SMALL BOWEL *VERSUS* GASTRIC SURGERY FOR GASTROINTESTINAL STROMAL TUMORS

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ABSTRACT

Objectives. The aim of the study was to compare the postoperative and oncologic outcomes of small bowel versus gastric surgery for gastrointestinal stromal tumors (GISTs).

Background. The feasibility of the small bowel resection for GIST has been demonstrated; however, its impact on outcomes, particularly its oncologic safety for tumors greater than 5 cm, remains unknown.

Methods. Among 93 patients treated for a stromal tumor in SUUB between 2001 and 2015, patients who underwent primary resection for a gGIST smaller than 20 cm (N = 66), by either small bowel (group S, n = 28) or gastric surgery (group G, n = 38), were compared. Multivariable analyses and propensity score matching were used to compensate for differences in baseline characteristics.

Results. Inhospital mortality and morbidity rates in groups S and G were 0.0% versus 2.6% (P = 0.086) and 10.7% vs 18.4% (P = 0.004), respectively. Small bowel resection was independently protective against in-hospital morbidity (odds ratio 0.54, P = 0.014). The rate of R0 resection was 96.4% in group S and 92.1% in group G (P = 0.103). After 1:1 propensity score matching (n= 22), the groups were comparable according to age, sex, tumor location and size, mitotic index, American Society of Anaesthesiology score, and the extent of surgical resection. After adjustment for BMI, overall morbidity (9.1% vs 19.6%; P = 0.005), surgical morbidity (4.5% vs 9.1%; P = 0.048), and medical morbidity (4.5% vs 13.6%; P = 0.01) were significantly lower in group S. Five year recurrence-free survival was significantly better in group S (89.3% vs 82.6%; P = 0.011). In tumors greater than 5 cm, in hospital morbidity and 5 year recurrence-free survival were similar between the groups (P = 0.255 and P = 0.423, respectively).

Conclusions. Small bowel resection for GISTs is associated with favourable short term outcomes without compromising oncologic results.

Keywords: GIST, small bowel resection, gastric surgery, morbidity, mortality, mitotic index, 5-year recurrence, 5-year recurrence-free survival, oncological outcomes

INTRODUCTION

Gastrointestinal stromal tumor (GIST) is the most common type of mesenchymal tumor of the gastrointestinal tract and is mostly located in the stomach (50-60%). (1) The standard treatment for localized GISTs is complete R0 surgical excision, avoiding tumor rupture and without the dissection of clinically negative lymph nodes. (2) Simple wedge resection, when feasible, has consequently become the preferred surgical approach in gastric GISTs (gGISTs).

Moreover, whereas the upper size limit for laparoscopic GIST resection has continuously been modified, reaching 5 cm in the recent National Comprehensive Cancer Network (NCCN) and Japanese guidelines, the value of the laparoscopic approach for gGISTs larger than 5 cm remains controversial regarding short term and oncologic outcomes. (4)

The aim of our study was therefore to compare postoperative outcomes and oncologic results of small bowel *versus* gastric surgery for GISTs.

METHODS

Study population

Data from 66 consecutive adult patients treated for a histopathologically confirmed GIST in SUUB between 2001 and 2015 were collected retrospectively through a dedicated analysis of patients charts. Data on patient demographics, clinical presentation, initial workup, operative technique, histopathology, postoperative course, and oncologic outcomes were gathered and analyzed. When missing,

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additional data were obtained from email exchanges or phone calls with the referral doctors or patients. Patients were not included if the surgical and/or tumoral data required for the analysis were missing.

Overall, 93 patients were treated for a GIST in the database. The criteria for inclusion in this study were the following: (1) patients undergoing elective primary surgical resection; (2) tumors < 20 cm in diameter; (3) no adjacent organ invasion (pancreas, colon, liver); (4) no distant metastasis; (5) duodenum tumors. Among the remaining population (N = 66), those patients who underwent a small bowel resection (group S, n = 28) were compared with those who underwent an gastric resection (group G, n = 38).

Pretreatment workup

Pretreatment investigations were standard and followed the international guidelines. Investigations routinely included a contrast enhanced abdominal computed tomography (CT) scan, a thorax CT scan, and an endoscopic examination with selective endoscopic ultrasound evaluation and biopsies.

