CLINICAL RESEARCH

e-ISSN 1643-3750 © Med Sci Monit, 2020; 26: e919003 DOI: 10.12659/MSM.919003

Received: 2019.07.25 Accepted: 2020.02.14 Available online: 2020.03.23 Published: 2020.05.09

The Retropancreatic Fusion Fascia Oriented Splenic Hilar Lymphadenectomy Versus Laparoscopic Approach In D2 Total Gastrectomy

uthor Da itatisi ata Ir scrip Liter Fun	s' Contribution: Study Design A ta Collection B tical Analysis C nterpretation D t Preparation E rature Search F ds Collection G	ABCDEF ABC ABCDE ABCD ABCDEFG	Mengyin Peng Jian Liu XiaoBo Yang ShiChen Liu Miao Wu	Department of Gastrointestinal Surgery, The Second People's Hospital of Yibin, Sichuan, Chengdu, P.R. China		
	Corresponding Sources of	g Author: support:	Miao Wu, e-mail: 13990905852@163.com Departmental sources			
Background:		ground:	The retropancreatic fusion fascia is recognized as the anatomical landmark during retropancreatic mobilization. However, its role in D2 total gastrectomy for proximal advanced gastric cancer (PAGC) remains unexplored. This study aimed to develop the retropancreatic fusion fascia-oriented <i>ex vivo</i> approach for splenic hilar lymphadenectomy (RP-SL) to avoid difficulty in using the total laparoscopic approach (TL-SL).			
	Material/Me	esults:	ical database and electronic medical records (E ratio for balance of the 2 groups. In sum, 84 matched patients were included in the with an average of 28.10. Sixteen patients were	estudy. There were 2360 retrieved lymph nodes (LNs), confirmed with positive splenic hilar lymphadenec-		
	Conclu	usions:	tomy, and the mean harvested lymph nodes (LNs) pared to the TL-SL group (3.07 vs. 2.29, P<0.001), P<0.001), and less blood loss (96.90 mL vs. 185.24 pital stay (6.55 days vs. 7.26 days), rate of morbid ¥64419.91) were comparable between the groups The landmark at the conjunction between the su atic margin made it feasible to identify the ret and efficient for splenic hilar lymphadenectomy	were significantly increased in the RP-SL group com- decreased operative time (193.21 min vs. 247.74 min, mL, P=0.001) in the RP-SL group. Postoperative hos- ity (9.50% vs. 11.91%), and overall costs (¥65255.64 vs. s (P>0.05). uperior mesenteric vessels and the inferior pancre- ropancreatic areolar. The RP-SL approach was safe <i>y</i> .		
MeSH Keywords:			Fascia • Hand-Assisted Laparoscopy • Lymph Node Excision • Stomach Neoplasms			
	Full-te	xt PDF:	https://www.medscimonit.com/abstract/index/	/idArt/919003		
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Background

The global incidence and mortality of gastric cancer have been steadily declining in consecutive decades, with similar trends in China [1,2]. The incidence of proximal gastric cancer, however, has steadily increased. Additionally, most patients were diagnosed at advanced stage due to the lack of wide-spread screening [2–5].

Radical surgery, standard as D2 total gastrectomy, still remains the cornerstone for patients with proximal advanced gastric cancer (PAGC), according to the Japanese gastric cancer treatment guidelines [6]. Several studies have reported that the metastatic rate of splenic hilar lymph node (SHLN) is 7.9% to 20.9% [7–9], which indicates the necessity of a thorough dissection of this group of lymph nodes (LNS). There has been much debate concerning the surgical approaches of splenic hilar lymphadenectomy (SHL) due to the narrow location and the variable vessels at the splenic hilum [10].

Synchronous splenectomy used to be the consensus to assure LN dissection, regardless of the tumor location and depth. Nevertheless, sufficient evidence has documented the unsatisfactory postoperative outcomes [11,12]. The JCOG 0110 trial also concluded that the 5-year survival rate was comparable between the splenectomy and the spleen preservation groups [13]. Because post-splenectomy immunosuppression carries a high risk of early recurrence or peritoneal/distal metastasis, surgeons are less likely to use a traumatic strategy [14].

