.513				0.284	0.824
Cardia	5 (8.2)	6 (3.1)	2 (3.5)			4 (7.8)	7 (13.7)	2 (3.9)		
Gastric fundus	18 (29.5)	77 (39.3)	21 (36.8)			17 (33.3)	15 (29.4)	19 (37.3)		
Gastric body	25 (41.0)	81 (41.3)	21 (36.8)			20 (39.2)	18 (35.3)	18 (35.3)		
Gastric antrum	9 (14.8)	27 (13.8)	10 (17.5)			6 (11.8)	7 (13.7)	9 (17.6)		
Pylorus	4 (6.6)	5 (2.6)	3 (5.3)			4 (7.8)	4 (7.8)	3 (5.9)		
Pathological diagnosis, n (%)				0.121	0.369				0.091	0.783
GIST	50 (82.0)	146 (74.5)	46 (80.7)			37 (72.5)	40 (78.4)	38 (74.5)		
Others[$]	11 (18.0)	50 (25.5)	11 (19.3)			14 (27.5)	11 (21.6)	13 (25.5)		
Tumour size (cm, mean ± SD)	4.4 ± 1.6	4.7 ± 1.7	5.4 ± 2.1	0.356	0.007	4.5 ± 1.4	5.0 ± 1.2	5.3 ± 2.2	0.324	0.052
Risk stratification[a], n (%)				0.329	0.193				0.236	0.816
Very low	5 (8.2)	19 (9.7)	11 (19.3)			5 (9.8)	9 (17.6)	10 (19.6)		
Low	29 (47.5)	83 (42.3)	23 (40.4)			23 (47.1)	23 (45.1)	20 (39.2)		
Intermediate	23 (37.7)	63 (32.1)	17 (29.8)			19 (37.3)	14 (27.5)	16 (31.4)		
High	4 (6.6)	31 (15.8)	6 (10.5)			4 (7.8)	5 (9.8)	5 (9.8)		
Mitotic index/50HPF				0.220	0.277				0.145	0.873
≤ 5	47 (77.0)	163 (83.2)	41 (71.9)			38 (74.5)	36 (70.6)	35 (68.6)		
6–10	7 (11.5)	22 (11.2)	10 (17.5)			6 (11.8)	8 (15.7)	10 (19.6)		
> 10	7 (11.5)	11 (5.6)	6 (10.5)			7 (13.7)	7 (13.7)	6 (11.8)		

RECS robotic and endoscopic cooperative surgery; *BMI* body mass index; *ASA* American society of anesthesiologists physical status classification;

[a]A risk category was assigned to all patients based on the application of the modified NIH criteria (2008 Edition); *HPF* high-powered fields; *SMD* standardized mean difference; *GIST* gastrointestinal stromal tumors;

[$]Leiomyoma, carcinoid, lipoma, and glomus tumor; *IQR* interquartile range

Comparison of short-term outcomes

Table 2 presents a comparison of the perioperative and postoperative outcomes among the three groups. The OPEN group demonstrated a shorter operative time than the other two groups: 90 (70–120) min versus 110 (90–135) min for LAP and 120 (100–150) min for RECS. The difference among the groups was significant (P < 0.001). Furthermore, intraoperative blood loss in the RECS group was significantly lower than that in both the LAP and OPEN groups (20 vs. 80 vs. 120 ml, respectively; P<0.001).

In the comparison of postoperative recovery, the time to first flatus was significantly shorter in the RECS group than in the LAP and OPEN groups, with values of 2 (1–3) vs. 2 (1–3) vs. 3 (2–3) days, respectively (P < 0.001). Similarly, the time to first liquid intake [2 (2–3) vs. 3 (2–4) vs. 4 (3–5) days, respectively; P < 0.001] and the postoperative hospital stay [5 (4–8) vs. 7 (5–9) vs. 9 (6–10) days, respectively; P < 0.001] were significantly shorter in the RECS group than in the LAP and OPEN groups. However, there were no significant differences in the postoperative complication rates or types of postoperative complications among the three groups.