Surgical approach

An upper midline laparotomy was performed through with wound protection. After exploration of the abdominal cavity, the tumor was resected by either small bowel resection or gastrectomy (total, subtotal, distal, or proximal), depending on the tumor size and location, and the surgeon's experience. The use of stapling devices or manual sutures was at the discretion of the surgeon. Perioperative care was based on the usual practices of the individual surgeons.

Postoperative course

Postoperative morbidity was divided into surgical complications (including anastomotic leak, intraabdominal abscess, surgical site infection and bleeding necessitating blood transfusions, reoperation, and others) and medical complications (including urologic, pulmonary, cardiovascular, thromboembolic, neurologic complications, and others). The severity of complications was assessed according to the Clavien-Dindo classification, and only complications of at least grade II were considered for the analysis of overall morbidity. (6) Grade III or IV complications (severe complications) were also assessed. (5)

Histopathologic analysis

A final diagnosis of GIST was based on histologic and immunohistochemical analysis with the selective use of mutational analysis in doubtful cases. Tumor histopathology was studied to determine size (cm) and mitotic index (number of mitoses per 5 mm^2). Resections were designated R0 when removal was complete both macroscopically and microscopically, and R1 in cases with a microscopically positive resection margin.

Adjuvant treatment and followup

Administration of adjuvant tyrosine kinase inhibitors (TKIs) was decided during multidisciplinary team meetings. A regular followup based on clinical examination and abdominal CT scan was recommended for at least 5 years, with a frequency depending on the recurrence risk according to the international guidelines. Disease recurrence was classified as either being a locoregional (within the regional resection area) or a distant recurrence. Mixed recurrences included concomitant locoregional and distant relapses.

Endpoints of the study

The primary objective was to evaluate inhospital overall morbidity. The secondary objectives were to analyze inhospital mortality, inhospital medical and surgical complications, grade III-IV complications, reoperation, and on the following oncologic outcomes: radicality of resection, 5 year recurrence rate, 5 year disease-free survival (DFS) and 5 year overall survival (OS).

Statistical analysis

Continuous variables are expressed as the mean ± SD, or the median (range) and categorical variables as a percentage. A Student *t* test or Mann-Whitney test was used for intergroup comparisons of continuous variables, where as a $\chi 2$ test or Fisher test was used to compare categorical data. Median followup was 45.4 months. Five year OS and DFS were estimated using the Kaplan-Meier method. The logrank test was used to compare survival curves. A binary logistic regression was used to identify predictors of inhospital overall morbidity.

In a second step, we conducted a propensity score matching analysis to compensate for the differences in some baseline characteristics between the S and G groups in the assessment of outcomes. First, we compared all available patient and tumor variables using a $\chi 2$ test. Next, a propensity score (the probability that a patient was assigned to the S or G group as a consequence of the individual profile of these factors in a nonrandomized patient population, range of 0-100%) was calculated using

TABLE 1. *Comparison of demographic, therapeutic, and pathological characteristics in the overall population and according to surgical approach before (n = 66) and after (n = 44) propensity score matching*