Combined with knowledge of the perigastric lymphatic system, spleen-preserving splenic hilar lymphadenectomy (SPSL) in D2 total gastrectomy has been widely accepted. The total laparoscopic splenic hilar lymphadenectomy (TL-SL) approach, however, is difficult and requires a highlevel technique. Several surgical techniques have been introduced to simplify the procedure, including the ultramodern Da-Vinci robotic system [15-21]. Hyung et al. reported the first laparoscopic SPSL strategy and suggested that the organ preservation strategy was safe and feasible, and obtained an adequate number of harvested LNs [22]. Since then, it has been instrumental in exploring the total laparoscopic approach. Li et al. proposed a modified approach, with acceptable surgical and short-term outcomes [18]. Both of these modular surgeries, however, involve intricate procedures for precise skeletonization and dissection. Similar dilemmas exist in the omnibearing method, as reported by Wang [21]. Huang's three-step maneuver is a modular surgical procedure, but it also demands delicate cooperation and has a steep learning curve [15]. To the best of our knowledge, epigastric minilaparotomy is required for specimen retraction, unless the Natural Orifice Specimen Extraction Surgery (NOSES) is performed in selected female patients.

The retropancreatic fusion fascia is an important anatomical landmark during retropancreatic mobilization in pancreaticoduodenectomy [23]. The fascial configuration of the retropancreatic suggests that the fusion fascia consist of peritoneal and retroperitoneal elements, and is unlikely to be a remnant of the peritoneum. The pancreatic nerve plexus is also thought to be located between the retropancreatic fusion fascia and the pancreatic capsule [24]. The renal vessels and nerves are beneath the Gerota fascia [25]. The avascular retropancreatic areolar between the 2 facias is a crucial surgical plane in pancreaticoduodenal cancer, but it is not reported in D2 total gastrectomy.

In the present study we explored a new procedure of SHL, always using minilaparotomy. We proposed that the retropancreatic fusion fascia-oriented *ex vivo* splenic hilar lymphadenectomy (RP-SL) simplifies the surgical procedure, and evaluated the effectiveness and the safety of this new technique compared to the TL-SL approach in D2 total gastrectomy.

Material and Methods

Patients

From December 2016 to December 2018, the clinical data of 84 patients who were diagnosed with PAGC and who underwent D2 total gastrectomy at the Second People's Hospital of Yibin, were retrospectively collected. None of them had received preoperative chemotherapy, but postoperative adjuvant chemotherapy was initiated with the intention of reducing recurrence following curative resection. There were 42 patients in the TL-SL group and 42 in the group using the retropancreatic fusion fascia-oriented *ex vivo* approach (RP-SL). The selection criteria were: 1) age \geq 18 years, without limitation of sex; 2) patients diagnosed as PAGC through postoperative biopsy; 3) tumor not invading the greater curvature or bulky LNs in the splenic hilum; and 4) all of the included surgeries were performed at the scheduled time.

The exclusion criteria were: 1) history of other malignancies or with confirmed distant metastasis; 2) history of previous major surgery involving the upper abdomen; 3) gastric stromal tumor or lymphoma; and 4) emergency surgery for severe bleeding, obstruction, or perforation.

Ethics and consent

The study protocol was approved by the Institutional Review Board and Human Ethics Committee of the Second People's Hospital of Yibin, Sichuan, China, and the study was performed in accordance with the 1975 Declaration of



Figure 1. The trocar position and the epigastric minilaparoytomy.

Helsinki (approval 2019.10.01). The requirement for written informed consent was exempted by the Ethics Committee because this was a retrospective study, and the patients' information was maintained with strict confidentiality.

Surgical technique

The perigastric LNs were classified according to the Japanese Classification of Gastric Carcinoma (JCGC) guidelines [10]. The RP-SL was proposed to simplify the procedure.

