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Impact of anatomical position of the pancreas on postoperative complications and drain amylase concentrations after laparoscopic distal gastrectomy for gastric cancer

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Abstract

Background Laparoscopic surgery for gastric cancer requires traction or compression of the pancreas, with the extent depending on the anatomical position of the pancreas. This study investigated the impact of the position of the pancreas on postoperative complications and drain amylase concentrations after laparoscopic distal gastrectomy (LDG).

Methods Gastric cancer patients who underwent LDG were assessed retrospectively. The following anatomical parameters were measured retrospectively in preoperative computed tomography sagittal projections: the length of the vertical line between the pancreas and the aorta (P–A length), representing the height of the slope looking down the celiac artery from the top of the pancreas, and the angle between a line drawn from the upper border of the pancreas to the root of the celiac artery and the aorta (UP–CA angle), representing the steepness of the slope. Correlations between each parameter and postoperative complications were analyzed by logistic regression analysis. Pearson's product–moment correlation coefficients were calculated for scatter diagrams for each parameter and drain amylase concentration on postoperative day 1.

Results Analyses were performed in 394 patients. P–A length [odds ratio (OR) 1.905; 95% confidence interval (CI) 1.100–3.300; $P=0.021$] was significantly correlated with pancreatic fistula. P–A length (OR 2.771; 95% CI 1.506–5.098; $P=0.001$), UP–CA angle (OR 2.323; 95% CI 1.251–4.314; $P=0.008$), and low preoperative serum albumin (OR 2.082; 95% CI 1.050–4.128; $P=0.036$) were significantly correlated with overall postoperative complications defined as Clavien–Dindo ≥ grade II. P–A length and UP–CA angle showed significant positive correlations with drain amylase concentration on postoperative day 1.

Conclusion The position of the pancreas is an independent predictor of pancreatic fistula and/or postoperative complications and correlates with drain amylase concentration after LDG for gastric cancer.

Keywords Stomach · Cancer · Pancreas · Complication · Anatomical position

Several recent studies have confirmed the advantages of laparoscopic gastrectomy (LAG) for gastric cancer, including less intraoperative bleeding, less pain, and shorter postoperative hospital stay [1–9]. Although postoperative complication rates are generally comparable between LAG and conventional open gastrectomy, a higher incidence of postoperative pancreatic fistula has been reported after LAG compared with open gastrectomy [10]. Possible causes of pancreatic injuries in LAG include lateral thermal damage to the pancreas by energy devices [11, 12], and the anatomical features or location of the pancreas [13, 14]. Gastric cancer surgery requires traction or compression of the pancreas to perform suprapancreatic lymph node dissection, and excessive compression may cause blunt trauma resulting in pancreatic fistula formation. Although various devices may be used to obtain a better operative view and avoid pancreas injury, assistants may still be forced to apply traction or compression of the pancreas during LAG.

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The anatomical position of the pancreas varies widely, and the distance between the pancreatic body surface and the root of the common hepatic artery, representing the position of the pancreas in the transverse direction, was identified as an independent predictor of the development of postoperative pancreatic fistula [14]. Given that the camera port is placed near the umbilicus in LAG and the camera has to look over the pancreas to visualize the celiac artery and its branches, which are at the center of suprapancreatic lymph node dissection, the position of the pancreas in the sagittal direction is also likely to influence the difficulty of the procedure.

Drain amylase concentrations after gastrectomy can be measured easily and used as a convenient predictor of pancreas-related complications in clinical practice. Several studies have reported associations between postoperative drain amylase concentrations and postoperative pancreatic fistula or inflammatory abdominal fluid collection, suggesting that postoperative drain amylase concentration may be used as an indicator of pancreas injury in LAG [10, 15–20].

The current study aimed to determine the correlations between the anatomical positions of the pancreas in both the transverse and sagittal directions and the occurrence of postoperative complications. Furthermore, we also analyzed the relationship between the anatomical position of the pancreas and postoperative drain amylase concentrations after LAG.

Materials and methods

Patients

Patients diagnosed preoperatively with Stage I gastric cancer who underwent laparoscopic distal gastrectomy (LDG) at the Cancer Institute Hospital from January 2013 to December 2015 were enrolled in the study. Patient data were retrieved retrospectively from our database and the patient's hospital records.

