Original Article

DOI: 10.5582/bst.2022.01522

Delayed gastric emptying after aggressive surgery for retroperitoneal sarcoma – Incidence, characteristics, and risk factors

Ang Lv[§], Rongze Sun[§], Hui Qiu, Jianhui Wu, Xiuyun Tian, Chunyi Hao[*]

Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education, Beijing), Department of Hepato-Pancreato-Biliary Surgery/ Sarcoma Center, Peking University Cancer Hospital & Institute, Beijing, China.

SUMMARY Delayed gastric emptying (DGE) after aggressive resection of retroperitoneal sarcoma (RPS) has rarely been described. This study aimed to determine the incidence and characteristics of DGE after surgery for RPS and explore its potential risk factors. Patients with RPS who had undergone surgery between January 2010 and February 2021 were retrospectively analyzed. DGE was defined and graded according to the International Study Group of Pancreatic Surgery classification and classified as primary or secondary to other complications. Patients with clinically relevant DGE (crDGE, grade B+C) were compared to those with no or mild DGE (grade A). Multivariate logistic regression analysis of clinicopathological and surgical parameters was performed to identify risk factors for crDGE. Of the 239 patients studied, 69 (28.9%) had experienced DGE and 54 (22.6%) had experienced crDGE. Patients with primary and secondary DGE accounted approximately half and half. The most common concurrent complications included abdominal infection, postoperative pancreatic fistula, and abdominal bleeding. Patients with crDGE were more likely to have multifocal tumors and the liposarcoma subtype, with a larger tumor size, longer operating time, more resected organs, and a history of combined resection of the stomach, pancreas, small intestine, and/or colon. In multivariate analysis, the tumor size, operating time, and combined pancreatic resection were independent risk factors for crDGE. In conclusion, the current results indicated that approximately one-fourth of patients experienced DGE after aggressive surgery for RPS and that DGE was primary or secondary to other underlying conditions. A large tumor involving long, difficult surgery and combined pancreatic resection highly predicted the incidence of crDGE. The prevention and management of DGE remain challenging.

Keywords delayed gastric emptying, retroperitoneal sarcoma, multivisceral resection, major complication, risk factor

1. Introduction

Retroperitoneal sarcomas (RPS) constitute a heterogeneous group of rare malignant tumors that often grow to a large size and involve adjacent organs before detection. Considering the overall limited effect of pharmacotherapy for most subtypes, surgery is the cornerstone of RPS management (*1,2*). Compared with simple tumor resection, aggressive multivisceral resection (MVR) en bloc with involved or adjacent organs is associated with a significantly decreased local recurrence rate and improved survival (*3-6*). However, aggressive surgery may inevitably lead to an increased risk of complications. Surgery for RPS has been found to have a major complication rate as high as approximately 15-31% and a mortality rate as high as approximately 3-7%, even in high-volume centers (*3,6-10*).

Delayed gastric emptying (DGE) is one of the predominant complications of major abdominal surgery, especially pancreatic and upper gastrointestinal surgery. DGE is diagnosed based on characteristic symptoms, the absence of gastric outlet obstruction, and evidence of an objective delay in gastric emptying (*11*). DGE delays oral intake, prolongs hospitalization, decreases quality of life, and increases the total cost of hospitalization (*12-15*). The exact etiology and pathogenesis of postoperative DGE remains unclear. The proposed risk factors and mechanisms are related to pre-existing conditions (such as diabetes mellitus and malnutrition), surgical procedures (such as

pyloric or antral ischemia, pylorospasm secondary to the disruption of the perigastric vagal nerves, and aggressive lymphadenectomy), and postoperative intra-abdominal complications (such as gastric dysrhythmias due to a postoperative pancreatic fistula [POPF], hemorrhage, or infection) (*14,16-20*).

The incidence of DGE reportedly ranges from 17.3% to 51.8% after pancreaticoduodenectomy (PD) (*21-24*), 5% to 24% after distal pancreatectomy (DP) (*25,26*), and 4.3% to 15.5% after distal gastrectomy (*27,28*). Considering the extensiveness, complexity, and high rate of intra-abdominal complications of aggressive surgery for RPS, DGE may be common after resection of RPS. However, the incidence and characteristics of and risk factors for DGE after surgery for RPS remain unclear. To the extent known, only one study has explicitly reported the incidence and severity of DGE after MVR for RPS (*29*); in that study, all 100 patients had primary RPS. As one of the largest specialized sarcoma centers in China, we established a treatment algorithm and performed aggressive surgery in patients with primary and recurrent RPS. This study aimed to investigate the incidence and characteristics of DGE after aggressive surgery for RPS using a larger sample of patients with either primary or recurrent disease and to analyze its potential risk factors.

2. Materials and Methods

2.1. Patients and data collection

We retrospectively analyzed a cohort of consecutive patients who had undergone surgery for RPS at the Peking University Cancer Hospital Sarcoma Center between January 2010 and February 2021. Patients with benign retroperitoneal tumors, desmoid-type fibromatosis, gastrointestinal stromal tumors, or subtypes other than RPS were excluded. Data on sex, age, body mass index (BMI), medical history, presentation status, pathological subtype, tumor grading, tumor size, tumor focality, surgical information (operating time, estimated blood loss, completeness of surgery, and the number and type of resected organs), and postoperative course (removal and re-insertion of a nasogastric tube, intensive care unit [ICU] admission, postoperative hospitalization, postoperative complications, and reoperation) were retrieved from electronic medical records.