The patients received general anesthesia and were placed in a supine position with legs set apart in a reverse Trendelenburg position. The surgeon was on the left side, the assistant was on the right side, and the camera assistant was positioned between the patient's legs. Five trocars were placed (Figure 1) for the manipulation.

Surgery commenced with the separation of the gastrocolic ligament, left to the splenic flexure and to the lower left corner of lesser omentum sac, and right to the hepatic flexure, expanding the anterior pancreaticoduodenal space oriented by the middle colonic vessel. The duodenum was transected 2 cm distal to the pylorus. The surgery continued along the common hepatic artery.

The stomach and omentum, fixed with a thread, were turned laterally and cephalad. Afterward, it was pivotal to enter the retropancreatic areolar by the anatomical landmark located



Figure 2. The landmark at the conjunction of the superior mesenteric vessels and inferior pancreatic margin.



Figure 3. The avascular retropancreatic areolar between the retropancreatic fusion fascia and the Gerota fascia.

at the conjunction between the superior mesenteric vessels and the inferior pancreatic margin (Figure 2). The assistant lifted the pancreas and maintained appropriate tension without intricate gesture alteration. The surgeon could mobilize and expand the avascular retropancreatic areolar along the retropancreatic fusion fascia using an electrotome, expanding to the confluence of the inferior mesenteric vein and the splenic vein, cephalad to the posterior gastric space and left to the spleen. The left subphrenic fundus gastric artery and the splenic ligaments were then snipped (Figure 3).

Thereafter, the stomach, omentum, spleen, and the pancreatic body and tail were retracted through the epigastric minilaparotomy for SHL, which was only used for specimen retraction in the TL-SL approach.

The LNs were dissected along the splenic hilum to the proximal splenic lobar vessels, and along the splenic artery toward the midline, up to the celiac trunk. Therefore, the No. 10a, No. 10p, No. 11da, and No. 11dp could be eliminated more efficiently and straightforward under direct vision. A Roux-en-Y esophagojejunostomy was performed in the digestive tract reconstruction.

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Table 1. Comparison of clinical characteristic between the two groups.

Variables	Ex	vivo group	In vivo group		P value
Gender					0.510
Male	17	(40.5%)	20	(47.6%)	
Female	25	(59.5%)	22	(52.4%)	
Smoking					0.826
Yes	24	(57.1%)	23	(54.8%)	
No	18	(42.9%)	19	(45.2%)	
Alcohol					0.113
Yes	12	(28.6%)	19	(45.2%)	
No	30	(71.4%)	23	(54.8%)	
ASA score					0.965
I	10	(23.8%)	10	(23.8%)	
II	21	(50.0%)	22	(52.4%)	
III	11	(26.2%)	10	(23.8%)	
Comorbidity					0.503
Yes	18	(42.9%)	15	(35.7%)	
No	24	(57.1%)	27	(64.3%)	
NRS2002 score					0.242
<3	37	(88.1%)	33	(78.6%)	
≥3	5	(11.9%)	9	(21.4%)	
Age	62.12±9.53		60.74±9.16		0.500
BMI	22.04±3.04		21.92±3.60		0.872
AFP (ng/mL)		3.66±3.02		3.80±2.83	0.879*
CEA (ng/mL)	2.58±2.36		2.71±2.63		0.879*
HGB (g/L)	109.91±27.19		113.12±22.56		0.558
ALB (g/L)	3	5.78±5.85	33	3.20±6.28	0.055

NRS2002 score within 24 hours of hospitalization. CEA – Carcinoembryonic antigen; AFP – alpha-fetoprotein; HGB – hemoglobin; ALB – albumin. * Mann-Whitney U test.

Statistical analysis

The IBM SPSS statistics software package (Version 24.0 for computer; IBM Corp., NY, USA) was used to conduct all of the statistical analyses. Continuous data were expressed as the mean±standard deviation values. Factors such as age, sex, body mass index (BMI), operation time, estimated blood loss, tumor size, location, histology, TNM staging, postoperative hospital stay (POD), comorbidity, and mortality were included in the final analyses. Categorical and continuous variables were appropriately analyzed using the chisquare test, Fisher's exact test, and t test, respectively, and the Mann-Whitney U test was used for the non-normally distributed data. A two-tailed P<0.05 was regarded as statistically significant.

