Transanal versus nontransanal surgery for the treatment of primary rectal gastrointestinal stromal tumors: a 10-year experience in a high-volume center

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Background: Rectal gastrointestinal stromal tumor (GIST) is a rare digestive disease that has a distinct malignant tendency compared to that of gastric-derived GIST. At present, there is still no standard, and the surgical approach to rectal GIST is controversial.

Methods: The clinicopathological data and prognosis of rectal GIST patients admitted to the Sixth Affiliated Hospital of Sun Yat-sen University from 1998.01.01 to 2018.12.31 were collected retrospectively. All cases were divided into either the transanal (TA) group or the nontransanal (NTA) group.

Results: A total of 537 GIST cases were treated in 10 years, including 82 rectal GIST cases (64 cases underwent surgical resection, including 29 cases in the TA group and 35 cases in the NTA group). Preoperative neoadjuvant therapy (P=0.003), postoperative adjuvant therapy (P=0.017), operative time (P=0.013), blood loss (P=0.038), anus-preserver (P=0.048), 30-day complication rate (P=0.000), time to flatus (P=0.036), hospital stays (P=0.011), distance from the anus (P=0.047), tumor size (P=0.002), mitotic count (P=0.035) and National Institutes of Health (NIH) criteria (P=0.000) were significantly different between these two groups (all P<0.05). The median follow-up time was 41 (range, 1–122) months. Twelve patients had recurrence and metastasis, and 4 patients died. The 5-year disease-free survival (DFS) and overall survival (OS) were 74.4% and 91.2%, respectively, in the whole group. There were no statistically significant differences between the TA group and the NTA group at 5-year DFS (81.3% *vs.* 79.0%, P=0.243) and OS (88.7% *vs.* 93.3%, P=0.308).

Conclusions: In the treatment of rectal GIST, TA resection has a minimally invasive effect, less postoperative complications, high anal sphincter preservation rate, and R0 resection rate and a better prognosis. How to improve the proportion of neoadjuvant therapy and choose the appropriate cases for TA surgery is still a challenge.

Keywords: Transanal (TA); nontransanal (NTA); rectal gastrointestinal stromal tumor (GIST)

Introduction

The gastrointestinal stromal tumor (GIST) is a tumor type with a malignant tendency originating from mesenchymal tissue. The incidence rate is 1–2/100,000, accounting for approximately 20% of all soft tissue sarcomas (1-3). Such tumors can occur throughout the digestive tract, with the stomach being the most common site, accounting for approximately 60%, while the rectum is relatively rare, accounting for approximately 5% (4,5). Because of the low incidence and lack of evidence from large-sample, prospective studies, predictive behavioral data in the National Comprehensive Cancer Network (NCCN) guidelines for rectal GIST are mainly derived from a retrospective study of 111 cases in 2006 (6,7). At present, the diagnosis and treatment of rectal GIST still refers to the guidelines of gastric GIST and a modified National Institutes of Health (NIH) risk grading system (index contains tumor site, tumor size, mitotic count and rupture), including very low-risk, low-risk, intermediate-risk and high-risk, was used to predict recurrence risk (8). In recent years, it is clear that this type of disease has a malignant tendency and is prone to recurrence, and the prognosis is worse than that of gastric GIST (9,10). At present, preoperative treatment, surgical approach, resection scope and prognosis of rectal GIST are still inconclusive, with much controversy (4,11). This study retrospectively collected 64 surgically resected rectal GISTs admitted to the Sixth Affiliated Hospital of Sun Yat-sen University from 1998 to 2018. All data were divided into two groups: the transanal (TA) group and the nontransanal (NTA) group. Then, clinicopathology and prognosis were compared in these two groups.

Methods

We received ethical approval for this case series from the Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China and obtained consent for publication from the patients.

Patients

A retrospective collection of rectal GIST cases was performed at the Sixth Affiliated Hospital of Sun Yat-sen University from 2008 to 2018. Enrollment criteria: (I) complete clinical information and follow-up and (II) primary GIST and pathological diagnosis. Exclusion criteria: (I) combined with other malignant tumors, (II) multiple GIST and (III) deaths due to other diseases.

