Retrospective Cohort Study

INTERNATIONAL JOURNAL OF SURGERY

OPEN

Development of a difficulty scoring system for laparoscopic pancreatoduodenectomy in the initial stage of the learning curve: a retrospective cohort study

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Background: It remains uncertain how surgeons can safely pass the learning curve of laparoscopic pancreatoduodenectomy (LPD) without potentially harming patients. We aimed to develop a difficulty scoring system (DSS) to select an appropriate patient for surgeons.

Materials and Methods: A total of 773 elective pancreatoduodenectomy surgeries between July 2014 and December 2019, including 346 LPD and 427 open pancreatoduodenectomy cases, were included. A 10-level DSS for LPD was developed, and an additional 77 consecutive LPD surgeries which could provide information of the learning stage I of LPD externally validated its performance between December 2019 and December 2021.

Results: The incidences of postoperative complications (Clavien–Dindo ≥ III) gradually decreased from the learning curve stage I–III (20.00, 10.94, 5.79%, $P = 0.008$, respectively). The DSS consisted of the following independent risk factors: (1) tumor location, (2) vascular resection and reconstruction, (3) learning curve stage, (4) prognostic nutritional index, (5) tumor size, and (6) benign or malignant tumor. The weighted Cohen's κ statistic of concordance between the reviewer's and calculated difficulty score index was 0.873. The *C*-statistics of DSS for postoperative complication (Clavien–Dindo ≥ III) were 0.818 in the learning curve stage I. The patients with DSS < 5 had lower postoperative complications (Clavien–Dindo ≥ III) than those with DSS ≥ 5 (4.35–41.18%, $P = 0.004$) in the training cohort and had a lower postoperative pancreatic fistula (19.23–57.14%, $P = 0.0352$), delayed gastric emptying (19.23–71.43%, $P = 0.001$), and bile leakage rate (0.00–21.43%, $P = 0.0368$) in validation cohort in the learning curve stage I.

Conclusion: We developed and validated a difficulty score model for patient selection, which could facilitate the stepwise adoption of LPD for surgeons at different stages of the learning curve.

Keywords: complications, difficulty scoring system, laparoscopic pancreatoduodenectomy, learning curve

Introduction

Pancreatoduodenectomy (PD), or the Whipple procedure, is a complex surgical procedure that has been accepted as the gold-standard treatment for resectable lesions of the pancreatic head and periampullary region[1]. Since Gagner introduced a laparoscopic approach to PD in 1994[2], LPD has been a generally accepted surgical treatment by high-volume pancreatic surgery centers. In addition, according to the Miami international evidence-based guidelines on minimally invasive pancreatic resections[3], minimally invasive pancreatectomy is preferred over OPD due to better surgical outcomes (i.e. shorter hospital stay, decreased blood loss, reduced pain, and comparable complication rates, oncological safety, and overall outcomes)[4–6].

Previous studies have demonstrated the safety and feasibility of LPD[7–9]. However, the procedure was considered a feasible, safe, and oncological equivalent approach only in high-volume centers and experienced hands[3,10]. The experience, surgical skills, and completion of the learning stages are still major obstacles to the extensive application of LPD[11]. Our previous multicentre research revealed three learning phases of LPD, which were phase I (1–40 cases), phase II (41–104 cases), and phase III (> 104

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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International Journal of Surgery (2023) 109:660–669

Received 1 September 2022; Accepted 29 December 2022

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www.journalsurgery.net.

Published online 3 April 2023

http://dx.doi.org/10.1097/JS9.0000000000000180

cases), and more than 104 procedures were needed to reach the learning curve plateau[12]. Despite the long training time for surgeons, there is no formal, universal, or standardized training program or certified curriculum for LPD. Previous studies that investigated LPD's learning curve used different metrics as their endpoint to measure proficiency[13–16]. For example, the primary endpoints used to measure operative expertise included the operative time, conversion rate, estimated blood loss, morbidity, and length of hospital stay. These outcomes also raise the question of how surgeons can safely pass the learning curve without potentially harming patients.

Furthermore, a complex surgical procedure can be influenced by different factors, such as patient characteristics, laparoscopic technical issues, lesion characteristics and location, and surgeon's skills and experience, which are significantly associated with perioperative and long-term outcomes of LPD. A difficulty scoring system (DSS) was used to graphically depict a statistical prognostic model to select an appropriate patient for a surgeon with different laparoscopic experience[17–19]. In this study, we aimed to develop and validate a DSS for patient selection by analyzing the clinical characteristics of patients and perioperative outcomes of LPD procedures, which could facilitate the safe and stepwise adoption of LPD for surgeons at a different stage of the learning curve. To the best of our knowledge, this is the first attempt to determine the patient selection, which can help surgeons navigate the steep learning curve of LPD.

HIGHLIGHTS

- The comprehensive data comparison of laparoscopic pancreatoduodenectomy (LPD) in different stages of learning curve versus open pancreatoduodenectomy (OPD).
- A difficulty scoring system (DSS) for LPD were established and validated.
- The patients with DSS < 5 had lower postoperative complications than those with DSS ≥ 5 in the learning curve stage I.
- It could facilitate the stepwise adoption of LPD for surgeons at initial stage of the learning curve.

Methods

Patients' data collection

From July 2014 to December 2019, 773 consecutive patients underwent PD for various diagnoses performed by a single surgeon at a Biliary-Pancreatic Surgery Department. Of which 346 and 427 were LPD and OPD cases, respectively. The 427 OPD cases were all in the mature stage. Whereas the 346 LPD cases covered the learning curve, with 1–40 cases being stage I, 41–104 cases being stage II, 105–346 cases being stage III. From December 2018 to December 2019, 77 consecutive LPD cases performed by another surgeon who had not reached the mature stage of the learning curve at the same department were collected for external validation. In this study, we focused on the learning stage I of LPD. Therefore, a surgeon who can provide his data of stage I could provide the validation performance of DSS. The patients' demographic and perioperative data were reviewed retrospectively. This study was approved by the Institutional Research Ethics committee of Tongji Hospital. The experiments were registered at ClinicalTrials (NCT05520606) and undertaken with the understanding and appropriate informed consent of each. Besides, the work has been reported in line with the STROCSS (Supplemental Digital Content 1, http://links.lww.com/JS9/A39) criteria[20].