This study's primary outcomes were the incidence and grade of DGE. To evaluate the clinical impact of DGE, patients experiencing clinically relevant DGE (grades B and C) were analyzed and compared to those with no or mild DGE (grade A). Patients who died of complications within 1 week of surgery were excluded because their DGE status could not be assessed.

This study was reported according to the STROBE guidelines. The study was approved by the Ethics Committee of Peking University Cancer Hospital and conducted in accordance with the 1975 Declaration of Helsinki, as revised in 2013. All patients provided written informed consent before surgery for the use of their anonymized data.

2.2. Perioperative management

All patients underwent surgery by the same surgical team led by Hao. The treatment algorithm and surgical procedures have been described previously (*3*). According to the general principles of surgical and supportive care, standard postoperative treatments were administered, including fluid balance, adequate electrolyte replacement, prophylactic anti-infection, and total parenteral nutrition.

A nasogastric tube was inserted during surgery when suturing repair, tangential resection, or anastomosis of the upper gastrointestinal tract was performed. If the amount of gastric juice was < 300 mL per day, the nasogastric tube was removed after flatus was expelled. When gastric retention, anastomotic leakage, or bowel obstruction was confirmed on abdominal radiography or upper gastroenterography, the nasogastric tube was re-inserted. Patients not undergoing resection or anastomosis of the gastrointestinal tract were permitted a liquid diet after flatus expulsion and subsequently transitioned to a semi-liquid and general diet. Patients undergoing resection or anastomosis of the stomach or duodenum were not permitted liquid diet intake until an upper gastroenterography had been performed on day 5-6 postoperatively to prevent anastomotic leakage, stricture, or DGE.

Upon diagnosis of DGE, efforts were made to mobilize the patient, use prokinetic agents, and aggressively treat any other complications, such as POPF and abdominal infection.

2.3. Definitions

DGE was defined and graded according to the standards published by the International Study Group of Pancreatic Surgery (ISGPS) (*14*). As alluded to above, grade B or C DGE was considered clinically relevant. DGE was classified as primary (unrelated to other complications) or secondary to other surgical complications. Other causes of aphagosis, such as anastomotic leakage and bowel obstruction, were carefully reviewed and ruled out. Complications other than DGE were graded using the Clavien–Dindo classification and considered "major" if graded III or higher (*30*). Pathological subtypes were classified according to the 2020 World Health Organization (Geneva) criteria for soft tissue tumors (*31*). Tumor grading was determined using the three-tiered grading system of the Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) criteria (*32*). Tumor size was defined as the sum of the largest

tumor diameters. Surgical resections were classified as macroscopically complete (R0/R1) or incomplete (R2) in accordance with most previous studies, because the large surface area and anatomical location of the RPS casts doubt on the use of a reliable microscopic margin assessment (*33*).

2.4. Statistical Analysis

Clinicopathological, surgical, and postoperative parameters are expressed as frequencies and percentages for categorical variables and medians and ranges for continuous variables. The chi-square test and *t*-test were used to compare categorical and continuous variables, respectively. Multivariate binary logistic regression with a forward LR strategy was used to analyze clinicopathological and surgical variables and explore the independent risk factors for clinically relevant DGE. Variables with *P*-values <0.1 from univariate analysis or clinical significance were incorporated into the multivariate model. Results were considered statistically significant if a two-sided *P*-value < 0.05 was obtained. Statistical analyses were performed using SPSS (version 26.0; SPSS Inc., Chicago, IL).

3. Results

Among 242 consecutive patients who underwent surgery for RPS, three patients were excluded because of death within 7 days postoperatively, and the remaining 239 patients were enrolled in this study. A flowchart illustrates the selection and subgrouping process (Figure 1).

Of the 239 enrolled patients, 69 (28.9%) experienced DGE and 54 (22.6%) experienced clinically relevant DGE. DGE was classified as grade A (15/69, 21.7%), B (21/69, 30.4%), or C (33/69, 47.8%) based on the ISGPS definition. DGE was primary in 34 (49.3%) patients (grade A in 10, grade B in 6, and grade C in 18) and secondary to other postoperative complications in 35 (50.7%) (grade A in 5, grade B in 15, and grade C in 15) (Figure 2A). Abdominal infection (n = 16),

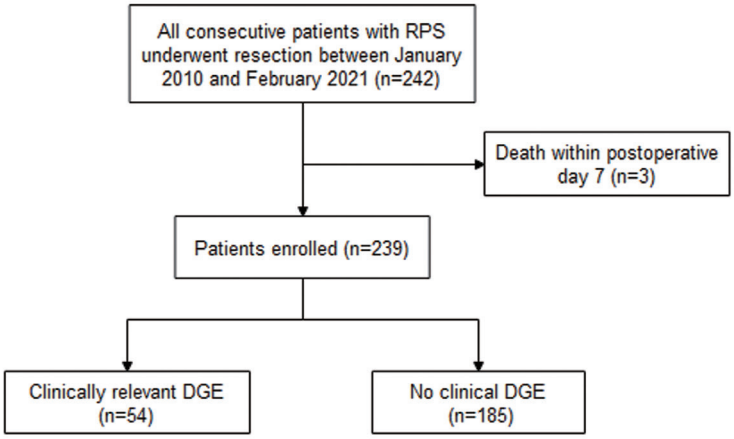

Figure 1. Flowchart for the selection and subgrouping process. DGE, delayed gastric emptying; RPS, retroperitoneal sarcoma.