Observation indicators and follow-up

For the surgical approach, the enrolled cases were divided into the TA group and the NTA group. According to previous surgical records, TA surgery was defined as the application of lithotomy or folding position, and local resection was performed under direct vision or utilizing a transanal endoscopy microsurgery (TEM) platform. NTA surgery was defined as trans-sacral or transabdominal partial resection or radical surgery (Dixon, Miles surgery) (*Figure 1*). The clinical and pathological parameters, including age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) score, genetic test, preoperative treatment, surgical and postoperative outcomes, and pathological outcomes were retrospectively analyzed. According to the modified NIH risk grading system in 2008 (12), the disease is classified into very low-risk, low-risk, intermediate-risk and high-risk. The mitotic index was counted per 50/high power field (HPF), and the above pathological examinations were approved by three experienced pathologists. The start time of the study was defined as the surgical time, and the last follow-up time was 2019-02-15.

Statistics

Statistical analyses were performed using SPSS 19.0. Quantitative data are reported as the mean ± standard deviation (SD) or median. Categorical data were compared by χ^2 tests or Fisher's exact test. Survival curves [overall survival (OS) and disease-free survival (DFS)] were derived from Kaplan-Meier estimates, and the curves were compared by the log-rank test. A P value <0.05 was considered statistically significant.

Results

Patients

A total of 537 GIST cases were collected from the Sixth Affiliated Hospital of Sun Yat-sen University from 2008 to 2018. A total of 82 patients with rectal GIST who met the criteria for inclusion in this study accounted for 15.3% (82/537) of the total. There were 64 surgical resection cases, 29 cases in the TA group, and 35 cases in the NTA group
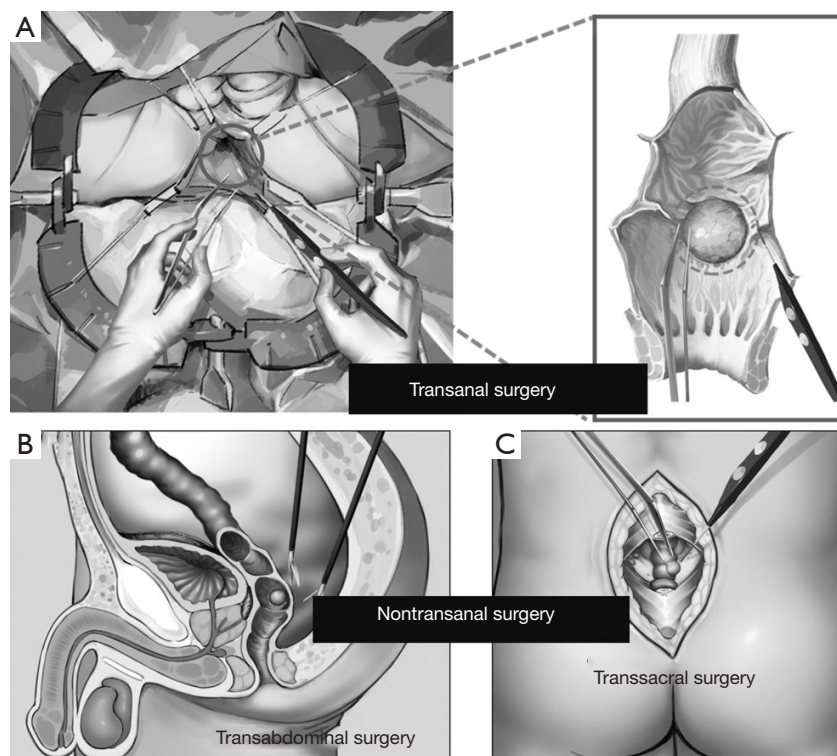
Figure 1 Description of (A) TA and (B,C) NTA surgery. TA, transanal; NTA, nontransanal.
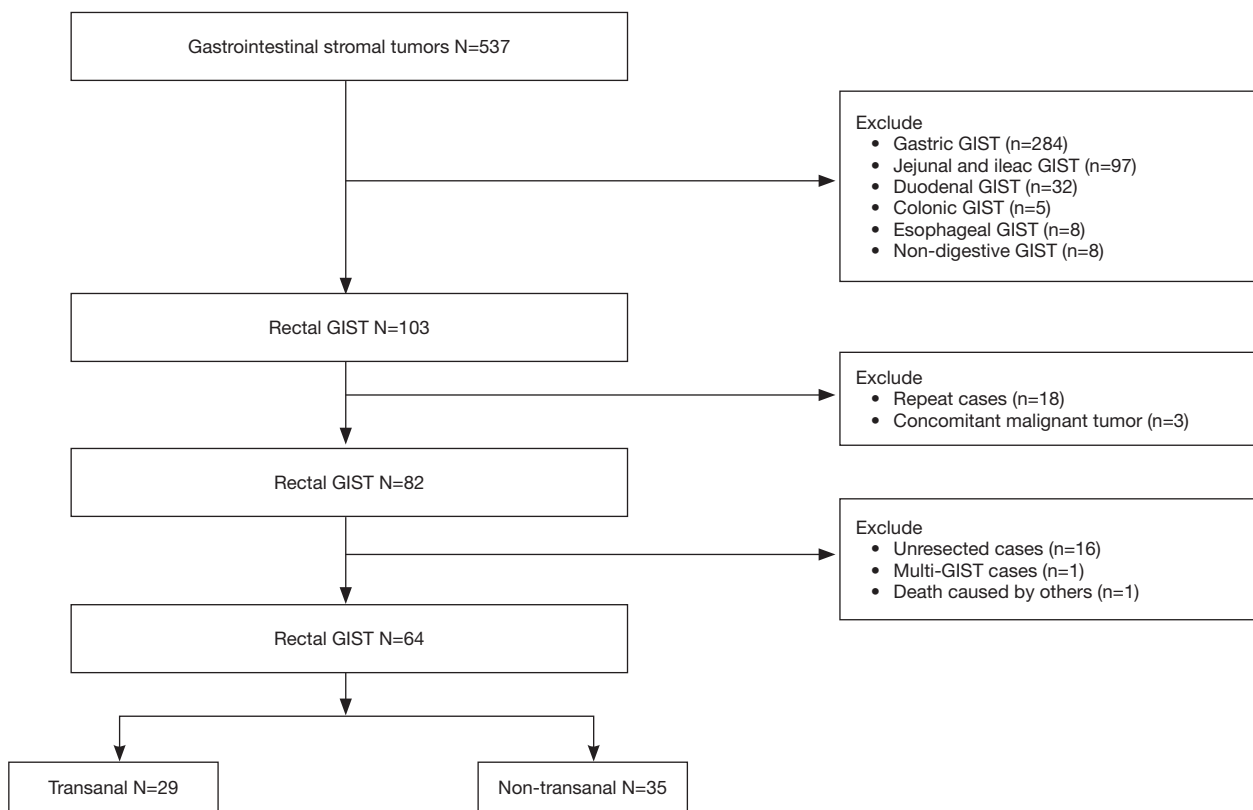
(*Figure 2*).

