Original Article

Check for updates

OPEN ACCESS

Received: Nov 2, 2019 Revised: Jan 2, 2020 Accepted: Feb 7, 2020

Correspondence to Ping Chen

Department of General Surgery, HwaMei Hospital, University of Chinese Academy of Sciences, Northwest Street 41, Haishu District, Ningbo 315010, China.

E-mail: chenpinghwamei@163.com

*Lihu Gu and Kang Zhang contributed equally to this work.

Copyright © 2020. Korean Gastric Cancer Association

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (https:// creativecommons.org/licenses/by-nc/4.0) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs

Lihu Gu https://orcid.org/0000-0003-3750-2939 Kang Zhang https://orcid.org/0000-0002-8521-0247 Zefeng Shen https://orcid.org/0000-0003-1233-2275 Xianfa Wang https://orcid.org/0000-0002-3761-9291 Hepan Zhu https://orcid.org/0000-0002-3761-9291 Junhai Pan https://orcid.org/0000-0002-4862-757X

Risk Factors for Duodenal Stump Leakage after Laparoscopic Gastrectomy for Gastric Cancer

Lihu Gu (¹)^{1,*}, Kang Zhang ¹)^{2,*}, Zefeng Shen ¹)³, Xianfa Wang ¹)³, Hepan Zhu ¹)³, Junhai Pan ¹)³, Xin Zhong ¹)³, Parikshit Asutosh Khadaroo ¹)⁴, Ping Chen ¹)¹

¹Department of General Surgery, HwaMei Hospital, University of Chinese Academy of Sciences, Ningbo, China

²Department of Clinical Medicine, Medical College of Ningbo University, Ningbo, China ³Department of General Surgery, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, China

⁴Department of Clinical Medicine, Monash University School of Medicine, Nursing and Health Sciences, Melbourne, Australia

ABSTRACT

Purpose: Duodenal stump leakage (DSL) is a potentially fatal complication that can occur after gastrectomy, but its underlying risk factors are unclear. This study aimed to investigate the risk factors and management of DSL after laparoscopic radical gastrectomy for gastric cancer (GC). **Materials and Methods:** Relevant data were collected from several prospective databases to retrospectively analyze the data of GC patients who underwent Billroth II (B-II) or Roux-

en-Y (R-Y) reconstruction after laparoscopic gastrectomy from 2 institutions (Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, and HwaMei Hospital, University of Chinese Academy of Sciences). The DSL risk factors were analyzed using univariate and multivariate analysis regression.

Results: A total of 810 patients were eligible for our analysis (426 with R-Y, 384 with B-II with Braun). Eleven patients had DSL (1.36%). Body mass index (BMI), elevated preoperative C-reactive protein (CRP) level, and unreinforced duodenal stump were the independent risk factors for DSL. DSL was diagnosed in 2–12 days, with a median of 8 days. Seven patients received conservative treatment, 3 patients received puncture treatment, and only 1 patient required reoperation. All patients recovered successfully after treatment.

Conclusions: The risk factors of DSL were BMI \geq 24 kg/m², elevated preoperative CRP level, and unreinforced duodenal stump. Nonsurgical treatments for DSL are preferred.

Keywords: Gastric cancer; Laparoscopic gastrectomy; Duodenal stump leakage; Risk factors

INTRODUCTION

Gastric cancer (GC) is the world's most common malignant disease and among the leading causes of cancer mortality [1]. Radical gastrectomy with lymph node dissection is currently the only potentially curative treatment method for patients with resectable GC [2]. Laparoscopic gastrectomy combined with lymph node dissection has become the preferred treatment for early GC [3,4]. Recent large multicenter randomized clinical trials have demonstrated that laparoscopic gastrectomy is both safe and effective for the treatment of advanced GC [5-7].

81

Journal of

. Gastric

Cancer

Xin Zhong 匝

https://orcid.org/0000-0002-8903-819X Parikshit Asutosh Khadaroo (b) https://orcid.org/0000-0003-4615-8551 Ping Chen (b) https://orcid.org/0000-0003-1440-0331

Author Contributions

Conceptualization: C.P.; Data curation: G.L., Z.K., Z.H., P.J., Z.X.; Formal analysis: K.P.A.; Investigation: G.L., Z.K., S.Z., S.Z., W.X., Z.H., P.J., Z.X., K.P.A., C.P.; Writing - original draft: G.L., S.Z., W.X.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Although the complications and mortality rates of laparoscopic gastrectomy have been very low with improvements in surgical techniques, periprocedural complications must be monitored [8,9]. Duodenal stump leakage (DSL), one of the most serious complications during gastrectomy, is a rare complication with up to 20% mortality rate [10]. DSL mainly occurs in patients undergoing Billroth II (B-II) and Roux-en-Y (R-Y) reconstructions in which a duodenal stump exists. Due to the higher requirements inherent to laparoscopic surgeries, difficulty persists regarding duodenal stump management and no consensual agreement has been reached regarding it in laparoscopic gastrectomy for GC.