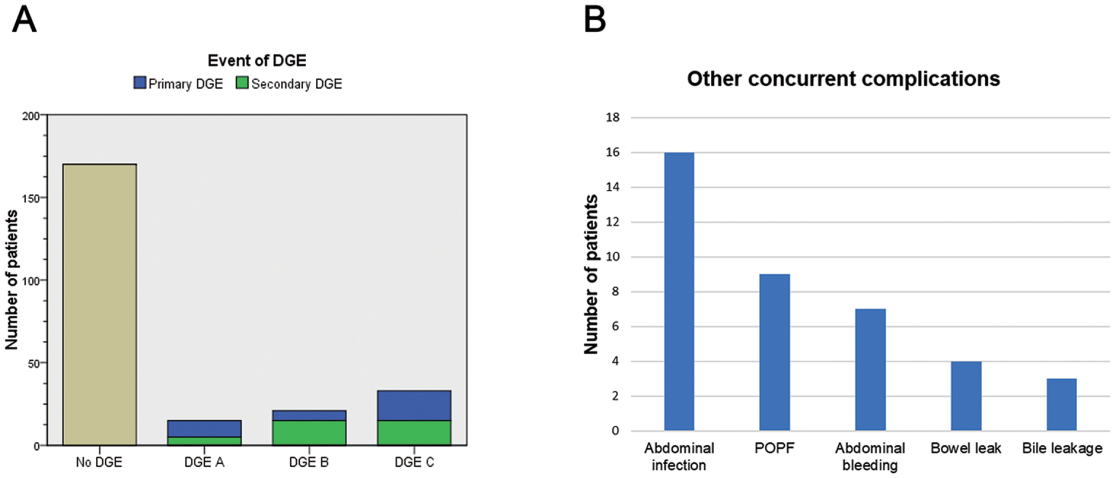

Figure 2. Grade and category of DGE (**A**) and its most common concurrent complications (**B**). DGE, delayed gastric emptying; POPF, postoperative pancreatic fistula.

POPF (n = 9), abdominal bleeding (n = 7), bowel leak (n = 4), and bile leakage (n = 3) were the predominant concurrent complications associated with clinically relevant DGE (Figure 2B).

Patient clinicopathological characteristics are shown in Table 1. Sex, age, BMI, previous diabetes, presentation status, and FNLCC grade were not associated with clinical DGE. Compared to patients not experiencing clinical DGE, those who experienced clinically relevant DGE had a larger tumor size (median 26.5 cm *vs*. 17.0 cm, $P < 0.001$) and higher proportion of multifocal tumors (25/54, 46.3% *vs*. 58/185, 31.3%, $P = 0.042$) and dedifferentiated liposarcoma subtypes (57.4% *vs*. 34.6%, $P = 0.021$). In terms of pathological subtypes, the incidence rate of clinical DGE was highest in liposarcomas (40/128, 31.3%) and lowest in leiomyosarcomas (3/40, 7.5%).

The surgical characteristics of patients are shown in Table 2. A significantly longer operating time (median: 551 min *vs*. 406 min, $P < 0.001$), greater estimated blood loss (median: 2000 mL *vs*. 800 mL, $P = 0.002$), and a greater number of organs removed during surgery (median: 7 *vs*. 5, $P < 0.001$) were noted in patients who experienced clinically relevant DGE. Moreover, combined gastric resection (23/54, 42.6% *vs*. 31/185, 16.8%; $P < 0.001$), pancreatic resection (33/54, 61.1% *vs*. 54/185, 29.2%; $P < 0.001$), major colon resection (49/54, 90.7% *vs*. 117/185, 63.2%; $P < 0.001$), and small intestine resection (23/54, 42.6% *vs*. 33/185, 17.8%; $P < 0.001$) were significantly more common in patients with clinical DGE. Patients who had undergone PD were more likely to experience clinical DGE than those who had undergone DP ($P = 0.016$). The completeness of resection and resection of the kidney

Table 1. Clinicopathological characteristics of patients

Parameter	Total (n = 239)	No clinical DGE (n = 185)	Clinical DGE (n = 54)	P
Sex ratio, n (male:female)	124:115	92:93	32:22	0.218
Age (years)*	55 (16-86)	55 (16-83)	58 (20-86)	0.208
BMI (kg/m^2)*	23.4 (15.6-39.0)	23.4 (15.6-39.0)	23.3 (16.9-32.2)	0.594
Diabetes, n (%)	24 (10.0%)	17 (9.2%)	7 (13.0%)	0.125
Presentation status, n (primary:recurrent)	144:95	117:68	27:27	0.080
Pathological subtypes, n (%)				0.021
DDLPS	95 (39.7%)	64 (34.6%)	31 (57.4%)	
WDLPS	33 (13.8%)	24 (13.0%)	9 (16.7%)	
LMS	40 (16.7%)	37 (20.0%)	3 (5.6%)	
UPS	17 (7.1%)	14 (7.6%)	3 (5.6%)	
SFT	16 (6.7%)	14 (7.6%)	2 (3.7%)	
Other	38 (15.9%)	32 (17.2%)	6 (11.0%)	
FNCLCC grade, n (%)				0.243
1	43 (18.0%)	36 (19.5%)	7 (13.0%)	
2	99 (41.4%)	79 (42.7%)	20 (37.0%)	
3	97 (40.6%)	70 (37.8%)	27 (50.0%)	
Tumor size (cm)*	19.0 (1.6-69.0)	17.0 (3.5-69.0)	26.5 (1.6-69.0)	< 0.001
Tumor focality, n (single:multifocal)	156:83	127:58	29:25	0.042

*Median with range. DGE, delayed gastric emptying; BMI, body mass index; P-POSSUM, physiological and operative severity score for the enumeration of mortality and morbidity; DDLPS, dedifferentiated liposarcoma; WDLPS, well-differentiated liposarcoma; LMS, leiomyosarcoma; UPS, undifferentiated pleomorphic sarcoma; SFT, solitary fibrous tumor; FNCLCC, Fédération Nationale des Centres de Lutte Contre le Cancer.