Clinical information

The median age was 59 years old in the whole group. For sex, the male: female ratio was 41:23. The mean BMI was 22.3 ± 2.4 kg/m^2. For the ASA score, grade I: 5 cases (7.8%), grade II: 45 cases (70.3%), and grade III: 14 cases (21.9%). There were 41 cases with clinical symptoms in the whole group, including bloody stool (14 cases), anal pain (13 cases), abdominal pain (8 cases), difficulty in defecation (3 cases), change of bowel habits (2 cases), and frequent urination (1 case). In the diagnostic workup, 24 cases (37.5%) were diagnosed by needle biopsy, 38 cases (59.4%) were diagnosed by resection, and 2 cases (3.1%) were diagnosed by endoscopy. There were 30 cases (46.9%) with postoperative adjuvant therapy in the whole group. Ten cases (15.9%) underwent genetic tests. Twelve cases had a recurrence. There was no significant difference in age (P=1.000), gender (P=0.443), BMI (P=0.171), presenting symptoms (P=0.667), diagnostic workup (P=0.457), genetic test (P=0.490) and recurrence (P=1.000) between the TA and NTA groups. However, for the preoperative adjuvant treatment, 7 cases were in the TA group and 22 cases were in the NTA group, and there was a significant difference between the two groups (P=0.003). For the postoperative adjuvant treatment, 9 cases were in the TA group and 21 cases were in the NTA group, and there was a significant difference between the two groups (P=0.017) (*Table 1*).