Some studies stated that laparoscopic surgery would increase the incidence of DSL, therefore reinforcing that the duodenal stump can reduce DSL occurrence [11]. In contrast, most researchers believe that routine duodenal stump reinforcement was not necessary for gastrectomy [12-14]. A recent study of 965 patients from Japan showed that laparoscopic duodenal stump reinforcement reduced the incidence of DSL during R-Y reconstruction [15]. However, the study was limited to patients with early GC, and 70 patients had an unreinforced duodenal stump. Furthermore, reconstruction was limited to R-Y, as B-II was rarely performed in Japan. Therefore, this study lacked guiding significance by not including advanced GC and is not relevant for locations that perform B-II of reconstruction. Therefore, our study further investigated the risk factors of DSL after laparoscopic radical gastrectomy for GC and included patients with advanced GC and both reconstruction methods R-Y and B-II (B-II with Braun).

MATERIALS AND METHODS

Study population

The data of all patients diagnosed with GC who underwent laparoscopic gastrectomy with R-Y or B-II with Braun reconstruction between January 2013 and December 2018 at Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, and between January 2014 and December 2018 at HwaMei Hospital, University of Chinese Academy of Sciences, were extracted from a prospectively collected database and retrospectively analyzed in this study. The inclusion criteria were 1) with histologically proven primary gastric adenocarcinoma; 2) no history of gastrectomy or other malignant tumor; 3) pathologically negative resection margins (RO resection) and lymphadenectomy (D1+ or more); and 4) no combined viscera resection. This study was approved by the research Ethics Committee of Zhejiang University School of Medicine Sir Run Run Shaw Hospital and HwaMei Hospital, University of Chinese Academy of Sciences (NO.PJ-SRRSH-KY-2019-1-21-21 and NO.PJ-NBEY-KY-2019-032-15).

Surgical procedures

According to the Japanese Gastric Cancer Association guidelines, all patients underwent radical gastrectomy with lymphadenectomy (D1+ or D2–3) [16]. The duodenal stump was cut to about 2 cm long using a linear stapler. In the unreinforced group, no additional treatment was performed of the duodenal stump. In the reinforcement group, the duodenal stump was reinforced using several different methods, including continuous suture, interrupted suture, semi-pouch suture, and complete-pouch suture under laparoscopy, with all suturing performed by hand. The suture depth included the full or seromuscular layer. One or two abdominal drainage tubes were routinely left in the abdominal cavity after surgery [13,17-19].

Journal of Gastric Cancer



Surgical complications

DSL was defined as follows: presence of fluid in the surgical abdominal drain or after radiological drainage with at least 3 times higher bilirubin or amylase concentrations than normal serum value; or leakage through the abdominal wall regardless of its clinical impact confirmed by abdomen computed tomography (CT) and/or fistulography [20]. Complications were identified when they occurred in the first 30 days after surgery or during the postoperative hospital stay. The severity of surgical complications was evaluated according to Clavien-Dindo classification (C-D). Complications of C-D grade 3a and above were considered events [21].

Statistical analysis

Continuous data are presented as mean and standard deviation or median and range, while categorical data are presented as percentages. The potentially relevant factors obtained from the univariate analysis were assessed in the multivariate model using logistic regression. Odds ratios (OR) and 95% confidence intervals (CIs) were calculated. All statistical tests were performed 2-sided, and values of P<0.05 were considered statistically significant. The analyses were performed using SPSS software (version 25.0; SPSS Inc., Chicago, IL, USA).

RESULTS

From January 2013 to December 2018, 926 patients underwent laparoscopic gastrectomy at Zhejiang University School of Medicine Sir Run Shaw Hospital, and from January 2014 to December 2018, 668 patients underwent laparoscopic gastrectomy at HwaMei Hospital, University of Chinese Academy of Sciences. Among them, a total of 784 patients were excluded according to the inclusion criteria. Finally, 810 patients were eligible for the analysis (426 patients with R-Y, 384 patients with B-II with Braun) (**Fig. 1**).

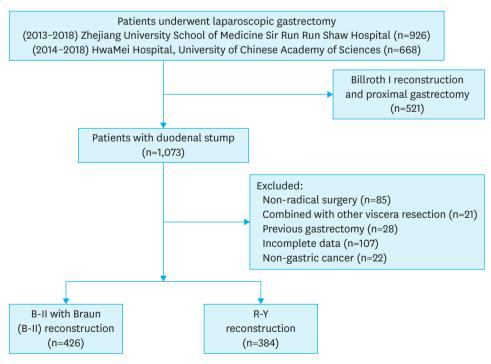


Fig. 1. Flow chart of the study population. B-II = Billroth II; R-Y = Roux-en-Y.



Regarding clinical features, there were more than twice as many males as females, and the vast majority (94%) of patients were American Society of Anesthesiologists (ASA) grade 1–2. Approximately one-third (26.8%) of the patients were overweight or obese, while one-third had (32.2%) varying degrees of anemia. Analysis of the surgical procedure was as follows: patients with distal gastrectomy and total gastrectomy were comparable, and the most common methods of reconstruction were R-Y and B-II with Braun. The median operation time was about 4 hours and the median blood loss was 70 mL. Of the cohort, 527 (65.1%) received duodenal stump reinforcement, while the remaining 283 patients did not receive duodenal stump reinforcement. Additionally, two-thirds of the patients had advanced GC (stages II–IIII) (**Table 1**).