Characteristics	Overall Population [n = 66 (%)]	Before Matching		*P*	After Matching		*P*
		S Group [n = 28 (%)]	G Group [n = 38 (%)]		S Group [n = 22 (%)]	G Group [n = 22 (%)]	
Year of intervention*							
Before 2009	34 (51.5)	12 (42.85)	22 (57.8)	0.001	10 (45.45)	11 (50.0)	0.705
After 2009	32 (48.5)	16 (57.14)	16 (42.2)		12 (54.54)	11 (50.0)	
Age*							
≤60 years	24 (36.36)	10 (35.71)	14 (36.84)	0.784	8 (36.36)	7 (31.81)	0.766
>60 years	42 (63.63)	18 (64.28)	24 (63.15)		14 (63.63)	15 (68.18)	
Sex*							
Male	35 (53.03)	14 (50.0)	21 (55.26)	0.079	11 (50.0)	11 (50.0)	0.850
Female	31 (46.96)	14 (50.0)	17 (44.73)		11 (50.0)	11 (50.0)	
BMI†							
<30 kg/m^2	51 (77.3)	22 (78.57)	29 (76.31)	<0.001	18 (81.81)	17 (77.27)	0.001
≥30 kg/m^2	9 (14.0)	5 (17.85)	4 (10.52)		3 (13.63)	2 (9.09)	
Missing	6 (9.09)	1 (3.57)	5 (13.15)		1 (4.54)	3 (13.63)	
Tumor location*							
Proximal	6 (9.09)	3 (10.71)	4 (10.52)	0.019	2 (9.09)	2 (9.09)	0.986
Midl	50 (75.75)	22 (78.57)	28 (73.68)		18 (81.81)	18 (81.81)	
Distal	10 (15.15)	3 (10.71)	7 (18.42)		2 (9.09)	2 (9.09)	
Surgical access‡							
Difficult	33 (50.0)	12 (42.85)	20 (52.63)	0.003	9 (40.90)	11 (50.0)	0.129
Easy	35 (53.03)	16 (57.14)	18 (47.36)		13 (59.09)	11 (50.0)	
Operative time mean (±SD) (min)	142±76	130±70	150±79	0.003	133±72	123±63	0.164
Blood loss mean (±SD) (mL)	110±333	48±128	159±424	<0.001	60±147	109±352	0.125
Tumor size (cm)*							
≤5	36 (54.54)	19 (67.85)	17 (44.73)	<0.001	13 (59.09)	13 (59.09)	0.759
>5-10	24 (36.36)	8 (28.57)	16 (42.1)		8 (36.36)	8 (36.36)	
>10	6 (9.09)	1 (3.57)	5 (13.15)		1 (4.54)	1 (4.54)	
Mitotic index (per 5 mm^2)*							
≤5	50 (75.75)	22 (78.57)	28 (73.68)	0.374	16 (72.72)	18 (81.81)	0.400
6-10	8 (12.12)	3 (10.71)	5 (13.15)		3 (13.63)	2 (9.09)	
>10	8 (12.12)	3 (10.71)	5 (13.15)		3 (13.63)	2 (9.09)	
Resection type							
R0	62 (93.93)	27 (96.42)	35 (92.1)	0.103	21 (95.45)	21 (95.45)	0.791†
R1	4 (6.06)	1 (3.57)	3 (7.89)		1 (4.54)	1 (4.54)	
Recurrence risk 15							
Very low risk	5 (7.57)	3 (10.71)	2 (5.26)	<0.001	2 (9.09)	2 (9.09)	0.938
Low risk	25 (37.87)	13 (46.42)	12 (31.57)		9 (40.90)	9 (40.90)	
Intermediate risk	20 (30.30)	8 (28.57)	12 (31.57)		7 (31.81)	7 (31.81)	
High risk	16 (24.24)	4 (14.28)	12 (31.57)		4 (18.18)	4 (18.18)	

*Variables used for propensity matching process.
†Results after matching are given adjusted on body mass index.
‡Difficult to access: lesser curvature of the body or antrum, near the cardia, or at the prepyloric region, near Treitz angle or ileocecal valve;
BMI – body mass index; S – small bowel; NA – not applicable because of very low number of events; G – gastric.

a logistic regression with unbalanced variables or conditioning variables of surgical approach or oncologic outcomes (variables used for propensity matching process are showed in Table 1). Finally, all patients in group S were matched 1:1 according to propensity scores of patients who underwent an gastric surgery (group G), leading to an even distribution of potential confounding factors between the treatment groups. Due to some missing data regarding body mass index (BMI), it was not possible to include this variable in the propensity score construction. Consequently, an adjustment for BMI was systematically performed. (7)

The factors associated with 5 year DFS were analyzed by Cox proportional hazard regression analysis using a stepwise procedure; the 0.1 level

TABLE 2. *Perioperative and Postoperative Outcomes in the Overall Population (n = 66) and According to Treatment Groups Before and After Propensity Score Matching (n = 44)*