Comparison of long-term outcomes

The median follow-up duration was 50 months (range: 12 to 108 months). During the follow-up period, a total of 17 patients died, including four from the RECS group, six from the LAP group, and seven from the OPEN group. Additionally, disease recurrence was observed in 13 patients, with three in the RECS group, five in the LAP group, and five in the OPEN group. Specifically, liver recurrence occurred in seven patients, whereas peritoneal recurrence was noted in six patients. The Kaplan−Meier survival curves for OS and RFS are presented in Fig. 1. There were no significant differences in the 5 year OS rates (91.4% vs. 87.8% vs. 80.0%, P = 0.686) or 5 year RFS rates (92.3% vs. 91.0% vs. 88.4%, P = 0.986) among the three groups.

Comparison of postoperative gastrointestinal symptoms

Figure 2 shows the comparison of GSRS scores among the patients in different groups at various follow-up times after surgery. Gastrointestinal symptoms improved over time in all groups. At 3 months after surgery, patients in the RECS group presented milder gastrointestinal symptoms than did those in the LAP and OPEN groups, with scores of 4.7 ± 1.0, 6.0 ± 1.4, and 8.3 ± 1.9, respectively (P < 0.001). Similar trends were observed at 6 months, with

Table 2 Comparison of perioperative outcomes among three groups after propensity score matching

Characteristics	RECS (n = 51)	LAP (n = 51)	OPEN (n = 51)	P-value
Type of operation, no. (%)				< 0.001
RECS	51 (100.0)	0 (0.0)	0 (0.0)	
Wedge resection	0 (0.0)	45 (88.2)	41 (80.4)	
Partial gastrectomy	0 (0.0)	3 (5.9)	4 (7.8)	
Total gastrectomy	0 (0.0)	3 (5.9)	6 (11.8)	
Operation time (min), median (IQR)	120 (100–150)	110 (90–135)	90 (70–120)	< 0.001
Estimated blood loss (ml), median (IQR)	20 (5–50)	80 (30–100)	120 (75–150)	< 0.001
Days to first flatus (days), median (IQR)	2 (1–3)	2 (1–3)	3 (2–3)	< 0.001
Days to soft diet (days), median (IQR)	2 (2–3)	3 (2–4)	4 (3–5)	< 0.001
Postoperative hospital stay (days), median (IQR)	5 (4–8)	7 (5–9)	9 (6–10)	< 0.001
Postoperative complication, no. (%)	5 (9.8)	9 (17.6)	13 (25.5)	0.115
Major complications§	0 (0.0)	1 (2.0)	2 (3.9)	0.361
Pneumonia	2 (3.9)	1 (2.0)	2 (3.9)	0.813
Wound infection	1 (2.0)	2 (3.9)	3 (5.9)	0.594
Urinary tract infection	1 (2.0)	2 (3.9)	2 (3.9)	0.813
Gastric emptying disorder	0 (0.0)	2 (3.9)	2 (3.9)	0.358
Intestinal obstruction	1 (2.0)	1 (2.0)	1 (2.0)	1.000
Abdominal infection	0 (0.0)	1 (2.0)	1 (2.0)	0.603
Anastomotic bleeding	0 (0.0)	1 (2.0)	1 (2.0)	0.603
Anastomotic fistula	0 (0.0)	0 (0.0)	1 (2.0)	0.365

RECS robotic and endoscopic cooperative surgery; §Clavien-Dindo classification III or more; *IQR* interquartile range

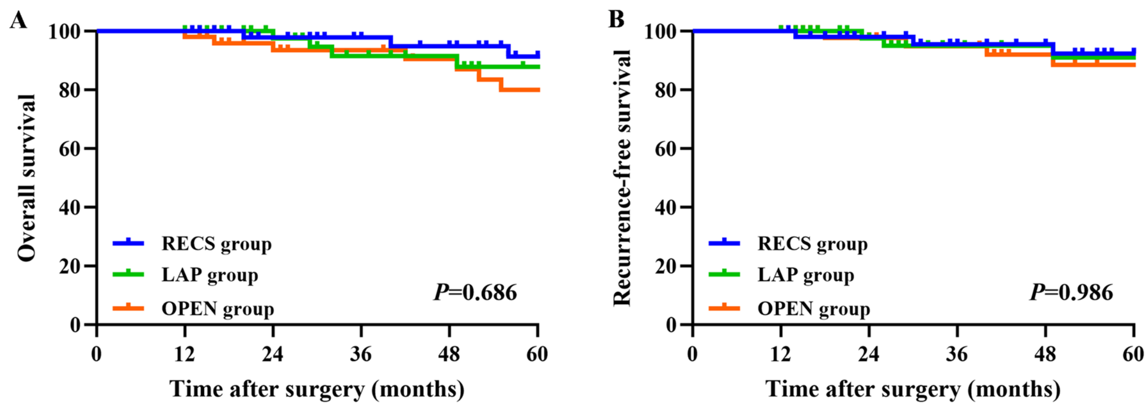

Fig. 1 Overall survival curves (**A**) and relapse-free survival curves (**B**) of patients with GSMTs according to the different surgery type