Characteristics	Values
Age (yr)	62.5±12.9
Sex	
Male	596 (73.6)
Female	214 (26.4)
American Society of Anesthesiologists	
≤2	761 (94.0)
>2	49 (6.0)
Body mass index (kg/m²)	
<24	593 (73.2)
≥24	217 (26.8)
Neoadjuvant chemotherapy	
Absence	791 (97.7)
Presence	19 (2.3)
Carcinoembryonic antigen (ng/mL)	
≤5	757 (93.5)
>5	53 (6.5)
Preoperative C-reactive protein	()
Normal	708 (87.4)
Elevated	102 (12.6)
Neutrophil-to-lymphocyte ratio	.02 (.2.0)
≤3	569 (70.2)
>3	241 (29.8)
Preoperative hemoglobin (g/L)	2.1.(2010)
>120	549 (67.8)
90–120	174 (21.5)
<90	87 (10.7)
Preoperative albumin (g/L)	
>35	671 (82.8)
28-35	129 (15.9)
<28	10 (1.2)
Type of gastrectomy	()
Distal	480 (59.3)
Total	330 (40.7)
Reconstruction methods	
B-II	120 (14.8)
B-II with Braun	306 (37.8)
Roux-en-Y	384 (47.4)
Operation time (min)	230 (180–540)
≤210	364 (44.9)
>210	446 (55.1)
Intraoperative blood loss (mL)	70 (20–350)
≤50	. ,
	606 (74.8)
>50	204 (25.2)

Table 1. Baseline clinicopathological characteristics

Values are presented as mean±standard deviation or median (range), or number (%).

(continued to the next page)



Characteristics	Values
Reinforcement of duodenal stump	
Absence	283 (34.9)
Presence	527 (65.1)
No. of lymph nodes retrieved	27 (8–100)
<30	597 (73.7)
≥30	213 (26.3)
Tumor location	
Upper third	113 (14.0)
Middle third	177 (21.9)
Lower third	473 (58.4)
Two-thirds or more	47 (5.8)
Tumor size (cm)	4.8±2.7
≤5	594 (73.3)
>5	216 (26.7)
Histologic type	
Differentiated	367 (45.3)
Undifferentiated	443 (54.7)
Perineural invasion	
Absence	456 (56.3)
Presence	354 (43.7)
Lymphovascular invasion	
Absence	415 (51.2)
Presence	395 (48.8)
T category	
T1	220 (27.2)
T2	98 (12.1)
Т3	151 (18.6)
T4a	292 (36.0)
T4b	49 (6.0)
N category	
NO	353 (43.6)
N1	133 (16.4)
N2	132 (16.3)
N3a	158 (19.5)
N3b	34 (4.2)
TNM stage	
Stage I	261 (32.2)
Stage II	172 (21.2)
Stage III	377 (46.5)

Table 1. (Continued) Baseline clinicopathological characteristics

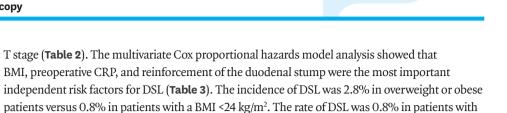
Values are presented as mean±standard deviation or median (range), or number (%).

Surgical complications

Complications of C-D grade 3–5 occurred in 90 patients (11.1%), including grade 3a in 73 cases, grade 3b in 13 cases, grade 4 in 2 cases, and grade 5 in 2 cases. Pulmonary complications occurred in 44 patients (5.4%). Other complications included anastomosis or stump leakage (n = 14), intestinal obstruction (n = 10), intra-abdominal abscess (n = 9), postoperative bleeding (n = 6), wound complications (n = 4), pancreatitis (n = 2), and cerebral infarction (n = 1). One patient died of a systemic infection secondary to an intra-abdominal abscess, while another died of respiratory failure. The overall mortality rate was 0.25%.

Risk factors for DSL

A total of 11 patients with DSL (1.36%) were observed. Twenty-four variable parameters were analyzed. On the univariate analysis, the following 5 clinicopathological characteristics were demonstrated to be potentially associated with DSL: body mass index (BMI), preoperative C-reactive protein (CRP), preoperative albumin, reinforcement of the duodenal stump, and



Journal of Gastric Cancer

Table 2. Univariate analysis of risk factors for duodenal stump leakage

normal CRP and 4.9% in patients with an elevated CRP (>6 mg/L). The DSL incidence in the duodenal stump reinforcement and unreinforced groups was 0.6% and 2.8%, respectively.

Characteristics	OR	95% CI	P-value
Age (yr)			
<60	Reference		
≥60	1.00	0.29-3.45	0.997
Sex			
Male	Reference		
Female	0.28	0.04-2.16	0.220
American Society of Anesthesiologists			
< <u>2</u>	Reference		
>2	1.25	0.44-3.53	0.673
Body mass index (kg/m²)			
<24	Reference		
≥24	2.22	1.19-4.12	0.012
Neoadjuvant chemotherapy			
Absence	Reference		
Presence	NA		
Carcinoembryonic antigen (ng/mL)			
≤5	Reference		
>5	2.58	0.32-20.80	0.375
Preoperative C-reactive protein			
Normal	Reference		
Elevated	6.03	1.81-20.14	0.003
Neutrophil-to-lymphocyte ratio			
≤3	Reference		
>3	0.52	0.11-2.43	0.406
Preoperative hemoglobin (g/L)			
>120	Reference		
90-120	1.05	0.21-5.26	0.950
<90	3.23	0.79-13.17	0.102
Preoperative albumin (g/L)			
>35	Reference		
28-35	1.31	0.27-6.22	0.619
<28	9.21	1.04-81.50	0.046
Type of gastrectomy			
Distal	Reference		
Total	1.27	0.54-2.00	0.621
Reconstruction methods			
B-II with Braun	Reference		
Roux-en-Y	1.34	0.41-4.42	0.634
Operation time (min)			
≤210	Reference		
>210	9.80	0.30-3.23	0.972
ntraoperative blood loss (mL)	0.00		
≤50	Reference		
>50	0.66	0.14-3.07	0.593
Reinforcement of duodenal stump	0.00		0.000
Absence	Reference		
Presence	0.20	0.05-0.75	0.017
No. of lymph nodes retrieved	0.20	0.05-0.75	0.017
<30	Reference		
≥30	1.61	0.47-5.57	0.449
200	not available.	0.4/-3.3/	0.449

OR = odds ratio; CI = confidence interval; NA = not available.