Definitions of variables

Postoperative complications and morbidity were defined and categorized according to the Clavien–Dindo (CD) classification; a CD ≥ III was defined as severe. Postoperative comorbidities, such as postpancreatectomy hemorrhage (PPH), postoperative pancreatic fistula (POPF), and delayed gastric emptying (DGE), were defined according to definitions outlined by the International Study Group of Pancreatic Surgery (ISGPF). The prognostic nutritional index (PNI) was calculated as $10 \times$ serum albumin (g/dl) $+ 0.005 \times$ total lymphocytes count (per mm^3)[21]. The neutrophil-to-lymphocyte ratio was calculated by dividing neutrophil count by lymphocyte count. The platelet-to-lymphocyte ratio was estimated as platelet count divided by lymphocyte count. The validation cohort data was collected in the same way as the training data.

Difficulty index definitions

A 10-level difficulty index was developed using a scale of 1–10, with 1 being the least difficult and 10 being the most difficult. The index was subsequently divided into the following three subgroups: 1–3 (low difficulty), 4–6 (intermediate difficulty), and 7–10 (high difficulty). The difficulty of each LPD surgery was determined using individual slides of the patient's profile and operation videos and scored by three experienced surgeons, who skilled in pancreatic surgery and has completed more than 500 OPD procedures, using the 10-level difficulty index. Open discussion between the surgeon and reviewers was allowed before assigning the score. The idiographic surgical information, such as surgical approach, surrounding condition of the tumor, pancreatic characteristics (i.e. soft or hard), anastomotic methods, and other details, were used to confirm the difficulty level. Each expert reviewer made a separate score evaluation, and the median of their scores were computed as the difficulty score (DS).

Statistical analysis

Data from all cases were combined to perform univariable and subsequent multiple linear regression analyses to assess the clinical parameters of DS and develop a DSS that reflects clinical practice. Continuous variables were presented as a median and interquartile range, whereas categorical variables were presented as percentages. Continuous variables were compared using the Student's t-test (two independent groups) or analysis of variance analysis (three independent groups), and categorical data were compared using the χ^2 test or Fisher's exact test. The interrater concordance between the reviewer's DS and the calculated DS index was computed using the weighted Cohen's κ, which evaluates the degree of disagreement by accounting for the differences in the importance of disagreement.

Table 1

Characteristics of patients in the laparoscopic and open pancreatoduodenectomy groups

	n (%)		
Variables	**LPD (N = 346)**	**OPD (N = 427)**	***P***
Age [mean (SD)] (years)	55.99 (10.87)	55.25 (10.55)	0.3366
Female	147 (42.49)	163 (38.17)	0.2238
BMI > 24 kg/m^2	242 (69.94)	245 (57.38)	
ASA			0.4066
I	36 (10.40)	41 (9.60)	
II	248 (71.68)	293 (68.62)	
III	62 (17.92)	93 (21.78)	
Diabetes	20 (5.78)	22 (5.15)	0.7017
Surgical history	101 (29.19)	144 (33.72)	0.178
Alb [median (IQR)] (g/l)	38.30 (35.60–40.80)	37.90 (34.90–41.00)	0.3909
Tbil [median (IQR)] (μmol/l)	27.00 (10.80–133.80)	44.90 (11.10–151.40)	0.2358
CA19-9 [median (IQR)] (U/ml)	36.29 (12.37–180.10)	55.32 (13.20–307.80)	0.0132
PTCD	126 (36.42)	156 (36.53)	0.973
Vascular resection	11 (3.18)	54 (12.65)	< 0.0001
Tumor location			< 0.0001
Distal biliary duct	27 (7.80)	42 (9.84)	
Ampullary	36 (10.40)	40 (9.37)	
Duodenal papillary	136 (39.31)	74 (17.33)	
Pancreatic head	147 (42.49)	166 (38.87)	
AJCC			0.2913
IA	90 (36.14)	91 (28.26)	
IB	66 (26.51)	99 (30.75)	
IIA	19 (7.63)	25 (7.76)	
IIB	58 (23.29)	88 (27.33)	
III	15 (6.02)	15 (4.66)	
IV	1 (0.40)	4 (1.24)	
Tumor size [median (IQR)] (cm)	2.50 (1.90–3.30)	2.90 (2.00–4.00)	0.0001
Operative time [median (IQR)] (min)	300.00 (250.00–380.00)	370.00 (290.00–430.00)	< 0.0001
EIBL [median (IQR)] (ml)	100.00 (50.00–300.00)	300.00 (200.00–600.00)	< 0.0001
Lymph nodes harvested [median (IQR)]	17.00 (6.00–25.00)	18.00 (7.00–28.00)	0.1821
R0 resection	324 (93.64)	388 (90.87)	0.1547
30-day mortality	13 (3.76)	17 (3.98)	0.8726
90-day mortality	17 (4.91)	28 (6.56)	0.3317
Clavien–Dindo ≥ III	29 (8.38)	40 (9.37)	0.6325
POPF of B/C grade	30 (8.67)	19 (4.45)	0.0166
PPH of B/C grade	24 (6.94)	26 (6.09)	0.6339
DGE of B/C grade	79 (22.83)	115 (26.93)	0.1911
Bile leakage	18 (5.20)	31 (7.26)	0.243
Abdominal infection	33 (9.54)	21 (4.92)	0.0122
Hepatic failure	0 (0.00)	5 (1.17)	0.0434
Renal failure	2 (0.58)	5 (1.17)	0.3869
Pulmonary infection	11 (3.18)	10 (2.34)	0.4765
Cardiac dysfunction	4 (1.16)	10 (2.34)	0.4765
LOS [median (IQR)] (days)	18.00 (15.00–22.00)	20.00 (16.00–26.00)	0.0002

AJCC, American Joint Committee on Cancer; Alb, albumin; ASA, American Society of Anesthesiologists physical status classes; CA19-9, cancer antigen 19-9; DGE, delayed gastric emptying; EIBL, estimated intraoperative blood loss; IQR, interquartile range; LOS, length of stay; LPD, laparoscopic pancreatoduodenectomy; OPD, open pancreatoduodenectomy; POPF, postoperative pancreatic fistula; PPH, postpancreatectomy hemorrhage; PTCD, percutaneous transhepatic cholangial drain; Tbil, total bilirubin