Table 2. Operative data on patients

Parameter	Total (n = 239)	No clinical DGE (n = 185)	Clinical DGE (n = 54)	P
Operating time (min)*	432 (71-1030)	406 (71-1030)	551 (300-995)	< 0.001
Estimated blood loss (mL)*	1000 (10-16000)	800 (10-16000)	2000 (100-15600)	0.002
No. of resected organs*	5 (0-14)	5 (0-14)	7 (1-13)	< 0.001
Complete resection (R0/R1), n (%)	215 (90.0%)	170 (91.9%)	45 (83.3%)	0.066
Partial gastric resection, n (%)	54 (22.6%)	31 (16.8%)	23 (42.6%)	< 0.001
Pancreatic resection, n (%)	87 (36.4%)	54 (29.2%)	33 (61.1%)	< 0.001
Type of pancreatic resection, n (%)				0.016
Pancreaticoduodenectomy	31 (35.6%)	14 (25.9%)	17 (51.5%)	
Distal pancreatectomy	56 (64.4%)	40 (74.1%)	16 (48.5%)	
Colon resection, n (%)	166 (69.5%)	117 (63.2%)	49 (90.7%)	< 0.001
Small intestine resection, n (%)	56 (23.4%)	33 (17.8%)	23 (42.6%)	< 0.001
Kidney resection, n (%)	130 (54.4%)	96 (51.9%)	34 (63.0%)	0.151
Major vessel resection, n (%)	61 (25.5%)	45 (24.3%)	16 (29.6%)	0.431

*Median with range. DGE: delayed gastric emptying.

or major vessels were not associated with clinical DGE.

Multivariate analysis, which included the aforementioned clinicopathological and surgical variables, indicated that the tumor size (odds ratio [OR]: 1.034; 95% confidence interval [CI]: 1.006-1.062; $P = 0.016$), operating time (OR: 1.003; 95% CI: 1.001-1.005; $P = 0.003$), and combined pancreatic resection (OR: 2.521; 95% CI: 1.243-5.113; $P = 0.010$) were independent risk factors for clinical DGE (Table 3). To further explore the independent risk factors for primary clinically relevant DGE, univariate and multivariate analyses of clinicopathological and surgical variables were also performed. The tumor size ($P = 0.016$), operating time ($P = 0.033$), and the number of resected organs ($P = 0.048$) were found to be associated with primary clinically relevant DGE in univariate analysis, and the tumor size (OR: 1.035; 95% CI: 1.006-1.066; $P = 0.019$) was identified as the unique independent risk factor in multivariate analysis.

The patients' postoperative courses are shown in Table 4. The rates of nasogastric tube insertion during surgery (43/54, 79.6% *vs*. 64/185, 34.6%, $P < 0.001$), delayed nasogastric tube removal (median: 9 *vs*. 5 days, $P < 0.001$), and nasogastric tube re-insertion (25/54, 46.3% *vs*. 11/185, 5.9%, $P < 0.001$) were significantly higher in patients experiencing clinical DGE. In addition, rates of ICU admission (37/54, 68.5% *vs*. 52/185, 28.1%, $P < 0.001$), major complications (26/54, 48.1% *vs*. 27/185, 14.6%, $P < 0.001$), reoperation (16/54, 29.6% *vs*. 9/185, 4.9%, $P < 0.001$), and 90-day postoperative mortality (5/54, 9.3% *vs*. 5/185, 2.7%, $P = 0.034$) were significantly higher in patients with clinical DGE. Accordingly, the total duration of hospitalization was longer in patients with clinical DGE (median: 34 *vs*. 16 days; $P < 0.001$).

4. Discussion

Postoperative DGE was first described by Warshaw *et al*. (*34*). Considering the rarity and complexity of surgery for RPS, only one study has specifically reported DGE after MVR for RPS in the English literature to date (*29*). The current study, which included 239 patients, is potentially the largest single-center case series thus far. In addition, to the extent known, this study is the first to compare patients experiencing clinically relevant DGE to those experiencing no or mild DGE in patients both with primary and recurrent RPS.

Rather than those potential life-threatening risks, the key threats to patients with DGE are delayed oral intake, prolonged hospitalization, and an increased

Table 3. Multivariate regression analysis of the clinicopathological and surgical factors influencing clinically relevant DGE

Clinicopathological parameters	Clinical DGE		Surgical parameters	Clinical DGE	
	OR (95% CI)	*P*		OR (95% CI)	*P*
Presentation status (primary*: recurrent)			Operating time	1.003 (1.001-1.005)	0.003
Pathology			Estimated blood loss		
DDLPS:Other*			No. of resected organs		
WDLPS:Other*			Complete resection (yes:no*)		
LMS:Other*			Partial gastric resection (yes:no*)		
Tumor size	1.034 (1.006-1.062)	0.016	Pancreatic resection (yes:no*)	2.521 (1.243-5.113)	0.010
Tumor focality (multifocal:single*)			Small intestine resection (yes:no*)		
			Colon resection (yes:no*)		

*is for reference. CI, confidence interval; OR, odds ratio; DGE, delayed gastric emptying; DDLPS, dedifferentiated liposarcoma; WDLPS, well-differentiated liposarcoma; LMS, leiomyosarcoma; P-POSSUM, physiological and operative severity score for enumeration of mortality and morbidity.