Characteristics	Overall Population [n = 66 (%)]	Before Matching			After Matching		
		S Group [n = 28 (%)]	G Group [n = 38 (%)]	*P*	S Group [n = 22 (%)]	G Group [n = 22 (%)]	*P**
Perioperative complication							
No	62 (93.93)	27 (96.42)	35 (92.1)	0.003	21 (95.45)	21 (95.45)	0.860†
Yes	4 (6.06)	1 (3.57)	3 (7.89)		1 (4.54)	1 (4.54)	
Tumor effraction							
No	64 (96.96)	27 (96.42)	37 (97.36)	0.112	21 (95.45)	21 (95.45)	NA
Yes	2 (3.03)	1 (3.57)	1 (2.63)		1 (4.54)	1 (4.54)	
Inhospital morbidity							
No	56 (84.84)	25 (89.28)	31 (81.57)	0.004	20 (90.91)	18 (80.4)	0.005
Yes	10 (15.15)	3 (10.71)	7 (18.42)		2 (9.09)	4 (19.6)	
Inhospital severe morbidity							
No	63 (95.45)	27 (96.42)	36 (94.73)	0.008	21 (95.45)	21 (95.45)	NA
Yes	3 (4.54)	1 (3.57)	2 (5.2)		1 (4.54)	1 (4.54)	
Inhospital surgical complication							
No	61 (92.42)	26 (92.85)	35 (92.1)	0.115	21 (95.45)	20 (90.91)	0.049
Yes	5 (7.57)	2 (7.14)	3 (7.89)		1 (4.54)	2 (9.09)	
Anastomotic leakage							
No	65 (98.48)	28 (100)	37 (97.36)	0.086	22 (100)	21 (95.45)	NA
Yes	1 (1.51)	0 (0.4)	1 (2.63)		0 (0)	1 (4.54)	
Surgical site infection							
No	64 (96.96)	27 (96.42)	37 (97.36)	0.025	22 (100)	21 (95.45)	0.054
Yes	2 (3.03)	1 (3.57)	1 (2.63)		0 (0)	1 (4.54)	
Reoperation							
No	64 (96.96)	28 (100)	36 (94.73)	0.080	22 (100)	21 (95.45)	0.178
Yes	2 (3.03)	0 (0)	2 (5.2)		0 (0)	1 (4.54)	
Inhospital medical complication							
No	59 (89.39)	26 (92.85)	33 (86.84)	0.002	21 (95.45)	19 (86.37)	0.009
Yes	7 (10.60)	2 (7.14)	5 (13.15)		1 (4.54)	3 (13.64)	
Pulmonary complications							
No	64 (96.96)	28 (100)	36 (94.73)	0.043	22 (100)	21 (95.45)	0.357
Yes	2 (3.03)	0 (0)	2 (5.2)		0 (0)	1 (4.54)	
Cardiovascular complications†							
No	65 (98.48)	28 (100)	37 (97.36)	0.156	22 (100)	22 (100)	NA
Yes	1 (1.51)	0 (0)	1 (2.63)		0 (0)	0 (0)	
Extra surgical site infection							
No	61 (92.42)	26 (92.85)	35 (92.1)	0.106	21 (95.45)	20 (90.91)	0.278
Yes	5 (7.57)	2 (7.14)	3 (7.89)		1 (4.54)	2 (9.09)	
Per and postoperative transfusion							
No	62 (93.93)	27 (96.42)	35 (92.1)	0.097	21 (95.45)	21 (95.45)	0.817
Yes	4 (6.06)	1 (3.57)	3 (7.89)		1 (4.54)	1 (4.54)	
Length of stay median [range]	9 [2–103]	7 [3–100]	11 [2–103]	<0.001	7 [3–103]	10 [2–103]	<0.001
Adjuvant treatment (65)							
No	55 (83.33)	24 (85.71)	31 (81.57)	0.161	19 (86.37)	20 (90.91)	0.111
Yes	10 (15.15)	4 (14.28)	6 (15.78)		3 (13.64)	2 (9.09)	

*All results after matching are given adjusted on body mass index.
†Included cardiac complications, thromboembolic events, and stroke.
S – small bowel; NA – not applicable because of very low number of events; G – gastric.