Multivariable linear regression analysis was used to determine the independent factors associated with technical difficulty. Factors with *P*-value less than 0.1 in the univariate regression analysis were included in the multivariate analysis. Subsequently, the final linear regression model was constructed using factors with *P*-value less than 0.05 in the multivariate regression analysis. Then, a scoring system was developed by assigning a weight to each risk factor based on the β coefficients from the final linear regression model, referred to as the Framingham study risk-score functions[22]. For the internal validation of the risk-scoring system, bootstrap resampling was performed by fitting the risk-scoring system in a bootstrap sample of 1000 subjects, which was drawn with a replacement from the original sample. For missing data analysis, a variable was excluded if it had missing data more than 20%. For the remaining data, the missingness was less than 10% and the complete analysis was used without any imputation. All calculations were performed with a R statistical software, version 4.1.2 and SAS 9.4, (http://www.r-project.org/) and a *P*-value less than 0.05 was considered statistically significant in a two-tailed test.

Table 2

Characteristics of patients according to three learning stages of laparoscopic pancreatoduodenectomy

	n (%)			
Variables	**Stage I (N = 40)**	**Stage II (N = 64)**	**Stage III (N = 242)**	***P***
Age [mean (SD)] (years)	57.78 (9.63)	54.89 (12.31)	55.99 (10.66)	0.4215
Female	16 (40.00)	28 (43.75)	103 (42.56)	0.9307
BMI [mean (SD)] (kg/m^2)	21.46 (2.43)	21.11 (2.76)	22.17 (2.82)	0.0148
Tumor size [median (IQR)] (cm)	2.10 (1.50–3.15)	2.15 (1.80–3.00)	2.50 (2.00–3.50)	0.0139
RDW_CV [median (IQR)] (%)	14.40 (13.35–15.55)	14.70 (13.45–15.90)	13.90 (13.10–15.00)	0.0174
PNI [median (IQR)] ((%))	44.13 (39.43–46.58)	44.35 (40.28–47.63)	46.95 (43.45–50.30)	0.0002
NLR [median (IQR)]	41.92 (33.34–60.10)	46.96 (30.70–57.62)	38.24 (29.94–51.13)	0.0424
PLR [median (IQR)]	167.38 (113.12–222.35)	163.94 (126.25–237.47)	136.11 (96.93–184.35)	0.0011
CONUT [median (IQR)]	3.00 (1.00–4.00)	2.00 (1.00–3.50)	2.00 (1.00–3.00)	0.0248
Creatinine [median (IQR)] (μmol/l)	60.00 (52.00–67.50)	63.00 (53.00–77.00)	65.50 (56.00–77.00)	0.0342
TG [median (IQR)] (mmol/l)	0.00 (0.00–0.95)	0.00 (0.00–0.94)	0.54 (0.00–1.55)	0.0129
Plt [median (IQR)] (10^9/l)	224.50 (171.50–289.00)	236.50 (194.50–320.00)	211.00 (169.00–266.00)	0.0189
ALT [median (IQR)] (U/l)	92.50 (28.00–260.00)	81.00 (16.50–216.00)	53.00 (18.00–154.00)	0.1472
AST [median (IQR)] (U/l)	68.00 (25.00–151.00)	54.00 (20.50–154.00)	47.00 (19.00–106.00)	0.1499
Alb [median (IQR)] (g/l)	36.65 (33.90–38.45)	37.45 (34.40–40.10)	38.75 (36.30–41.20)	0.0005
Tbil [median (IQR)] (μmol/l)	63.30 (15.95–159.60)	57.10 (12.35–173.45)	22.10 (9.90–118.70)	0.0328
CA19-9 [median (IQR)] (U/ml)	27.91 (8.16–198.74)	35.26 (11.64–150.25)	39.17 (13.05–184.90)	0.6302
PTCD	15 (37.50)	25 (39.06)	86 (35.54)	0.863
Vascular resection	0 (0.00)	0 (0.00)	11 (4.55)	0.0871[a]
Tumor location				0.2213
Distal biliary duct	4 (13.33)	6 (9.38)	32 (13.22)	
Ampullary	5 (16.67)	16 (25.00)	34 (14.05)	
Duodenal papillary	16 (53.33)	24 (37.50)	96 (39.67)	
Pancreatic head	5 (16.67)	18 (28.13)	80 (33.06)	
ASA				0.3467
I	3 (7.50)	11 (17.19)	22 (9.09)	
II	31 (77.50)	43 (67.19)	174 (71.90)	
III	6 (15.00)	10 (15.63)	46 (19.01)	
AJCC				0.8568[a]
IA	15 (42.86)	15 (35.71)	60 (34.88)	
IB	12 (34.29)	10 (23.81)	44 (25.58)	
IIA	3 (8.57)	4 (9.52)	12 (6.98)	
IIB	4 (11.43)	10 (23.81)	44 (25.58)	
III	1 (2.86)	3 (7.14)	11 (6.40)	
IV	0 (0.00)	0 (0.00)	1 (0.58)	
Operative time [median (IQR)] (min)	460.00 (400.00–540.00)	338.50 (260.00–425.00)	280.00 (250.00–330.00)	< 0.0001
EIBL [median (IQR)] (ml)	100.00 (50.00–200.00)	100.00 (80.00–200.00)	125.00 (50.00–300.00)	0.3261
Lymph nodes harvested [median (IQR)]	18.00 (7.0–21.00)	18.00 (7.0–25.0)	19.0 (6.0–28.0)	0.6752
R0 resection	2 (5.00)	6 (9.38)	14 (5.79)	0.5391[a]
30-day mortality	2 (5.00)	1 (1.56)	10 (4.13)	0.5719[a]
90-day mortality	2 (5.00)	1 (1.56)	14 (5.79)	0.3805[a]
Clavien–Dindo ≥ III	8 (20.00)	7 (10.94)	14 (5.79)	0.0078
POPF of B/C grade	8 (20.00)	10 (15.63)	12 (4.96)	< 0.001
PPH of B/C grade	8 (20.00)	5 (7.81)	11 (4.55)	0.0017
DGE of B/C grade	15 (37.50)	17 (26.56)	47 (19.42)	0.0304
Bile leakage	6 (15.00)	5 (7.81)	7 (2.89)	0.0035
Abdominal infection	10 (25.00)	8 (12.50)	15 (6.20)	0.0006[a]
Hepatic failure	0 (0.00)	0 (0.00)	0 (0.00)	–
Renal failure	0 (0.00)	0 (0.00)	2 (0.83)	0.649[a]
Pulmonary infection	3 (7.50)	2 (3.13)	6 (2.48)	0.2452[a]
Cardiac dysfunction	0 (0.00)	0 (0.00)	4 (1.65)	0.2452[a]
LOS [median (IQR)] (days)	21.00 (14.00–31.00)	18.00 (14.50–24.00)	18.00 (15.00–21.00)	0.1156