Surgical and postoperative outcomes

In terms of surgical index, the TA group had less operative time (40.0 ± 7.1 vs. 160.0 ± 63.2 min, P=0.013), less blood loss (12.5 ± 10.6 vs. 80.0 ± 40.0 mL, P=0.038), and a high anus-preserver rate (P=0.048). In the NTA group, there were 2 cases with combined-organ resection, one with combined-urinary bladder resection and one with combined-ovary resection. The overall postoperative 30-day complication rate was 25.0% (16/64), including 2 cases of hemorrhage, 4 cases of anastomotic leakage, 2 cases of incision infection, 2 cases of abscess, 2 cases of anal fistula, 1 case of small intestinal obstruction, and 1 case of sphincter damage. The 30-day postoperative complication rate was lower in the TA group than in the NTA group (P=0.000). In terms of the postoperative recovery index, the TA group had an earlier

Figure 2 Study flowchart. Rectal GIST in the Sixth Affiliated Hospital of Sun Yat-sen University from 2008–2018. GIST, gastrointestinal stromal tumor.

flatus time (1.5±0.7 *vs.* 3.5±0.6 days, P=0.036) and a shorter hospital stay (4.0±1.4 *vs.* 10.2±7.9 days, P=0.011). There was no postoperative morbidity within 30 days in the two groups (*Table 2*).

Pathological outcomes

In terms of tumor size, there were 8 cases (12.5%) ≤2 cm, 38 cases (59.4%) >2 & ≤5 cm, and 18 cases (28.1%) >5 & ≤10 cm. The tumors in the TA group were smaller than those in the NTA group, and there was a significant difference between the two groups (P=0.002). The distance from the anus in the TA group was shorter than that in the NTA group (4.2±0.9 *vs.* 5.8±2.1 cm, P=0.047). For tumor location, 26 cases (40.6%) were located in the anterior wall, 5 cases (7.8%) were located in the posterior wall, and 33 cases (51.6%) were located in the sidewall. In histopathological classification, there were 56 cases (87.5%) of spindle cell type, 7 cases (10.9%) of epithelial cell type, and 1 case (1.6%) of mixed type. Immunohistochemistry

(IHC) was performed in all cases, including 52 cases of CD34(+), 60 cases of CD117(+), and 52 cases of Dog-1(+). There were only 10 cases with genetic mutation detection in the whole group, including 9 cases of c-Kit 11 mutation and 1 case of platelet-derived growth factor receptor alpha (PDGFRA) 12 mutation. Only one patient in the whole group had intraoperative tumor rupture. Only one case had a positive surgical margin and this case was treated by Imatinib later, now still be alive. There was no significant difference in tumor position (P=0.234), histopathological classification (P=0.623), IHC (P=0.442), genetic mutation test (P=0.347), tumor rupture (P=0.997) and surgical margin (P=0.997) between the TA group and the NTA group. However, for the mitotic count (P=0.035) and NIH criteria (P=0.000), there was a statistically significant difference between the TA group and the NTA group (*Table 3*).

Some clinical information in different periods

The time between 2008 and 2018 was divided into

Table 1 Clinical information about rectal GIST

Clinical information	No. of cases (%)	TA (n=29)	NTA (n=35)	P value
Age				1.000
>60 years	30 (46.9)	14	16	
≤60 years	34 (53.1)	15	19	
Sex				0.443
Male	41 (64.1)	17	24	
Female	23 (35.9)	12	11	
BMI (kg/m^2)		22.0±2.7	22.9±2.4	0.171
ASA score				0.667
I	5 (7.8)	2	3	
II	45 (70.3)	20	25	
III	14 (21.9)	7	7	
Presenting symptom				0.457
Yes	41 (64.1)	18	23	
No	23 (35.9)	11	12	
Diagnostic workup				0.215
Needle biopsy	24 (37.5)	9	15	
Resection	38 (59.4)	20	18	
Endoscopy	2 (3.1)	0	2	
Preoperative adjuvant therapy				0.003
Yes	29 (45.3)	7	22	
No	35 (54.7)	22	13	
Postoperative adjuvant therapy				0.017
Yes	30 (46.9)	9	21	
No	34 (53.1)	20	14	
Genetic test				0.490
Yes	10 (15.6)	3	7	
No	54 (84.4)	26	28	
Recurrence	12 (18.8)	5	7	1.000

GIST, gastrointestinal stromal tumor; TA, transanal; NTA, nontransanal; BMI, body mass index; ASA, American Society of Anesthesiology.

four periods: 2008–2009, 2010–2012, 2013–2015, and 2016–2018. From *Table 4*, the resected cases gradually increased, which was 2 cases, 15 cases, 16 cases, and 31 cases, respectively, in the four different periods. The cases (%) that underwent trans-sacral surgery were 0 (0%), 1 (6.7%), 7 (43.8%) and 9 (29.0%), respectively, while the cases (%) of extensive resection were 0 (0%), 4 (26.7%), 5 (31.3%) and 6 (19.4%), respectively. In the whole group, only 2 cases (12.5%) were in 2013–2015, and 8 cases (25.8%) in 2016–2018 performed a genetic test. The cases (%) of neoadjuvant therapy in the four-time periods were 0 (0%), 4 (26.7%), 9 (56.3%), and 16 (51.6%), respectively, and