Clinical classification of tumor depth (cT) and nodal involvement (cN) was determined by preoperative evaluations, including barium radiography, gastroscopy, computed tomography (CT), and endoscopic ultrasonography. All tumors were diagnosed histologically as adenocarcinomas or signet ring cell carcinoma. A clinical stage of cT1N0, cT2N0 or cT1N1 was an indication for LDG, in accordance with Japanese gastric cancer treatment guidelines [21]. D1+ lymphadenectomy was applied for cT1N0 cancer and D2 was applied for cT2N0 or cT1N1 cancer.

Information on patient age and gender, body mass index (BMI), serum total protein, serum albumin, serum prealbumin, reconstruction method, operation time, estimated intraoperative blood loss, and postoperative complications was extracted from the database and patient records.

Measurement of anatomical parameters related to the pancreas

The maximum length of the vertical line between the pancreas body surface and the aorta (P–A length), representing the height of the slope looking down the root

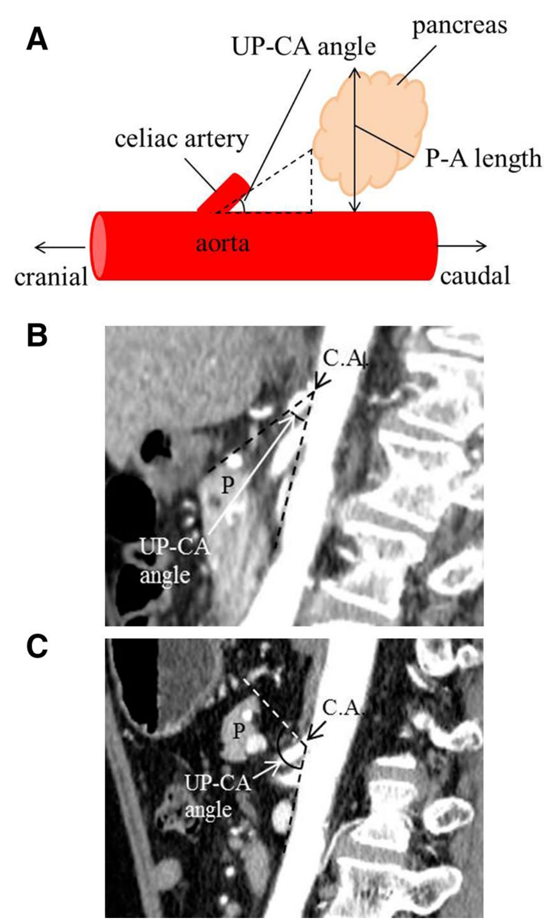

Fig. 1 Anatomical position of the pancreas in sagittal projections on CT scans. **A** Measurement of anatomical parameters related to the pancreas. The following parameters were measured in sagittal projections on preoperative CT scans: maximum length of the vertical line between the surface of the pancreas and the aorta (P–A length) and the angle produced by the meeting of the line drawn from the upper border of the pancreas to the root of the celiac artery and the aorta (UP–CA angle). **B, C** Variations in sagittal position of the pancreas. The pancreas could be located caudal (**B**) or cranial (**C**) to the root of the celiac artery. UP–CA angle was 40.1° in one patient (**B**) and 118.9° in another patient (**C**). *P* pancreas, *CA* celiac artery

of the celiac artery from the top of the pancreas, and the angle between a line drawn from the upper border of the pancreas to the root of the celiac artery and the aorta (UP–CA angle), representing the steepness of the slope, were measured in sagittal projections on preoperative CT scans (Fig. 1A).