TABLE 3. *Univariable and Multivariable Analyses of Predictive Factors of Postoperative Morbidity for Patients in the Overall Population (n = 66)*

Variables	No. Postoperative Morbidity (n = 56)	Postoperative Morbidity (n = 10)	Univariate Analysis (*P*)	Multivariable Analysis Considering Variables Available at the Time of Surgery	
				P	OR (95% CI)
Year of intervention [n (%)]					
Before 2009	26 (83.9)	5 (16.1)	0.013	0.006	1
After 2009	30 (85.7)	5 (14.3)			0.54 (0.34-0.84)
Case volume					
Low	12 (85.7)	2 (14.3)			0.69 (0.42-1.12)
High	44 (84.6)	8 (15.4)			
Age [n (%)]					
≤60 years	22 (88.0)	3 (12.0)	0.025	0.260	1
>60 years	34 (82.9)	7 (17.1)			1.34 (0.81-2.22)
Sex [n (%)]					
Male	28 (82.4)	6 (17.6)	0.002		0.56 (0.35-0.88)
Female	28 (87.5)	4 (12.5)			
BMI (kg/m^2) [n (%)]					
<30	43 (86.0)	7 (14.0)	0.340		
≥30	8 (80.0)	2 (20.0)			
NP	5 (83.3)	1 (16.7)			
ASA score [n (%)]					
I-II	20 (95.2)	1 (4.8)	0.001	0.026	1
III-IV	27 (84.4)	5 (15.6)		0.056	1.73 (0.99-3.04)
V-VI	9 (69.2)	4 (30.8)		0.007	2.45 (1.27-4.72)
Tumor location [n (%)]					
Proximal	5 (71.4)	2 (28.6)	0.165		
Midl	42 (85.7)	7 (14.3)			
Distal	9 (90.0)	1 (10.0)			
Surgical access*					
Difficult	26 (46.4)	6 (60.0)			
Easy	30 (53.6)	4 (40.0)			
Approach [n (%)]					
Group G	31 (79.5)	8 (20.5)	0.004	0.014	1
Group S	25 (92.6)	2 (7.4)			0.54 (0.33-0.88)
Tumor size (cm) [n (%)]					
≤5	30 (85.7)	5 (14.3)	0.044	0.152	1
>5-10	21 (87.5)	3 (12.5)		0.272	0.76 (0.47-1.24)
>10	5 (71.4)	2 (28.6)		0.234	1.52 (0.76-3.02)
Mitotic index [n (/5 mm^2)] (%)					
≤5	43 (87.8)	6 (12.2)	0.127		
6-10	7 (77.8)	2 (22.2)			
>10	6 (75.0)	2 (25.0)			
Tumor effraction [n (%)]					
No	54 (84.4)	10 (15.6)	0.075	0.561	1
Yes	2 (100.0)	0 (0.0)			
Recurrence risk 15 [n (%)]					
Very low risk	4 (80.0)	1 (20.0)	0.212		
Low risk	21 (91.3)	2 (8.7)			
Intermediate risk	18 (85.7)	3 (14.3)			
High risk	13 (76.5)	4 (23.5)			
Resection type [n (%)]					
R0	53 (85.5)	9 (14.5)	<0.001		
R1	3 (75.0)	1 (52.0)			

*Difficult to access: lesser curvature of the body or antrum, near the cardia, or at the prepyloric region, near Treitz angle or ileocecal valve. ASA indicates American Society of Anaesthesiologists; CI – confidence interval; S – small bowel; G – gastric; OR – odds ratio.

was defined for entry into the model. All tests were 2 sided and the threshold for statistical significance was set to $P < 0.05$. Analyses were performed using SPSS version 19.0 software (IBM Corp., Armonk, NY).

RESULTS

Demographic and therapeutic characteristics

The characteristics of the overall population (N = 66) are summarized in Table 1. The patients' median BMI was 25 kg/m^2 (range 14-51). The vast majority of patients were symptomatic (65%). Most of the tumors were located in the body of the stomach (73.68%). Gastrectomies were total, subtotal, distal, and proximal in 26 (68.4%), 9 (23.7%), 2 (5.3), and 1 (2.6%), respectively. Perioperative tumor effraction occurred in 3% of cases.

Patients in group S had a lower BMI and surgery before 2009, compared with group G ($P < 0.05$). Mean operative time was significantly longer in group G ($P = 0.003$), with higher blood loss ($P < 0.001$).

Histopathologic results

The median size of the tumors was 5 cm (range 0.5-20) and the median mitotic index was 3 (range 0-150). The R0 resection rate was 94% (62). Before matching, significant differences were observed between the groups. Despite a similar mitotic rate ($P = 0.374$), the tumors in group S were smaller and had a lower risk of recurrence ($P < 0.05$).

