



# Short-term outcomes after duodenal surgery for mesenchymal tumors: a retrospective analysis from a single tertiary referral center

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## Abstract

Duodenal resections are sometimes necessary for radical surgery. We analyzed technical aspects and post-operative outcomes in patients with RPS and GIST involving duodenum. We identified patients who underwent duodenal resection for RPS and GIST at our Institute between 2000 and 2016. Clinical, pathological and treatment variables were analyzed. Thirty patients were treated: 15 for GIST, 15 for RPS. Sixteen duodenal wedge resections (WR) and 14 segmental resections (SR) were performed. Multi-organ resection was frequently performed (63.4%). Median time to flatus was 3 days (range 1–6), to oral refeeding 4.5 (range 2–15). Overall postoperative morbidity rate was 53% (16/30): Clavien Dindo grade  $\leq$  II: 10; duodenum-related complication rate was 33% (10/30), Clavien Dindo grade  $\leq$  II: 9. Morbidity rates were higher in SR than WR. Duodenal resections for RPS and GIST have significant morbidity rate and whenever it is possible, WR is preferable to SR because of the lower morbidity rate.

**Keywords** Retroperitoneal sarcoma · Gastrointestinal stromal tumors · Surgical complications · Duodenal resection

## Introduction

Surgery is the mainstay in the treatment of mesenchymal tumors such as retroperitoneal sarcomas (RPS) and gastrointestinal stromal tumors (GIST).

GISTs are the most common mesenchymal tumors of the digestive tract and represent 1–3% of all digestive tract neoplasms [1]. They commonly originate in the stomach (40–60%), and only rarely from the duodenum (5% of all GISTs); however, they are responsible for 30% of all the primary malignancies of the duodenum [2].

RPS are rare tumors; the mean annual incidence is approximately 2.7 cases/1 million without significant oscillations over time [3]. Retroperitoneal localization accounts for approximately 12% of all soft tissue sarcomas and the

most common histology is represented by liposarcoma and leiomyosarcoma [4].

A complete surgical resection, often requiring multi-organ resection, is the mainstay of the treatment of RPS, representing the only chance for cure. It was shown that aggressive surgical approach to these tumors is associated with an improved local control [5], and duodenal resections are sometimes necessary to achieve radical surgery in the treatment of RPS. The anatomic complexity of the duodenum makes surgical management challenging, also limited resections may result to be technically demanding. Depending on the site and on the characteristics of the tumor, both wedge resection (WR) and segmental resection (SR) may fit on the oncological point of view, allowing the surgeon to obtain clear margins. However, studies investigating short-term outcomes of duodenal resection are few and short-term outcomes still remain unclear and, therefore, the surgical management of duodenum, including the optimal procedure and techniques of reconstruction, is not well defined due to the lack of data and rarity of disease.

The aim of this study was to review our experience in patients with RPS and GIST involving the duodenum to analyze surgical technique and post-operative short-term outcomes.

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## Materials and methods

We identified all the patients who underwent surgery with duodenal resection for RPS and GIST, at the Surgical Oncology Unit of Humanitas Clinical and Research Center in Milan, between January 2000 and December 2016. Patients who underwent pancreaticoduodenectomy were excluded. Patient files, operative reports, radiological charts and pathology were reviewed. Demographics, clinical, pathological and treatment variables were analyzed. All the patients included in the study underwent surgery with curative intent. Standard surgical approach for GIST was complete excision of the lesion, with an en bloc resection when adjacent organs were involved. In patients affected by RPS, our surgical policy was to remove the tumor with wide healthy margins. The practical application of this approach changed over time, leading, in later years, to associated multivisceral resection in all primary cases, even when gross visceral infiltration by the tumor mass was not recognized. The type of surgical approach on the duodenum was WR or SR according to tumor site and size, based on the intraoperative judgment of the surgeon. Patients were grouped according to the histology of the tumor (GIST and RPS) and to the type of duodenal surgery (WR and SR). Postoperative complications were defined as all adverse events occurred within 30 days after surgery or during the same hospitalization. Duodenum-related complications were defined as surgical adverse events exclusively resulting from duodenal resection. The severity of complications was scored according to Clavien–Dindo Classification (CDC) [6] and Comprehensive Complication Index (CCI) [7]. In the latter score, all complications and the correspondent treatment are taken into consideration thus representing the overall burden of post-operative morbidity. Descriptive statistics were computed and all the continuous variables were reported as median value with relative ranges.

