Association of textbook outcomes with improved survival in pancreatic ductal adenocarcinoma following pancreaticoduodenectomy: a retrospective study

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Background: Assessing the perioperative outcomes of pancreaticoduodenectomy (PD) based solely on individual complications is not comprehensive, and the association between perioperative outcomes and the long-term prognosis of individuals diagnosed with pancreatic ductal adenocarcinoma (PDAC) remains uncertain. Our study is designed to evaluate the impact of a novel composite indicator, textbook outcomes (TO), on the long-term prognosis of patients undergoing PD for PDAC.

Methods: This study conducted a retrospective analysis of 139 patients who underwent PD for pathologically confirmed PDAC at our hospital between January 2018 and December 2021. After applying exclusion criteria, a total of 111 patients were included in the subsequent analysis. These patients were categorized into two groups: the non-TO group (n=42) and the TO group (n=69). The Kaplan-Meier survival curve was employed to describe the relationship between TO and disease-free survival (DFS) and overall survival (OS). Cox regression was employed to assess the impact of achieving TO on long-term survival. Logistic regression was employed to investigate the risk factors affecting the achievement of TO.

Results: Out of the 111 PDAC patients, 69 (62.2%) achieved TO following PD. The achievement of TO significantly improved the OS of PDAC patients [P=0.03; hazard ratio (HR) =0.60; 95% confidence interval (CI): 0.37–0.83]. Cox regression analysis indicated that achieving TO was a protective factor for OS (P=0.04; HR =4.08; 95% CI: 1.07–15.61). Logistic regression analysis indicated that high amylase in drainage fluid on the third day after surgery (>1,300 U/L) was detrimental to achieve TO [odds ratio (OR) =0.10; 95% CI: 0.02–0.58; P=0.01], longer surgery durations (≥6.25 hours) was detrimental to achieve TO (OR =0.19; 95% CI: 0.06–0.54; P=0.002), and soft pancreatic texture was detrimental to achieve TO (OR =0.31; 95% CI: 0.10–0.93, P=0.04).

Conclusions: Achievement of TO significantly improves the OS of PDAC patients and has the potential to serve as a robust prognostic indicator. Looking ahead, it is highly necessary for TO to become a standard surgical quality control measure in hospitals.

Keywords: Pancreaticoduodenectomy (PD); pancreatic ductal adenocarcinoma (PDAC); textbook outcomes (TO); prognosis

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Introduction

Pancreaticoduodenectomy (PD) is one of the most complex and challenging surgery. Radical resection represents the core component of its comprehensive treatment process for pancreatic cancer. However, given that the diverse and risky character of its surgical complications, the quality of the surgery directly determines the short-term prognosis of patients, influencing the implementation of postoperative multimodal therapy or adjuvant treatment, and it is highly likely to have an impact on long-term prognosis (1-4). Currently, the assessment of surgical quality for PD predominantly relies on a model that evaluates individual complications. Despite the International Study Group of Pancreatic Surgery (ISGPS) providing comprehensive definitions and revisions for postoperative complications like postoperative pancreatic fistula (POPF) (5,6), postoperative hemorrhage (PPH) (7) and postoperative bile leak (8), which has significantly advanced the management and prevention of postoperative complications, analyzing individual complications may not comprehensively cover the entire surgical process. The standardization and normalization of its evaluation are susceptible to potential confounding factors. Recent research indicates that assessing surgical procedures by integrating multiple factors helps enhance the overall quality of complex surgeries. This approach guides both patients and healthcare providers, fostering more favorable medical outcomes (9,10). Additionally, research centered around achieving "textbook outcomes" (TO) has emerged in this context (11,12).

In 2013, the concept of TO was first proposed and applied to assess the quality of colon cancer surgeries which is achieved when none of the unexpected events occurred. It has been used to evaluate the quality of surgeries across different hospitals with different capacities by comparing the achievement rate of TO in colon cancer surgeries (13). Subsequently, this concept has been widely explored and applied to other surgical procedures such as liver resections (14,15), esophageal surgeries (16), heart transplant surgeries (17) and so on. In the field of pancreatic surgery, Merath *et al.* conducted an initial exploration of TO for pancreatic surgery which included four indicators: no postoperative complications, no prolonged hospital stays, no postoperative mortality, and no readmissions within 90 days after discharge. The TO rates for pancreatic surgery varied from 11.1% to 69.6% across different hospitals (18). Mehta *et al.* used the same concept to define TO and found that achieving TO was more likely in specialized cancer hospitals (19). This highlights that TO can be used to assess the quality of surgical outcomes in different hospitals and can help guide patients in choosing where to seek medical care. In 2020, Heidsma *et al.* evaluated TO for surgery of pancreatic neuroendocrine tumors and found that achieving TO was beneficial for improving the long-term prognosis of patients, as it had a protective effect on disease-free survival (DFS) [odds ratio (OR) =0.54; 95% confidence interval (CI): 0.35–0.81; P=0.003]. What set this study apart from the previous research was that it included R0 resection as part of the TO definition (20). As of 2020, the Dutch Pancreatic Cancer Group (DPCG) defined TO for pancreatic surgery as follows: no in-hospital mortality, no Clavien-Dindo complications of grade III or higher, no clinically relevant pancreatic fistula, no postoperative bleeding, no bile leakage, and no readmission within 30 days. This definition was established after a review by 24 pancreatic surgeons from ten different countries, providing a relatively authoritative reference for the application of TO in pancreatic surgery (21).

Subsequently, more meticulously designed studies have emerged in the field of pancreatic surgery, particularly in

Highlight box

Key findings

- In this cohort of 111 patients undergoing pancreaticoduodenectomy (PD) for pancreatic ductal adenocarcinoma (PDAC), 62.2% (69/111) achieved textbook outcomes (TO).
- Patients who achieved TO following PD had longer overall survival (OS).
- Factors related to postoperative pancreatic fistula, prolonged surgical time, and seriouspostoperative inflammatory response may not be conducive to the achievement of TO.
- Failure to achieve TO is an independent risk factor for PDAC patients' OS.

What is known and what is new?

- Previous researches demonstrated that achievement of TO significantly improved the long-term prognosis for gastric and colorectal cancers.
- This study, for the first time, reveals that achievement of TO can also notably improve the long-term prognosis of PDAC. Furthermore, it suggests that TO may serve as a comprehensive perioperative indicator for predicting long-term prognosis in PDAC patients.

What is the implication, and what should change now?

- TO shows significant guidance value in identifying patients benefiting from surgery and predicting long-term prognosis, and it should become a key indicator in the surgical quality control of medical institutions.

the context of PD (22-25). Nicholas *et al.* applied the new standard of TO in pancreatic surgery for the first time. They studied 182 patients who underwent PD from 2005 to 2020 and found that 58% of them achieved TO. The study also compared the probability of achieving TO in different years, summarizing the treatment experience of the single center (22). Wu *et al.* conducted a multicenter retrospective study from the Chinese mainland, which included a total of 1,029 patients who underwent laparoscopic pancreaticoduodenectomy (LPD). The study revealed an achievement rate of 68.9% for TO and identified narrow main pancreatic duct diameter, advanced age, and the presence of cardiovascular disease as risk factors for not achieving TO (23). Furthermore, the researchers used TO as a primary indicator to evaluate the short-term surgical outcomes of Laparoscopic duodenum-preserving pancreatic head resection (LDPPHR-t) and found that POPF was the primary barrier to achieving TO after LDPPHR-t. Placement of an endoscopic nasobiliary drainage (ENBD) tube was recognized as the only significant independent risk factor for developing POPF following LDPPHR-t surgery. Their researches used TO to explore possible avenues for improving the quality of PD (24). The widespread adoption of neoadjuvant therapy in unresectable pancreatic ductal adenocarcinoma (PDAC) has made pancreatic surgery more complex and challenging. A prospective study conducted by Zhu *et al.* revealed that there was no difference in achieving TO between the neoadjuvant chemotherapy group and the direct surgery group. This provided evidence at the perioperative management level to support the safety of neoadjuvant chemotherapy for PDAC patients (25). Numerous studies have conducted exploratory research on the application of the new concept of TO in pancreatic surgery, with different emphases. These studies have demonstrated the feasibility and wide applicability of TO in the field of pancreatic surgery. Establishing an evaluation system centered around TO in pancreatic surgery holds great promise for further enhancing surgical techniques and quality, particularly in the context of PD.

It is worth noting that this definition does not include pathological indicators such as the achievement of R0 resection, intraoperative lymph node clearance, postoperative adjuvant therapy and so on. Within the existing standards that do not incorporate oncological assessment indicators, it remains unclear whether the achievement of TO in pancreatic surgery has an impact on the long-term prognosis of malignant tumor patients, and whether the definition of TO is applicable in Asian medical and cultural environments. To address these scientific questions, our research aims to explore the achievement of TO following PD for PDAC within the Asian medical background and to investigate whether the achievement of TO has an impact on the long-term prognosis of patients with PDAC, and to explore the risk factors affecting TO. This study was presented in strict accordance with the STROBE reporting checklist (26) (available at https://tgh.amegroups.com/article/view/10.21037/tgh-23-112/rc).