(continued to the next page)

Characteristics	OR	95% CI	P-value
Tumor location			
Upper third	Reference		
Middle third	0.96	0.16-5.82	0.962
Lower third	0.59	0.11-3.10	0.391
Two-thirds or more	1.21	0.11-13.64	0.879
Tumor size (cm)			
≤5	Reference		
>5	1.03	0.27-3.93	0.963
Histologic type			
Differentiated	Reference		
Undifferentiated	1.22	0.34-4.34	0.764
Perineural invasion			
Absence	Reference		
Presence	1.55	0.47-5.13	0.471
Lymphovascular invasion			
Absence	Reference		
Presence	1.27	0.38-4.18	0.700
T category			
T1	Reference		
T2	4.56	0.41-50.92	0.218
T3	NA		
T4a	3.82	0.44-32.89	0.223
T4b	14.28	1.45-140.39	0.023
N category			
NO	Reference		
N1	1.61	0.38-6.82	0.521
N2	NA		
N3a	0.89	0.17-4.65	0.892
N3b	2.11	0.24-18.59	0.502
TNM stage			
Stage I	Reference		
Stage II	2.30	0.38-13.90	0.365
Stage III	2.09	0.42-10.46	0.368

Table 2. (Continued) Univariate analysis of risk factors for duodenal stump leakage

OR = odds ratio; CI = confidence interval; NA = not available.

Details of patients with DSL

Among the patients with DSL, 10 were male and one was female. One patient had an ASA of 3 and the rest were ASA 1–2. The mean BMI was 23.9 kg/m²; 6 patients were overweight or obese (BMI >24 kg/m²). CRP was elevated in 5 patients before surgery. The duodenal stump was not reinforced in 8 cases. DSL was diagnosed in 2–12 days, with a median of 8 days. Seven patients received conservative treatment, 3 received puncture treatment, and 1 underwent reoperation. All patients recovered after treatment. The average postoperative hospitalization stay was 21 days (**Table 4**).

DISCUSSION

DSL is a rare complication of gastrectomy that has a high mortality rate. It can lead to intraabdominal infections and hemorrhage, significantly lengthening the postoperative hospital stay and increasing treatment costs and mortality rates [22,23]. In laparotomy, the duodenal stump is usually reinforced. Presently, minimally invasive techniques, especially laparoscopy, have been widely used in the surgical treatment of GC, but no consensus has been reached regarding duodenal stump management. Furthermore, the risk factors of DSL during a laparoscopic radical gastrectomy are controversial.



Table 3. Multivariate analysis of risk factors for duodenal stump leakage

Characteristics	OR	95% CI	P-value
Body mass index (kg/m²)			
<24	Reference		
≥24	2.39	1.27-4.52	0.007
Preoperative C-reactive protein			
Normal	Reference		
Elevated	7.44	2.12-26.11	0.002
Preoperative hemoglobin (g/L)			
>120	Reference		
90–120	NA		
<90	NA		
Preoperative albumin (g/L)			
>35	Reference		
28-35	NA		
<28	NA		
Reinforcement of duodenal stump			
Absence	Reference		
Presence	0.17	0.04-0.67	0.011
T category			
T1	Reference		
T2	NA		
Т3	NA		
T4a	NA		
T4b	NA		

OR = odds ratio; CI = confidence interval; NA = not available.

Bold words on behalf of the difference is statistically significant (p<0.05).

Table 4. Details of patients with DSL

No.*	Age	Sex	ASA	BMI (kg/m²)	CRP (mg/L)	HB (g/L)	Albumin (g/L)	Surgery	Reinforcement	Diagnostic time	TNM (8th)	Complications [†]	Treatment [‡]	PHD
1	75	Male	1	23.9	9.5	89	26.5	DG/B-II	Absence	POD 2	IIIB	Intraabdominal abscess, pulmonary infection	Puncture treatment	18
2	60	Male	1	26.1	45.5	137	36.7	TG/R-Y	Absence	POD 9	IIIB	Pulmonary infection	Puncture treatment	13
3	65	Male	1	23.2	2.3	87	39.0	TG/R-Y	Presence	PDO 3	IB	Pulmonary infection	Puncture treatment	17
4	71	Male	1	22.9	1.1	117	42.6	DG/B-II with Braun	Presence	POD 12	IIB	Intraabdominal abscess, pulmonary infection	Reoperation	29
5	70	Female	2	25.8	14.5	91	33.0	TG/R-Y	Presence	POD 9	IIIA	Pulmonary infection	Conservative treatment	23
6	74	Male	2	17.7	0.5	130	40.0	TG/R-Y	Absence	POD 6	IIB	Intraabdominal abscess, pulmonary infection	Conservative treatment	50
7	58	Male	2	24.7	8.3	85	34.9	TG/R-Y	Absence	POD 8	IIIC	Pulmonary infection; intestinal obstruction	Conservative treatment	30
8	59	Male	1	24.6	0.8	157	49.7	DG/B-II with Braun	Absence	POD 9	IIIB	Pulmonary infection	Conservative treatment	13
9	44	Male	1	27.7	1.0	141	46.2	DG/B-II with Braun	Absence	POD 2	IA		Conservative treatment	17
10	69	Male	3	24.6	1.2	123	43.3	DG/B-II with Braun	Absence	POD 9	IIA		Conservative treatment	13
11	62	Male	1	22.1	13.0	155	40.2	DG/R-Y	Absence	POD 4	IIIB		Conservative treatment	11