## Results

Thirty patients were treated with WR or SR for mesenchymal tumors (RPS or GIST) with a duodenal involvement. Main demographics, clinical and surgical data are summarized in Table 1. Histopathological analyses identified 15 GIST (50%) and 15 RPS (50%), of which 7 were defined as dedifferentiated liposarcoma (47% of RPS), 5 as well-differentiated liposarcoma (33% of RPS), and 3 as undifferentiated pleomorphic cell sarcoma (UPS) (20%). Five patients received preoperative treatment: chemotherapy was administered to four patients (13.3%) diagnosed with

**Table 1** Characteristics of the patients

	GIST # (%)	RPS # (%)	All patients # (%)
Sex			
m	10 (66.7)	9 (60.0)	19 (63.4)
f	5 (33.3)	6 (40.0)	11 (36.6)
Median age			
Years [range]	57 [14–78]	64 [40–81]	59 [14–81]
Preoperative treatment			
Yes	1 (6.6)	4 (26.6)	5 (16.7)
No	14 (93.4)	11 (73.4)	25 (83.3)
Previous abdominal surgery			
Yes	1 (6.6)	10 (66.7)	11 (36.6)
No	14 (93.4)	5 (33.3)	19 (63.4)
Involved duodenal segment			
First	2 (13.3)	1 (6.6)	3 (10.0)
Second	3 (20.0)	3 (20.0)	6 (20.0)
Third	2 (13.3)	1 (6.6)	3 (10.0)
Fourth	5 (33.4)	6 (40.0)	11 (36.7)
Multiple	3 (20.0)	4 (26.8)	7 (23.3)
Type of surgery			
Wedge resection	8 (53.3)	8 (53.3)	16 (53.3)
Segmental resection	7 (46.7)	7 (46.7)	14 (46.7)
Multivisceral resection			
Yes	7 (46.7)	12 (80.0)	19 (63.4)
No	8 (53.3)	3 (20.0)	11 (36.6)
Residual disease (R)			
0	12 (80.0)	10 (66.6)	22 (73.4)
1	3 (20.0)	4 (26.8)	7 (23.3)
2	0 (0.0)	1 (6.6)	1 (3.3)
Median CCI			
<i>n</i> [range]	8.7 [0–34.8]	20.9 [0–58.3]	8.7 [0–58.3]
Clavien–Dindo classification			
I	3 (20.0)	0 (0.0)	3 (10.0)
II	3 (20.0)	4 (26.8)	7 (23.3)
IIIa	1 (6.6)	0 (0.0)	1 (3.3)
IIIb	1 (6.6)	3 (20.0)	4 (13.3)
IV	0 (0.0)	1 (6.6)	1 (3.3)
V	0 (0.0)	0 (0.0)	0 (0.0)
Post-operative morbidity			
Overall complications	8 (53.3)	8 (53.3)	16 (53.3)
Only duodenal	3 (20.0)	4 (26.8)	7 (23.3)
Duodenal and others	1 (6.6)	2 (13.3)	3 (10.0)
Only others	4 (26.8)	2 (13.3)	6 (20.0)

sarcoma, while imatinib mesilate was given to one patient (3.3%) affected by GIST. No patient received preoperative radiotherapy prior to the index surgical procedure. However, five (16.6%) patients received chemo-, radio- or chemoradiotherapy in their past for other tumors. Eleven