AJCC, American Joint Committee on Cancer; Alb, albumin; ALT, alanine aminotransferase; ASA, American Society of Anesthesiologists physical status classes; AST, aspartate aminotransferase; CA19-9, cancer antigen 19-9; CONUT, Controlling Nutritional status score; DGE, delayed gastric emptying; EIBL, estimated intraoperative blood loss; IQR, interquartile range; LOS, length of stay; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; Plt, platelet; PNI, prognostic nutritional index; POPF, postoperative pancreatic fistula; PPH, postpancreatectomy hemorrhage; PTCD, percutaneous transhepatic cholangial drainage; RDW_CV, red blood cell distribution width CV; Tbil, total bilirubin; TG, triglyceride.

[a]Fisher exact test.

Results

Characteristics of patients in the laparoscopic and open pancreatoduodenectomy groups

The baseline and perioperative characteristics of 346 LPD and 427 OPD cases are described in Table 1 and Supplementary Table 1 (Supplemental Digital Content 2, http://links.lww.com/JS9/A40). There were no differences between the two groups for age, sex, BMI, American Society of Anaesthesiologists physical status score, American Joint Committee on Cancer (AJCC) stage, and medical or surgical history ($P > 0.05$). The length of stay, tumor diameter, level of cancer antigen 19-9, and rate of vascular resection and reconstruction in the LPD group were significantly lower than those of the OPD group. The most common tumor types of the LPD and OPD groups were tumor in the duodenal papilla and pancreatic head, respectively. In addition, there were no differences between the groups for the number of harvested and positive lymph nodes, pancreatojejunostomy methods, rate of positive resected margin and R0 resection, postoperative complication (CD ≥ III), and mortality within 30 and 90 days. The operative time, estimated intraoperative blood loss, and intraoperative infusion quantity of the LPD group were lower than in the OPD group.

Patient's characteristics of the three-level difficulty stages of the learning curve

To investigate the differences between the learning stages of LPD, 346 LPD cases were categorized according to the definition of the learning curve of LPD, and patients' characteristics between the three stages were compared. The results are shown in Table 2 and Supplementary Table 2 (Supplemental Digital Content 3, http://links.lww.com/JS9/A41). There were no differences between the three stages for age, sex, BMI, American Society of Anaesthesiologists score, length of stay, level of cancer antigen 19-9, and AJCC stage ($P > 0.05$). The tumor diameter, red cell volume distribution width, PNI, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, controlling nutritional status, creatinine, total bilirubin, and history of diabetes in LPD cases were statistically significant between the three stages. The incidences of postoperative complications (CD ≥ III) gradually decreased from stage I to III (20.00, 10.94, 5.79%, respectively, $P = 0.008$), including POPF of B/C grade (20.00, 15.63, 4.96%, respectively, $P = 0.001$), PPH of B/C grade (20.00, 7.81, 4.55%, respectively, $P = 0.002$), biliary leakage (15.00, 7.81, 2.89%, respectively, $P = 0.004$), and DGE of B/C grade (37.50, 26.56, 19.42%, respectively, $P = 0.030$).

Difficulty scoring system for inchoate learning curve phase

Based on the reviewer's difficulty 10-level index evaluation, 346 LPD cases were assigned a different value corresponding to their difficulty level. Using the automatic linear modeling tool, the following six clinical factors that significantly affected the difficulty level of LPD were identified: (1) tumor location, (2) vascular resection and reconstruction, (3) learning curve stage, (4) PNI, (5) tumor size, and (6) benign or malignant tumor (Table 3). The concordance between the reviewer's 10-level difficulty index and DS calculated by the linear modeling index is shown in Figure 1. From the linear modeling DS system, we developed a simpler and more practical scoring system, wherein index scores were assigned based on the difference between the computed values in a category and rounded off to the closest whole number. The short-term postoperative outcomes of the cases were postoperative complications (CD ≥ III).

Table 3

Linear modeling of the 10-level difficulty index for laparoscopic pancreatoduodenectomy

Factors	Coefficient (95% CI)	*P*	Importance	Score
Intercept	–0.033 (–0.088 to 0.155)	0.5933		
Location				
Other	0		0.1942	1
Pancreatic	1.214 (1.150–1.278)	< 0.0001		2
Cut artery				
No	0		0.0113	0
Yes	1.036 (0.868–1.205)	< 0.0001		1
Stage				
1	0		0.5804	1
2	2.632 (2.523–2.742)	< 0.0001		3
3	3.548 (3.454–3.641)	< 0.0001		4
PNI				
PNI ≥ 49	0		0.0741	0
PNI < 49	0.669 (0.603–0.734)	< 0.0001		1
Tumor size(cm)				
0–2	0		0.0247	0
> 2	0.661 (0.599–0.723)	< 0.0001		1
Malignant				
0	0		0.1153	0
1	1.062 (0.992–1.133)	< 0.0001		1

Weighted κ coefficient (95% CI): 0.873 (0.844–0.901), $R^2 = 0.966$.
Correlation index, $r = 0.9558$ ($P < 0.0001$).
CI, confidence interval; PNI, prognostic nutritional index.