Results

The present study included 84 patients with a 1:1 ratio in the RT-SL and L-SL groups. Evidence of ascites in 8 patients was confirmed to be negative. All of the laparoscopic splenic hilar lymphadenectomy procedures were performed without conversion, but splenic lobar artery injury occurred in 1 patient. The clinicopathological characteristics, surgical information, and postoperative short-term outcomes were compared, as shown in the tables. There were no significant differences in age, BMI, NRS2002 scores (Table 1), differentiation, tumor size, depth of tumor invasion, and TNM staging between the 2 groups (Table 2). There were 2360 harvested LNs, with an average of 28.1. A total of 527 (22.33%) LNs were confirmed to be positive. In total, 69 (82.14%) patients were confirmed with positive perigastric LNs, and 16 (19.05%) cases were confirmed with positive SHLN.

The conjunction between the superior mesenteric vessels and inferior pancreatic margin was a conspicuous anatomical landmark to identify the retropancreatic areolar, which was located between the posterior pancreatic fusion fascia and the Gerota fascia. None of the 42 RP-SL patients had intraoperative injury. There was a significant difference in the operation time between the groups (193.21±50.03 min vs. 247.74±72.29 min, P<0.001), as well as in the intraoperative blood loss (96.90±23.58 mL vs. 185.24±140.70 mL, P<0.001) (Table 2). The length of the epigastric minilaparotomy was 6.25±1.29 cm and 6.12±0.99 cm, respectively. In addition, the mean number of retrieved LNs was 28.1, and the harvested splenic hilar LNs was 3.07±0.84 and 2.29±0.86 in the 2 groups. Sixteen patients were confirmed with positive SHLN, consisting of 13 patients (15.48%) with positive No. 10a and 4 patients (4.76%) with positive No. 10p. For the postoperative outcomes in the RP-SL group (Table 3), the time to first flatus, time to remove the naso-jejunum nutrition tube, and time to eating solid food were 3.14±0.68 d, 7.12±2.31 d, and 4.17±1.25 d, respectively.

The degree classification of the perioperative complications was based on the Clavien-Dindo system [26]. The Clavien-Dindo II or severe morbidities occurred in 4 patients (9.5%) and 5 patients (11.9%) in the 2 groups, including 1 intraoperative splenic lobar artery injury, 2 intraperitoneal pancreatic thermal injury, 1 surgical wound infection, one

 Table 2. Comparison of postoperative outcomes between the two groups.

Variables	Ex vi	vo group	In vi	vo group	P value
OT (min)	193.	21±50.03	247.	74±72.29	<0.001*
BLV (mL)	96.	96.90±23.58		24±140.70	<0.001*
Max D (cm)	4.	68±1.24	4.83±1.66		0.650
LOI (cm)	6.	25±1.29	6.12±0.99		0.699*
No. 10 LNs	3.	3.07±0.84		29±0.86	<0.001*
No. 10+ LNs	0.50±0.94		0.2	26±0.665	0.233*
Ascites					0.434
Yes	8	(19.0%)	11	(26.2%)	
No	34	(91.0%)	31	(73.8%)	
Differentiated					0.620
Moderate/high	12	(28.6%)	10	(23.8%)	
Low	30	(71.4%)	32	(76.2%)	
Т					0.152
T2	9	(21.4%)	17	(40.5%)	
T3	23	(54.8%)	16	(38.1%)	
T4	10	(23.8%)	9	(21.4%)	
N					0.453
NO	9	(21.4%)	6	(14.3%)	
N1	3	(7.1%)	7	(16.7%)	
N2	11	(26.2%)	13	(31.0%)	
N3	19	(45.2%)	16	(38.1%)	
TNM*					0.775
I	3	(7.1%)	3	(7.1%)	
II	12	(28.6%)	15	(35.7%)	
III	27	(64.3%)	24	(57.1%)	

OT – operation time; BLV – volume of blood loss; Max D – maximum diameter of the tumor; LOI – length of incision. The eighth AJCC TNM system for gastric cancer. * Mann-Whitney U test.

intraperitoneal infection, one pulmonary infection, and 3 deep venous thromboses. No pancreatic fistula, splenic vessels torsion, splenic infarction, or mortality occurred.