Surgery

Under general anesthesia, the first port was placed exactly on the umbilicus using the open technique and a pneumoperitoneum was created by injecting carbon dioxide (10–12 mmHg). A 10-mm 30° oblique rigid laparoscope was inserted through the umbilical port. Under laparoscopic imaging, four ports (each 5–12 mm) were placed in the left upper (12 mm), left lower (12 mm), right upper (5 mm), and right lower (12 mm) quadrants, respectively. The port in the right lower quadrant was placed on a line between the right upper port and the umbilicus, and most of the suprapancreatic lymph node dissection was performed through this port using an energy device held in the operator's right hand. Dissection procedures were carried out using a THUNDERBEAT (Olympus, Tokyo, Japan), HARMONIC ACE®+ Shears (Ethicon Endo-Surgery, LLC., Cincinnati, OH, USA), or a Sonicision™ 39 cm Cordless Ultrasonic Dissection Device (Medtronic plc., Dublin, Ireland). Suction and coagulation were carried out using an electrosurgical unit (VIO 300D; Erbe Elektromedizin, Tubingen, Germany) connected to a Hi-Q suction cup (Olympus, Tokyo, Japan). The operators were standing on each side of the patient and the camera operator was standing between the patient's legs. The procedure was initiated by opening the omental bursa. Lymph node dissection was performed according to the standard procedure established by Hiki et al. [22], including additional dissection of station 11p in D1+ gastrectomy. During suprapancreatic lymph node dissection, traction or compression of the pancreas was applied by the assistant using gauze or sponges. After completion of lymphadenectomy, the stomach was dissected with two firings of an Endo GIA™ 60 mm Purple Reload with Tri-Staple™ Technology (Medtronic plc.) or ECHELON FLEX™ Powered ENDOPATH® Stapler (Ethicon Endo-Surgery, LLC.), blue, 60 mm. Billroth-I intracorporeal gastroduodenostomy with a delta-shaped anastomosis or antecolic Roux-en-Y intracorporeal gastrojejunostomy was performed, as described previously [23, 24]. In Roux-en-Y reconstruction, the staple line of the duodenal stump was routinely invaginated with three or four interrupted seromuscular sutures, and Petersen's defect and the mesenteric defect at the jejunojejunostomy were closed with continuous and interrupted sutures, respectively, to prevent internal herniation.

Postoperative complications

The severity of postoperative complications was graded according to the Japan Clinical Oncology Group Postoperative Complications (JCOG PC) criteria, which provide detailed grading criteria for each postoperative complication in accordance with the general grading rules of the Clavien–Dindo classification [25–27]. In this study, postoperative complications of grade II or above were defined as overall complications. According to the JCOG PC criteria, grade I pancreatic fistula was defined as drainage fluid amylase levels on or after postoperative day 3 of ≥ 3 times the upper limit of institutional normal, but without the need for intervention. We therefore defined pancreatic fistula in this study as drainage fluid amylase levels on postoperative day 3 ≥ 396 IU, given that the upper normal limit in our institution was 132 IU.

Clinicopathological and anatomical factors

Clinicopathological or anatomical parameters that might correlate with pancreatic fistula or postoperative overall complications were evaluated by univariate and multivariate logistic regression analyses. The cut-off value for each factor or parameter in logistic regression analysis was determined using the quartile values, because these were considered to be more objective than values obtained by other methods, such as receiver operating characteristic curves. Factors or parameters with $P < 0.1$ in univariate analysis were selected as covariables in the subsequent multivariate analysis. Multivariate logistic regression analysis was performed with backward elimination for variable selection with $\alpha = 0.10$.

Correlations between drain amylase concentrations and anatomical parameters related to the pancreas

Scatter diagrams of drain amylase concentration on postoperative day 1 and each anatomical parameter related to the pancreas were drawn and Pearson's product–moment correlation coefficient was calculated for each parameter.

Statistical analysis

All data are presented as the number of patients or as median (range). Statistical analyses were performed as described above for each analysis using SPSS version 11.0 (SPSS, Chicago, IL, USA). Significance was established at $P < 0.05$.

Results

A total of 530 patients underwent LDG with D1+ or D2 lymphadenectomy for gastric cancer at the Cancer Institute Hospital during the study period. 39 patients who underwent combined surgery with other organs were excluded. Data for 394 patients in whom sagittal projections of preoperative CT were available were analyzed.

Clinicopathological and anatomical parameters related to the pancreas

The patient characteristics and the anatomical parameters related to the pancreas are shown in Table 1. Surgical data for LDG are shown in Table 2. The sagittal position of the pancreas differed greatly among individuals (Fig. 1B, C).