Table 4. Postoperative course of patients

Parameter	Total ($n = 239$)	No clinical DGE ($n = 185$)	Clinical DGE ($n = 54$)	*P*
Nasogastric tube placement intraoperatively, *n* (%)	107 (44.8%)	64 (34.6%)	43 (79.6%)	< 0.001
Removal of a nasogastric tube (POD)*	6 (2-57)	5 (2-18)	9 (2-57)	< 0.001
Re-insertion of a nasogastric tube, *n* (%)	36 (15.1%)	11 (5.9%)	25 (46.3%)	< 0.001
ICU admission, *n* (%)	89 (37.2%)	52 (28.1%)	37 (68.5%)	< 0.001
ICU days*	4 (1-35)	3 (1-35)	5 (2-21)	0.274
Postoperative hospitalization (day)*	19 (6-149)	16 (6-105)	34 (15-149)	< 0.001
Major complications other than DGE, *n* (%)	53 (22.2%)	27 (14.6%)	26 (48.1%)	< 0.001
Re-operation, *n* (%)	25 (10.5%)	9 (4.9%)	16 (29.6%)	< 0.001
90-day postoperative mortality, *n* (%)	10 (4.2%)	5 (2.7%)	5 (9.3%)	0.034

*Median with range. DGE, delayed gastric emptying; POD, days postoperatively; ICU, intensive care unit.

total cost of hospitalization. Therefore, when reporting major complications of surgery for RPS, DGE is often overlooked, even in high-volume centers, such as the Transatlantic Australasian RPS Working Group (*35,36*), resulting in a lack of data on the incidence and severity of DGE after surgery for RPS. Based on the widely accepted definition and grading standards proposed by the ISGPS, the incidence of DGE was 28.9% (69/239) and that of clinically relevant DGE was 22.6% (54/239); the rates were slightly lower than those reported by Baia *et al*. (42% and 28%, respectively) (*29*). In this case series, patients with primary and secondary DGE accounted approximately half and half, while DGE secondary to other complications was more often observed in patients with clinical DGE (30/54, 55.6%) than in those with mild DGE (5/15, 33.3%). A similar trend was also observed in other studies, in which the proportion of patients with secondary clinical DGE reached 64.3% (18/28) after surgery for RPS (*29*) and 84.1% (37/44) after pancreatic surgery (*23*). Accordingly, abdominal infection, POPF, and abdominal bleeding (*23,24,29*) were the most common concurrent complications associated with clinically relevant DGE in the current study.

The influence of intra-abdominal complications on the incidence of postoperative DGE was first reported by Henegouwen *et al*. (*37*) in 1997. In that prospective study, the incidence of DGE after standard PD (n = 100) was compared to that after pylorus-preserving PD (n = 100). With a postoperative DGE prevalence of 65%, the study demonstrated that the presence of postoperative intra-abdominal complications was the predominant risk factor for DGE ($P < 0.0001$). Subsequently, several studies, including meta-analyses, yielded similar results (*16,23,29,38*). Therefore, some researchers have suggested that, without any obvious etiology, DGE could be regarded as a sentinel event of severe complications in pancreatic and RPS surgery (*23,39*). Moreover, Baia *et al*. reported that satisfactory outcomes (a resumption of oral feeding) were potentially achievable after the treatment of complications causing secondary DGE (*29*). In addition to major complications, the current results indicated that the rates of ICU admission (68.5% *vs*. 28.1%), reoperation (29.6% *vs*. 4.9%), and 90-day mortality (9.3% *vs*. 2.7%) were also significantly higher in patients with clinically relevant DGE. The possible reasons for the link between the presence of major complications or other adverse postoperative courses and the incidence of DGE remain unclear. This indicates that clinical DGE may be considered the result of local inflammation and a manifestation of the patient's poor condition overall.

While analyzing the relationship between postoperative course and DGE, we looked for independent risk factors among clinicopathological and surgical variables. In multivariate analysis, the tumor size, operating time, and combined pancreatic resection were independent factors associated with clinical DGE. Pancreatic resection itself, regardless of PD or DP, is a relatively high-risk operation, and DGE is one of its most common complications (*21-26*). During resection of RPS, removal of the pancreas is sometimes necessary for oncological or technical reasons. However, compared to combined resection of other organs (such as the colon and kidney), combined resection of the pancreas for RPS is more controversial due to the potentially high risk of morbidity and mortality (*40-43*). In the current study, the prominent complications after combined pancreatic resection included POPF, abdominal infection, and abdominal bleeding, which were also found to be the most common complications leading to DGE. This potentially explains why a combined pancreatic resection increases the risk of clinical DGE.