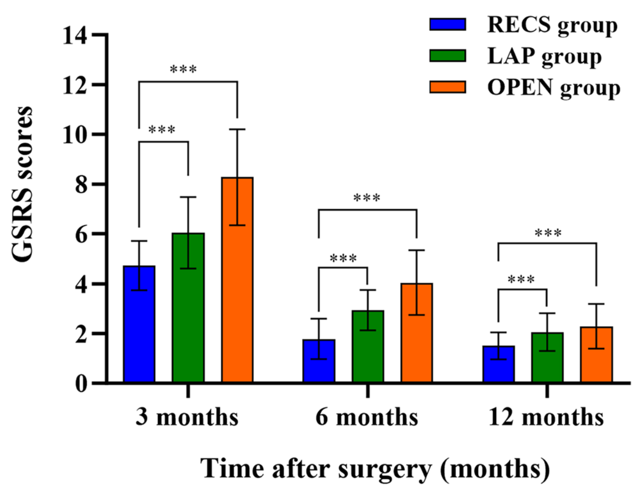

Fig. 2 Changes in gastrointestinal symptoms in the three groups after 3, 6, and 12 months of surgery. ***Significant differences between groups

scores of 1.8 ± 0.8 for RECS, 2.9 ± 0.8 for LAP, and 4.0 ± 1.3 for OPEN ($P < 0.001$), and at 12 months, with scores of 1.5 ± 0.5, 2.1 ± 0.8, and 2.3 ± 0.9, respectively ($P < 0.001$). Figure 3 presents the patients' scores across the 15 dimensions of the GSRS questionnaire at 3 months postsurgery. Notably, at this time, group differences in gastrointestinal symptoms were primarily observed in the decreased passage of stools, abdominal distention, and abdominal pain (all $P < 0.05$). Further comparisons of the different dimensions of the GSRS scale among the groups 6 and 12 months after surgery are shown in Supplementary Figs. 2 and 3.

Cost-effectiveness analysis

Table 3 presents a comparison of medical costs among the three surgical methods. The total medical costs for the RECS group were significantly greater than those for the LAP and OPEN groups [60.1 (52.7–67.4) vs. 50.3 (43.6–55.7) vs.

Fig. 3 Radar chart of scores on 15 dimensions of GSRS questionnaire among patients with GSMTs at three months after surgery according to the different surgery type