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Table 2 Surgical and postoperative outcomes regarding rectal GIST

Surgical outcomes	No. of cases (%)	TA (n=29)	NTA (n=35)	P value
Operative time (min)	–	40.0±7.1	160.0±63.2	0.013
Blood loss (mL)	–	12.5±10.6	80.0±40.0	0.038
Anus-preserver				0.048
Yes	59	29	30	
No	5	0	5	
Combined-organ resection	2	0	2	0.143
Defunctioning stoma	–	0	2	0.143
30-day complication rate	16 (25.0)	2	14	0.000
Bleeding	2	1	1	
Leakage	4	0	4	
Incision infection	2	0	2	
Abscess	2	0	2	
Anal fistula	2	0	2	
Obstruction	1	0	1	
Sphincter damage	3	1	2	
Time to flatus (day)	–	1.5±0.7	3.5±0.6	0.036
Time to diet (day)	–	3.0±1.4	3.5±1.2	0.685
Hospital stays (day)	–	4.0±1.4	10.2±7.9	0.011
Postoperative morbidity within 30 days	0	0	0	1.000

GIST, gastrointestinal stromal tumor; TA, transanal; NTA, nontransanal.

the cases (%) of postoperative adjuvant treatments were 1 (50.0%), 1 (6.7%), 8 (50.0%), and 20 (64.5%), respectively.

Prognosis

The mean overall follow-up time was 46 (range, 1–122) months. Disease recurrence over the entire follow-up period was observed in 17.2% (n=5) of patients in the TA group and 20.0% (n=7) of patients in the NTA group, without a significant difference between these two groups (P=1.000) (*Table 1*). Among the 12 recurrence cases, 10 cases were recurrent *in situ*, 1 case had liver metastasis and recurrence *in situ*, and 1 case had prostate and seminal vesicle metastasis. Among the recurrent cases, there were 10 high-risk cases and 7 cases treated with imatinib. There was no significant difference between the TA and NTA groups in terms of DFS and OS. The 3- and 5-year DFS rates were 81.3% and 65.1% for the TA group and 79.0% and 65.9% for the NTA group, respectively (P=0.243) (*Figure 3*). There were 4 deaths in the whole group, and 3 cases were high-risk cases. The 3- and 5-year OS rates were 95.0% and 88.7% for the TA group and 93.3% and 93.3% for the NTA group (P=0.308) (*Figure 4*). Univariate analysis showed that tumor size, mitotic count and NIH risk were the factors influencing DFS. However, multivariate analysis did not find any independent risk factors affecting DFS. For OS, univariate and multivariate analysis found no prognostic factors or independent risk factors (*Table 5*).

Discussion

This study was a single-center, retrospective study that collected 82 pathologically confirmed rectal GIST cases (*Figure 1*), accounting for 15.3% (82/537) of all GIST

**Table 3** Pathological outcomes regarding rectal GIST

Pathological outcomes	No. of cases (%)	TA (n=29)	NTA (n=35)	P value
Distance from the anus (cm)	–	4.2±0.9	5.8±2.1	0.047
Tumor size*				0.002
≤2 cm	8 (12.5)	8	0	
>2 & ≤5 cm	38 (59.4)	16	22	
>5 & ≤10 cm	18 (28.1)	5	13	
Tumor location				0.234
Anterior wall	26 (40.6)	12	14	
Posterior wall	5 (7.8)	4	1	
Sidewall	33 (51.6)	13	20	
Mitotic count				0.035
≤5/50 HPF	48 (75.0)	25	23	
>5 & ≤10/50 HPF	15 (23.4)	3	12	
>10/50 HPF	1 (1.6)	1	0	
Histopathological classification				0.623
Spindle	56 (87.5)	26	30	
Epithelioid	7 (10.9)	3	4	
Mixed	1 (1.6)	0	1	
IHC				0.442
CD34(+)	52 (81.3)	24	28	
CD117(+)	60 (93.8)	27	33	
Dog-1(+)	52 (81.3)	23	29	
Genetic mutation test (total =10)				0.347
c-Kit 11	9	3	6	
PDGFRA 12	1	1	0	
Others	0	0	0	
Tumor rupture				0.997
Yes	1	0	1	
Surgical margin				0.997
Positive	1	0	1	
NIH criteria				0.000
Very low	8 (12.5)	8	0	
Low	14 (21.9)	9	5	
High	42 (65.6)	12	30	

*, Tumor size means the preoperative size with or without any neoadjuvant treatment. GIST, gastrointestinal stromal tumor; TA, transanal; NTA, nontransanal; HPF, high power field; IHC, immunohistochemistry; NIH, National Institute of Health.