Postoperative complications

Pancreatic fistula, defined as a drainage fluid amylase level on postoperative day 3 ≥ 396 IU, was observed in 118 patients (29.9%). Postoperative complications classified as grade II or above in accordance with the JCOG PC criteria are shown in Table 3. No grade IV or V complications were observed during the study period. Overall complications defined as grade II or above were observed in 54 patients (13.7%) and severe complications defined as grade III were observed in 23 patients (5.9%). Among the grade III complications, pancreatic fistula (3.0%) was the most frequent complication.

Table 1 Characteristics of patients undergoing LDG for gastric cancer

Characteristic	Value
Number of patients	394
Age (years)	67 [25–91]
Sex ratio (M:F)	253:141
BMI (kg/m^2)	22.6 [14.5–39.1]
P–A length (mm)	38.9 [12.9–69.8]
UP–CA angle (°)	73.3 [8.6–149.4]
ASA-PS (1/2/3)	238/151/5
Hemoglobin (g/dl)	13.4 [8.4–16.7]
Total protein (g/dl)	6.8 [5.1–8.1]
Albumin (g/dl)	4.1 [2.6–4.9]
Prealbumin (mg/dl)	26.6 [11.6–48.7]
PNI	49.8 [28.4–61.6]
cStage IA:IB	332:62

Data are presented as median [range]

LDG laparoscopic distal gastrectomy, *BMI* body mass index, *P–A* pancreas–aorta, *UP–CA* upper border of the pancreas–celiac artery, *ASA-PS* American Society of Anesthesiologists physical status, *PNI* prognostic nutritional index

Table 2 Surgical data of LDG for gastric cancer

Variable	Value
Operation time (min)	280 [156–492]
Blood loss (ml)	20 [0–500]
Reconstruction	
Roux-en-Y	252 (64.0)
Billroth-I	142 (36.0)
Lymph node dissection	
D1+	243 (61.7)
D2	151 (38.3)

Data are presented as median [range]. Values in parentheses are percentages

LDG laparoscopic distal gastrectomy

Table 3 Postoperative complications after LDG for gastric cancer

Patient-oriented Maximum grade of the complications	Number of patients ($N = 394$)
Grade II	31 (7.8)
Grade IIIa	20 (5.1)
Grade IIIb	3 (0.8)
Total	54 (13.7)
Complication-oriented Complication	**Number of complications**
Grade II	
Pancreatic fistula	13 (3.3)
Intraabdominal abscess	7 (1.8)
Pneumonia	3 (0.8)
Postoperative hemorrhage	1 (0.3)
Others	9 (2.3)
Grade IIIa	
Pancreatic fistula	12 (3.0)
Intraabdominal abscess	10 (2.5)
Postoperative hemorrhage	4 (1.0)
Anastomotic leak	2 (0.5)
Pulmonary fistula	2 (0.5)
Anastomotic stenosis	1 (0.3)
Grade IIIb	
Intestinal obstruction	2 (0.5)
Anastomotic leak	1 (0.3)
Postoperative hemorrhage	1 (0.3)

Each grade was based on the Japan Clinical Oncology Group postoperative complications criteria. Values in parentheses are percentages

LDG Laparoscopic distal gastrectomy

Based on JCOG criteria, 14 of 118 (11.9%) patients with pancreatic fistula developed postoperative complications classified as Clavien–Dindo grade III or above, compared with 4 of 134 (3.0%) patients without pancreatic fistula

Table 4 Univariate analysis of risk factors for pancreatic fistula and postoperative complications after LDG