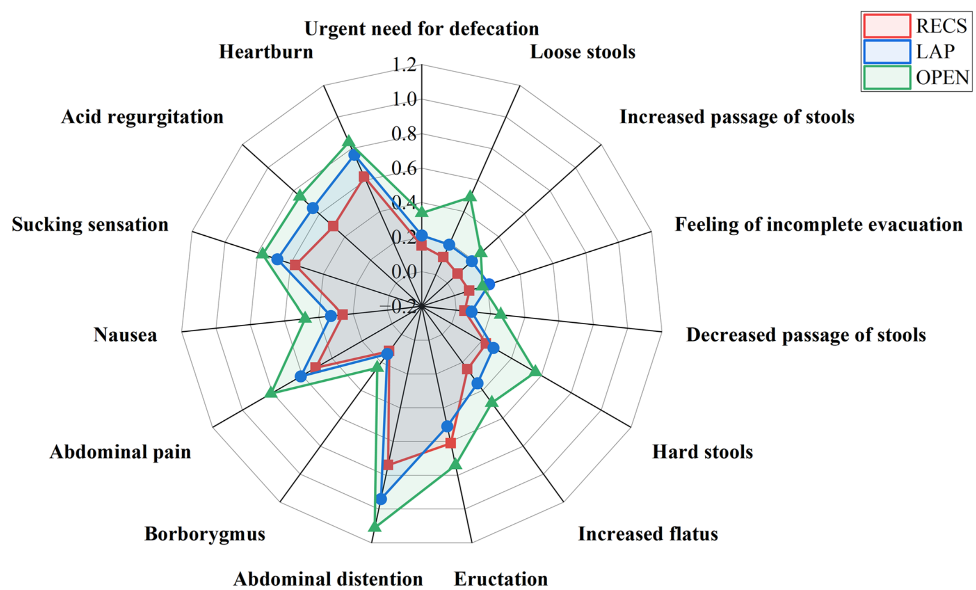

Table 3 Hospitalization expenses among three groups after propensity score matching

Costs in ¥*	RECS (*n* = 51)	LAP (*n* = 51)	OPEN (*n* = 51)	*P*-value
Total hospital costs§	60.1 (52.7–67.4)	50.3 (43.6–55.7)	41.9 (36.5–47.4)	< 0.001
Surgery costs	29.1 (24.1–30.9)	16.1 (13.9–19.9)	10.2 (8.9–11.5)	< 0.001
Surgical ward costs	3.5 (1.9–5.9)	3.7 (1.6–6.3)	4.0 (1.8–6.3)	0.147
Drug costs	11.1 (7.7–16.9)	12.3 (8.6–16.3)	11.7 (8.3–15.3)	0.437
Laboratory and imaging test costs	6.6 (5.1–8.2)	6.3 (5.3–8.0)	6.1 (5.2–8.1)	0.739
Nursing costs	2.7 (2.2–3.5)	3.2 (2.7–3.9)	3.4 (2.7–4.1)	0.019
Other costs	8.3 (7.0–9.3)	8.5 (7.2–10.0)	8.1 (6.2–8.8)	0.365

*All costs were adjusted for inflation for 2023

§Cost data are presented in RMB (thousand yuan) as median (IQR)

41.9 (36.5–47.4) thousand yuan, $P < 0.001$]. Further analysis revealed that the cost disparity primarily stemmed from surgical expenses [29.1 (24.1–30.9) vs. 16.1 (13.9–19.9) vs. 10.2 (8.9–11.5) thousand yuan, $P < 0.001$]. A detailed analysis of the surgical costs revealed that the main source of the cost difference was the cost of instruments and consumables (Supplementary Table 1). Additionally, patients in the RECS group incurred significantly lower nursing costs than those in the other two groups did [2.7 (2.2–3.5) vs. 3.2 (2.7–3.9) vs. 3.4 (2.7–4.1) thousand yuan, $P = 0.019$].

The cost−utility plane for the three cohorts is illustrated in Fig. 4A. Compared with the RECS group, both the LAP and OPEN groups presented negative incremental costs and effects. Figure 4B presents the ICERs and 95% confidence intervals for the pairwise comparisons among the three groups. Specifically, the incremental costs and benefits of RECS relative to laparoscopic surgery were ¥10,764 and 0.59 QALYs, respectively, whereas those relative to open surgery were ¥19,920 and 0.35 QALYs, respectively. The INMB and CEAC curves as a function of the WTP are depicted in Fig. 5A, B. Analysis of the INMB curves indicates that as WTP increases, both open and laparoscopic surgeries yield greater economic benefits than the RECS method does. Additionally, analysis of the CEAC curves demonstrates that the LAP and OPEN methods have an 8% and 3% probability of being more cost-effective than RECS across all WTP thresholds. Further deterministic sensitivity analysis revealed that the results were robust to fluctuations in utility weights, inflation and WTP (Supplementary Fig. 4).

Discussion

Minimally invasive surgical techniques are becoming increasingly prevalent in the treatment of GSMTs. In recent decades, numerous surgeons have made substantial efforts to improve surgical techniques to achieve more desirable