Table 4 Clinical information about rectal GIST in 6 different periods

Period	Cases	Micro-surgery[a], n (%)	Trans-sacral surgery, n (%)	Extensive resection[b], n (%)	Genetic test, n (%)	Intermediate/high risk, n (%)	Neoadjuvant therapy, n (%)	Adjuvant therapy[c], n (%)
2008–2009	2	2 (100.0)	0	0	0	1 (50.0)	0	1 (50.0)
2010–2012	15	7 (46.7)	1 (6.7)	4 (26.7)	0	9 (60.0)	4 (26.7)	1 (6.7)
2013–2015	16	6 (37.5)	7 (43.8)	5 (31.3)	2 (12.5)	12 (75.0)	9 (56.3)	8 (50.0)
2016–2018	31	14 (45.7)	9 (29.0)	6 (19.4)	8 (25.8)	20 (64.5)	16 (51.6)	20 (64.5)
Total	64	29 (45.3)	17 (26.6)	15 (23.4)	10 (15.6)	42 (65.6)	29 (45.3)	30 (46.9)

[a], micro-surgery: local resection; [b], extensive resection: Miles + Dixon + Parks; [c], the intermediate and high-risk cases accepted postoperative adjuvant therapy. GIST, gastrointestinal stromal tumor.
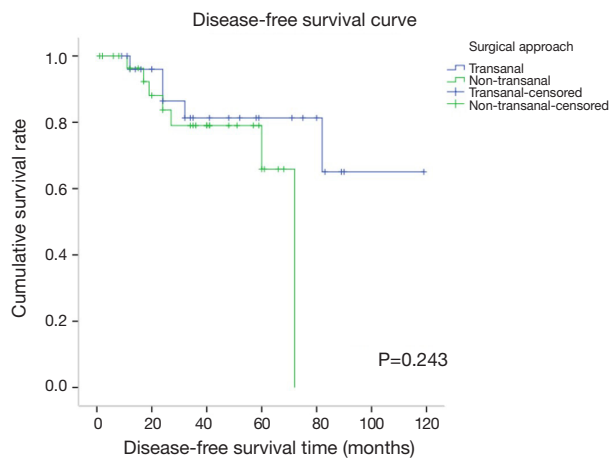
Figure 3 The 3- and 5-year DFS rates were 81.3% and 65.1%, respectively, for the TA group and 79.0% and 65.9%, respectively, for the NTA group. There was no difference between the TA and NTA groups (P=0.243). DFS, disease-free survival; TA, transanal; NTA, nontransanal.
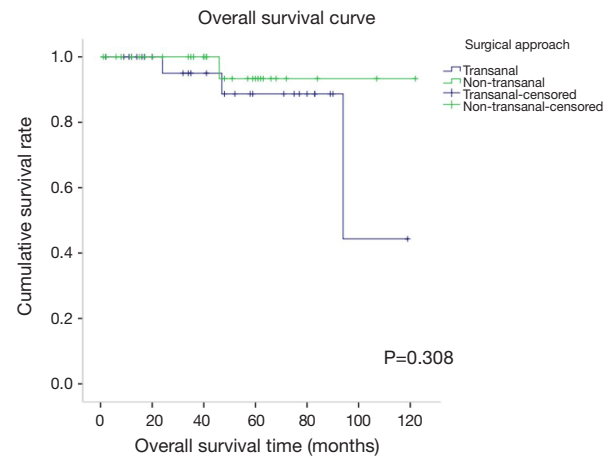
Figure 4 The 3- and 5-year OS rates were 95.0% and 88.7%, respectively, for the TA group and 93.3% and 93.3%, respectively, for the NTA group. There was no difference between the TA and NTA groups (P=0.308). OS, overall survival; TA, transanal; NTA, nontransanal.