Discussion

In recent decades, gastric carcinoma has become the leading cause of tumor incidence and cancer-related deaths

 Table 3. Comparison of short term outcomes between the two groups.

Variables	Ex vivo group	In vivo group	P value
AD (d)	5.14±2.01	4.64±2.20	0.235*
NJNT (d)	7.12±2.31	4.64±2.19	0.900*
Flatus (d)	3.14±0.68	3.07±0.92	0.431*
Diet (d)	4.17±1.25	3.86±0.93	0.256*
Complications			1.000
Yes	4 (9.5%)	5 (11.9%)	
No	38(90.5%)	37(88.1%)	
POD (d)	6.55±1.73	7.26±1.71	0.066*
Cost (RMB)	65255.64±11358.31	64419.90±14308.93	0.514*

AD – abdominal drainage; NJNT – Nasojejunal nutrient tube; Complication – Clavien-Dindo II or severer; POD – Postoperative hospital stay. * Mann-Whitney U test.

worldwide [1]. According to the JCGC guidelines [6], total gastrectomy with D2 lymphadenectomy is the standard radical surgery performed in patients with PAGC [4].

LN metastasis is an independent risk factor for early recurrence and oncological survival [27]. The incidence of SHLN metastasis is 7.9% to 20.9% [28–30], with a similar incidence in the present study (22.3%). The SHL allows for a similar long-term prognosis with perigastric LNs dissection [27]. Moreover, the SHL was necessary to achieve the radical surgery (R0) according to the JCGC cancer treatment guidelines [6].

In the laparotomy era, synchronous splenectomy was necessary to ensure the SHL in D2 total gastrectomy. The JCOG 0110 trial, however, has reported their final results showing that the 5-year survival rates were 75.1% and 76.4% in the splenectomy and spleen preservation group, respectively, with no significant difference, demonstrating the noninferiority of spleen preservation [13]. Another study focusing on tumor invading the greater curvature also suggested that the SHLNs should be part of D2 lymphadenectomy, although this may not necessarily involve splenectomy [30]. The SPSL, therefore, was gradually accepted.

Various factors affect *in vivo* SHL, including the tortuous splenic vessels, the various types of splenic lobar arteries, and the visual defect. It is essential to avoid secondary injury, especially while learning to perform the procedure. Since Hyung et al. first reported the total laparoscopic SPSL in 2008 [22], several surgical procedures for improving the TL-SL have been recently reported, with the advantages

of minimally invasive surgery [15–18]. A study of the middle approach by Hyung et al. reported that the mean number of retrieved SHLNs was 2.7 (1–5), which was similar to laparotomy [22], and they also suggested that the SHL was more difficult without mobilization of the whole spleen.

The retropancreatic fusion fascia was initially described as a morphological entity by Androulakis [31]. It is well recognized that the fusion fascia, which lies between the pancreatic parenchyma and retroperitoneal organs, acts as a barrier in pancreatic tumors. The mobilization of the retropancreatic areolar, along the fusion fascia, is essential because of the nerve preservation in pancreaticoduodenectomy [23].

There is no available approach combining the retropancreatic fusion fascia with the SHL in gastrectomy.