The tumor size and operating time were other independent risk factors for postoperative DGE. Considering that all patients underwent surgery by the same experienced surgical team led by Hao, operating time could be regarded as an indicator of the surgery's complexity. Owing to its biological characteristics and anatomic location, RPS often grows to a vast size and involves adjacent organs before being detected. When a large tumor is located in the upper quadrant, compression of the stomach, duodenum, or small intestine is common. The changes caused by long-term compression and relief of the upper gastrointestinal tract after tumor removal may also be a possible reason for postoperative DGE (*29*). Moreover, the incidence of DGE varies among subtypes. The highest incidence was noted with liposarcoma, in approximately 1/3 of patients (40/128), and the lowest with leiomyosarcoma, at a rate of 7.5% (3/40). This may be because leiomyosarcoma typically arises from retroperitoneal vessels, such as the inferior vena cava or renal/gonadal/iliac vein; therefore, it is usually smaller in size and seldom requires gastrointestinal or pancreatic resection. In contrast, liposarcomas are generally larger in size, with a more indistinct border and a greater tendency to involve other organs (*44*), and they present as intra-abdominal multifocal recurrence rather than distant metastasis. Patients with larger and multifocal tumors involving adjacent organs usually undergo longer surgeries, more complex surgical procedures, and the resection of more organs, possibly explaining why these patients are at a higher risk of developing clinically relevant DGE.

The prevention and management of DGE remain challenging because the results of the current analysis indicated that the incidence of clinical DGE may depend more on the characteristics of the tumor rather than the surgical procedure. Considering the overall high recurrence tendency of RPS, from the perspective of local control, long hours of extensive MVR are

usually necessary for a large invasive tumor. Given that no specific agent can provide a faster recovery, the potential measures could include: effective preoperative systemic therapy to shrink the tumor and make it easier to remove, selection of an appropriate surgical approach and skilled surgical techniques to reduce the operating time as much as possible, a personalized histology-specific surgical strategy to determine the possibility of pancreatic-preserving resection, and timely appropriate treatment to control underlying complications. All of these measures above are predicated on an experienced multidisciplinary team, and this is a significant reason why patient management in a high-volume specialized sarcoma center is strongly recommended (*45,46*).

The main limitations of this study include its retrospective nature and the inclusion of patients from a single institution over a long period of time exceeding 10 years. Nonetheless, this study has analyzed the largest case series to date and it provides meaningful insights into the characteristics of, risk factors for, and management of DGE after aggressive surgery for RPS. The current findings could help to understand this issue and improve clinical decision-making.

In conclusion, the current study found that approximately one-fourth of patients have DGE after aggressive surgery for RPS and that DGE was primary or secondary to other underlying conditions. A large tumor involving long, difficult surgery and combined pancreatic resection highly predicted the incidence of clinically relevant DGE. The prevention and management of DGE remain challenging.

Funding: This work was supported by the Capital Health Research and Development of Special Funds (approval no. 2020-1-1021), Beijing Excellent Talent Training Project (approval no. 2018000021469G269), Beijing Municipal Administration of Hospital's Ascent Plan (approval no. DFL20181104), and Beijing Municipal Administration of Hospitals' Youth Program (approval no. QML20181104).

Conflict of Interest: The authors have no conflicts of interest to disclose.

Author contributions: Lv A and Hao CY contributed to the conception and design of the study. Lv A, Sun RZ, Qiu H, Wu JH, and Tian XY collected, analyzed, and interpreted patient data. Lv A and Sun RZ wrote the first draft of this manuscript. Qiu H, Wu JH, and Tian XY wrote the manuscript. All authors contributed to manuscript revision and read and approved the submitted version.

References

1. Swallow CJ, Strauss DC, Bonvalot S, *et al*. Management of primary retroperitoneal sarcoma (RPS) in the adult: An updated consensus approach from the Transatlantic Australasian RPS Working Group. Ann Surg Oncol. 2021; 28:7873-7888.
2. Trans-Atlantic RPS Working Group. Management of recurrent retroperitoneal sarcoma (RPS) in the adult: A consensus approach from the Trans-Atlantic RPS Working Group. Ann Surg Oncol. 2016; 23:3531-3540.
3. Lv A, Li Y, Li ZW, Mao LL, Tian XY, Hao CY. Treatment algorithm and surgical outcome for primary and recurrent retroperitoneal sarcomas: A long-term single-center experience of 242 cases. J Surg Oncol. 2022; 126:1288-1298.
4. Fairweather M, Gonzalez RJ, Strauss D, Raut CP. Current principles of surgery for retroperitoneal sarcomas. J Surg Oncol. 2018; 117:33-41.
5. Gronchi A, Miceli R, Allard MA, *et al*. Personalizing the approach to retroperitoneal soft tissue sarcoma: histology-specific patterns of failure and postrelapse outcome after primary extended resection. Ann Surg Oncol. 2015; 22:1447-1454.
6. Bonvalot S, Miceli R, Berselli M, Causeret S, Colombo C, Mariani L, Bouzaiene H, Le Péchoux C, Casali PG, Le Cesne A, Fiore M, Gronchi A. Aggressive surgery in retroperitoneal soft tissue sarcoma carried out at high-volume centers is safe and is associated with improved local control. Ann Surg Oncol. 2010; 17:1507-1514.
7. Gronchi A, Strauss DC, Miceli R, *et al*. Variability in patterns of recurrence after resection of primary retroperitoneal sarcoma (RPS): A report on 1007 patients from the multi-institutional collaborative RPS working group. Ann Surg. 2016; 263:1002-1009.
8. Smith HG, Panchalingam D, Hannay JA, Smith MJ, Thomas JM, Hayes AJ, Strauss DC. Outcome following resection of retroperitoneal sarcoma. Br J Surg. 2015; 102:1698-1709.
9. Lehnert T, Cardona S, Hinz U, Willeke F, Mechtersheimer G, Treiber M, Herfarth C, Buechler MW, Schwarzbach MH. Primary and locally recurrent retroperitoneal soft-tissue sarcoma: local control and survival. Eur J Surg Oncol. 2009; 35:986-993.
10. Hamilton TD, Cannell AJ, Kim M, Catton CN, Blackstein ME, Dickson BC, Gladdy RA, Swallow CJ. Results of resection for recurrent or residual retroperitoneal sarcoma after failed primary treatment. Ann Surg Oncol. 2017; 24:211-218.
11. Navas CM, Wadas ED, Zbib NH, Crowell MD, Lacy BE. Gastroparesis and severity of delayed gastric emptying: comparison of patient characteristics, treatments and medication adverse events. Dig Dis Sci. 2021; 66:526-534.
12. Akizuki E, Kimura Y, Nobuoka T, Imamura M, Nagayama M, Sonoda T, Hirata K. Reconsideration of postoperative oral intake tolerance after pancreaticoduodenectomy: Prospective consecutive analysis of delayed gastric emptying according to the ISGPS definition and the amount of dietary intake. Ann Surg. 2009; 249:986-994.
13. Kawai M, Tani M, Hirono S, Okada K, Miyazawa M, Yamaue H. Pylorus-resecting pancreaticoduodenectomy offers long-term outcomes similar to those of pylorus-preserving pancreaticoduodenectomy: Results of a prospective study. World J Surg. 2014; 38:1476-1483.
14. Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, Neoptolemos JP, Padbury RT, Sarr MG, Traverso LW, Yeo CJ, Büchler MW. Delayed gastric emptying (DGE) after pancreatic surgery: A suggested

definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery. 2007; 142:761-768.
15. Welsch T, Borm M, Degrate L, Hinz U, Büchler MW, Wente MN. Evaluation of the International Study Group of Pancreatic Surgery definition of delayed gastric emptying after pancreatoduodenectomy in a high-volume center. Br J Surg. 2010; 97:1043-1050.
16. Qu H, Sun GR, Zhou SQ, He QS. Clinical risk factors of delayed gastric emptying in patients after pancreaticoduodenectomy: a systematic review and meta-analysis. Eur J Surg Oncol. 2013; 39:213-223.
17. Park YC, Kim SW, Jang JY, Ahn YJ, Park YH. Factors influencing delayed gastric emptying after pylorus-preserving pancreatoduodenectomy. J Am Coll Surg. 2003; 196:859-865.
18. Kim DK, Hindenburg AA, Sharma SK, Suk CH, Gress FG, Staszewski H, Grendell JH, Reed WP. Is pylorospasm a cause of delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy? Ann Surg Oncol. 2005; 12:222-227.
19. Futagawa Y, Kanehira M, Furukawa K, Kitamura H, Yoshida S, Usuba T, Misawa T, Okamoto T, Yanaga K. Impact of delayed gastric emptying after pancreaticoduodenectomy on survival. J Hepatobiliary Pancreat Sci. 2017; 24:466-474.
20. Khan AS, Williams G, Woolsey C, Liu J, Fields RC, Doyle MMB, Hawkins WG, Strasberg SM. Flange gastroenterostomy results in reduction in delayed gastric emptying after standard pancreaticoduodenectomy: a prospective cohort study. J Am Coll Surg. 2017; 225:498-507.
21. Mirrielees JA, Weber SM, Abbott DE, Greenberg CC, Minter RM, Scarborough JE. Pancreatic fistula and delayed gastric emptying are the highest-impact complications after Whipple. J Surg Res. 2020; 250:80-87.
22. Eshuis WJ, van Eijck CH, Gerhards MF, Coene PP, de Hingh IH, Karsten TM, Bonsing BA, Gerritsen JJ, Bosscha K, Spillenaar Bilgen EJ, Haverkamp JA, Busch OR, van Gulik TM, Reitsma JB, Gouma DJ. Antecolic versus retrocolic route of the gastroenteric anastomosis after pancreatoduodenectomy: A randomized controlled trial. Ann Surg. 2014; 259:45-51.
23. Vandermeeren C, Loi P, Closset J. Does pancreaticogastrostomy decrease the occurrence of delayed gastric emptying after pancreatoduodenectomy? Pancreas. 2017; 46:1064-1068.
24. Hayama S, Senmaru N, Hirano S. Delayed gastric emptying after pancreatoduodenectomy: comparison between invaginated pancreatogastrostomy and pancreatojejunostomy. BMC Surg. 2020; 20:60.
25. Glowka TR, von Websky M, Pantelis D, Manekeller S, Standop J, Kalff JC, Schäfer N. Risk factors for delayed gastric emptying following distal pancreatectomy. Langenbeck's Arch Surg. 2016; 401:161-167.
26. Degisors S, Caiazzo R, Dokmak S, Truant S, Aussilhou B, Eveno C, Pattou F, El Amrani M, Piessen G, Sauvanet A. Delayed gastric emptying following distal pancreatectomy: incidence and predisposing factors. HPB (Oxford). 2022; 24:772-781.
27. Matsumoto S, Wakatsuki K, Migita K, Ito M, Nakade H, Kunishige T, Kitano M, Nakatani M, Sho M. Predictive factors for delayed gastric emptying after distal gastrectomy with Roux-en-Y reconstruction. Am Surg. 2018; 84:1086-1090.
28. Hirao M, Fujitani K, Tsujinaka T. Delayed gastric emptying after distal gastrectomy for gastric cancer. Hepatogastroenterology. 2005; 52:305-309.
29. Baia M, Conti L, Pasquali S, Sarre-Lazcano C, Abatini C, Cioffi SPB, Della Valle S, Greco G, Vigorito R, Casirati A, Proto P, Gavazzi C, Gronchi A, Fiore M. Delayed gastric emptying after multivisceral resection for retroperitoneal sarcoma. Ann Surg Oncol. 2022; 29:3264-3270.
30. Dindo D, Demartines N, Clavien P-A. Classification of surgical complications: A new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004; 240:205-213.
31. WHO Classification of Tumours Editorial Board. Soft Tissue and Bone Tumours. International Agency for Research on Cancer, Lyon, France, 2020.
32. Trojani M, Contesso G, Coindre JM, Rouesse J, Bui NB, de Mascarel A, Goussot JF, David M, Bonichon F, Lagarde C. Soft-tissue sarcomas of adults; study of pathological prognostic variables and definition of a histopathological grading system. Int J Cancer. 1984; 33:37-42.
33. Anaya DA, Lev DC, Pollock RE. The role of surgical margin status in retroperitoneal sarcoma. J Surg Oncol. 2008; 98:607-610.
34. Warshaw AL, Torchiana DL. Delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy. Surg Gynecol Obstet. 1985; 160:1-4.
35. MacNeill AJ, Gronchi A, Miceli R, *et al*. Postoperative morbidity after radical resection of primary retroperitoneal sarcoma: a report from the Transatlantic RPS Working Group. Ann Surg. 2018; 267:959-964.
36. Nessim C, Raut CP, Callegaro D, *et al*. Postoperative morbidity after resection of recurrent retroperitoneal sarcoma: a report from the Transatlantic Australasian RPS Working Group (TARPSWG). Ann Surg Oncol. 2021; 28:2705-2714.
37. van Berge Henegouwen MI, van Gulik TM, DeWit LT, Allema JH, Rauws EA, Obertop H, Gouma DJ. Delayed gastric emptying after standard pancreaticoduodenectomy versus pylorus-preserving pancreaticoduodenectomy: An analysis of 200 consecutive patients. J Am Coll Surg. 1997; 185:373-379.
38. Riediger H, Makowiec F, Schareck WD, Hopt UT, Adam U. Delayed gastric emptying after pylorus-preserving pancreatoduodenectomy is strongly related to other postoperative complications. J Gastrointest Surg. 2003; 7:758-765.
39. Baia M, Pasquali S, Fiore M. ASO Author Reflection: Delayed gastric emptying as a sentinel event of severe complications in retroperitoneal sarcoma surgery. Ann Surg Oncol. 2022; 29:3271-3272.
40. Lv A, Liu DN, Wang Z, Li CP, Liu BN, Liu Q, Tian XY, Hao CY. Short- and long-term surgical outcomes of pancreatic resection for retroperitoneal sarcoma: a long-term single-center experience of 90 cases. J Surg Oncol. 2022; 1-12.
41. Tseng WW, Tsao-Wei DD, Callegaro D, *et al*. Pancreaticoduodenectomy in the surgical management of primary retroperitoneal sarcoma. Eur J Surg Oncol. 2018; 44:810-815.
42. Flacs M, Faron M, Mir O, Mihoubi F, Sourouille I, Haddag-Miliani L, Dumont S, Terrier P, Levy A, Dousset B, Boudou-Rouquette P, Le Cesne A, Gaujoux S, Honoré C. Postoperative outcome of surgery with pancreatic resection for retroperitoneal soft tissue sarcoma: Results