patients (36.6%) had previous abdominal surgery for other diseases. Sixteen patients (53.3%) underwent duodenal WR, while the remaining 14 patients (46.7%) had SR (12 of which included Treitz’s loop resection) with a duodeno-jejunosomy. In particular, 8 out of the 15 patients with GIST (53.3%) were operated by WR and the remaining 7 patients (46.7%) underwent SR. Median diameter of the tumor was 21 mm (range 13–90) in the WR group and 37 mm in SR group (range 25–130); type of resection (WR vs SR) was not influenced by the involved duodenal portion. Similarly, in 8 out of the 15 RPS (53.3%) WR was performed, while the remaining 7 patients (46.7%) underwent SR. Median diameter of the tumor was 59.5 mm (range 31–240) in the former group and 50 mm (range 34–200) in the latter; no tumors involving the third duodenal segment were observed in patients who underwent WR for RPS, and no tumors involving the second duodenal portion were reported in the SR group.

Multi-organ resection was performed in 19 patients (63.4% of cases); the median number of resected organs en bloc with the tumor was 2 (range 1–4) (Table 2). As expected, most of multi-visceral resections (12/19, 63%) were performed in the RPS group. Anastomoses were mostly hand-sewn (13/14, 92.8%); this was a technical decision based on the surgeon experience about duodenal anastomosis. Side-to-side anastomosis was sewn in five patients (35.7%), end-to-side in three patients (21.4%), end-to-end in three patients (21.4%), while Roux-en-Y anastomosis was used to reconstruct the gastrointestinal tract in two patients (14.3%). Only one mechanical anastomosis (7.2%) was performed and it was end-to-side fashioned.

As regards RPS subgroup, the histopathologic invasion of the duodenum was confirmed in ten patients (66.6%). Overall, R0 resections were observed in 22 patients (73.4%), R1 resections in 7 patients (23.3%), and R2 in 1 patient (3.3%)

with residual disease on the mesenteric axis. Considering only duodenal margin, its infiltration was reported in 3 patients (2 RPS and 1 GIST) and all of them underwent WR.

Median time to flatus and to bowel movement was 3 (range 1–6) and 5 days (range 3–19), respectively. Nasogastric tube was removed after a median of 3 days (range 0–35) and for four patients (13.3%) it was necessary to replace the tube for nausea or vomiting. Oral refeeding started after a median of 4.5 days (range 2–15), after nasogastric tube removal and in absence of nausea or vomiting. Median post-operative stay was 10.5 days (range 5–97).

The overall 30-day postoperative morbidity rate was 53.3% (16/30). According to CDC, grade I complications were recorded in three patients (10%), grade II in seven (23.3%), grade IIIa in one (3.3%), grade IIIb in four (13.3%) and grade IVa in one patient (3.3%). Severe complications (CDC ≥ III) occurred in six (19.9%) patients. There was no postoperative mortality. As regards duodenum-related complications: six patients had delayed gastric emptying/paralytic ileus (three grade I and three grade II, according to CDC), in three patients we observed duodenal leakage (grade II), and one patient had a mechanical ileus caused by an intestinal volvulus involving the duodeno-jejunal anastomosis (grade IIIb). Median CCI in the WR group was of 0 (range 0–39.7) and 20.9 (range 0–58.3) in the SR group. Morbidity rate was higher in SR group (11/14, 79%) compared to WR (5/16, 31%). Particularly for duodenum-related complications, duodenal leak occurred only in SR group (3/14, 21% versus 0/16, 0%); delayed gastric emptying/paralytic ileus occurred in 5/14 SR (36%) versus 1/16 WR (6%); intestinal volvulus affected 1 patient (7%) in SR group versus 0 (0%) in WR group. All the three patients with duodenal leak had previous abdominal surgery and two of them also received chemotherapy. Three out of three patients (100%) with a duodenal leak, four out of five patients (80%) with delayed gastric emptying/paralytic ileus and the patient with intestinal volvulus received a multivisceral resection. Other observed complications were minor wound complications (2/30, 6.7%), atrial fibrillation (1/30, 3.3%), pneumonia (1/30, 3.3%), leak of the colo-colic anastomosis (1/30, 3.3%), urinary tract infection (1/30, 3.3%) and colitis sustained by *Clostridium difficile* (1/30, 3.3%). No correlation was found between type of anastomosis and complications.