Methods

This study was conducted in accordance with the principles of the Helsinki Declaration (as revised in 2013). The study was reviewed and approved by the Ethics Committee of Sun Yat-sen Memorial Hospital, Sun Yat-sen University (approval ID: SYSKY-2023-1076-01) and was registered in the Chinese Clinical Trial Registry (registration No. MR-44-23-046152). All participating patients provided informed consent prior to surgery, authorizing the confidential use of their medical data for research purposes.

Inclusion and exclusion criteria

This retrospective cohort study included 139 patients following PD at our medical institution from January 2018 to December 2021, and postoperative pathology reports validated the presence of PDAC. Among these 139 patients, nine patients had concurrent liver resection for preoperative liver metastasis, six patients had concurrent colonic resection for preoperative colon invasion, six patients received neoadjuvant therapy, and seven patients were lost to follow-up. Excluding the 28 patients who had undergone concurrent other organs resection, received neoadjuvant therapy, and lost to follow up, the study ultimately included 111 patients who underwent standard PD for PDAC, and no distant metastases were detected in these patients before and during surgery. Based on the presence of complications, the 111 patients were categorized into two groups, namely the TO group (n=69) and the non-TO group (n=42). Three patients in the non-TO group who died during the perioperative period were not included in subsequent prognosis analyses (*Figure 1*).

Data collection

All perioperative medical data for patients were meticulously recorded. Basic characteristics including age, gender, body

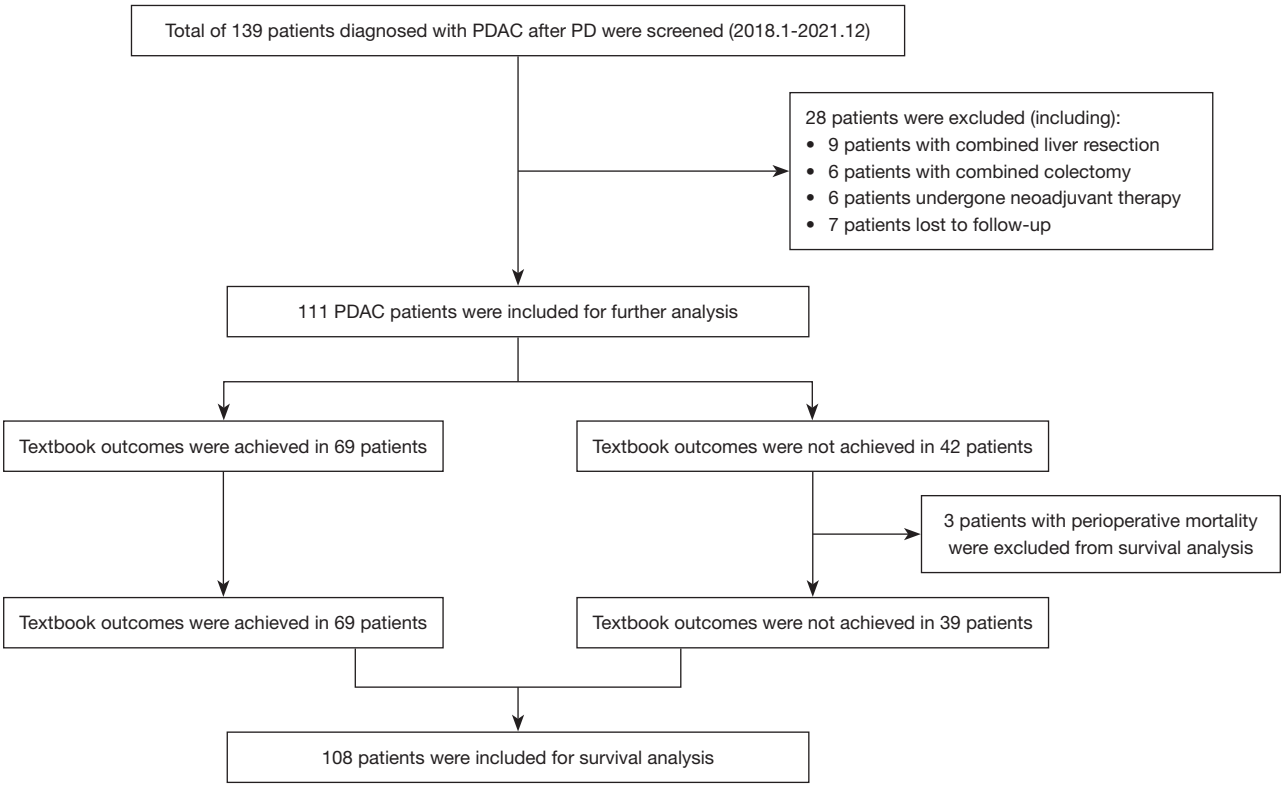

Figure 1 Inclusion and exclusion criteria. PDAC, pancreatic ductal adenocarcinoma; PD, pancreaticoduodenectomy.

mass index (BMI), Charlson comorbidity index (CCI), American Society of Anesthesiologists (ASA) score, and preoperative biliary drainage procedures were collected. Preoperative oncological indicators [carbohydrate antigen 199 (CA199), CA125, and CA724], blood biochemistry parameters, blood cell analysis parameters, amylase levels in drainage fluid on the first and third postoperative days, and serum amylase on the first postoperative day were collected for all patients. Pathological results including tumor size, tumor differentiation, TNM (AJCC 8th) stage, R0 resection (defined as a surgical margin of at least 1 mm free of tumor tissue under the microscope), the number of lymph nodes dissected and numbers of metastases, microscopic perineural invasion, microscopic adipose tissue invasion, microscopic vascular tumor emboli and whether postoperative adjuvant therapy has been completed [defined as postoperative adjuvant therapy cycles (PATc) ≥6] were collected (27,28). Surgical parameters, such as surgical type, duration, vascular repairment or reconstruction, pancreaticojejunostomy method, estimated blood loss, intraoperative transfusion, pancreatic texture, main pancreatic duct diameter, and bile duct diameter, were collected for all patients.

Assessment of resectability

In accordance with the NCCN (National Comprehensive Cancer Network) Guidelines for PDAC (28), resectability was assessed preoperatively by radiologists and hepatobiliary surgeons utilizing enhanced computed tomography (CT) or magnetic resonance imaging (MRI) scans of the abdomen, chest, head, and pelvis. The resectable tumor was defined as no contact with the major arteries [celiac axis (CA), superior mesenteric artery (SMA), or common hepatic artery (CHA)], and no contact with major veins [superior mesenteric vein (SMV) or portal vein (PV)] or ≤180° contact without major vein contour irregularity, and no metastases. The borderline resectable tumor was defined as contact with the CHA without extension to the CA or hepatic artery bifurcation or abutment and no extension to SMA or variant artery, and >180° contact major vein (SMV or PV) with contour irregularity or tumor thrombus but vascular resection and reconstruction are still feasible.

Nevertheless, considering a multitude of factors, clinical

practices often extend beyond established guidelines. For instance, the PDAC patients with metastases (liver or colon) who were in suitable overall health condition and exhibit a strong willingness for surgical intervention might undergo PD in conjunction with resection of additional organs. Surgery was contingent upon thorough deliberation during a multidisciplinary team (MDT) conference. To ensure uniformity and comparability, we had strictly included patients diagnosed with resectable and borderline resectable PDAC.

Follow-up of patients

Patients were followed up using outpatient visits and telephone contacts, with the last follow-up conducted up to October 15, 2023. Overall survival (OS) was determined as the duration from the surgical procedure to the occurrence of decease or the date of the last follow-up. DFS was characterized as the duration from the surgical procedure to the recurrence of tumors or the date of the last follow-up. The presence of tumor recurrence or progression is determined based on postoperative enhanced CT or MRI scans of patients and the trends in serum tumor markers. According to the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) standards, disease progression can be confirmed when the measurable total volume of the pancreas and surrounding tissues has increased by 20% or more compared to the previously recorded minimum total volume, or when new lesions or organ metastases are observed (29).

Definition of TO

Following the definition of TO by the DPCG in 2020, we have also defined TO as the following criteria: no POPF, no PPH, no bile leakage (all ISGPS grade B/C), no severe complications (Clavien-Dindo grade ≥ III), no in-hospital or 30-day mortality, and no readmission within 30 days after discharge (21). When all six of these criteria are fully met, the case is recognized as having achieved a TO in the surgery. Postoperative complications are assessed and graded using the Clavien-Dindo complication grading system (30) and the definitions of postoperative complications by ISGPS (6-8).