ASA = American Society of Anesthesiologists; BMI = body mass index; CRP = C-reactive protein; HB = hemoglobin; DG = distal gastrectomy; TG = total gastrectomy; R-Y = Roux-en-Y; B-II = Billroth II; POD = postoperative day; PHD = postoperative hospitalization days; DSL = duodenal stump leakage. *No patients received neoadjuvant chemotherapy; [†]Complications other than DSL (C-D grade 3–5); [‡]All patients recovered after treatment.



In this study, patients who received a laparoscopic radical gastrectomy with R-Y or B-II with Braun reconstruction for GC had a duodenal stump. The results showed that the incidence of DSL was 1.36%, consistent with previous studies. Cozzaglio et al. [11] analyzed more than 8,000 cases of GC (7,987 by the laparotomy, 281 by laparoscopy) and found that laparoscopic surgery increased the risk of DSL (OR, 5.6). On the contrary, Paik et al. [24] and Ali et al. [20], among most researchers, reported that laparoscopic gastrectomy was not related to the occurrence of DSL.

A series of clinical factors were analyzed in this study, and the results showed that age, sex, ASA score, carcinoembryonic antigen level, neutrophil-to-lymphocyte ratio, hemoglobin level, and albumin level were not significantly correlated with DSL. Interestingly, preoperative elevated CRP and overweight or obesity status were positively correlated with the incidence of DSL after laparoscopic gastrectomy. Some studies suggested that patients with multiple comorbidities and nutritional impairments might have a higher risk of DSL [23,24]. However, Ri's results were the same as ours [15], and the ASA score and nutritional status were not associated with DSL after laparoscopic gastrectomy. The reason may be due to the small number of patients with comorbidities and nutritional impairments included in this study. Obesity makes surgery more difficult and increases operative time. Moreover, patients with a higher BMI may be at higher risk of developing metabolic diseases such as type 2 diabetes or hypertension, which can also lead to a reduced ability to heal after surgery and ultimately increasing the risk of DSL. Although many previous studies reported no link between BMI and DSL [23,24,26], a recent study found that a BMI \ge 23 kg/m² could increase the risk of DSL with an OR of 9.26 [25]. Other complications have also been shown to increase in patients who were obese or had a high BMI [27,28].

Most importantly, our study showed that an elevated preoperative CRP level was one of the risk factors of DSL after laparoscopic gastrectomy. After reviewing previous studies, this is the first report of this phenomenon. However, the concrete mechanism for this remains unclear. Many previous studies have shown that the preoperative CRP level was an independent and significant indicator for elevated morbidity and mortality, including pulmonary resection [29], pancreaticoduodenectomy [30], and cardiac surgery [31]. In addition, other studies demonstrated that preoperative CRP could predict long-term survival for diseases such as colorectal cancer [32], GC [33,34], and renal cancer [35]. A recent randomized clinical trial showed that the preoperative CRP-albumin ratio was a promising predictor of early recurrence and postoperative adjuvant chemotherapy response [36]. However, the underlying molecular biological mechanism has not yet been elucidated.

The relationship between surgical parameters and DSL is controversial. Orsenigo et al. [24], Ri et al. [25], and Ramos et al. [26] suggested that the D2 lymph node dissection and subtotal gastrectomy were the risk factors for DSL, but our results were similar to those of most studies except for duodenal stump reinforcement, other factors including gastrectomy type, reconstruction method, operative time, intraoperative blood loss, and lymph node dissection had no direct relationship with DSL occurrence. A phase 2 clinical trial involving 100 patients showed that laparoscopic reinforcement suturing prevented DSL [37]. Two previous studies showed that laparoscopic duodenal stump reinforcement reduced the risk of DSL. Nonetheless, R-Y was used in these 2 studies [24,25]. Furthermore, duodenal stump reinforcement could not only reduce the incidence of DSL, it could reduce its severity after laparoscopic gastrectomy. Duodenal stump reinforcement increased the duration of surgery but did not increase the risk of intraoperative blood loss or other complications. A linear stapling device with bioabsorbable



polyglycolic acid sheets could be used to reinforce the duodenal stump without the need for manual suturing, ultimately reducing the incidence of DSL [38].

No association between tumor characteristics (including location, size, differentiation, and Tumor Node Metastasis stage) and DSL was found in this study. According to Ramos et al. [26], a tumor in the distal stomach was a risk factor for DSL. More importantly, DSL might reduce long-term survival for patients with GC. Gastric outlet obstruction was thought to increase the occurrence of DSL in Paik's study [23]. The underlying mechanism may be that tumors located in the distal stomach are more prone to gastric outlet obstruction, which increases the risk of mucosal edema and impaired systemic nutrition, all of which increase the risk of DSL.