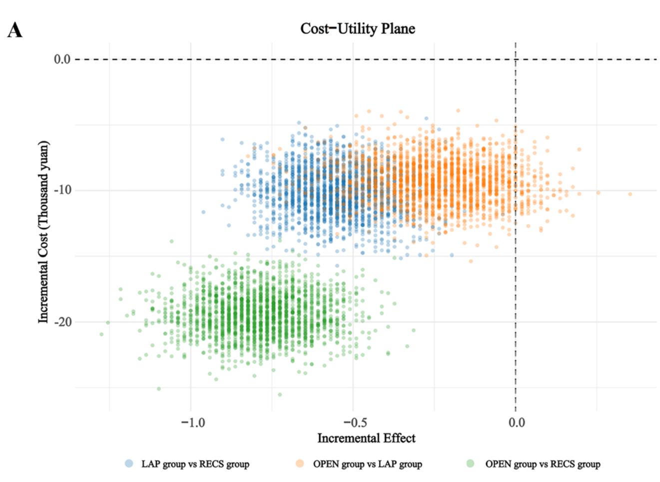

Fig. 4 **A** Cost-effectiveness scatterplot of 2000 bootstrap replicates for incremental cost and incremental effectiveness of pairwise comparisons among the three groups. **B** The incremental cost-effectiveness ratio slope with 95% confidence interval of pairwise comparisons among the three groups

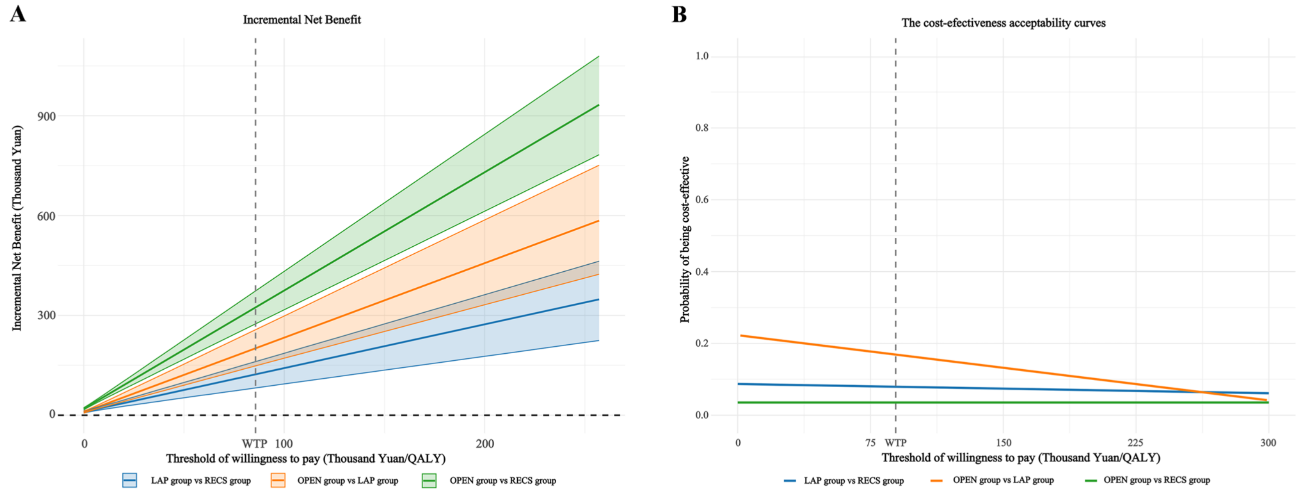

Fig. 5 **A** Incremental net monetary benefit with 95% confidence interval of pairwise comparisons among the three groups. **B** Cost-effectiveness acceptability curves of pairwise comparisons among the three groups. *WTP* willingness to pay

clinical outcomes for patients with GSMTs [16–18]. This study demonstrated that compared with conventional laparoscopic and open surgeries, RECS resulted in lower intraoperative blood loss, expedited postoperative recovery, and sustained improvements in gastrointestinal symptoms in the treatment of GSMTs. Given the increasing financial costs of healthcare, there is a pressing need for cost–benefit analyses, particularly concerning new devices and technologies. This study is the first to report the results of a cost-effectiveness analysis of different surgical modalities in the treatment of GSMTs. The findings indicated that although the total cost of hospitalization was significantly greater in the RECS group, the likelihood of RECS being more cost-effective than the other methods exceeded 90% across all WTP thresholds.

