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International Reference Values for Surgical Outcomes of Total Pancreatectomy

Philip C. Müller, MD; Caroline Berchtold, MD; Christoph Kuemmerli, MD, MSc; Eva Breuer, MD; Zhihao Li, MD; Alessia Vallorani, MD; Carsten Hansen, MD; Cristiano Guidetti, MD; Janina Eden, MD; Brady A. Campbell, MD; Pengfei Wu, MD; Sara Nicole Cecchetto, MD; Hallbera Gudmundsdottir, MD; Michael Kendrick, MD; Patrick P. Starlinger, MD, PhD; Nicolò Pecorelli, MD; Giovanni Guarneri, MD; Waqas Farooqui, MD; Christoph Tschuor, MD, PhD; Stefan Kobbelgaard Burgdorf, MD; Julia Mühlhäusser, MD; Jörn-Markus Gass, MD; Brian K. P. Goh, MD; Ye-Xin Koh, MD; Artur Rebelo, MD; Jörg Kleeff, MD; Tomas Seip, MD; Martin Santibanes, MD, PhD; Letizia Todeschini, MD; Giovanni Marchegiani, MD, PhD; Nadiya Belfil, MD; Mickaël Lesurtel, MD; Marcel Machado, MD; Ugo Boggi, MD; Emanuele Kauffmann, MD; Marie Cappelle, MD; Bas Groot Koerkamp, MD, PhD; Fabrizio Di Benedetto, MD; Keith Roberts, MD, PhD; Avinoam Nevler, MD; Harish Lavu, MD; Philipp Dutkowski, MD; Felix Nickel, MD, MME; Thilo Hackert, MD; Jin He, MD; Massimo Falconi, MD; Mark Truty, MD; Adrian T. Billeter, MD, PhD; Beat P. Müller, MD; and the Outcomes for Total Pancreatectomy Group

IMPORTANCE Total pancreatectomy (TP) is indicated for advanced pancreatic cancer or multifocal tumors. Furthermore, TP may be performed to avoid the risk of pancreatic fistula in selected patients to improve the perioperative risk profile.

OBJECTIVE To define reference values for TP based on a low-risk cohort treated at expert centers.

DESIGN, SETTING, AND PARTICIPANTS This multicenter study analyzed outcomes from patients undergoing primary TP for malignant or benign lesions from 25 international expert centers from January 2017 to November 2023. Low-risk patients undergoing TP (LR-TP) were without vascular resections or significant comorbidities.

EXPOSURES TP.

MAIN OUTCOMES AND MEASURES Twenty reference values were derived from the 75th or the 25th percentile of the median values of all centers. Outcomes of LR-TP were compared with a cohort of TP with vascular resection, TP due to high-risk pancreatic anastomosis, and the benchmark values for low-risk pancreatoduodenectomy.

RESULTS Of 994 patients, 333 (33.5%; median [IQR] age, 66 [58-72] years; 171 male [51.4%]) qualified as the LR-TP cohort. Reference values included blood loss (≤1000 mL), major complications (≤37%), 3-month postoperative mortality (<6%), and retrieved lymph nodes (≥29). Compared with TP with vascular resections, reference cutoffs were not met for major complications (51% vs LR-TP ≤37%) and 90-day mortality (11% vs LR-TP ≤6%). For TP due to high-risk anastomosis, failure to rescue rate (38% vs ≤6%) and 90-day mortality (11% vs LR-TP ≤6%) were not met. Compared with pancreatoduodenectomy, reference values for postoperative mortality were 3 times higher for LR-TP (≤2% vs ≤6%) and less for resected lymph nodes (≥16 vs ≥29).

CONCLUSIONS AND RELEVANCE This case-control study provided global reference values for TP, indicating significantly higher postoperative morbidity and mortality compared with pancreatoduodenectomy. Perioperative morbidity of TP was especially increased in patients with vascular resections. These reference values can serve for quality control of pancreatic surgery.