DSL is one of the most serious complications; fortunately, all patients recovered after treatment in this study. Numerous studies including this one showed that although DSL can occur at different periods after surgery, the most common period is about 1 week postoperative. A systematic review of 20 studies including 294 patients with DSL showed that the DSL diagnosis occurred between the fifth and tenth postoperative days [39]. Many patients with DSL developed more than one complication, including but not limited to sepsis, abdominal abscess, wound infection, pneumonia, and intra-abdominal bleeding. In this study, some patients with DSL had other complications, but none were serious. Our experience was that early intervention was needed once these complications occurred.

For example, if the patient has a small amount of abdominal fluid with a low-grade fever or normal body temperature, especially if the drainage tube can successfully drain fluids around the duodenal stump, conservative treatment (antibiotics and enhanced nutritional support) may be appropriate. Additionally, if the patient's abdominal cavity effusion can be resolved using puncture treatment, a conservative treatment approach can be selected. Surgical treatment decisions should be based on a patient's situation and symptoms. If the patient has recurrent or increased abdominal effusion or continues to suffer from a repeated high fever and fails to respond to antibiotic treatment, guided ultrasound or CT puncture drainage should be used and the drainage fluid should be cultured to develop a specific treatment plan. In the event that conservative or puncture treatment fails and fluid accumulation is increased excessively or if the fluid accumulation in the abdominal cavity is intractable despite measures taken, surgical treatment should be provided as soon as possible. It must be emphasized that patients must be kept under close observation to reduce the possibility of conservative treatment-induced aggravations.

The treatment of DSL includes conservative, percutaneous, endoscopic, and surgical treatments. Nonsurgical treatments are typically the preferred choice. The surgical approach should be reserved for severe cases or those in which nonsurgical approaches fail. Cornejo et al. [40] believed that conservative management had better outcomes than surgery. Paik et al. [23] reported 16 cases of DSL, 3 of which were treated with reoperation; all patients had to undergo reoperation 1–2 days after surgery. Ali et al. [19] reported that all patients with DSL (n = 19) were successfully treated nonsurgically and no patients died. A study included 10 patients with DSL, 4 of whom received unreinforced duodenal stump and underwent reoperation after DSL. In contrast, 6 patients were treated with duodenal stump reinforcement after the diagnosis of DSL; of them, only 1 needed reoperation, while the rest received conservative treatment [25]. Other studies reported the use of endoscopic clipping in the treatment of DSL [41].



This study is of particular importance in China as 1 to 2 intra-abdominal drainage tubes are routinely indurated after gastrectomy, one close to the duodenal stump, if present. DSL can be diagnosed according to the amylase level of the drainage tube fluid. Moreover, once the diagnosis is made, this drainage tube can continue to drain the fluid around the stump, reducing the risk of intra-abdominal infection and facilitating duodenal stump healing. As a result, the proportion of patients receiving conservative treatment in this study was significantly higher. However, Schots et al. [42] believed that abdominal drainage and amylase measurement did not influence the early recognition and management of leakage in GC, but his study included only 3 patients with DSL. Therefore, we recommend that the duodenal stump be reinforced during laparoscopic radical gastrectomy to reduce the risk of DSL, especially for patients with risk factors.

Although we adopted a scientific and rigorous method for analysis, the study still has shortcomings. It was a retrospective study with some inevitable defects, including selection bias and recall bias. In addition, the patients included in this study were from China, a region with a high incidence of GC; thus, this conclusion might not be directly applicable to Western countries. Most importantly, because this was a retrospective study, the indications for duodenal stump reinforcement are unclear and mostly determined by surgeon experience. This study aimed to confirm the significance of duodenal stump reinforcement and clarify its necessity. Finally, the methods of duodenal stump reinforcement varied, and their differences could not be analyzed. Therefore, the conclusions of this study must be further verified by large multicenter clinical trials.

In conclusion, our research shows that DSL after laparoscopic radical gastrectomy for GC is rare. The main risk factors for DSL are obesity, increased preoperative CRP level, and an unreinforced duodenal stump.

REFERENCES

- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
 PUBMED | CROSSREF
- Sasako M, Sano T, Yamamoto S, Kurokawa Y, Nashimoto A, Kurita A, et al. D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer. N Engl J Med 2008;359:453-462.
 PUBMED | CROSSREF
- Lee CM, Park S, Park SH, Jung SW, Choe JW, Sul JY, et al. Sentinel node mapping using a fluorescent dye and visible light during laparoscopic gastrectomy for early gastric cancer: result of a prospective study from a single institute. Ann Surg 2017;265:766-773.
 PUBMED | CROSSREF
- Jung DH, Lee Y, Kim DW, Park YS, Ahn SH, Park DJ, et al. Laparoscopic proximal gastrectomy with double tract reconstruction is superior to laparoscopic total gastrectomy for proximal early gastric cancer. Surg Endosc 2017;31:3961-3969.
 PUBMED | CROSSREF
- Yu J, Huang C, Sun Y, Su X, Cao H, Hu J, et al. Effect of laparoscopic vs open distal gastrectomy on 3-year disease-free survival in patients with locally advanced gastric cancer: the CLASS-01 randomized clinical trial. JAMA 2019;321:1983-1992.
 PUBMED | CROSSREF
- Lee HJ, Hyung WJ, Yang HK, Han SU, Park YK, An JY, et al. Short-term outcomes of a multicenter randomized controlled trial comparing laparoscopic distal gastrectomy with D2 lymphadenectomy to open distal gastrectomy for locally advanced gastric cancer (KLASS-02-RCT). Ann Surg 2019;270:983-991.
 PUBMED | CROSSREF