Postoperative course

In the overall population, the rate of inhospital mortality was 1.5% and the rate of inhospital overall morbidity was 15.1%, including a 4.5% rate of grade III-IV morbidity. The inhospital mortality rate was 2.6% in group G versus 3.6% in group S ($P = 0.086$). The inhospital overall morbidity rate was lower in group S (10.7% vs 18.4%; $P = 0.004$), as was the inhospital grade III-IV morbidity rate (3.6% vs 5.2%; $P = 0.008$). In comparison to group S, the medical complication rate was significantly higher in group G (13.1% vs 7.1%; $P = 0.002$). The median length of stay was 9.0 days (range 2-103) and was significantly shorter in the S group [7 (range 1-176) vs 11 (range 1-219) days; $P < 0.001$].

Preoperative and perioperative factors significantly linked to inhospital overall morbidity in univariable analysis were surgery before 2009, age > 60 years, male sex, gastric surgical approach, tumor size, and R1 resection. By multivariable analysis, the predictors of inhospital overall morbidity were surgery before 2009 and male sex, whereas a small bowel resection (group S) was protective against inhospital overall morbidity.

Postoperative Outcomes After Matching

After propensity score matching, groups G and S were well balanced. Inhospital overall morbidity rates were 9.1% versus 19.6% ($P = 0.005$), with the same severe complications (4.54%). Both medical and surgical complication rates were lower in group S (4.54% vs 13.64%; $P = 0.043$ and 4.54% vs 9.1%; $P = 0.049$, respectively). The difference in surgical complication rates was mainly attributable to surgical site infection ($P = 0.054$).

Oncologic Outcomes After Matching

The risk of 5year recurrence after adjustment for BMI was similar between groups S and G (3.9% vs 5.6%; $P = 0.583$, respectively), with no significant difference in terms of locoregional (2.9% vs 3.1%), metastatic (2.9% vs 4.3%), and mixed recurrence (0.8% vs 1.6%) rates. Five year DFS [89.3% vs 82.6%; $P = 0.011$ (Fig. 1) and OS (93.6% vs 87.8%; $P = 0.014$) were superior in group S. By multivariable analysis, the small bowel location was associated with a favorable 5 year DFS [hazard ratio (HR) 0.489, 93% confidence interval (CI) 0.269-0.975, $P = 0.046$], whereas overall inhospital overall morbidity (HR 2.694, 95% CI 1.321–5.624, $P = 0.004$), high ASA scores ($P = 0.003$), and high mitotic index ($P < 0.001$) were associated with a dismal 5 year DFS.

Postoperative and Oncologic Outcomes After Matching in Patients With Tumors Larger Than 5 cm

In a subgroup analysis of patients operated for tumors larger than 5 cm (n = 18), the demographic and tumor characteristics shown in between patients who underwent a small bowel resection (n = 9) and a gastric resection (n = 9) remained well balanced ($P > 0.186$). The inhospital overall morbidity (9.1% vs 19.6%; $P = 0.235$), grade III-IV morbidity, and mortality rates were similar between the two groups. The surgical complication, medical complication, and reoperation rates were also comparable. The 5 year recurrence rate was similar between the groups ($P = 0.591$), as were the rates for 5 year DFS ($P = 0.423$) and 5 year OS ($P = 0.490$).