Surgical procedure and postoperative management

In our medical institution, PD can be performed using open surgery, laparoscopic assistance, or robot-assisted techniques. The surgical procedure follows these principles: under general anesthesia, an initial abdominal exploration is carried out to rule out any metastases. Then, gallbladder is removed. Distal stomach is transected using a stapler. The hepatic common artery is meticulously dissected, and the 8th group of lymph nodes is cleared. After ligating and dividing the gastroduodenal artery and right gastric vessels, the hepatoduodenal ligament is incised. The 12th group of lymph nodes is cleared, and then the common hepatic duct is transected using a sharp scalpel or scissors. The body and neck of the pancreas are adequately exposed, and the pancreas is transected horizontally and cauterized using an ultrasonic scalpel or bipolar coagulation. The jejunum is transected about 15 cm away from the Treitz ligament using a stapler. After thoroughly addressing the mesenteric vessels and the pancreatic stump, the reconstruction of the gastrointestinal tract is performed using the Child order. The surgeon decides during the procedure whether to perform an end-to-side mucosa-to-mucosa pancreaticojejunostomy or an end-to-end pancreaticojejunostomy. Subsequently, an end-to-side choledochojejunostomy is performed about 10 cm distal to the pancreaticojejunostomy, and finally, a gastrojejunostomy is done about 40 cm distal to the choledochojejunostomy using either a stapler or hand-sewn technique, with reinforcement of the seromuscular layer of the stomach and jejunum using absorbable sutures.

Drains are routinely placed anterior and posterior to the pancreaticojejunostomy anastomosis to prevent leakage. In cases of biliary stricture, a T-tube drainage may be inserted. To prevent POPF, prophylactic measures are taken, which include the use of somatostatin or its analogs. Postoperatively, the drainage fluid amylase levels are regularly monitored. Drains are removed when there is a decrease in drainage fluid volume and clinical signs of severe complications such as POPF or bile leakage have been ruled out.

Statistical analysis

All statistical analyses were performed using R software (4.2.2). To compare the baseline data between two groups (non-TO group *vs.* TO group), Student's *t*-test or analysis of variance (ANOVA) was applied for continuous variables presented as means with standard deviations, while Chi-squared test was employed for categorical variables presented as medians with interquartile ranges (IQRs) or ranges. The Kaplan Meier (K-M) analysis was employed

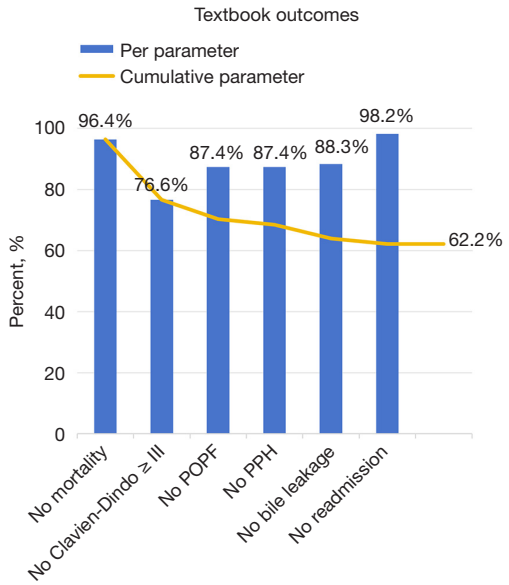

Figure 2 Achievement of textbook outcomes after PD in 111 patients with PDAC. The blue bar chart represents the proportion achieved by each parameter, and the yellow line shows the cumulative achievement ratio of all parameters. POPF, postoperative pancreatic fistula; PPH, postoperative hemorrhage; PD, pancreaticoduodenectomy; PDAC, pancreatic ductal adenocarcinoma.

to assess DFS and OS between the two groups. Median follow-up time was calculated using the reverse K-M analysis, and the results included reporting the median follow-up time, median survival time, as well as the 1-year and 2-year survival rates. Cox regression analysis was utilized to investigate the relationship between achieving TO and long-term survival. Logistic regression analysis was employed to explore potential factors associated with the attainment of TO. Variables were included in the multivariate logistic regression analysis if the independent variables' P value was less than 0.1 in the univariate analysis. Continuous independent variables were transformed into binary variables for subsequent analysis using the Youden index as a cutoff value. A P value less than 0.05 was deemed significant.

Results

TO achievement rate and distribution of the primary reasons for not achieving TO

In the 111 cases of PDAC patients, 69 cases (62.2%) achieved TO. *Figure 2* displays the distribution and cumulative occurrence of the six individual outcome indicators. The most common parameter preventing the achievement of TO was "No Clavien-Dindo ≥ Grade III complications" (76.6%), followed by "No PPH" and "No POPF" (87.4%). The least common indicator was "No readmission within 30 days" (98.2%).

Table 1 presents the distribution of the primary reasons

Table 1 Reasons for the failure to achieve TO

TO metric	Non-TO group (N=42)
Perioperative mortality, n (%)	3 (7.1)
PPH	2 (4.8)
Pancreatic fistula-associated abdominal infection	1 (2.4)
Clavien-Dindo ≥ III, n (%)	25 (59.5)
Hypovolemic shock	10 (23.8)
Septic shock	7 (16.7)
Abdominal infection	5 (11.9)
Pneumonia	2 (4.8)
Reopen operation	6 (14.3)
Bleeding	3 (7.1)
Pancreatoenteric anastomotic fistula	1 (2.4)
Gastrointestinal anastomotic fistula	1 (2.4)
Output loop obstruction	1 (2.4)
Hemostasia with interventional embolization	4 (9.5)
Unscheduled ICU admission	3 (7.1)
Hepatic failure	2 (4.8)
Delayed gastric emptying	2 (4.8)
Cardiac failure	1 (2.4)
Pulmonary embolism	1 (2.4)
Abdominal chylous fistula	1 (2.4)
POPF ≥ B, n (%)	14 (33.3)
PPH ≥ B, n (%)	14 (33.3)
Bile leakage ≥ B, n (%)	13 (30.9)
Readmission within 30 days, n (%)	2 (4.8)
Delayed gastric emptying	1 (2.4)
Biliary tract infection	1 (2.4)

TO, textbook outcomes; PPH, postoperative hemorrhage; ICU, intensive care unit; POPF, postoperative pancreatic fistula.

for not achieving TO, with the most significant factor being the occurrence of Clavien-Dindo ≥ Grade III complications (25/42, 59.5%). The top three common reasons were hypovolemic shock (10/42, 23.8%), septic shock (7/42, 16.7%), and reoperation (6/42, 14.3%). Additionally, three patients experienced perioperative mortality, with two cases due to PPH and one case due to severe abdominal infection caused by POPF. However, only two patients were readmitted within 30 days after discharging due to gastric emptying disorders and biliary infection.

Comparison of baseline data between the non-TO and TO groups

Table 2 shows the comparison of partial baseline characteristics among the 111 PDAC patients. Significant distinctions (P<0.05) were observed between the non-TO and TO groups in parameters such as ASA score, laboratory parameters on the third day after surgery [including activated partial thromboplastin time (APTT), percentage of neutrophil, percentage of lymphocyte, percentage of monocyte, and neutrophil/lymphocyte ratio (NLR)], postoperative amylase levels in drainage fluid, pancreatic texture, main pancreatic duct diameter, length of postoperative hospital stay (LOS), and length of time to the first adjuvant therapy (LOFAT).

However, no statistically significant distinctions (P>0.05) were noted in terms of gender, age, BMI, CCI, resectability, other laboratory test results, operation duration, operation type, intraoperative blood loss, vascular reconstruction, pancreaticoenteric anastomosis method, TNM stage, tumor differentiation, tumor size, the number of lymph nodes dissected and numbers of metastases, and diameter of the transected common bile duct, PATc and completed postoperative adjuvant therapy (CPAT; PATc ≥6). A comprehensive dataset with detailed baseline information for all patients is available in the Table S1. Moreover, it is noteworthy that four patients in the non-TO group did not receive adjuvant therapy, with three of them experiencing perioperative mortality, while one patient was unable to tolerate chemotherapy due to severe renal dysfunction.