The RECS technique we proposed previously is a novel surgical approach that integrates endoscopic techniques, the third space, and robotic surgery. During the RECS procedure, endoscopists perform submucosal injections to delineate the surgical resection area and create a submucosal space. This allows the surgeons to assess the extent of tumor resection accurately on the basis of the established resection line, thereby minimizing the risk of stenosis or deformity resulting from excessive resection of the gastric wall as well as the risk of leaving positive resection margins due to an insufficient resection. Previous studies have confirmed that the submucosal space, also referred to as the third space, is a critical surgical area in the diagnosis and treatment of GSMTs [19, 20]. With the complete establishment of the third space, both the structure of the gastric wall and the location of the tumor can be thoroughly visualized, allowing precise tumor dissection within the robot's field of view. Furthermore, third-space surgery maximizes preservation of the mucosal layer and prevents communication between the abdominal and gastric cavities; maintaining an intact mucosal layer significantly reduces the risk of intra-abdominal infection and gastric perforation. Previous studies have reported that the incidence of complications associated with laparoscopic endoscopic cooperative surgery (LECS) ranges from 3.5% to 27.8%, among which intra-abdominal infection (5.8%), bleeding (3.2%), and perforation (2.2%) are the most frequently observed [21]. The reliability of the RECS technique is underscored by the lack of such complications in our patient cohort. Thus, the results of this study can be used as a reference for selecting the surgical approach for patients with GSMTs during the formulation of the surgical strategy. For example, for GSMTs without mucosal invasion, RECS can be considered, whereas for GSMTs accompanied by mucosal ulcers or bleeding, endoscopic techniques or conventional surgery should be considered according to the clinicopathological characteristics of the patient.

Owing to its technical advantages, Da Vinci robotic surgery has been rapidly adopted for specific surgical approaches. Compared with laparoscopic surgery, robotic surgery provides several technical benefits, including a seven degree-of-freedom arm, 3D magnified vision, tremor filtering, and enhanced ergonomic features, all of which result in greater flexibility and accuracy during confined third-space surgery. Furthermore, the technological superiority of robotic surgery, particularly regarding tissue dissociation and the protection of neurovascular structures in gastric tumor surgeries, has been substantiated in multiple studies [22–24]. In 2010, Buchs et al. first reported the initial results of robotic surgery in the treatment of five large gastrointestinal stromal tumors (GISTs), concluding that this approach is both safe and effective [25]. Subsequent studies of the robotic treatment of gastric GISTs have mostly been case reports and small case series [26, 27].

In our study, use of the RECS technique was associated with longer operative times, reduced intraoperative blood loss, and expedited postoperative recovery with respect to laparoscopic and open surgeries. The longer operative time for RECS relative to the other two techniques may be attributed to the need to make robotic arm adjustments and perform the endoscopic procedures. In the study conducted by Graziano et al., a total of 45 patients underwent robotic resection for GISTs, including 42 who underwent wedge resections and three who underwent partial gastrectomies [28]. The median operative time for the robotic group in that study was 151 min (range: 75–300 min), which was longer than that observed in our study. Furthermore, previous studies have reported operative times for classic LECS (193 min) [29], inverted LECS (215 min) [30] and closed LECS (253 min) [31] that were significantly longer than those of our RECS group (120 min). This discrepancy may be attributed to technical differences; LECS involves endoscopic mucosal dissection followed by laparoscopic serosal muscle dissection, which is a meticulous and time-consuming process, whereas RECS technology allows all anatomical operations to be performed solely by robotic systems, resulting in a simpler and more efficient procedure. With respect to other operation-related outcomes, the amount of intraoperative bleeding and the indicators of postoperative recovery were comparable to those reported in previous LECS studies. However, owing to differences in inclusion criteria and the absence of direct comparative studies, this conclusion requires further validation through additional research.

Currently, research on the long-term outcomes of patients who have undergone robotic surgery for GSMTs is limited. Only Solaini and colleagues have investigated the clinical outcomes of patients who have undergone robotic surgery compared with those of patients treated with laparoscopic and open surgeries for gastric GISTs [11]. They performed 19 robotic wedge resections and 5 robotic partial gastrectomies, achieving complete resection in all patients. During a median follow-up period of 24 months, none of the patients who underwent robotic surgery experienced local recurrence. In this study, there was no significant difference in the 5 year RFS rates among the RECS, LAP, and OPEN groups (92.3% vs. 91.0% vs. 88.4%, $P=0.986$). A total of three patients in the RECS group developed local recurrence during follow-up, which was eventually managed with surgical treatment. In these patients, recurrence was likely not attributable to the surgical procedure but rather to the clinicopathological features of the patients, including a tumor diameter greater than 5 cm and a high mitotic index, both of which are associated with an increased risk of recurrence. Thus, our experience suggests that RECS is a safe and effective approach for the treatment of GSMTs, yielding excellent long-term oncologic results with respect to traditional surgical methods.