cases in a single-center, which is higher than the 4–5% reported in previous studies (2,7). This discrepancy may be because our center is one of the largest colorectal clinics in South China. As the current diagnosis and treatment of rectal GIST is still controversial and difficult, more rectal GIST cases may be admitted to our center. As in previous literature reports (13-16), the asymptomatic rate of patients with rectal GIST was between 9.5% and 36.2%. In our study, 23 cases (35.9%, 23/64) had no specific clinical symptoms before surgery, suggesting that rectal GIST is full of challenges in early diagnosis. Therefore, how to screen asymptomatic groups in a timely manner is the main effort

for colorectal surgeons in the future. In this study, only 10 (15.6%, 10/64) cases performed a genetic test, which was lower than the 36.8% (7/19) and 34.0% (16/47) of cases reported by Wilkinson (11) and Cavnar (16). Genetic testing is an essential means in the era of precision therapy (17). The lower rate of genetic testing in our study may be related to the lower prevalence rate in the past and higher test costs.

Preoperative neoadjuvant treatment is a promising concept that has been successful in a variety of solid tumors (18-20). Preoperative neoadjuvant treatment can shrink the tumor, reduce the risk of subsequent surgery and

Table 5 Univariate and multivariate analysis of DFS and OS for rectal GIST

Variables	DFS		OS	
	Univariate analysis (P value)	Multivariate analysis (P value)	Univariate analysis (P value)	Multivariate analysis (P value)
Sex (male, female)	0.576	–	0.925	–
Age (>60, ≤60), years	0.928	–	0.395	–
Tumor size (≤5, >5), cm	0.312	–	0.763	–
Mitotic count (≤5, >5), /50 HPF	0.035	–	0.982	–
NIH risk (very low and low, high)	0.024	0.745	0.487	–
Preoperative Adjuvant therapy (yes, no)	0.016	0.358	0.262	–
Postoperative Adjuvant therapy (yes, no)	0.519	–	0.428	–
Surgical approach TA, NTA	0.243	–	0.308	–

*, only three factors that were significant in univariate analysis and two factors were included for the multivariate analysis for DFS. DFS, disease-free survival; OS, overall survival; GIST, gastrointestinal stromal tumor; NIH, National Institutes of Health. TA, transanal; NTA, nontransanal.

the incidence of complications. Otherwise, preoperative neoadjuvant treatment can improve the R0 resection rate, verify the drug response and improve the prognosis (21). Previous studies (22) have shown that preoperative neoadjuvant therapy has a response rate (%) of 42–100%, a sphincter-preserving rate (%) of 33.3–100% and an R0 resection rate of 77.3–100%. The 5-year OS rate can reach 90%. In this study, 29 cases (45.3%, 29/64) were treated with preoperative neoadjuvant therapy. As reported in previous studies (11,13-16,23-25) (*Table 6*) on surgically resected rectal GIST, the neoadjuvant rate was 0–81.8%. Additionally, the preoperative neoadjuvant therapy in this study was significantly different between the TA and NTA groups (P=0.003), 7 cases in the TA group and 22 in the NTA group, which was similar to the study reported by Cavnar (16). This result is mainly related to the preoperative tumor size (15). Tumor size is an objective criterion for clinicians to assess whether preoperative neoadjuvant therapy is available. The tumor size in the NTA group was larger than that in the TA group (P=0.002) (*Table 3*). Thus, tumor size is the consideration for surgeons to choose a suitable surgical approach in the resection of rectal GIST (13,23,25). How to shrink the tumor by effective preoperative neoadjuvant treatment and choose a less traumatic surgical approach is the future direction of research.

Based on the clinical practice and conclusions of related research, TA surgery has the advantages of small surgical trauma, high anus-preserver rate, high R0 resection rate,

and low complication rate, so this strategy is one of the choices for the surgical resection of rectal GIST (11). Previous studies have shown that the rate of TA resection in all surgical cases is 6.3–48.9% (13-16,23,24). In this study, 29 cases underwent TA surgery, and 35 cases underwent NTA surgery. The TA resection rate accounted for 45.3% of all surgical resection cases. Higher rates of TA surgery may be related to advancements in surgical techniques and the development of surgical platforms and the role of preoperative neoadjuvant therapy. Previous studies have confirmed that TA surgery can achieve ideal DFS and OS for rectal GIST. In our study, we also observed that the operation time was shorter (P=0.013), the blood loss was less (P=0.038), the anus-preserver rate was higher (P=0.048), the 30-day complication rate was lower (P=0.000) and hospital stays were shorter (P=0.011) in the TA group. Therefore, if a good prognosis can be achieved, TA surgery is worthy of clinical promotion (11,26). As mentioned above, tumor size is the consideration for surgeons to choose the surgical approach, and the distance of the tumor from the anus is also a problem that surgeons need to consider. In this study, the distance from the anus was shorter in the TA group than in the NTA group (4.2±0.9 *vs.* 5.8±1.1, P=0.047), which is consistent with a previous study (15).