Variables	Pancreatic fistula (D-AMY on POD 3 ≥ 396 IU)				Overall complications (≥ grade II)			
	N = 118				N = 54			
	OR	95% CI		P	OR	95% CI		P
		Lower	Upper			Lower	Upper	
Age								
≥ 75	0.917	0.494	1.699	0.782	1.383	0.723	2.645	0.328
< 75	1				1			
Sex								
Male	1.618	0.943	2.776	0.081	1.531	0.811	2.888	0.189
Female	1				1			
BMI (kg/m^2)								
≥ 24.5	1.671	0.937	2.979	0.082	2.388	1.311	4.351	0.004
< 24.5	1				1			
P–A length (mm)								
≥ 45	1.905	1.100	3.300	0.021	2.827	1.559	5.124	0.001
< 45	1				1			
UP–CA angle (°)								
≥ 97	1.729	0.978	3.057	0.060	2.348	1.29	4.276	0.005
< 97	1				1			
ASA-PS								
2, 3	0.800	0.486	1.318	0.382	0.732	0.399	1.341	0.313
1	1				1			
Hemoglobin (g/dl)								
< 12.5	0.600	0.336	1.073	0.085	0.700	0.346	1.416	0.321
≥ 12.5	1				1			
Total protein (g/dl)								
< 6.5	0.926	0.500	1.718	0.808	1.006	0.504	2.007	0.987
≥ 6.5	1				1			
Albumin (g/dl)								
< 3.9	1.395	0.720	2.694	0.322	1.753	0.909	3.381	0.094
≥ 3.9	1				1			
Prealbumin (mg/dl)								
< 23.4	0.895	0.488	1.639	0.718	1.010	0.516	1.977	0.977
≥ 23.4	1				1			
PNI								
< 47.0	1.043	0.589	1.847	0.884	0.857	0.431	1.704	0.660
≥ 47.0	1				1			
cStage								
IB	1.074	0.593	1.947	0.813	0.921	0.412	2.061	0.841
IA	1				1			
D-number								
D2	1.136	0.656	1.966	0.649	0.835	0.405	1.724	0.627
D1+	1				1			
Reconstruction								
Roux-en-Y	0.848	0.507	1.419	0.530	0.664	0.372	1.188	0.168
Billroth-I	1				1			

LDG laparoscopic distal gastrectomy, *POD* postoperative day, *OR* odds ratio, *BMI* body mass index, *P–A* pancreas–aorta, *UP–CA* upper border of the pancreas–celiac artery, *ASA-PS* American Society of Anesthesiologists physical status, *PNI* prognostic nutritional index

($P = 0.013$). The median lengths of postoperative hospital stay (range) in patients with and without pancreatic fistula based on JCOG criteria were 10 (7–39) and 10 (6–67) days, respectively, with no significant difference between the groups ($P = 0.312$).

Risk factors for pancreatic fistula

P–A length (≥ 45 mm) was significantly associated with pancreatic fistula after LDG according to univariate analysis (Table 4). Factors with $P < 0.1$ were then selected as covariables in multivariate analysis. Multiple logistic regression analysis also identified P–A length [odds ratio (OR) 1.905, 95% confidence interval (CI) 1.100–3.300, $P = 0.021$] as an independent predictor of a higher incidence of pancreatic fistula (Table 5).

Risk factors for postoperative overall complications

BMI (≥ 24.5 kg/m^2), P–A length (≥ 45 mm), UP–CA angle (≥ 97°), and preoperative serum albumin (< 3.9 g/dl) were significantly associated with overall complications after LDG according to univariate analysis (Table 4). Factors with $P < 0.1$ were then selected as covariables in multivariate analysis. Multiple logistic regression analysis identified P–A length (OR 2.771, 95% CI 1.506–5.098, $P = 0.001$), UP–CA angle (OR 2.323, 95% CI 1.251–4.314, $P = 0.008$), and preoperative serum albumin (OR 2.082, 95% CI 1.050–4.128, $P = 0.036$) as independent predictors of a higher postoperative complication rate (Table 5).

Associations between postoperative drain amylase concentrations on postoperative day 1 and anatomical parameters related to the pancreas

Scatter diagrams of drain amylase concentration on postoperative day 1 and each anatomical parameter related to the pancreas are shown in Fig. 2. Drain amylase concentration on postoperative day 1 was significantly positively correlated with P–A length and UP–CA angle (Fig. 2).

Discussion

This study revealed that the anatomical position of the pancreas was significantly associated with the occurrence of pancreatic fistula and overall postoperative complications after LDG, and also affected drain amylase concentrations on postoperative day 1.