Table 2 Part of baseline characteristics of PDAC patients with or without achieving textbook outcomes following PD

Characteristics	Non-textbook outcome group (n=42)	Textbook outcome group (n=69)	P value
Gender (female/male)	19 (45.2)/23 (54.8)	30 (43.5)/39 (56.5)	>0.99
Age (years)	62.7 (12.3)	60.2 (9.32)	0.28
BMI (kg/m^2)	22.1 (3.34)	21.7 (2.70)	0.45
ASA			0.044
1	3 (7.1)	7 (10.1)	
2	13 (31.0)	30 (43.5)	
3	22 (52.4)	32 (46.4)	
4	4 (9.5)	0 (0.0)	
Resectability			0.83
Resectable	32 (76.2)	50 (72.5)	
Borderline	10 (23.8)	19 (27.5)	
CA199 (U/mL)	222 [0.600, 4,370]	181 [0.600, >10,000]	0.35
APTT† (s)	31.9 (6.92)	28.0 (5.52)	0.002
Neutrophils† (%)	83.6 [67.9, 93.1]	78.8 [62.7, 95.4]	<0.001
Lymphocyte† (%)	7.65 [2.70, 17.4]	9.70 [2.40, 22.8]	0.02
Monocyte† (%)	5.80 [1.00, 12.5]	7.20 [2.10, 17.8]	0.03
NLR†	10.8 [4.15, 33.5]	8.20 [2.78, 39.8]	0.02

Table 2 (*continued*)

Table 2 (*continued*)

Characteristics	Non-textbook outcome group (n=42)	Textbook outcome group (n=69)	P value
DFA POD‡ (U/L)	450 [3.00, 36,100]	211 [11.0, 13,300]	0.046
DFA POD† (U/L)	184 [6.00, 65,000]	83.0 [6.00, 15,100]	0.005
Operation duration (hours)	7.00 [3.60, 12.0]	6.00 [2.15, 12.0]	0.13
Operation type			0.80
L	17 (40.5)	27 (39.1)	
L→O	7 (16.7)	9 (13.0)	
O	15 (35.7)	30 (43.5)	
R	3 (7.1)	3 (4.3)	
Pancreatic anastomosis			>0.99
Duct-to-mucosa	34 (81.0)	55 (79.7)	
End-to-end	8 (19.0)	14 (20.3)	
Estimated blood loss (mL)	200 [20.0, 16,000]	150 [20.0, 4,800]	0.38
Blood transfusion (mL)	400 [200, 7,100]	800 [200, 2,400]	0.71
None§	23 (54.8)	37 (53.6)	
TNM (AJCC 8th)			0.85
I	6 (14.3)	12 (17.4)	
II	7 (16.7)	13 (18.8)	
III	29 (69.0)	44 (63.8)	
Tumor size (cm)	3.00 [1.40, 6.40]	3.00 [1.00, 10.3]	0.65
Resected lymph nodes	15.5 [5.00, 37.0]	16.0 [3.00, 50.0]	0.32
Pancreatic texture (hard/soft)	21 (50.0)/21 (50.0)	55 (79.7)/14 (20.3)	0.002
Pancreatic duct diameter (cm)	0.27 [0.11, 0.67]	0.34 [0.15, 0.81]	0.02
LOS (days)	22 [4, 97]	12 [6, 37]	<0.001
LOFAT (days)	69 [39, 135]	47 [26, 87]	<0.001
Missing	4 (9.5)	0 (0.0)	
PATc	6 [1, 16]	8 [1, 22]	0.08
Missing	4 (9.5)	0 (0.0)	
CPAT (PATc ≥6)			0.37
No	12 (28.6)	15 (21.7)	
Yes	26 (61.9)	54 (78.3)	
Missing	4 (9.5)	0 (0.0)	

Data are presented as n (%), mean (standard deviation), medium [minimum, maximum]. †, postoperative day 3 level; ‡, postoperative first day level; §, no blood transfusion. Missing: absence value. PDAC, pancreatic ductal adenocarcinoma; PD, pancreaticoduodenectomy; BMI, body mass index; ASA, American Society of Anesthesiologists; CA199, carbohydrate antigen 199; APTT, activated partial thromboplastin time; NLR, neutrophil/lymphocyte ratio; DFA, drainage fluid amylase; POD, postoperative day; L, laparoscopic surgery; O, open surgery; L→O, laparoscopic surgery transit open; R, robotic surgery; TNM (AJCC 8th), TNM stage of American Joint Committee on Cancer (eighth edition); LOS, length of postoperative hospital stay; LOFAT, length of time to the first adjuvant therapy; PATc, postoperative adjuvant therapy cycles; CPAT, completed postoperative adjuvant therapy.

Comparison of indicators that may potentially affect prognosis between the non-TO group and TO group

Table 3 presents the comparison of prognostic parameters among 108 PDAC patients. Insignificant distinctions (P>0.05) were observed between the non-TO and TO groups in parameters such as age, gender, CA199 levels, resectability, TNM stage, tumor differentiation, microscopic perineural invasion, microscopic adipose tissue invasion, microscopic vascular tumor emboli, the site of first recurrence and whether postoperative adjuvant therapy has been completed. Additionally, all surgeries in this cohort achieved R0 resection. The relatively balanced distribution of prognostic risk factors in this cohort suggests strong comparability between the non-TO and TO groups of PDAC patients, ensuring the reliability of the outcomes. Furthermore, it should be noted that the postoperative adjuvant therapy completion rate in the TO cohort exceeded that of the non-TO cohort. Despite a negative statistical significance (TO:non-TO =78.3%:66.7%, P=0.28), it may imply that the achievement of TO is conducive to the implementation of postoperative adjuvant therapy.

Relationship between TO and survival results

The objective of the survival analysis was to evaluate tumor recurrence and prognosis between the TO and non-TO groups, therefore, three patients who experienced perioperative mortality were excluded. It is important to note that perioperative deaths are also considered one of the criteria for achieving TO, which may have a potential impact on the survival analysis. The survival analysis included the remaining 108 PDAC patients, with 39 in the non-TO group and 69 in the TO group. The median follow-up time for this cohort was 44.2 (IQR, 36.7–64.1) months, and the median survival time was 23.4 (IQR, 17.8–28.7) months. In the non-TO group, the 1-year and 2-year survival rates for PDAC patients were 64.1% and 35.9% respectively. However, it reached 78.2% and 56.4% in the TO group.

The TO group had a longer DFS, with a median recurrence time of 14.2 (IQR, 10.8–23.4) and 9.4 (IQR, 7.2–14.7) months in the non-TO group [P=0.09; hazard ratio (HR) =0.69; 95% CI: 0.48–0.91] (*Figure 3A*). The TO group also had a longer OS, with a median survival time of 27.3 (IQR, 20.3–53.2) and 18 (IQR, 12.4–26.9) months in the non-TO group (P=0.03; HR =0.60; 95% CI: 0.37–0.83) (*Figure 3B*). This suggests that achieving TO following PD is associated with an extension in the survival duration for PDAC patients, but there is currently insufficient evidence to suggest that it reduces the risk of tumor recurrence.

The impact of achieving a TO on long-term prognosis

In unadjusted analyses, univariate Cox regression demonstrated that achieving a TO was advantageous for patients' long-term survival (P=0.02; HR =4.38; 95% CI: 1.28–14.97). Meanwhile, CA199 ≥200 U/L and TNM stage 3 were both statistically significant risk factors for patient survival (*Figure 4A*). To minimize the confounding effects of other influencing factors, a subsequent multivariate Cox regression analysis was performed, indicating that achieving TO remained beneficial for patients' survival (P=0.04; HR =4.08; 95% CI: 1.07–15.61) (*Figure 4B*). In conclusion, the Cox regression analysis suggests that achieving TO is a protective factor for survival, and the TO have the potential to be included in predicting the prognosis of PDAC patients.

Risk factors affecting the achievement of TO

Univariate and multivariate analyses indicated that high amylase in drainage fluid on the third day after surgery (>1,300 U/L), longer surgery duration (≥6.25 hours), and soft pancreatic texture were independently associated with the failure to achieve a TO. Patients with high amylase in drainage fluid on the third day after surgery was detrimental to achieve TO (OR =0.10; 95% CI: 0.02–0.58; P=0.01), patients with surgery durations of ≥6.25 hours was detrimental to achieve TO (OR =0.19; 95% CI: 0.06–0.54; P=0.002), and patients with soft pancreatic texture was detrimental to achieve TO (OR =0.31; 95% CI: 0.10–0.93, P=0.04) (*Table 4*). Elevated amylase in postoperative drainage fluid and soft pancreatic texture are both risk factors for the occurrence and development of POPF. A longer surgery duration often indicates a more challenging surgery, which has a strong correlation with the inclusion criteria for TO. On the other hand, advanced age (≥65 years) and high amylase in drainage fluid on the first postoperative day (>1,300 U/L) were significantly unfavorable for achieving a TO in univariate analysis but had no significant significance in multivariate analysis. Low NLR on the third postoperative day (<7.9) and a wide diameter of the main pancreatic duct (≥0.3 cm) were significantly favorable for achieving a TO in univariate analysis but had no significant significance in multivariate analysis (*Table 4*). In summary,