Surgeons aim to achieve optimal functional protection for patients while ensuring complete tumor resection. In this study, the GSRS was utilized to evaluate postoperative gastrointestinal symptoms. We found that the improvements in gastrointestinal symptom control achieved with RECS over laparoscopic and open surgery were durable and remained significant 1 year after surgery. Given that GSMTs are encompassed by the normal gastric wall, excessive gastric wall resection may result in postoperative gastric transformation and stasis. The RECS technique minimizes excessive resection of the gastric wall, preserving the mucosal layer entirely and thereby maximizing the maintenance of gastric volume and functional integrity. Furthermore, for tumors located in anatomically challenging locations such as the esophagogastric junction and pylorus, the 720 degree wrist configuration of the robotic arm facilitates meticulous dissection of neoplastic tissue with minimal manipulation, which helps preserve the integrity of the gastric anatomy to the greatest extent possible.

High acquisition and operating costs may hinder the widespread adoption and application of robotic surgery. As indicated by the analysis of total medical expenditures, the RECS procedure was more expensive than both the laparoscopic and open approaches were, which is consistent with findings from previous studies [32]. As shown in Table 3, the disparity in total hospitalization costs was primarily due to differences in surgical costs. However, the results also indicated that the RECS technique can reduce nursing costs by facilitating faster postoperative recovery. According to the cost−utility analysis conducted in our study, compared with laparoscopic and open surgery, RECS yielded additional QALYs. Moreover, the results of CEAC curve and sensitivity analysis further demonstrated the acceptability and stability of this advantage. However, although we controlled for the effect of annual inflation rates on our results, changes in reimbursement rules for robotic surgery or national health care reform provisions could also have affected our results. Thus, future studies in which cost-effect analyses are performed on the basis of medical policy changes may be warranted, potentially providing a new reference for treatment decision-making for patients with GSMTs. In addition, it should be noted that the upcoming expiration of certain manufacturing licenses and the introduction of new robotic systems from various companies may decrease the overall costs of robotic systems, thereby increasing the prospects for the clinical application of RECS technology.

This study had several limitations. First, the relatively small sample size may have resulted in insufficient statistical power for the conclusions drawn. Therefore, a high-quality, multicenter, prospective study with a larger sample size is needed to validate the results of this study. Second, the differences in clinical outcomes in this study were due mainly to the different surgical techniques used. Patients who underwent endoscopic resection techniques, such as tunneling resection, submucosal dissection and LECS, were not included in the study. Future comparisons involving these and other endoscopic techniques are warranted to further define the sources of the improvements in clinical outcomes observed in these studies. Finally, the cost-effectiveness analyses in this study were based on the direct medical costs of the patients; direct nonmedical costs and indirect costs, such as lost work-days due to illness, economic expenses due to quality of life changes, and follow-up costs, were not collected and analyzed. Hence, a multidimensional, prospective study is warranted to obtain an exhaustive collection of data and perform a comprehensive evaluation.

Conclusion

In this study, we demonstrated that our proposed RECS technique facilitates precise GSMT resection, leading to significant improvements in perioperative clinical outcomes and a reduction in postoperative gastrointestinal symptoms. Although the total medical costs are relatively high, the high probability that RECS is cost-effective makes it an enticing surgical option. Therefore, surgeons should tailor surgical strategies to the individual patient's clinicopathological characteristics, their quality of life requirements, and their economic situation.

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Author contributions JJS was involved in study design. LM, RHL, and CHH collected the data. CHH, LZ and PHQ analyzed the data. LM wrote the paper. LM, RHL, and JJS edited the paper. All authors approved the final manuscript.

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Data availability Requests for raw data and supporting materials can be made by contacting the corresponding author.

Declarations

Disclosures Lei Ma, Ruihan Liu, Chenhao Hu, Lei Zhang, Penghong Qu, and Junjun She have no conflicts of interest or financial ties to disclose.

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