We used the median as the cutoff value (e.g. DSS = 5 for stage I and DSS = 6 for stage II). The areas under the receiver operating characteristic curve of DSS to CD were 0.818 and 0.675 in learning curve stages I and II, respectively (Supplementary Table 3, Supplemental Digital Content 4, http://links.lww.com/JS9/A42). To

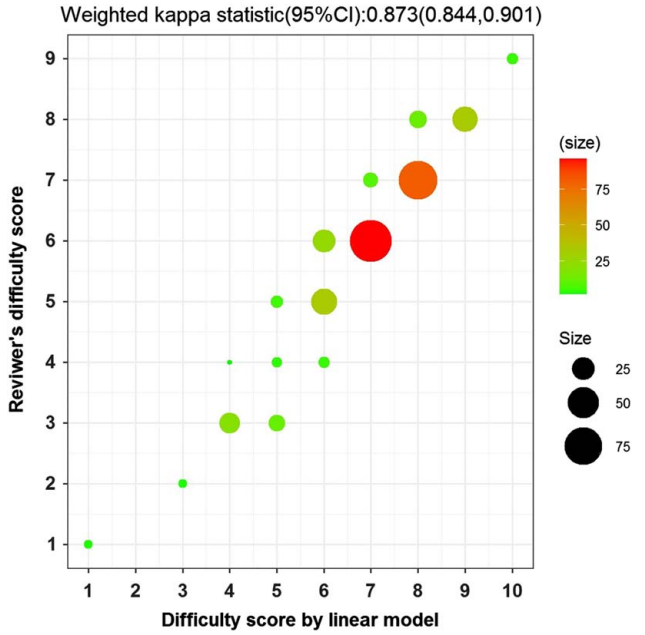

Figure 1. The κ value of the calculated and reviewer's difficulty score. Weighted κ coefficient (95% CI): 0.873 (0.844–0.901), $R^2 = 0.966$, $r = 0.9558$ ($P < 0.0001$). CI, confidence interval.

Table 4

Outcomes according to the difficulty scoring system in learning curve stage I in the training cohort

	n (%)		
Variables	**DSS < 5 (N = 23)**	**DSS ≥ 5 (N = 17)**	***P***
Age [mean (SD)] (years)	56.83 (11.07)	59.06 (7.38)	0.4756
Female	9 (39.13)	7 (41.18)	0.8961
ASA			0.2944
1	3 (13.04)	0 (0.00)	
2	17 (73.91)	14 (82.35)	
3	3 (13.04)	3 (17.65)	
BMI [mean (SD)] (kg/m^2)	21.32 (2.07)	21.65 (2.90)	0.6697
LOS [median (IQR)] (days)	21.00 (14.00–25.00)	25.00 (17.00–32.00)	0.6252
Tumor size [median (IQR)] (cm)	1.80 (1.20–2.00)	2.90 (2.50–3.50)	0.0005
Lym [median (IQR)] (10^9/l)	1.55 (1.15–1.81)	1.28 (0.86–1.50)	0.0835
RDW [median (IQR)]	13.80 (13.00–14.40)	15.40 (14.50–16.50)	0.0277
PNI [median (IQR)]	45.40 (43.65–49.35)	39.70 (37.40–43.50)	0.0012
NLR [median (IQR)]	36.39 (31.36–47.93)	50.81 (40.54–71.15)	0.2077
PLR [median (IQR)]	151.32 (112.90–211.88)	176.19 (113.33–239.53)	0.4282
CONUT [median (IQR)]	2.00 (1.00–3.00)	3.00 (1.00–4.00)	0.1227
Creatinine [median (IQR)] (mmol/l)	65.00 (58.00–72.00)	52.00 (47.00–58.00)	0.0071
BUN [median (IQR)] (mmol/l)	4.21 (2.99–5.41)	4.73 (3.96–5.51)	0.6838
CRP [median (IQR)] (mg/l)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.9315
TC [median (IQR)] (mmol/l)	4.47 (3.70–5.62)	5.69 (4.47–6.46)	0.0453
WBC [median (IQR)] (10^9/l)	5.35 (4.71–6.36)	5.64 (4.65–6.83)	0.3251
Neu [median (IQR)] (%)	57.30 (52.90–63.90)	62.80 (58.20–66.90)	0.1283
RBC [median (IQR)] (10^{12}/l)	4.04 (3.82–4.43)	3.89 (3.57–4.21)	0.1212
Hb [median (IQR)] (g/l)	124.00 (117.00–136.00)	111.00 (108.00–118.00)	0.0115
ALT [median (IQR)] (U/l)	67.00 (16.00–277.00)	136.00 (68.00–253.00)	0.5951
AST [median (IQR)] (U/l)	51.00 (17.00–138.00)	97.00 (51.00–174.00)	0.2418
γ-GT [median (IQR)] (U/l)	239.00 (22.00–546.00)	633.00 (365.00–1082.00)	0.0099
Alb [median (IQR)] (g/l)	37.50 (35.90–41.40)	34.50 (30.90–36.70)	0.0024
Tbil [median (IQR)] (μmol/l)	19.80 (11.50–78.60)	133.80 (69.40–202.60)	0.0191
Dbil [median (IQR)] (μmol/l)	10.90 (4.10–63.80)	109.40 (51.90–153.30)	0.0168
CA19-9 [median (IQR)] (U/ml)	14.88 (7.24–166.82)	80.19 (20.16–210.31)	0.9972
CEA [median (IQR)] (ng/l)	2.51 (1.29–3.45)	3.03 (1.87–4.22)	0.2859
CA125 [median (IQR)] (U/ml)	17.50 (9.60–22.37)	14.70 (9.10–19.00)	0.8509
AFP [median (IQR)] (ng/ml)	3.17 (1.76–4.97)	2.46 (2.15–3.16)	0.080
Operative time [median (IQR)] (min)	480.00 (390.00–600.00)	431.00 (400.00–530.00)	0.3571
EIBL [median (IQR)] (ml)	100.00 (50.00–400.00)	100.00 (30.00–200.00)	0.1927
IFIV [median (IQR)] (ml)	3500.00 (3000.00–4500.00)	3500.00 (2500.00–4500.00)	0.283
Intraoperative urine [median (IQR)] (ml)	1400.00 (1000.00–2000.00)	1200.00 (1000.00–1500.00)	0.7652
Lymph nodes harvested [median (IQR)]	16.00 (10.00–21.00)	17.00 (11.00–20.00)	0.3176
Positive lymph nodes [median (IQR)]	0.00 (0.00–1.00)	0.00 (0.00–1.00)	0.8812
PTCD	5 (21.74)	10 (58.82)	0.0166
Vascular resection	23 (100.00)	17 (100.00)	
Tumor location			0.4074[a]
Distal biliary duct	4 (17.39)	1 (5.88)	
Ampullary	3 (13.04)	2 (11.76)	
Duodenal papillary	12 (52.17)	8 (47.06)	
Pancreatic head	4 (17.39)	6 (35.29)	
Tumor characteristic			0.0877[a]
Benign	5 (21.74)	1 (5.88)	
Malignant	21 (78.26)	16 (94.11)	
AJCC			< 0.0001
IA	15 (78.95)	0 (0.00)	
IB	0 (0.00)	12 (75.00)	
IIA	1 (5.26)	2 (12.50)	
IIB	2 (10.53)	2 (12.50)	
III	1 (5.26)	0 (0.00)	
R0 resection			0.826[a]
R0	22 (95.65)	16 (94.12)	
R1	1 (4.35)	1 (5.88)	
30-day mortality	0 (0.00)	2 (11.76)	0.092[a]
90-day mortality	0 (0.00)	2 (11.76)	0.092[a]
Clavien–Dindo ≥ III	1 (4.35)	7 (41.18)	0.004[a]