To evaluate the clinical value of a surgical approach, in addition to considering its safety and feasibility, it is also important to evaluate the impact of this approach on prognosis (16). In this study, although the tumor was larger,

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Table 6 Studies about surgical resection for rectal GIST

Year	Country	Center	TA: NTA (cases)	Tumor size (cm)	Pre-IM treatment, n (%)	Recurrence and metastasis, n (%)	DFS (TA *vs.* NTA or total)	OS (TA *vs.* NTA or total)
2004 (23)	Korea	Single	13:29	4.5 *vs.* 7.2	0	27 (64.3)	92.3%±7.4% *vs.* 92.1%±9.2% (2-year DFS, P=0.98)	100% *vs.* 91.0%±6.1% (2-year OS, P=0.25)
2007 (13)	China	Single	13:16	2.9 *vs.* 7.9	–	12 (41.4)	58.6% (5-year DFS)	82.8% (5-year OS)
2013 (14)	Netherlands	Multi	2:30	5.5 (average)	22 (68.8)	13 (40.6)	78.1% (3-year DFS)	93.8% (3-year OS)
2013 (24)	China	Single	5:16	7.5±6.4	0	15 (71.4)	33% (5-year DFS)	46% (5-year OS)
2014 (15)	China	Single	8:13	3.7±2.3 *vs.* 7.0±3.2	5 (23.8)	7 (33.3)	95.2±6.6 *vs.* 34.9± 8.7 months, P=0.006	46% (5-year OS)
2015 (11)	UK	Single	2:11	7.6 (mean)	9 (81.8)	2 (15.3)	38 (range, 20–129) months	62 (range, 39–162) months
2017 (16)	USA	Single	23:24	4.5 (average)	17 (36.2)	27 (57.4)	31.9% (5-year DFS)	55.3% (5-year OS)
2017 (25)	USA	Multi	163:168	2.5 *vs.* 6.2	59 (17.7)	–	–	80.1% *vs.* 74.1% (5-year OS, P=0.04)

GIST, gastrointestinal stromal tumor; TA, transanal; NTA, nontransanal; Pre-IM, preoperative imatinib treatment; DFS, disease-free survival; OS, overall survival.

the mitotic count was higher and the number of high-risk cases was higher in the NTA group, but there was no significant difference between the two groups in DFS or OS, which may be related to the proportion of preoperative neoadjuvant therapy being higher and 70% (21/30) of the high-risk cases receiving postoperative adjuvant therapy in the NTA group. In the study of Liu (15), the TA group achieved a better DFS, and the results may be related to more high-risk cases in the NTA group but a lower proportion of adjuvant treatments (25%). Many previous studies have confirmed (8,27,28) that perioperative imatinib treatment can improve DFS and OS in patients with GIST.

In the previous discussion, our study demonstrated that distance from the anus and tumor size were important considerations for surgeons in choosing TA or NTA surgery. Therefore, we recommend that patients within 5 cm from the anus and with a tumor size of less than 5 cm may undergo TA surgery in an experienced center. However, in the context of the rapid development of TEM, TME, other surgical operating platforms and surgical energy instruments, sometimes distance from the anus and tumor size are not completely necessary indicators for surgeons

to choose surgical methods (29-31). The limitation of this study is that it is a single-center, small-sample, retrospective study. However, this study is currently the largest sample of studies on the surgical approach to rectal GIST selection in China, which can provide some information and guidance for clinical practice.

Conclusions

TA surgery is an effective approach for the resection of rectal GIST because of its minimally invasive advantages, such as short operation time, less blood loss, rapid recovery, and low complication rate. In addition, TA surgery has an ideal rate of anal sphincter preservation, achieving a good DFS and OS, which is worthy of clinical promotion. However, this study is only a retrospective, single-center, small-sample study, and the conclusions still need to be confirmed by a prospective, multicenter, large-sample study. Moreover, how to select the appropriate rectal GIST cases for preoperative neoadjuvant therapy and improve the proportion of TA resection is the direction that still needs to be studied in the future.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the Research Ethics Committee, the Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China (No. 2018ZSLYEC-099). Informed consent for participation in the study was obtained either directly, or from a guardian of each patient.

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