Table 3 Comparison of indicators that may potentially affect prognosis

Characteristics	Non-textbook outcome group (n=39)	Textbook outcome group (n=69)	P value
Age (<65/≥65 years)	19 (48.7)/20 (51.3)	44 (63.8)/25 (36.2)	0.19
Gender (female/male)	16 (41.0)/23 (59.0)	31 (44.9)/38 (55.1)	0.85
CA199 (<200/≥200 U/L)	19 (48.7)/20 (51.3)	38 (55.1)/31 (44.9)	0.66
Resectability			>0.99
Resectable	29 (74.4)	50 (72.5)	
Borderline	10 (25.6)	19 (27.5)	
pT stage			0.89
1	4 (10.3)	5 (7.2)	
2	13 (33.3)	27 (39.1)	
3	18 (46.2)	29 (42.0)	
4	4 (10.3)	8 (11.6)	
pN stage			0.60
0	15 (38.5)	28 (40.6)	
1	17 (43.6)	24 (34.8)	
2	7 (17.9)	17 (24.6)	
TNM (AJCC 8th)			0.95
I	6 (15.4)	12 (17.4)	
II	7 (17.9)	13 (18.8)	
III	26 (66.7)	44 (63.8)	
Differentiation degree			0.98
Well	2 (5.1)	3 (4.3)	
Poor	9 (23.1)	16 (23.2)	
Medium	28 (71.8)	50 (72.5)	
Perineural invasion (no/yes)	3 (7.7)/36 (92.3)	7 (10.1)/62 (89.9)	0.94
Adipose tissue invasion (no/yes)	10 (25.6)/29 (74.4)	12 (17.4)/57 (82.6)	0.44
Vascular cancer thrombus (no/yes)	14 (35.9)/25 (64.1)	14 (20.3)/55 (79.7)	0.12
Initial recurrence site			0.33
Abdomen or retroperitoneal metastasis	5 (12.8)	9 (13.0)	
Liver	14 (35.9)	23 (33.3)	
Local recurrence	5 (12.8)	13 (18.8)	
Lung	6 (15.4)	7 (10.1)	
Multiple	6 (15.4)	4 (5.8)	
None	3 (7.7)	13 (18.8)	
CPAT (PATc ≥6)			0.28
No	13 (33.3)	15 (21.7)	
Yes	26 (66.7)	54 (78.3)	

Data are presented as n (%). CA199, carbohydrate antigen 199; pT stage, pathological T stage; pN stage, pathological N stage; TNM (AJCC 8th), TNM stage of American Joint Committee on Cancer (eighth edition); CPAT, completed postoperative adjuvant therapy; PATc, postoperative adjuvant therapy cycles.

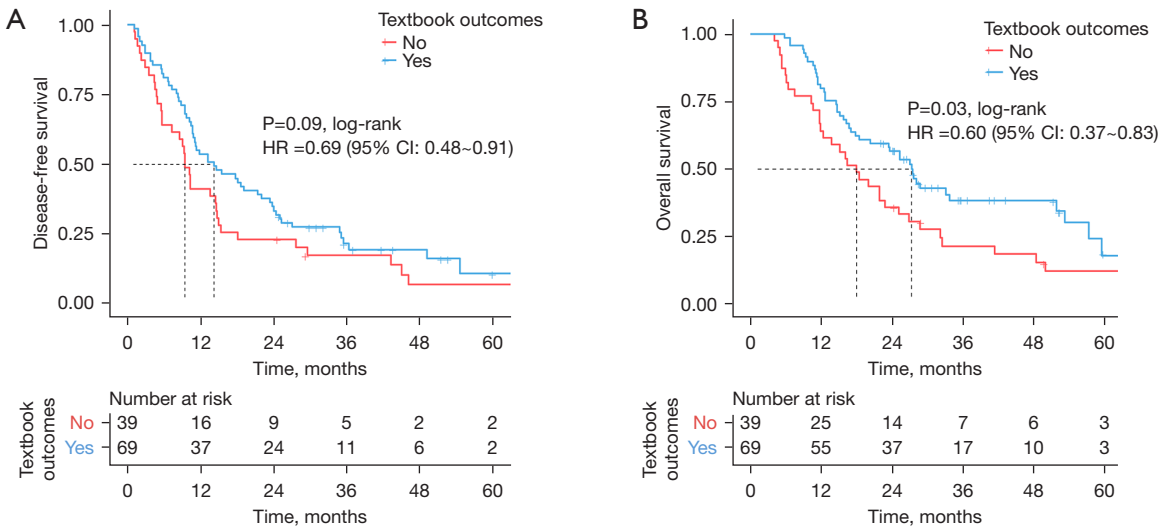

Figure 3 Effect of achieving textbook outcomes for PD on long-term prognosis in patients with PDAC. (A) Kaplan-Meier curve of DFS between the TO and non-TO group. (B) Kaplan-Meier curve of OS between the TO and non-TO group. HR, hazard ratio; CI, confidence interval; PD, pancreaticoduodenectomy; TO, textbook outcomes; PDAC, pancreatic ductal adenocarcinoma; DFS, disease-free survival; OS, overall survival.

these results suggest that advanced age, risk factors related to POPF, infection, and high surgical difficulty are potential risk factors in achieving a TO, emphasizing the importance of enhancing perioperative management for improving the surgical treatment of PD.

Discussion

As a composite parameter that can reflect the overall perioperative outcomes of surgery, the achievement of TO is highly likely to impact the prognosis of malignant tumor patients. Since the DPCG proposed a relatively authoritative definition of TO for pancreatic surgery in 2020, there is still no research evaluating the impact of achieving a surgical TO on the long-term prognosis of patients with PDAC. This study is the first to assess the impact of achieving TO following PD on the prognosis of PDAC patients according to the currently accepted standards. It holds significant clinical relevance.

Our study cohort adopted the pancreatic surgery TO definition proposed by the DPCG, which includes the following criteria: no clinically relevant POPF, no PPH, and no bile leakage (all classified as ISGPS grade B/C), no severe complications (Clavien-Dindo grade ≥ III), no in-hospital or 30-day mortality, and no readmission within 30 days after discharge (21). Considering that the extended hospital stay in our center was more often due to delayed removal of abdominal drainage tubes caused by POPF, including biochemical leakage (BL), rather than delayed gastric emptying (DGE), we did not include the prolongation of LOS as a criterion for the definition of TO (31).

PD plays a pivotal role in the curative treatment of pancreatic malignancies, and the quality of the surgery often determines the short-term prognosis of patients. The European Society for Medical Oncology (ESMO) guidelines recommend that all pancreatic cancer patients should undergo regular and adequate adjuvant therapy after surgery (27). However, the occurrence of severe postoperative complications can delay the execution of subsequent treatments, which is detrimental to the long-term prognosis of patients. The above-mentioned studies indicate that a comprehensive metric called "textbook outcomes" can be used to assess the quality of surgery. However, it has not yet been validated whether TO can impact the long-term prognosis of malignant tumors, particularly in the context of pancreatic cancer treatment. Existing research shows that achieving a TO is beneficial for improving the RFS and OS of patients with gastric and colon cancers (32,33). Nevertheless, the criteria for achieving TO in curative surgery for gastric and colon cancers include pathological parameters, such as the adequacy of dissected lymph nodes and achievement of R0 resection, however, it is well-known that pathological parameters are associated with long-term prognosis for cancer patients. Similarly, the research by Heidsma *et al.*