of a retrospective bicentric analysis on 50 consecutive patients. J Gastrointest Surg. 2021; 25:2299-2306.
43. Bagaria SP, Swallow C, Suraweera H, *et al*. Morbidity and outcomes after distal pancreatectomy for primary retroperitoneal sarcoma: an analysis by the Trans-Atlantic Australasian Retroperitoneal Sarcoma Working Group. Ann Surg Oncol. 2021; 28:6882-6889.
44. Wang Z, Wu J, Lv A, Li C, Li Z, Zhao M, Hao C. Infiltration characteristics and influencing factors of retroperitoneal liposarcoma: Novel evidence for extended surgery and a tumor grading system. Biosci Trends. 2018; 12:185-192.
45. Bagaria SP, Neville M, Gray RJ, Gabriel E, Ashman JB, Attia S, Wasif N. The volume-outcome relationship in retroperitoneal soft tissue sarcoma: Evidence of improved short- and long-term outcomes at high-volume institutions. Sarcoma. 2018; 2018:3056562.
46. Keung EZ, Chiang YJ, Cormier JN, Torres KE, Hunt KK, Feig BW, Roland CL. Treatment at low-volume hospitals is associated with reduced short-term and long-term outcomes for patients with retroperitoneal sarcoma. Cancer. 2018; 124:4495-4503.

Received December 15, 2022; Revised January 27, 2023; Accepted February 5, 2023.

[§]These authors contributed equally to this work.

**Address correspondence to:*
Chunyi Hao, Department of Hepato-Pancreato-Biliary Surgery/Sarcoma Center, Peking University Cancer Hospital & Institute, No. 52, Fucheng Road, Haidian District, Beijing 100142, China.
E-mail: haochunyi@bjmu.edu.cn

Released online in J-STAGE as advance publication February 10, 2023.