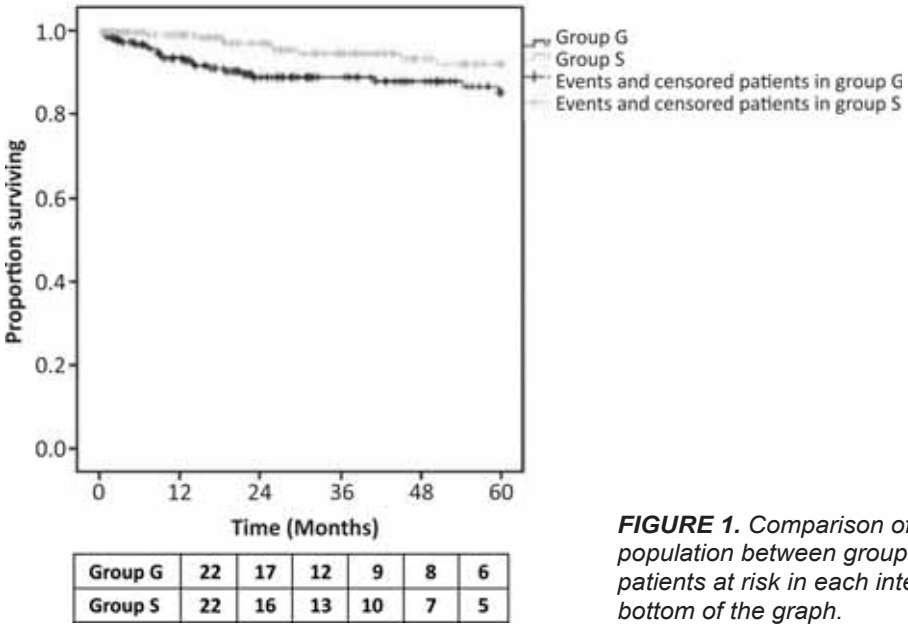

FIGURE 1. *Comparison of disease free survival in the matched population between group G and group S. The number of patients at risk in each interval is shown in the table at the bottom of the graph.*

DISCUSSIONS

In the present study, having enrolled more than 66 patients who underwent resection for a GIST, we observed a significant 42% decrease of inhospital overall morbidity associated with the small bowel GIST and identified the small bowel surgery as protective against inhospital overall morbidity, using both propensity score matching and multivariable analyses. Moreover, in the matched cohort populations, we observed that the radicality of the resection and the risk and patterns of recurrence were similar between the groups with an even better 5 year overall and DFS in group S. In the subgroup of patients operated on for tumors larger than 5 cm, no adverse impact of small bowel location was observed.

To date, there has been no prospective randomized trial directly comparing small bowel and gastric surgery for GIST. Metaanalyses of comparative retrospective series suggested that the small bowel location be associated with smaller diameter tumors, which yielded a similar operation time and favored a small bowel surgery with its decreased intraoperative blood loss, and earlier recovery including time to first flatus, time to oral feeding, and decreased length of stay. Conflicting data were reported regarding postoperative morbidity and oncologic results that were either similar or better in the small bowel group, with a marginal impact on medical complications and a similar risk of surgical and grade III-IV complications. From a methodological perspective, a metaanalysis of nonrandomized cohorts with no allocation concealment carries a potential risk of overstating the intervention effect by 30-41%. (8) In addition to the problem of the tumor size that clearly influences both the surgical technique and prognosis, most studies were not designed for oncologic purposes with missing or inconsistent data regarding the mitotic index or TKI administration and a limited followup. (3)

In accordance with the most recently published metaanalyses, the present study demonstrated a significant reduction of overall morbidity in group S. In addition to a marked reduction of medical complications (56%) with a collective implication of infectious and noninfectious complications, we demonstrated through the propensity matched population analysis that grade III-IV complications were lowered by 65% in the S group, with a 50% reduction in surgical morbidity and more specifically surgical site infection.

The impact of the small bowel location of GIST on oncologic outcomes was evaluated in only the matched cohort population in which the risk of recurrence according to the NCCN criteria was similar ($P = 0.938$). (6) If the R0 resection rate and the pattern and incidence of recurrence were similar between the groups, the 5 year recurrence-free and OS were even better in group S.

This study has some limitations. As with all retrospective surveys, this study was exposed to selection bias. Even if a large number of variables considered as pertinent in the dedicated literature have been taken into account with evaluation of their impact on outcomes through multivariable analy-

sis, we acknowledge that some other variables might have been not considered. This is, however, the case of all retrospective studies. This prompted us to use propensity score matching. Taking into account all known variables potentially related to postoperative morbidity and oncologic outcomes allowed highly comparable groups and reinforced the conclusions of the present study. Due to the retrospective nature of our study, no power calculation was performed. However, our use of the Clavien-Dindo classification strongly mitigated against variation in defining complications. To limit problems with consistency, only medically relevant complications, defined as Clavien-Dindo grade ≥ II, were included in the analysis.

CONCLUSIONS

In conclusion, in this study, small bowel location of GISTs after the radical resection principles of surgery is associated with favorable short term outcomes without compromising oncologic results.

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