In the present RP-SL approach, it is important to identify the retropancreatic areolar between the retropancreatic fusion fascia and Gerota fascia, and the expansion continues along the avascular plane. Li et al. reported a modified approach based on the peripancreatic structures [18], but they did not mention the retropancreatic fusion fascia. The limitations include the change of position and additional trocar use, preventing use by the novice. Huang's three-step maneuver [15] offers benefits for the novice, but is still extremely demanding. In general, TL-SL is difficult, and good team cooperation is essential. In the present approach, the mobilization of the pancreas and the spleen was straightforward along the retropancreatic fusion fascia, which is an envelope structure wrapping around the whole pancreas. The main point is recognizing the anatomical landmark at the conjunction between the superior mesenteric vessels and the inferior pancreatic margin.

The SHL is beneficial and important in light of the high metastatic incidence of splenic hilar LNs [28,29], in accordance with the Japanese Gastric Cancer Guidelines [6].

The splenic lobar arteries (SLA) have been classified into 4 types, consisting of concentrated and distributed types [32]. Moreover, the wide variation of the SLA and the distance between the pancreatic tail and spleen are the main disadvantages of the TL-SL. In the present study, the mobilized pancreas and spleen were retracted through the minilaparotomy and the interrelation was also unchanged. In our results, a mean of 2.29 SHLNs were harvested in the TL-SL group, which is similar to the findings in previous reports [15,18,22], and also does not obviously differ from the open strategy [13]. However, a significant difference was found compared to the RP-SL group (3.07±0.84, 2.29±0.86, P<0.001). Furthermore, results suggest that the tactile procedure can improve the integrity of the lymphatic specimen under direct vision.

To the best of our knowledge, there are only a few studies that evaluated the safety and feasibility of splenic hilar lymphadenectomy. Hu et al. found that the ex vivo SPSL results in more harvested splenic hilar LNs at the cost of surgery time [28]. The obvious advantages of the ex vivo approach are better exposure and direct vision, facilitating the complete clearance of LNs located at the posterior splenic lobar arteries and the blood vessels protection. Ji et al. made a similar recommendation, saying that the ex vivo procedure was more efficient, without influencing the safety and oncological prognosis [7]. No surgical plane, however, was mentioned in either of these studies. Compared to previous studies [28], the surgery time was shorter due to the lack of nerves and vessels in the surgical plane with the present technique, and the team performance was also clearly improved.

It is difficult to deal with surgical bleeding in splenic lobar artery injury, which might be the main cause of the longer surgery time in the TL-SL group. The robotic procedure can allow manipulation at the deep and narrow hilum, without mobilization of the pancreas and spleen, thus repairing the vascular injury quickly [19]. However, its use is quite limited for multiple reasons.

Another advantage of laparoscopic surgery is the shorter incision and less postoperative pain compared to laparotomy. We found no significant difference in the length of minilaparotomy between the RP-SL group and the TL-SL group (6.25±1.29 cm vs. 6.12±0.99 cm, P=0.616). Splenic infarction can be avoided once the spleen is properly put back into the splenic hilum. Our results also support the high effectiveness of the retropancreatic fusion fascia-oriented *ex vivo* splenic hilar lymphadenectomy, without sacrificing surgical time and safety.

There are several limitations in this study. First, the possible selection bias, detection bias, and performance of analysis bias are inevitable in any retrospective study. For instance, the *in vivo* procedure might not be selected for extremely obese patients or patients with broad adhesion at the splenic hilum. Second, the long-term outcomes were not available because the follow-up period was too short to draw a conclusion. The first patient was recruited in December 2016, with the longest follow-up of 26 months. Careful follow-up will include assessment of the oncological prognosis and long-term outcomes in order to evaluate the clinical value of RP-SL. Furthermore, this was a single-arm study, which might have resulted in a lower level of confidence.

Conclusions

The RP-SL and TL-SL procedures for SHL are both safe and feasible. However, the retropancreatic fusion fascia-oriented *ex vivo* approach has higher effectiveness, produces more harvested splenic hilar LNs, has shorter surgery time, and improved the learning curve of the SPSL. Due to the limited

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follow-up time and small sample size of the present study, a well-designed multicenter, large-scale, randomized, controlled trial is necessary to verify our results.

Conflict of interest

None.

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