- Kinoshita T, Uyama I, Terashima M, Noshiro H, Nagai E, Obama K, et al. Long-term outcomes of laparoscopic versus open surgery for clinical stage II/III gastric cancer: a multicenter cohort study in Japan (LOC-A Study). Ann Surg 2019;269:887-894.
 PUBMED | CROSSREF
- Lee MS, Ahn SH, Lee JH, Park DJ, Lee HJ, Kim HH, et al. What is the best reconstruction method after distal gastrectomy for gastric cancer? Surg Endosc 2012;26:1539-1547.
- Kawamura H, Ohno Y, Ichikawa N, Yoshida T, Homma S, Takahashi M, et al. Anastomotic complications after laparoscopic total gastrectomy with esophagojejunostomy constructed by circular stapler (OrVil[™]) versus linear stapler (overlap method). Surg Endosc 2017;31:5175-5182.
 PUBMED | CROSSREF
- Aurello P, Sirimarco D, Magistri P, Petrucciani N, Berardi G, Amato S, et al. Management of duodenal stump fistula after gastrectomy for gastric cancer: systematic review. World J Gastroenterol 2015;21:7571-7576.
 PUBMED | CROSSREF
- Cozzaglio L, Giovenzana M, Biffi R, Cobianchi L, Coniglio A, Framarini M, et al. Surgical management of duodenal stump fistula after elective gastrectomy for malignancy: an Italian retrospective multicenter study. Gastric Cancer 2016;19:273-279.
 PUBMED | CROSSREF
- Inokuchi M, Nakagawa M, Tanioka T, Okuno K, Gokita K, Kojima K. Long- and short-term outcomes of laparoscopic gastrectomy versus open gastrectomy in patients with clinically and pathological locally advanced gastric cancer: a propensity-score matching analysis. Surg Endosc 2018;32:735-742.
 PUBMED
- Kim CH, Song KY, Park CH, Seo YJ, Park SM, Kim JJ. A comparison of outcomes of three reconstruction methods after laparoscopic distal gastrectomy. J Gastric Cancer 2015;15:46-52.
 PUBMED | CROSSREF
- Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2010 (ver. 3). Gastric Cancer 2011;14:113-123.
 PUBMED | CROSSREF
- Ri M, Hiki N, Ishizuka N, Ida S, Kumagai K, Nunobe S, et al.. Duodenal stump reinforcement might reduce both incidence and severity of duodenal stump leakage after laparoscopic gastrectomy with Rouxen-Y reconstruction for gastric cancer. Gastric Cancer 2019;22:1053-1059.
 PUBMED | CROSSREF
- Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2014 (ver. 4). Gastric Cancer 2017;20:1-19.
 PUBMED | CROSSREF
- Komatsu S, Ichikawa D, Kubota T, Okamoto K, Shiozaki A, Fujiwara H, et al. Clinical outcomes and quality of life according to types of reconstruction following laparoscopy-assisted distal gastrectomy for gastric cancer. Surg Laparosc Endosc Percutan Tech 2015;25:69-73.
 PUBMED | CROSSREF
- Okuno K, Nakagawa M, Kojima K, Kanemoto E, Gokita K, Tanioka T, et al. Long-term functional outcomes of Roux-en-Y versus Billroth I reconstructions after laparoscopic distal gastrectomy for gastric cancer: a propensity-score matching analysis. Surg Endosc 2018;32:4465-4471.

 PUBMED | CROSSREF
- Songun I, Putter H, Kranenbarg EM, Sasako M, van de Velde CJ. Surgical treatment of gastric cancer: 15year follow-up results of the randomised nationwide Dutch D1D2 trial. Lancet Oncol 2010;11:439-449.
 PUBMED | CROSSREF
- Ali BI, Park CH, Song KY. Outcomes of non-operative treatment for duodenal stump leakage after gastrectomy in patients with gastric cancer. J Gastric Cancer 2016;16:28-33.
 PUBMED | CROSSREF
- Dindo D, Demartines N, Clavien PA. 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.
 PUBMED | CROSSREF
- Cozzaglio L, Cimino M, Mauri G, Ardito A, Pedicini V, Poretti D, et al. Percutaneous transhepatic biliary drainage and occlusion balloon in the management of duodenal stump fistula. J Gastrointest Surg 2011;15:1977-1981.
 PUBMED | CROSSREF
- Kang KC, Cho GS, Han SU, Kim W, Kim HH, Kim MC, et al. Comparison of Billroth I and Billroth II reconstructions after laparoscopy-assisted distal gastrectomy: a retrospective analysis of large-scale multicenter results from Korea. Surg Endosc 2011;25:1953-1961.
 PUBMED | CROSSREF