**Table 2** Details of multivisceral resection

Histology	Number of multi-visceral resections (%)	Resected organs	#
Sarcoma	12 (63.0)	Colon	7
		Kidney	5
		Ileum	2
		Stomach	1
		Spleen	1
		Pancreas (tail)	1
		Other	3
		GIST	7 (27.0)
		kidney	1
		Pancreas (tail)	1
		Ileum	1
		Liver	1

## Discussion

In the absence of metastatic disease, surgical resection is the main curative approach to treat GIST with or without perioperative administration of tyrosine kinase inhibitor [8, 9]. As regards RPS, in the recent literature, an aggressive surgical approach has been advocated, comprising en bloc resection of most of the adjacent organs when in proximity

of the tumor surface (i.e., kidney, colon, psoas muscle, small bowel, left pancreas, spleen, and diaphragm), while other organs' resection (duodenum, head of the pancreas, liver, stomach, major abdominal vessels and nerves, bone) is acknowledged only if direct infiltration is present [5, 10, 11]. However, the optimal surgical management of the duodenum still represents a matter of debate since studies analyzing short-term outcomes of this kind of surgery are few and still far from being conclusive. It is well known that duodenal surgery significantly influences post-operative morbidity; due to the narrow and complex anatomy of the pancreaticoduodenal area with the proximity to the pancreas, the bile duct, the mesenteric root, the portal vein and the papilla of Vater, clear resection margins often measure only few millimeters. Such anatomical limits may sometimes indicate pancreaticoduodenectomy, and different authors already compared both surgical and oncological outcomes between this procedure and limited resection, i.e., pancreas-sparing duodenectomy [1], but no data focusing on SR versus WR are available.

In our study, duodenal surgery confirmed to affect significantly postoperative morbidity; in fact, we reported an overall 30-day postoperative morbidity rate of 53%; when we did not consider duodenum-related complications, the overall 30-day postoperative morbidity rate decreased (37% vs 53%). The high morbidity associated with duodenal surgery was also evident when postoperative complications were evaluated using the CCI; considering a CCI of 34.8 as median value in patients with one duodenal complication and at least one other, the median CCI resulted to be 20.9 (range 8.7–42.7) when duodenum-related complications were excluded. Particularly, CCI observed in WR group was lower when compared to SR group although the difference between the two groups decreased when duodenum-related morbidity was excluded. However, these complications were mostly minor ones, being the rate of severe complication 20%, and no mortality was observed; such percentages are in line with those reported in the literature for major surgery. Duodenum-related complications were classified as minor (Clavien–Dindo II or less) in 70% of cases. Therefore, SR or WR could be considered feasible in referral centers with expertise on this type of surgery.

As discussed above, in RPS surgery, duodenal resection is usually indicated only if gross infiltration is present, and the possibility to achieve free resection margins has to be carefully weighted and discussed for each single patient since duodenal surgery is characterized by a high morbidity rate [5]. In our series, three patients had R1 wedge resection; one patient was diagnosed with GIST while other two patients were diagnosed with sarcoma. All of them required resection of the second part of the duodenum, and WR was chosen in an attempt to reduce perioperative morbidity, avoiding more aggressive approach. Therefore, we believe that in

these patients R1 resection was mainly due by the site of disease. However, whenever it is possible, WR should be the preferred approach, as long it may guarantee free resection margins. Considering resection for primary duodenal GIST, the size of the tumor can influence the surgical choice, with WR being the preferable procedure for smaller tumors; our results did not show a correlation between type of surgery and location of the GIST; however, it seems reasonable that also this variable has to be taken into account. In fact, different authors suggested WR as the preferable procedure for small lesions if the resulting lumen is adequate and the ampulla of Vater can be preserved [12, 13], while SR can be performed for larger tumors located at third and fourth (infra-ampullary) portion of duodenum. Even if both procedures are less invasive and easier to perform than pancreaticoduodenectomy, risk of anastomotic leakage or stenosis is present [12], confirming again the high morbidity rate of duodenal surgery. In this context, the possible neoadjuvant use of the tyrosine kinase inhibitor imatinib in selected cases of locally advanced GIST with the aim to downsize the tumor—and, therefore, changing the surgical strategy—has to be considered; as Tielen and colleagues report in their study, tumor shrinkage enhances the likelihood of an organ preserving surgery [14]; moreover, imatinib reduces the risk of tumor rupture during its manipulation, thus decreasing the risk of developing abdominal metastases [15].