Invited Commentary

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The members of the Outcomes for Total Pancreatectomy Group appear at the end of this article.

Corresponding Author: Philip C. Müller, MD (philip.mueller@clarunis.ch), and Beat P. Müller, MD (beat.mueller@clarunis.ch), Department of Surgery, Clarunis—University Digestive Health Care Center, University Hospital Basel, Spitalstrasse 21, 4031 Basel, Switzerland.

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Total pancreatectomy (TP) is indicated for patients with advanced pancreatic cancer or multifocal pancreatic tumors. Furthermore, TP has recently gained interest in mitigating the risk of postoperative pancreatic fistula (POPF) after pancreatoduodenectomy with high-risk pancreatic anastomosis. Furthermore, in patients undergoing pancreatoduodenectomy with vascular resections, TP is suggested to mitigate the perioperative risk, especially regarding vascular complications combined with POPF.[1-3] However, despite centralization efforts toward expert centers, TP remains an overall rarely performed procedure with significant morbidity and mortality compared with pancreatoduodenectomy. Similar to pancreatoduodenectomy, postoperative complications after TP depend on the extent of resection with regard to concomitant venous, arterial, and multivisceral resections.[4] To provide reference values, a differentiated analysis of TP taking the corresponding levels of surgical complexity into account is pivotal.

Assessment of quality requires tangible parameters; therefore, benchmarking, defining outcomes for standardized patients and subgroups, has become an essential tool to compare outcomes between centers within a health care system or to centralize medical care for high-risk procedures.[5] Because improving quality is one of the key approaches to cut down on complications, the single most relevant cost driving factor, better outcomes will also save health care spending and make health care more cost-efficient.[6] Defining standard outcomes for various subgroups of patients allows quality assessment and objective comparisons between different surgeons, centers, and health care systems. Especially for highly complex procedures performed at dedicated centers, objectifiable and internationally standardized quality assessment is pivotal. Defining reference values in well-defined low-risk cohorts from worldwide expert centers can be used for comparison in the field.

The aim of this multicenter study was to define the international reference values for TP. The data of patients undergoing TP that was performed at 25 international centers were included to provide cutoffs for future comparisons.

Key Points

Question What are international reference values for total pancreatectomy based on a low-risk cohort treated at expert centers?

Findings In this international, multicenter, case-control study including 994 patients from 25 reference centers, 20 surgical and oncological reference values for total pancreatectomy were defined and included a relevant rate of major complications and 90-day postoperative mortality.

Meaning This study found global reference values for total pancreatectomy, which indicate significantly higher postoperative morbidity and mortality as compared with pancreatoduodenectomy, especially in patients with vascular resections.

Methods

Study Design

This retrospective multicenter case-control study analyzed outcomes from low-risk patients undergoing primary TP for benign or malignant disease at 25 international expert centers. Ethical approval was obtained from the Ethics Committee of Northwestern Switzerland. General informed consent was obtained at the respective centers. International high-volume centers with a case load of at least 50 pancreatic resections per year and a maintained prospective patient database covering minimum 1-year follow-up were included. The final collaborative group consisted of 25 expert centers from 3 continents: including 1 from Asia, 7 from the Americas and 17 from Europe, from which 20 reference values were identified to define best practice for TP.[7-10] The anonymized data were collected and stored in an encrypted online data registry provided by the University Hospital Basel.[11] This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.