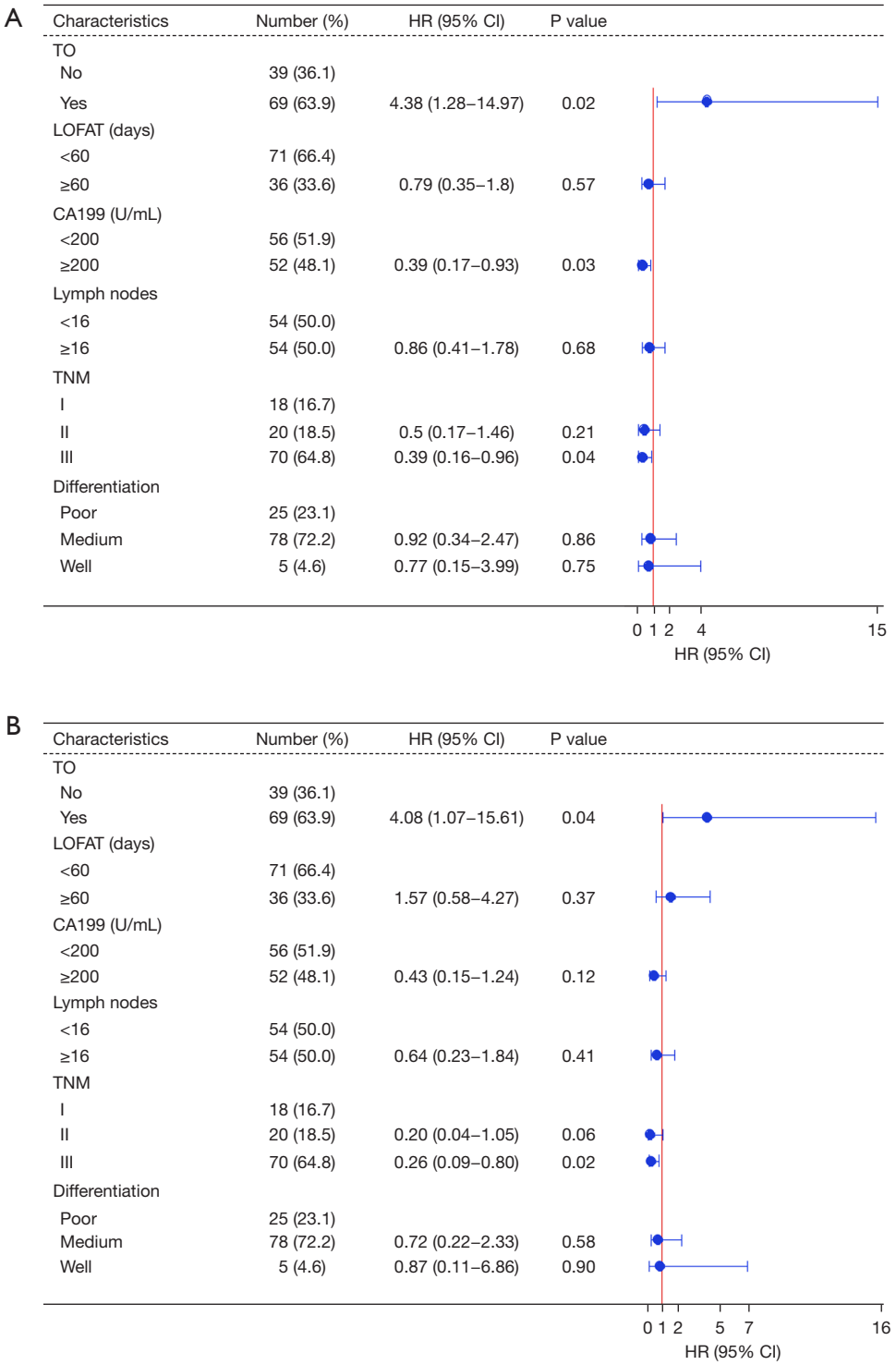

Figure 4 Forest plots of univariate and multivariate Cox regression analysis of overall survival in 108 patients with PDAC. Univariate (A) and multivariate (B) Cox regression analysis of relevant parameters affecting the overall survival of the PDAC patients. HR, hazard ratio; CI, confidence interval; TO, textbook outcomes; LOFAT, length of time to the first adjuvant therapy; CA199, carbohydrate antigen 199; TNM, TNM stage of American Joint Committee on Cancer (eighth edition); PDAC, pancreatic ductal adenocarcinoma.

Table 4 Logistic regression analysis of factors potentially influencing TO

Characteristics	Non-TO group (n=42), n (%)	TO group (n=69), n (%)	Univariable analysis		Multivariable analysis	
			OR (95% CI)	P value	OR (95% CI)	P value
Gender						
Female	19 (45.2)	30 (43.5)	–	–	–	–
Male	23 (54.8)	39 (56.5)	1.07 (0.50–2.32)	0.86	–	–
Age (years)						
<65	20 (47.6)	46 (66.7)	–	–	–	–
≥65	22 (52.4)	23 (33.3)	0.45 (0.21–1.00)	0.049	0.66 (0.25–1.76)	0.40
BMI (kg/m^2)						
<18.5	6 (14.3)	10 (14.5)	–	–	–	–
18.5–24	29 (69.0)	46 (66.7)	0.95 (0.31–2.90)	0.93	–	–
>24	7 (16.7)	13 (18.8)	1.11 (0.28–4.37)	0.88	–	–
Resectability						
Resectable	32 (76.2)	50 (72.5)	–	–	–	–
Borderline	10 (23.8)	19 (27.5)	0.82 (0.34–1.99)	0.67	–	–
CCI						
<5	12 (28.6)	24 (34.8)	–	–	–	–
≥5	30 (71.4)	45 (65.2)	0.75 (0.33–1.72)	0.50	–	–
ASA						
1+2	16 (38.1)	37 (53.6)	–	–	–	–
3+4	26 (61.9)	32 (46.4)	0.53 (0.24–1.16)	0.11	–	–
NLR†						
High	32 (76.2)	35 (50.7)	–	–	–	–
Low	10 (23.8)	34 (49.3)	3.11 (1.33–7.29)	0.009	1.66 (0.46–6.04)	0.44
PLR†						
High	32 (76.2)	42 (60.9)	–	–	–	–
Low	10 (23.8)	27 (39.1)	2.06 (0.87–4.86)	0.10	2.25 (0.72–6.98)	0.16
MLR†						
High	16 (38.1)	15 (21.7)	–	–	–	–
Low	26 (61.9)	54 (78.3)	2.22 (0.95–5.16)	0.07	1.29 (0.39–4.22)	0.67
Neutrophils† (%)						
<85	25 (59.5)	55 (79.7)	–	–	–	–
≥85	17 (40.5)	14 (20.3)	0.37 (0.16–0.88)	0.02	1.53 (0.40–5.85)	0.54
AMY POD‡ (U/L)						
<130	22 (52.4)	40 (58.0)	–	–	–	–
≥130	20 (47.6)	29 (42.0)	0.80 (0.37–1.72)	0.57	–	–

Table 4 (*continued*)

Table 4 (*continued*)

Characteristics	Non-TO group (n=42), n (%)	TO group (n=69), n (%)	Univariable analysis		Multivariable analysis	
			OR (95% CI)	P value	OR (95% CI)	P value
DFA POD‡ (U/L)						
<390	19 (45.2)	42 (60.9)	–	–	–	–
390–1,300	7 (16.7)	13 (18.8)	0.84 (0.29–2.44)	0.75	1.53 (0.37–6.29)	0.55
>1,300	16 (38.1)	14 (20.3)	0.40 (0.16–0.97)	0.043	1.56 (0.31–7.96)	0.59
DFA POD† (U/L)						
<390	22 (52.4)	52 (75.4)	–	–	–	–
390–1,300	4 (9.5)	12 (17.4)	1.27 (0.37–4.37)	0.71	1.14 (0.22–5.96)	0.88
>1,300	16 (38.1)	5 (7.2)	0.13 (0.04–0.41)	<0.001	0.10 (0.02–0.58)	0.01
Estimated blood loss (mL)						
<300	28 (66.7)	43 (62.3)	–	–	–	–
≥300	14 (33.3)	26 (37.7)	1.21 (0.54–2.71)	0.64	–	–
Operation duration (hours)						
<6.25	15 (35.7)	41 (59.4)	–	–	–	–
≥6.25	27 (64.3)	28 (40.6)	0.38 (0.17–0.84)	0.02	0.19 (0.06–0.54)	0.002
Pancreatic texture						
Hard	21 (50.0)	55 (79.7)	–	–	–	–
Soft	21 (50.0)	14 (20.3)	0.25 (0.11–0.59)	0.002	0.31 (0.10–0.93)	0.04
Dilated pancreatic duct (cm)						
<0.3	23 (54.8)	17 (24.6)	–	–	–	–
≥0.3	19 (45.2)	52 (75.4)	3.70 (1.63–8.39)	0.002	1.53 (0.50–4.68)	0.45

†, postoperative day 3 level; ‡, postoperative first day level. TO, textbook outcomes; OR, odds ratio; CI, confidence interval; BMI, body mass index; CCI, Charlson comorbidity index; ASA, American Society of Anesthesiologists; NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio; MLR, monocytes/lymphocyte ratio; AMY, serum amylase; POD, postoperative day; DFA, drainage fluid amylase.

indicated that achieving TO after pancreatic surgery for pancreatic neuroendocrine tumors improved long-term outcomes (20). However, when defining TO, they included the achievement of R0 resection, and with a non-R0 resection rate of 14.7% (20). In our cohort, consisting of 111 patients who underwent PD for PDAC, 69 individuals (62.2%) achieved TO. After excluding three patients who died during the perioperative period, we performed survival analysis. The TO group had longer DFS and OS, with a significant statistical difference observed in OS (P=0.025; HR =0.025; 95% CI: 0.37–0.83). Previous studies have indicated that CA199 ≥200 U/L (34), peripancreatic nerve invasion (35), and different sites of initial recurrence (36,37) might influence the long-term prognosis of PDAC. There were no statistically significant differences in pathological data between the two groups before conducting survival analysis, and all patients achieved R0 resection, which helped minimize the interference of confounding factors with the research results. We further utilized Cox regression analysis to assess the impact of achieving TO on the long-term prognosis of PDAC patients, and the results demonstrated that achieving TO is a protective factor for patient survival (P=0.04; HR =4.08; 95% CI: 1.07–15.61). Our study suggests that achieving TO in PDAC leads to improved OS rates, and TO holds promise as a robust indicator for predicting long-term prognosis after PDAC surgery.