Age, operation time, total gastrectomy, and pancreatectomy have been reported as risk factors for complications following radical lymphadenectomies for gastric cancer [28]. In terms of laparoscopic surgery, LAG is known to be more difficult in obese patients. BMI has been used as an indicator of obesity, and high BMI was reported to be a risk factor for complications after LAG [29]. In the current study, however, multivariate analysis identified the position of the pancreas in sagittal and transverse directions as being significantly associated with postoperative pancreatic fistula and overall complications after LDG. This identified predictor of pancreatic fistula was in accord with the report by Migita et al., though the definition of pancreatic fistula and method of measuring the position of the pancreas differed from the present study [14]. Compression and mobilization of the pancreas may be required to perform suprapancreatic

Table 5 Multivariate analysis of risk factors for pancreatic fistula and postoperative complications after LDG

Variables	Pancreatic fistula (D-AMY on POD 3 ≥ 396 IU)				Overall complications (≥ grade II)			
	N = 118				*N* = 54			
	OR	95% CI		*P*	OR	95% CI		*P*
		Lower	Upper			Lower	Upper	
P–A length (mm)								
≥ 45	1.905	1.100	3.300	0.021	2.771	1.506	5.098	0.001
< 45	1				1			
UP–CA angle (°)								
≥ 97					2.323	1.251	4.314	0.008
< 97					1			
Albumin (g/dl)								
< 3.9					2.082	1.050	4.128	0.036
≥ 3.9					1			

LDG laparoscopic distal gastrectomy, *POD* postoperative day, *OR* odds ratio, *P–A* pancreas–aorta, *UP–CA* upper border of the pancreas–celiac artery

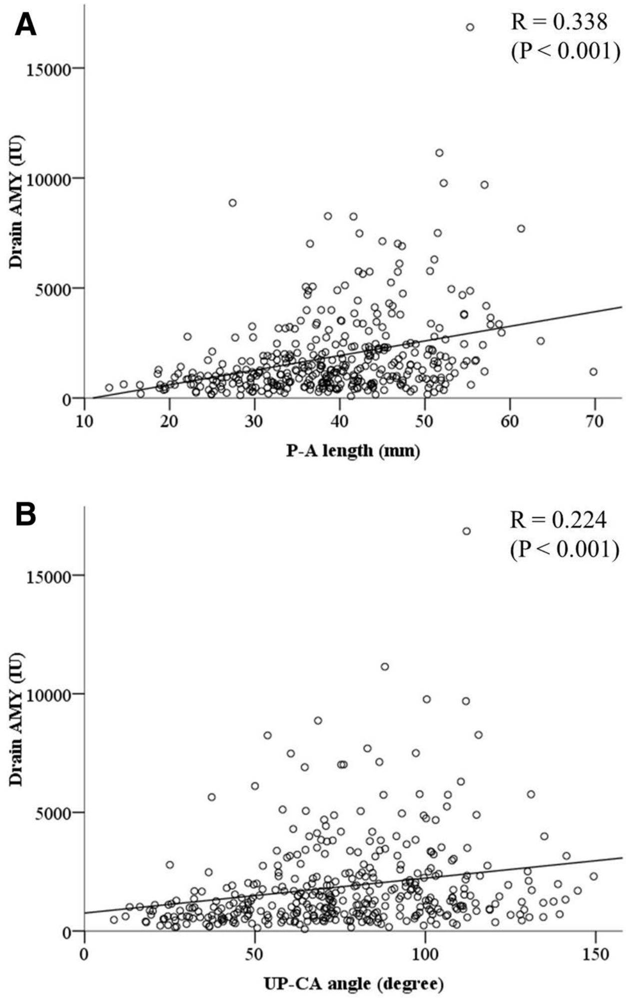

Fig. 2 Associations between drain amylase concentration on postoperative day 1 and **A** P–A length and **B** UP–CA angle. P–A length, maximum length of the vertical line between the surface of the pancreas and the aorta; UP–CA angle, angle produced by the meeting of the line drawn from the upper border of the pancreas to the root of the celiac artery and the aorta; *AMY* amylase

lymph node dissection in the patients with long P–A length, and these may damage the pancreas, potentially resulting in the occurrence of a pancreatic fistula. Looking down the celiac artery and its branches over the pancreas using a scope inserted in the umbilicus is a specific part of the procedure in LAG, and it is therefore interesting that the position of the pancreas in the sagittal direction was also predictive of postoperative complications after LDG. Procedural difficulties in LDG may be related to the individual patient's body shape, represented by the anatomical position of the pancreas. Further studies are needed to determine the direct mechanisms responsible for the increase in postoperative complications in patients with these risk factors.