Table 4

(*Continued*)

Variables	n (%)		
	DSS < 5 (N = 23)	DSS ≥ 5 (N = 17)	*P*
POPF of B/C grade	5 (21.74)	3 (17.65)	0.749[a]
PPH of B/C grade	4 (17.39)	4 (23.53)	0.631[a]
DGE of B/C grade	10 (43.48)	5 (29.41)	0.364[a]
Bile leakage	2 (8.70)	4 (23.53)	0.194[a]
Abdominal infection	2 (8.70)	8 (47.06)	0.006[a]
Hepatic failure	0 (0.00)	0 (0.00)	–
Renal failure	0 (0.00)	0 (0.00)	–
Pulmonary infection	1 (4.35)	2 (11.76)	0.379[a]
Cardiac dysfunction	0 (0.00)	0 (0.00)	–

AFP, alpha-fetoprotein; Alb, albumin; AJCC, American Joint Committee on Cancer; ALT, alanine aminotransferase; ASA, American Society of Anesthesiologists physical status classes; AST, aspartate aminotransferase; BUN; blood urea nitrogen; CA19-9, cancer antigen 19-9; CA125, carbohydrate antigen 125; CEA, carcinoembryonic antigen; CONUT, Controlling Nutritional status score; CRP, C-reactive protein; Dbil, direct bilirubin; DGE, delayed gastric emptying; DSS, difficulty scoring system; EIBL, estimated intraoperative blood loss; γ-GT, gamma-glutamyl transpeptidase; Hb, hemoglobin; IFIV, intraoperative fluid infusion volume; IQR, interquartile range; LOS, length of stay; Lym, lymphocytes; Neu, neutrophils; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; PNI, prognostic nutritional index; POPF, postoperative pancreatic fistula; PPH, postpancreatectomy hemorrhage; PTCD, percutaneous transhepatic cholangial drainage; RBC, red blood cell; RDW, red blood cell distribution width; Tbil, total bilirubin; TC, serum total cholesterol; WBC; white blood cell.

[a]Fisher exact test.

further evaluate the outcomes of the learning cohort, we divided the 40 LPD cases in stage I into two subgroups (i.e. 23 cases, DSS < 5; 17 cases, DSS ≥ 5). The perioperative data and postoperative outcomes of these cases are shown in Table 4. The patients with DSS < 5 had lower postoperative complications (CD ≥ III) than those with DSS ≥ 5 (4.35–41.18%, $P = 0.004$).

Validation of difficulty scoring system

To verify DSS's accuracy and clinical application, we reviewed 77 LPD cases of another surgeon who had not reached the mature learning curve stage at the same center. Supplementary Table 4 (Supplemental Digital Content 5, http://links.lww.com/JS9/A43) summarizes the patients' baseline demographic, clinicopathologic, and perioperative and postoperative data across the two learning curve stages. Supplementary Table 5 (Supplemental Digital Content 6, http://links.lww.com/JS9/A44) summarizes the characteristics of LPD surgeries according to difficulty groups. Twenty-eight cases were classified as low, 41 as intermediate, and eight as high difficulty. There were no significant differences in sex, age, BMI, and preoperative laboratory testing results between the three groups. Operative time [390.00 (300.00–435.00), 400.00 (358.00–435.00), 489.50 (413.00–522.00) min, $P = 0.0197$], estimated blood loss [175.00 (50.00–300.00), 200.00 (150.00–300.00), 350.00 (300.00–900.00) ml, $P = 0.0046$] were progressively increased from low to high difficulty groups. The PPH of B/C grade rate (3.57, 9.76, 37.50%, respectively, $P = 0.0474$) and DGE of B/C grade rate (0.00, 17.50, 37.50%, respectively, $P = 0.0166$) were progressively increased from low to high difficulty groups. However, it was not statistically significant. The postoperative complications (CD ≥ III) rate was increased from low to high difficulty groups (3.57, 12.20, 25.00%, respectively, $P = 0.1316$).To further clarify the clinical application value, the 40 LPD cases in the first stage of the learning curve were divided into two groups according to the DSS score (26 cases for DSS < 5 and 14 cases for DSS ≥ 5). The POPF rate (19.23–57.14%, $P = 0.0352$), DGE rate (19.23–71.43%, $P = 0.001$), and bile leakage rate (0.00–21.43%, $P = 0.0368$) were increased as the DSS increases. The postoperative complications (CD ≥ III) rate in DSS ≥ 5 group was higher than those in DSS < 5 group (3.85–14.29%, $P = 0.2763$). There were no significant differences in other perioperative outcomes, such as postoperative morbidity, readmission rate, and hospitalization (Table 5).