Previous studies have suggested that the occurrence of postoperative complications may accelerate tumor recurrence

and affect long-term prognosis (38-40), potentially due to immunosuppression induced by surgical stress. Research by Coffey *et al.* demonstrated that postoperative immunosuppression, persisting for two weeks following surgery and peaking on the third day, facilitates the evasion of circulating tumor cells from the immune surveillance, promoting tumor proliferation (41). Studies have shown that elevated postoperative levels of inflammatory biomarkers, such as NLR, C-reactive protein (CRP), and interleukin-6 (IL-6), can hasten tumor recurrence and impact long-term prognosis (42-45). In our study cohort, on the third day post-surgery, the non-TO group exhibited a significantly lower percentage of lymphocytes [TO *vs.* non-TO =9.70% (2.40%, 22.8%) *vs.* 7.65% (2.70%, 17.4%), P=0.02] and a significantly higher NLR [TO *vs.* non-TO =8.20 (2.78, 39.8) *vs.* 10.8 (4.15, 33.5), P=0.02], which reflect, to a certain extent, the TO group patients might have a relatively milder postoperative stress response and a lower degree of immunosuppression. However, we did not observe a significant direct correlation between postoperative NLR levels and DFS or OS, and the above related results are displayed in Appendix 1. Nonetheless, it is undeniable that routine postoperative monitoring of biomarkers such as CRP and interleukins can guide subsequent treatment in patients with malignancies.

We further explored the factors influencing the achievement of TO. Before conducting logistic regression analysis regarding the outcome of achieving TO, we first compared the perioperative baseline data between the TO and non-TO group. Interestingly, we found statistically significant differences between the two groups in laboratory test results on the third day after surgery (including the proportion of neutrophils, amylase levels in drainage fluid, and other factors related to POPF). This suggests that POPF is a critical postoperative complication to be concerned about, which is consistent with the current high-priority scientific issues in PD (24,46). POPF is likely to act as a focal point and trigger for other postoperative complications, such as abdominal infections and PPH. This also indicates that although TO, as a composite metric, provides a holistic assessment of the entire surgical and perioperative management process and has the advantage of an overall evaluation, it should not disregard the prevention and treatment of individual complications, particularly POPF.

Subsequent univariate and multivariate logistic analyses indicated that prolonged surgery time (≥6.25 hours), soft pancreatic texture, and high amylase levels in postoperative drainage fluid (>1,300 U/L) were unfavorable factors for achieving TO. Prolonged surgery time often implies more complex procedures. For instance, during surgery, identifying suspected vascular invasion may necessitate more intricate vascular and lymph node dissection, or even vascular repairment or reconstruction. Extensive dissection and vascular reconstruction may increase the likelihood of postoperative complications. Soft pancreatic texture is a high-risk factor for POPF, with a probability of 20–40% for POPF to occur (47,48). Increased amylase level in postoperative drainage fluid is a classic indicator of POPF. All these factors suggest that high-risk factors for POPF are unfavorable for achieving TO. Many researchers have explored various methods of pancreaticojejunostomy, but there is still no consensus on which approach is effective in reducing the occurrence of POPF (49-51). This implies that improving the quality of pancreaticojejunostomy is advantageous in reducing POPF. Recently, Japanese researchers applied the linear staplers in the transverse section of soft pancreatic texture during PD. Out of 20 patients, only one experienced a grade B-POPF (52). Although further research is needed to explore the advantages and disadvantages of this approach, it offers a promising direction to reduce the incidence of POPF.

Additionally, within our study cohort, 26.1% (29/111) of patients were preoperatively classified as borderline resectable requiring vascular involvement, and no significant difference in resectability was noted between the two groups (TO *vs.* non-TO =27.5% *vs.* 23.8%, P=0.83). It is undeniable that vascular invasion increases the complexity of surgery. However, our research indicates that aggressive vascular resections in PD did not impact the achievement of TO, which may be related to the mature learning curve of our team. Naturally, the safety and efficacy of aggressive surgical treatment for PDAC patients with vascular invasion still need to be confirmed with larger-scale studies and TO may well serve as a "litmus test" for understanding this topic.

In fact, studying the relationship between surgical quality and the long-term prognosis of malignant tumors is a highly complex endeavor. It requires the specification of a particular type of surgery and malignant tumor and the need to balance baseline data that could potentially impact prognosis, such as using propensity score matching (PSM) and other methods. These conditions demand high standards from the research center, including factors such as the enough annual surgical volume, whether the surgical team has completed their learning curve, and the ability to collect an adequate sample size.

Our initial exploration and affirmation of the favorable impact of achieving TO in PD on the long-term prognosis of PDAC patients provide a new research direction and

clinical data for pancreatic surgery TO-related research. However, this study also has its limitations. Firstly, it is based on retrospective data collection, and it's challenging to avoid information bias that arises during the data collection process. Secondly, the sample size in this study is relatively small, and larger sample sizes or multicenter studies will be needed in the future. Thirdly, all patients in this study are of Asian populations, while the concept of TO was developed based on data from European populations. There are significant differences in medical practices between different healthcare cultures. For example, European patients often have their drainage tubes removed and are discharged approximately 7 days after surgery, while Asian patients frequently require drainage removal before being discharged. This leads to differences in the achievement of TO parameters. For instance, van Roessel *et al*.'s study reported a readmission rate of 83.1% (21) while our cohort had a rate of 98.2%. Fourthly, over time and with guideline updates, the changes in postoperative adjuvant treatment plans for patients add uncontrollable confounding factors to prognosis analysis. Nevertheless, our study still holds a certain level of pioneering value and could potentially make an impact in this field. It provides new insights for improving surgical quality and offers data on the application of pancreatic surgery TO in different cultural backgrounds.

Conclusions

This study demonstrates that achieving TO is a valuable indicator that can comprehensively reflect the effectiveness of perioperative treatment for patients from multiple dimensions. It provides a more holistic representation of the complete postoperative course. The attainment of TO significantly improves the OS of PDAC patients and has the potential to serve as a robust prognostic indicator. Looking ahead, it is highly necessary for TO to become a standard surgical quality control measure in hospitals. Launching clinical research worldwide with TO at its core might greatly enhance the treatment outcomes for malignant tumors.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tgh.amegroups.com/article/view/10.21037/tgh-23-112/rc

Data Sharing Statement: Available at https://tgh.amegroups.com/article/view/10.21037/tgh-23-112/dss

Peer Review File: Available at https://tgh.amegroups.com/article/view/10.21037/tgh-23-112/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tgh.amegroups.com/article/view/10.21037/tgh-23-112/coif). H.Z. reports having received funding from the Basic and Applied Basic Research Foundation of Guangdong Province (No. 2020A1515011379) for this manuscript. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the principles of the Helsinki Declaration (as revised in 2013). The study was reviewed and approved by the Ethics Committee of Sun Yat-sen Memorial Hospital, Sun Yat-sen University (approval ID: SYSKY-2023-1076-01) and was registered in the Chinese Clinical Trial Registry (registration No. MR-44-23-046152). All participating patients provided informed consent prior to surgery, authorizing the confidential use of their medical data for research purposes.