Both anatomical parameters related to the pancreas were significantly correlated with drain amylase concentrations on postoperative day 1, which was regarded as a marker of pancreatic injury caused by surgery, though the correlation strengths were low. Although high drain amylase concentration on postoperative day 1 does not necessarily reflect the occurrence of postoperative complications including pancreatic fistula, these results provide additional evidence to support the importance of the anatomical position of the pancreas in affecting the difficulty of accessing the operative field during suprapancreatic lymph node dissection in LDG.

It is therefore necessary to determine how to minimize or avoid the effects of the identified risk factors for postoperative complications following LDG. The use of a flexible laparoscope may provide better images when looking down the celiac artery and its branches over the pancreas, compared with a rigid laparoscope. However, rigid endoscopes generally provide superior image clarity. If the sharpness of the picture is prioritized, the camera port can be placed more cranially than the umbilicus, allowing the celiac artery and its branches to be visualized with less traction on the pancreas. The use of sponges or gauzes can also help to minimize pancreas injury, and assistants can exert traction on the pancreas through those devices. The best way to avoid pancreas injury is to avoid touching it during the procedure. The pancreas can be flipped over and the celiac artery and its branches visualized by compressing the lower border of the pancreas with sponges; however, pulling the fat tissue at the lower border of the pancreas can create the same view as flipping over the pancreas. These procedures have been introduced and their efficacy in reducing postoperative complications has already been reported [30].

There were some limitations to the present study. First, the results of this study were based on the standardized LDG procedure in our institution. The conclusions may therefore only be valid for patients operated on in our hospital, while different factors may correlate with complications in other hospitals using different methods. Second, pancreatic fistula was defined as a drainage fluid amylase level on or after postoperative day 3 of ≥ 3 times the upper limit of the institutional norm, in accordance with JCOG PC criteria. This criterion was used because it was regarded as more objective than other criteria. The incidence of pancreatic fistula was high (29.9%) compared with our daily clinical experience. However, among patients with postoperative complications classified as Clavien–Dindo grade III or above, significantly more patients with pancreatic fistula based on JCOG criteria required radiological or surgical re-intervention compared with those without (11.9 vs 3.0%, $P = 0.013$). This difference suggests that the definition of pancreatic fistula in accordance with the JCOG criteria reflects the situation seen in clinical practice to some extent, even though the difference did not affect the length of postoperative hospital stay. Finally, other parameters related to the pancreas that were not evaluated in the present study, such as pancreas volume or density, may be more strongly related to the development of postoperative pancreatic fistula than P–A length or UP–CA angle. However, the chosen parameters should be easily measurable utilizing procedures used in daily clinical practice, and the measured values should be consistent among different measurers. P–A length and UP–CA angle were therefore considered to be the most promising parameters in terms of simplicity and robustness.

In conclusion, anatomical parameters related to the pancreas, P–A length and UP–CA angle, may be independent predictors of pancreatic fistula and/or postoperative complications in patients undergoing LDG for gastric cancer. These parameters also correlate significantly with drain amylase concentrations on postoperative day 1. Procedures aimed at improving the operative view while avoiding pancreas injury during suprapancreatic lymph node dissection may help to reduce postoperative complications after LDG, specifically in patients with certain pancreatic anatomies.

Compliance with ethical standards

Disclosures Drs. Koshi Kumagai, Naoki Hiki, Souya Nunobe, Satoshi Kamiya, Masahiro Tsujiura, Satoshi Ida, Manabu Ohashi, Toshiharu Yamaguchi, and Takeshi Sano have no conflicts of interest or financial ties to disclose.

Ethical approval All procedures involving human participants were carried out in accordance with the ethical standards of the institutional and/or national research committee, and in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The entire study was conducted with the approval of the institutional review board at the Cancer Institute Hospital (No. 1737). Informed consent was obtained from all individual participants included in the study. This article does not contain any studies with animals performed by any of the authors.

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