Discussion

LPD has been accepted as a conventional surgical procedure for pancreatic head and ampullary tumors in large pancreatic surgery centers[23,24]. Owing to the complicated surgical procedure and high technical requirements of surgeons, LPD is considered the "Everest" of abdominal minimally invasive surgery. The initial phase of the learning curve is a prerequisite for inexperienced surgeons[25,26], and it has been shown that more than 30–50 cases are needed at this phase[27–29]. Many institutions select patients with periampullary disease without vascular invasion for surgeons in the initial learning stage of LPD[30]. However, the precise patient selection criteria for the initial learning curve stage of LPD has not been demonstrated, which is critical in reducing postoperative complications and facilitating the steep learning curve of LPD[14].

This study aimed to develop a DSS for LPD that can be used to select surgery cases based on the surgeon's experience and expertise, ensuring safe stepwise adoption of LPD. The difficulty of LPD depends not only on the technical complexity of resection and reestablishment but also on various factors, such as a patient's general condition, tumor size and location, and the degree of blood vessel invasion[31]. Moreover, 'difficulty' is a relative, subjective term that varies among individuals with different surgical skills. Several studies have attempted to grade the difficulty of a surgery and relevant risk factors, and the validation or clinical application of those models or risk factors has demonstrated that patient selection based on objective variables could improve the short-term outcome after surgery[32,33]. Unfortunately, only a few studies have examined patient selection during the initial stage of the learning curve of LPD.

In the present study, the difficulty levels of 346 LPD cases were assessed by experts who had mastered all LPD surgical procedures. Furthermore, we have identified a few known surgical difficulty indexes. First, tumor diameter larger than 2 cm. Tumor size is an independent risk factor for the prognosis of pancreatic

Table 5

Outcomes according to the difficulty scoring system in learning curve stage I in the validation cohort

	n (%)		
Variables	**DSS < 5 (N = 26)**	**DSS ≥ 5 (N = 14)**	***P***
Age [mean (SD)] (years)	54.92 (12.17)	59.71 (6.14)	0.1769
Female	11 (42.31)	8 (57.14)	0.3702
ASA			0.1306
1	1 (3.85)	1 (7.14)	
2	21 (80.77)	7 (50.00)	
3	4 (15.38)	6 (42.86)	
BMI [mean (SD)] (kg/m^2)	23.25 (2.85)	21.33 (2.33)	0.0369
LOS [median (IQR)] (days)	19.50 (15.00–25.00)	18.50 (17.00–26.00)	0.9202
Tumor size [median (IQR)] (cm)	1.65 (1.30–2.00)	2.50 (2.50–3.00)	0.0006
Lym [median (IQR)] ($10^9/l$)	1.55 (1.16–1.91)	1.21 (1.07–1.40)	0.0453
PNI [median (IQR)]	46.20 (40.90–49.90)	44.65 (38.40–48.15)	0.1573
WBC [median (IQR)] ($10^9/l$)	6.11 (4.94–6.90)	5.70 (5.09–6.28)	0.7543
Neu [median (IQR)] (%)	60.20 (55.80–68.20)	66.45 (63.30–69.90)	0.0662
RBC [median (IQR)] ($10^{12}/l$)	4.14 (4.00–4.28)	3.80 (3.23–4.10)	0.0016
Hb [median (IQR)] (g/l)	127.00 (115.00–134.00)	116.50 (94.00–122.00)	0.0114
Alb [median (IQR)] (g/l)	39.45 (34.50–40.80)	38.50 (31.30–42.80)	0.6054
Tbil [median (IQR)] (μmol/l)	26.75 (8.50–201.80)	55.10 (18.00–125.90)	0.9236
Operative time [median (IQR)] (min)	395.00 (300.00–450.00)	400.00 (360.00–430.00)	0.2424
EIBL [median (IQR)] (ml)	200.00 (50.00–300.00)	200.00 (150.00–300.00)	0.3161
IFIV [median (IQR)] (ml)	2500.00 (2000.00–3000.00)	2250.00 (2000.00–3000.00)	0.8304
Intraoperative urine [median (IQR)] (ml)	1000.00 (800.00–1200.00)	900.00 (700.00–1200.00)	0.843
Lymph nodes harvested [median (IQR)]	12 (9–14)	13 (9–15)	0.3461
Vascular resection	0 (0.00)	1 (7.14)	0.1675[a]
Tumor location			
Distal biliary duct	3 (11.54)	0 (0.00)	0.0042
Ampullary	3 (11.54)	2 (14.29)	
Duodenal papillary	14 (53.85)	1 (7.14)	
Pancreatic head	6 (23.08)	11 (78.57)	
Tumor characteristic			0.0344
Benign	10 (38.46)	1 (7.14)	
Malignant	16 (61.54)	13 (92.86)	
AJCC			0.0022
IA	17 (65.38)	0 (0.00)	
IB	4 (15.38)	5 (35.71)	
IIA	0 (0.00)	1 (7.14)	
IIB	4 (15.38)	6 (42.86)	
III	1 (3.85)	2 (14.29)	
Clavien–Dindo ≥ III	1 (3.85)	2 (14.29)	0.2763[a]
Pancreatic fistula	5 (19.23)	8 (57.14)	0.0352[a]
POPF of B/C grade	2 (7.69)	3 (21.43)	0.3223[a]
PPH	4 (15.38)	6 (42.86)	0.0520[a]
PPH of B/C grade	0 (0.00)	2 (14.29)	0.1167[a]
DGE	5 (19.23)	10 (71.43)	0.0010
DGE of B/C grade	1 (3.85)	2 (14.29)	0.2763[a]
Bile leakage	0 (0.00)	3 (21.43)	0.0368[a]
Abdominal infection	0 (0.00)	2 (14.29)	0.1167[a]
Hepatic failure	0 (0.00)	0 (0.00)	–
Renal failure	0 (0.00)	0 (0.00))	–
Pulmonary infection	0 (0.00)	0 (0.00)	–
Cardiac dysfunction	0 (0.00)	0 (0.00)	–

AJCC, American Joint Committee on Cancer; Alb, albumin; ASA, American Society of Anesthesiologists physical status classes; DGE, delayed gastric emptying; DSS, difficulty scoring system; EIBL, estimated intraoperative blood loss; Hb, hemoglobin; IFIV, intraoperative fluid infusion volume; IQR, interquartile range; LOS, length of stay; Lym, lymphocytes; Neu, neutrophils; PNI, prognostic nutritional index; POPF, postoperative pancreatic fistula; PPH, postpancreatectomy hemorrhage; RBC, red blood cell; Tbil, total bilirubin; WBC, white blood cell.