- Paik HJ, Lee SH, Choi CI, Kim DH, Jeon TY, Kim DH, et al. Duodenal stump fistula after gastrectomy for gastric cancer: risk factors, prevention, and management. Ann Surg Treat Res 2016;90:157-163.
 PUBMED | CROSSREF
- Orsenigo E, Bissolati M, Socci C, Chiari D, Muffatti F, Nifosi J, et al. Duodenal stump fistula after gastric surgery for malignancies: a retrospective analysis of risk factors in a single centre experience. Gastric Cancer 2014;17:733-744.
 PUBMED | CROSSREF
- 26. Ramos MF, Pereira MA, Barchi LC, Yagi OK, Dias AR, Szor DJ, et al. Duodenal fistula: the most lethal surgical complication in a case series of radical gastrectomy. Int J Surg 2018;53:366-370.
 PUBMED | CROSSREF
- Takeuchi M, Ishii K, Seki H, Yasui N, Sakata M, Shimada A, et al. Excessive visceral fat area as a risk factor for early postoperative complications of total gastrectomy for gastric cancer: a retrospective cohort study. BMC Surg 2016;16:54.
 PUBMED | CROSSREF
- McDermott FD, Heeney A, Kelly ME, Steele RJ, Carlson GL, Winter DC. Systematic review of preoperative, intraoperative and postoperative risk factors for colorectal anastomotic leaks. Br J Surg 2015;102:462-479.
 PUBMED | CROSSREF
- Lopez-Pastorini A, Riedel R, Koryllos A, Beckers F, Ludwig C, Stoelben E. The impact of preoperative elevated serum C-reactive protein on postoperative morbidity and mortality after anatomic resection for lung cancer. Lung Cancer 2017;109:68-73.
 PUBMED | CROSSREF
- Mansukhani V, Desai G, Shah R, Jagannath P. The role of preoperative C-reactive protein and procalcitonin as predictors of post-pancreaticoduodenectomy infective complications: a prospective observational study. Indian J Gastroenterol 2017;36:289-295.

 PUBMED | CROSSREF
- Perry TE, Muehlschlegel JD, Liu KY, Fox AA, Collard CD, Body SC, et al. Preoperative C-reactive protein predicts long-term mortality and hospital length of stay after primary, nonemergent coronary artery bypass grafting. Anesthesiology 2010;112:607-613.
 PUBMED | CROSSREF
- Egenvall M, Mörner M, Martling A, Gunnarsson U. Prediction of outcome after curative surgery for colorectal cancer: preoperative haemoglobin, C-reactive protein and albumin. Colorectal Dis 2018;20:26-34.
 PUBMED | CROSSREF
- 33. Kim EY, Yim HW, Park CH, Song KY. C-reactive protein can be an early predictor of postoperative complications after gastrectomy for gastric cancer. Surg Endosc 2017;31:445-454.
 PUBMED | CROSSREF
- 34. Crumley AB, McMillan DC, McKernan M, Going JJ, Shearer CJ, Stuart RC. An elevated C-reactive protein concentration, prior to surgery, predicts poor cancer-specific survival in patients undergoing resection for gastro-oesophageal cancer. Br J Cancer 2006;94:1568-1571. PUBMED | CROSSREF
- 35. Johnson TV, Abbasi A, Owen-Smith A, Young A, Ogan K, Pattaras J, et al. Absolute preoperative C-reactive protein predicts metastasis and mortality in the first year following potentially curative nephrectomy for clear cell renal cell carcinoma. J Urol 2010;183:480-485.
 PUBMED | CROSSREF
- 36. Xu BB, Lu J, Zheng ZF, Xie JW, Wang JB, Lin JX, et al. The predictive value of the preoperative C-reactive protein-albumin ratio for early recurrence and chemotherapy benefit in patients with gastric cancer after radical gastrectomy: using randomized phase III trial data. Gastric Cancer 2019;22:1016-1028. PUBMED | CROSSREF
- Kim MC, Kim SY, Kim KW. Laparoscopic reinforcement suture (LARS) on staple line of duodenal stump using barbed suture in laparoscopic gastrectomy for gastric cancer: a prospective single arm phase II study. J Gastric Cancer 2017;17:354-362.
 PUBMED | CROSSREF
- Misawa K, Yoshikawa T, Ito S, Cho H, Ito Y, Ogata T. Safety and feasibility of linear stapling device with bioabsorbable polyglycolic acid sheet for duodenal closure in gastric cancer surgery: a multi-institutional phase II study. World J Surg 2019;43:192-198.
 PUBMED | CROSSREF
- Zizzo M, Ugoletti L, Manzini L, Castro Ruiz C, Nita GE, Zanelli M, et al. Management of duodenal stump fistula after gastrectomy for malignant disease: a systematic review of the literature. BMC Surg 2019;19:55.
 PUBMED | CROSSREF

https://jgc-online.org



- Cornejo ML, Priego P, Ramos D, Coll M, Ballestero A, Galindo J, et al. Duodenal fistula after gastrectomy: retrospective study of 13 new cases. Rev Esp Enferm Dig 2016;108:20-26.
- Lee JY, Ryu KW, Cho SJ, Kim CG, Choi IJ, Kim MJ, et al. Endoscopic clipping of duodenal stump leakage after Billroth II gastrectomy in gastric cancer patient. J Surg Oncol 2009;100:80-81.
 PUBMED | CROSSREF
- Schots JP, Luyer MD, Nieuwenhuijzen GA. Abdominal drainage and amylase measurement for detection of leakage after gastrectomy for gastric cancer. J Gastrointest Surg 2018;22:1163-1170.
 PUBMED | CROSSREF