References

1. Siegel RL, Miller KD, Wagle NS, et al. Cancer statistics, 2023. CA Cancer J Clin 2023;73:17-48.

2. Strobel O, Neoptolemos J, Jäger D, et al. Optimizing the outcomes of pancreatic cancer surgery. Nat Rev Clin Oncol 2019;16:11-26.
3. Macfie R, Berger Y, Liu H, et al. Major Postoperative Complications Limit Adjuvant Therapy Administration in Patients Undergoing Pancreatoduodenectomy for Distal Cholangiocarcinoma or Pancreatic Ductal Adenocarcinoma. Ann Surg Oncol 2023;30:5027-34.
4. Kamarajah SK, Bundred JR, Alrawashdeh W, et al. A systematic review and network meta-analysis of phase III randomised controlled trials for adjuvant therapy following resection of pancreatic ductal adenocarcinoma (PDAC). HPB (Oxford) 2020;22:649-59.
5. Bassi C, Dervenis C, Butturini G, et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery 2005;138:8-13.
6. Bassi C, Marchegiani G, Dervenis C, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. Surgery 2017;161:584-91.
7. Wente MN, Veit JA, Bassi C, et al. Postpancreatectomy hemorrhage (PPH): an International Study Group of Pancreatic Surgery (ISGPS) definition. Surgery 2007;142:20-5.
8. Koch M, Garden OJ, Padbury R, et al. Bile leakage after hepatobiliary and pancreatic surgery: a definition and grading of severity by the International Study Group of Liver Surgery. Surgery 2011;149:680-8.
9. Tsilimigras DI, Pawlik TM, Moris D. Textbook outcomes in hepatobiliary and pancreatic surgery. World J Gastroenterol 2021;27:1524-30.
10. Dijs-Elsinga J, Otten W, Versluijs MM, et al. Choosing a hospital for surgery: the importance of information on quality of care. Med Decis Making 2010;30:544-55.
11. Beane JD, Borrebach JD, Zureikat AH, et al. Optimal Pancreatic Surgery: Are We Making Progress in North America? Ann Surg 2021;274:e355-63.
12. Görgec B, Benedetti Cacciaguerra A, Pawlik TM, et al. An International Expert Delphi Consensus on Defining Textbook Outcome in Liver Surgery (TOLS). Ann Surg 2023;277:821-8.
13. Kolfschoten NE, Kievit J, Gooiker GA, et al. Focusing on desired outcomes of care after colon cancer resections; hospital variations in 'textbook outcome'. Eur J Surg Oncol 2013;39:156-63.
14. Merath K, Chen Q, Bagante F, et al. A Multi-institutional International Analysis of Textbook Outcomes Among Patients Undergoing Curative-Intent Resection of Intrahepatic Cholangiocarcinoma. JAMA Surg 2019;154:e190571.
15. Voigt KR, Wullaert L, de Graaff MR, et al. Association between textbook outcome and long-term survival after surgery for colorectal liver metastases. Br J Surg 2023;110:1284-7.
16. Levy J, Gupta V, Amirazodi E, et al. Textbook Outcome and Survival in Patients With Gastric Cancer: An Analysis of the Population Registry of Esophageal and Stomach Tumours in Ontario (PRESTO). Ann Surg 2022;275:140-8.
17. Zakko J, Premkumar A, Logan AJ, et al. Textbook outcome: A novel metric in heart transplantation outcomes. J Thorac Cardiovasc Surg 2024;167:1077-1087.e13.
18. Merath K, Chen Q, Bagante F, et al. Textbook Outcomes Among Medicare Patients Undergoing Hepatopancreatic Surgery. Ann Surg 2020;271:1116-23.
19. Mehta R, Tsilimigras DI, Paredes AZ, et al. Dedicated Cancer Centers are More Likely to Achieve a Textbook Outcome Following Hepatopancreatic Surgery. Ann Surg Oncol 2020;27:1889-97.
20. Heidsma CM, Hyer M, Tsilimigras DI, et al. Incidence and impact of Textbook Outcome among patients undergoing resection of pancreatic neuroendocrine tumors: Results of the US Neuroendocrine Tumor Study Group. J Surg Oncol 2020;121:1201-8.
21. van Roessel S, Mackay TM, van Dieren S, et al. Textbook Outcome: Nationwide Analysis of a Novel Quality Measure in Pancreatic Surgery. Ann Surg 2020;271:155-62.
22. Nicholas E, van Roessel S, de Burlet K, et al. Using Textbook Outcomes to benchmark practice in pancreatic surgery. ANZ J Surg 2021;91:361-6.
23. Wu Y, Peng B, Liu J, et al. Textbook outcome as a composite outcome measure in laparoscopic pancreaticoduodenectomy: a multicenter retrospective cohort study. Int J Surg 2023;109:374-82.
24. Wu Y, Wujimaimaiti N, Yuan J, et al. Risk factors for achieving textbook outcome after laparoscopic duodenum-preserving total pancreatic head resection: a retrospective cohort study. Int J Surg 2023;109:698-706.
25. Zhu L, Fu Z, Liu X, et al. Textbook outcomes among patients undergoing curative resection of pancreatic ductal adenocarcinoma in the era of neoadjuvant therapy. Clinical Surgical Oncology 2023;2:100012.
26. Ghaferi AA, Schwartz TA, Pawlik TM. STROBE Reporting Guidelines for Observational Studies. JAMA Surg 2021;156:577-8.

27. Conroy T, Pfeiffer P, Vilgrain V, et al. Pancreatic cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol 2023;34:987-1002.
28. Tempero MA, Malafa MP, Al-Hawary M, et al. Pancreatic Adenocarcinoma, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2021;19:439-57.
29. Schwartz LH, Litière S, de Vries E, et al. RECIST 1.1-Update and clarification: From the RECIST committee. Eur J Cancer 2016;62:132-7.
30. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-13.
31. Smits FJ, Verweij ME, Daamen LA, et al. Impact of Complications After Pancreatoduodenectomy on Mortality, Organ Failure, Hospital Stay, and Readmission: Analysis of a Nationwide Audit. Ann Surg 2022;275:e222-8.
32. Çetinkaya-Hosgör C, Seika P, Raakow J, et al. Textbook Outcome after Gastrectomy for Gastric Cancer Is Associated with Improved Overall and Disease-Free Survival. J Clin Med 2023;12:5419.
33. Rubio García JJ, Mauri Barberá F, Villodre Tudela C, et al. Textbook outcome in colon carcinoma: implications for overall survival and disease-free survival. Langenbecks Arch Surg 2023;408:218.
34. Luo G, Jin K, Deng S, et al. Roles of CA19-9 in pancreatic cancer: Biomarker, predictor and promoter. Biochim Biophys Acta Rev Cancer 2021;1875:188409.
35. Schorn S, Demir IE, Haller B, et al. The influence of neural invasion on survival and tumor recurrence in pancreatic ductal adenocarcinoma - A systematic review and meta-analysis. Surg Oncol 2017;26:105-15.
36. Groot VP, Gemenetzis G, Blair AB, et al. Defining and Predicting Early Recurrence in 957 Patients With Resected Pancreatic Ductal Adenocarcinoma. Ann Surg 2019;269:1154-62.
37. Sperti C, Pasquali C, Piccoli A, et al. Recurrence after resection for ductal adenocarcinoma of the pancreas. World J Surg 1997;21:195-200.
38. Krarup PM, Nordholm-Carstensen A, Jorgensen LN, et al. Anastomotic leak increases distant recurrence and long-term mortality after curative resection for colonic cancer: a nationwide cohort study. Ann Surg 2014;259:930-8.
39. Hashimoto S, Tominaga T, Nonaka T, et al. Long-term outcomes and early recurrence after resection for metachronous pulmonary metastases from colorectal cancer. Langenbecks Arch Surg 2023;409:24.
40. Beecher SM, O'Leary DP, McLaughlin R, et al. The Impact of Surgical Complications on Cancer Recurrence Rates: A Literature Review. Oncol Res Treat 2018;41:478-82.
41. Coffey JC, Wang JH, Smith MJ, et al. Excisional surgery for cancer cure: therapy at a cost. Lancet Oncol 2003;4:760-8.
42. Jin F, Han A, Shi F, et al. The postoperative neutrophil-to-lymphocyte ratio and changes in this ratio predict survival after the complete resection of stage I non-small cell lung cancer. Onco Targets Ther 2016;9:6529-37.
43. Keyl J, Kasper S, Wiesweg M, et al. Multimodal survival prediction in advanced pancreatic cancer using machine learning. ESMO Open 2022;7:100555.
44. Wang J, Karime C, Majeed U, et al. Targeting leukemia inhibitory factor in pancreatic adenocarcinoma. Expert Opin Investig Drugs 2023;32:387-99.
45. Chung HH, Seo SH, Kim H, et al. Postoperative Prognostic Predictors of Bile Duct Cancers: Clinical Analysis and Immunoassays of Tissue Microarrays. Gut Liver 2023;17:159-69.
46. Schuh F, Mihaljevic AL, Probst P, et al. A Simple Classification of Pancreatic Duct Size and Texture Predicts Postoperative Pancreatic Fistula: A classification of the International Study Group of Pancreatic Surgery. Ann Surg 2023;277:e597-608.
47. Hirono S, Kawai M, Okada KI, et al. Modified Blumgart Mattress Suture Versus Conventional Interrupted Suture in Pancreaticojejunostomy During Pancreaticoduodenectomy: Randomized Controlled Trial. Ann Surg 2019;269:243-51.
48. Ahmad SA, Edwards MJ, Sutton JM, et al. Factors influencing readmission after pancreaticoduodenectomy: a multi-institutional study of 1302 patients. Ann Surg 2012;256:529-37.
49. Berger AC, Howard TJ, Kennedy EP, et al. Does type of pancreaticojejunostomy after pancreaticoduodenectomy decrease rate of pancreatic fistula? A randomized, prospective, dual-institution trial. J Am Coll Surg 2009;208:738-47; discussion 747-9.
50. Daamen LA, Smits FJ, Besselink MG, et al. A web-based overview, systematic review and meta-analysis of pancreatic anastomosis techniques following pancreatoduodenectomy. HPB (Oxford) 2018;20:777-85.
51. Cao Z, Luo W, Qiu J, et al. Is Invagination Anastomosis More Effective in Reducing Clinically Relevant Pancreatic Fistula for Soft Pancreas After Pancreaticoduodenectomy

Under Novel Fistula Criteria: A Systematic Review and Meta-Analysis. Front Oncol 2020;10:1637.
52. Kitahata Y, Okada KI, Miyazawa M, et al. Stapler Method for Transection of the Pancreatic Parenchyma During Pancreatoduodenectomy: Prospective Study. J Gastrointest Surg 2023;27:2215-7.

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