[a]Fisher exact test.

ductal adenocarcinoma (PDAC) after surgery. The AJCC eighth edition staging system for PDAC defined a maximum tumor diameter of 2 cm as the boundary point of T1 and T2 stages. A smaller tumor size indicates that the tumor is at an early stage of differentiation. Moreover, a previous study showed that tumor size more than 3 cm is independently associated with long-term survival[34]. Second, surgical procedures involving vascular resection and reconstruction. Patients with superior mesenteric

vein (SMV)/portal vein (PV) or hepatic artery invasion should be categorized as a more difficult case. The AJCC eighth edition staging system for PDAC has defined a tumor involving the celiac axis or superior mesenteric artery as a boundary point of T4 stage, regardless of tumor size. Furthermore, the ISGPS suggests that partial resection of the PV or SMV should be performed in case of their suspected involvement in tumor progression to achieve radical resection. However, postoperative complications after a venous resection appear to be contradictory. A recent observational study showed that venous resection is associated with increased mortality and poor survival[35]; however, another study examining 229 venous resections showed no differences in morbidity, mortality, and survival among the types of venous resection[36]. Third, pancreatic and malignant tumors. Tumors located on the pancreatic head or uncinate process are considered a more difficult surgery than those with tumors forming in other sites because the pancreatic head tumor can invade the SMV/PV more easily, especially if the tumor is malignant. The PNI, initially proposed by Buzby *et al.*[37] and refined by Onodera *et al.*[21], is calculated using the serum albumin concentration and total lymphocytes count in peripheral blood and is used to evaluate preoperative nutritional conditions and surgical complications in patients with gastrointestinal cancers. The significance of PNI as a prognostic predictor has been demonstrated in various types of human cancers[38–40]; low PNI may indicate hypoalbuminemia and/or lymphocytopenia. Hypoalbuminemia in patients after PD contributes to impaired liver function due to biliary obstruction. It is also associated with a sustained systemic inflammatory response from the tumor itself or host reaction. Contrarily, lymphocytes play important roles in the host immune response, postoperative tissue repair, and digestive system functional recovery. In most cases, the clinical and empirical patient selection based on PNI and other inflammatory indices do not reduce the complication rate. In our study, a linear model was generated by analyzing all clinical information and difficulty indexes, and a subsequent simpler 10-level scoring system was developed from the linear model. The weighted κ statistic was 0.873 for the 10-level difficulty index, showing an excellent agreement between the assessment by the reviewer and 10-level scoring system.

Furthermore, the clinical practice, usefulness, and applicability of the developed DSS were evaluated internally and externally. Compared with subjective and partial experiential selection criteria, the DSS developed in our study could provide a more accurate and objective-based selection for a surgeon who has been at the initial stage of the learning curve of LPD. The tumor's location, size, and characteristics could be assessed accurately before surgery. Moreover, factors such as PNI and the learning curve stage were considered objective clinical data. In stage I of the learning curve of LPD (0–40 cases), patients with DSS < 5 had lower postoperative complications (CD $\geq$ III) than those with DSS ≥ 5 after PD, including POPF, DGE, and bile leakage rate. Although due to sample size limitations of the validation cohort, there were no significant differences in the postoperative complications rate (CD $\geq$ III). Based on these results, we still recommend selecting cases with DSS < 5 in the learning curve stage I for surgeons to reduce postoperative complications and improve the outcomes. In addition, the six identified surgical difficulty indexes could aid surgeons in selecting the appropriate surgical method to improve patient fitness for surgery and the corresponding prognosis. Furthermore, it can also be used as a guide to build a useful curriculum for surgeons acquiring the technical skills of LPD in a stepwise manner.

This study has several limitations. First, although the learning and validation cohort data were from different surgeons, it was still a single-center study. The clinical application, rationality, and practicality of this DSS need to be verified in future studies. Besides, we developed the DSS only suitable for learning stage I of LPD. Therefore, in our future plans, the multicentric validation and more experience regarding learning stage I, learning stage II, and learning stage III will be conducted. Second, individual surgeons might have had some technical differences, including the surgical approach and strategy. Therefore, all the above were also risk factors for postoperative complications, and the influence of these subjective differences on our results needs to be verified further.

In conclusion, we developed a validated risk-scoring model for predicting the technical difficulty of LPD with satisfactory clinical usefulness. These results were based on objective variables, which could reduce postoperative complications and effectively replace the conventional subjective patient selection. We believe that our constructed DSS model can select more appropriate patients for surgeons at their initial learning stage of LPD, contributing to safer and more reliable short-term outcomes for surgeons.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Ethical approval

The study was approved by the institutional review board at each participating hospital, and the need for informed consent was waived due to the retrospective nature of the study.

Sources of funding

This study was supported by grants from The National Natural Science Foundation of China (81402443 to F.P.; 81772950 to R.Q.; 81773160 to M.W.), the HUBEI Natural Science Foundation (2017CFB467 to M.W.), the Tongji Hospital Science Fund for Distinguished Young Scholars (2016YQ08 to M.W.), and the Wuhan applied basic research project (2016060101010070 to R.Q.).

Authors' contribution

F.P.: conceptualization, methodology, data curation, investigation. R.H.: conceptualization, methodology, writing – original draft. H.W. and M.W.: conceptualization, methodology, software, formal analysis. H.Z.: conceptualization, methodology, software, formal analysis, visualization. T.Q.: writing – review and editing, project administration, resources, supervision. R.Q.: conceptualization, writing – review and editing, project administration, funding acquisition, supervision.

Conflicts of interest disclosure

The authors declare that they have no financial conflict of interest with regard to the content of this report.

Research registration unique identifying number (UIN)

NCT05520606.

Guarantor

Renyi Qin.

Acknowledgements

The authors thank Editage (www.editage.com) for English language editing.

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