In our experience, both end-to-end and end-to-side primary anastomoses can be used to safely restore intestinal continuity after SR, without differences in postoperative morbidity. Dorcaratto and colleagues reported similar results, with no significant differences in morbidity rates; however, they observed that the severity of complications was higher in the end-to-side group [16]. We found a correlation between duodenal leak and previous treatment (previous surgery or chemotherapy); in fact, all three patients with duodenal leak had previous abdominal surgery and, also chemotherapy.

Concerning the resected duodenal portion, we did not identify variations in complication rates in subgroups of patients. Occurrence of postoperative ileus was quite frequent (7/30 patients, 23.3%), as expected after major abdominal open surgery. If we exclude ileus because of a volvulus, five out of the six remaining patients suffering from postoperative ileus were among those who underwent SR, involving resection of the Treitz's loop in almost all of the cases (involvement of third or fourth duodenal portion). However, due to the rarity of both mesenchymal tumors and to the unstandardized approach to duodenal malignancies, it is hard to find comparable data in the literature since available studies are retrospective, with small samples and the proposed surgical options are different [2, 8, 12, 16].

Our study presents some limitations including its retrospective nature, with inherent bias regarding patient



selection. Also mixing two different histotypes and the relatively small number of patients involved in a long period (16 years) made it difficult to perform adequate statistical analysis to identify independent risk factors for complication after duodenal resection. However, retrospective studies may be of some value and deserve adequate consideration when regarding very rare disease. In addition, considering the rarity of mesenchymal tumors, our cohort could represent a not-negligible surgical series. For instance, in the very large series published by the Transatlantic RPS Working Group including 1007 patients, a duodenal or duodeno-jejunal junction resection was performed in only four cases [11]. Although presenting different tumor biology, both RPS and GIST are mainly treated by surgical resection; hence, we focused on technical aspects and post-operative morbidity providing detailed clinical and surgical information, without considering oncological and survival outcomes. Moreover, all data are also reported separately by subgroups of disease.

Despite the challenging location, GIST and RPS involving duodenum can be safely managed by surgery. The need to perform duodenectomy just to secure a disease-free margin should be evaluated on a case-by-case basis, with costs carefully weighed against the expected benefit. The type of procedure should be chosen according to the specific duodenal site of origin and tumor size, because of the significant rates of postoperative morbidity. WR should be considered as the first choice whenever technically feasible since it is associated with a lower morbidity rate. Patients should be referred to high-volume centers, where the best approach can be planned and a more limited risk expected. Long-term and comparative studies are needed to confirm the efficacy of this infrequently performed procedure. Giving the rarity of these diseases and the difficulty in designing prospective trial on this topic, further collaborative multicenter retrospective studies should be encouraged to define the best therapeutic approach.

**Author contributions** Substantial contributions were made to the conception or design of the work (FCMC, LR, and LS), the acquisition, analysis (LS, FS, DG, and EMM), interpretation of data for the work (FCMC, LR, LC, and VQ), drafting the work (FCMC, LR, and LS) or revising it critically for important intellectual content (FCMC, FS, DG, EMM, LC, and VQ), and final approval of the version to be published (FCMC, LR, LS, FS, DG, EMM, LC, and VQ). Agreement to be 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 (FCMC, LR, LS, FS, DG, EMM, LC, and VQ).

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## Compliance with ethical standards

**Conflict of interest** The authors declare they have no conflict of interest.

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