Study Population

Patients undergoing primary TP were included from January 2017 to November 2023 with a minimum follow-up of 1 year for each patient. Included were patients 18 years and older undergoing TP for benign or malignant disease. Excluded were cases of secondary completion pancreatectomy. Low-risk TP (LR-TP) was defined as those individuals without major comorbidities such as obesity (body mass index [BMI] >35, calculated as weight in kilograms divided by height in meters squared), chronic cardiovascular disease (congestive heart failure, myocardial infarction within 6 months preoperatively, atrial fibrillation, previous coronary intervention, or cardiac surgery), chronic obstructive pulmonary disease, or kidney diseases (Modification of Diet in Renal Disease equation ≥ stage 3); those not using medications for diabetes, antiplatelets, and anticoagulation; and those with American Society of Anesthesiologists classification 4 or greater.[7] Furthermore, only TP without venous or arterial resection were included in the LR-TP cohort (TP type 1 according to Loos et al[4]).[7] Patient race and ethnicity data were not collected for this study.

Indicators for Outcome

Fifteen critical perioperative parameters were analyzed as reference values for all cases. For patients with pancreatic ductal adenocarcinoma (PDAC), 5 additional oncologic criteria were analyzed. Like previous outcomes studies on pancreatic surgery, parameters were assessed at 3 months after surgery.[7] Additional, 12-month follow-up data and 3-year overall survival were also provided.

Outcome measures included procedure-related morbidity and mortality, pancreas specific morbidity (defined according to the International Study Group of Pancreatic Surgery [ISGPS]) such as postoperative hemorrhage (PPH),[8] delayed gastric emptying[9] and readmission. Morbidity was assessed with Clavien-Dindo (CD) classification and the comprehensive complication index at 3 months after surgery.[10] In addition, endocrine outcomes such as number and severity of hypoglycemic

events were analyzed for short- and long-term endocrine outcomes. Long-term glycemic control was additionally measured using hemoglobin A_{1c}.

For patients with PDAC, oncologic outcomes including R1 rate (<1-mm clearance or positive circumferential resection margin [CRM]),[12] number of resected lymph nodes, 1-year overall survival, and 3-year overall survival were assessed.

The failure to rescue rate was calculated by dividing the number of deaths in patients with a CD complication graded greater than II (numerator) by the total number of patients with a complication graded CD greater than II (denominator).[13]

Textbook outcome summarizes optimal surgical results after pancreatic surgery as a composite outcome and was defined by the absence of bile leak, PPH, major complications, readmission, and in-hospital mortality.[14]

The Pancreatic Surgery Composite Endpoint (PACE) was likewise developed as a standardized measure to assess ideal outcomes after pancreatic surgery. The PACE is positive if 1 of the following postoperative complications is present: PPH, reoperation, or reintervention. The PACE can be used to predict prolonged hospital stays and perioperative mortality.[15]

Outcome Comparisons

The applicability of the TP reference values was tested in 4 independent cohorts. Patients undergoing TP from the same 25 centers but classified as higher-risk TP cases due to relevant comorbidities were compared with the LR-TP values. Second, a comparison with patients undergoing TP with vascular resections (venous and/or arterial) was made, this cohort included both LR and higher-risk patients based on comorbidities. Third, because TP is a treatment alternative to mitigate the risk of POPF, TP due to a potential high-risk pancreas anastomosis were compared with LR-TP cutoffs. High-risk anastomosis was proposed as an ISGPS type C-D anastomosis (type C, soft texture and pancreatic duct >3 mm; type D, soft texture and pancreatic duct ≤3 mm).[16] All TPs in which in the operative note indicated that the main surgeon decided intraoperatively to perform a TP due to an expected high-risk pancreatic anastomosis were registered as high-risk anastomosis TP. Fourth, LR-TPs were compared with the published multinational benchmark values for pancreatoduodenectomy, which were developed by definition in low-risk patients.[7]

Statistical Analysis

Reference values were set at either the 75th or 25th percentile of the median outcome parameters of the centers. For poor outcomes, the 75th percentile, and for good outcomes, the 25th percentile, were chosen as previously applied and reported for other complex procedures in pancreatic, hepatobiliary and upper gastrointestinal surgery.[7,17-19] Statistical analysis was performed using descriptive statistics.

For the multivariable analysis, we used multiple imputation to address the missing at random pattern of missing data. Five datasets were generated using either logistic regression or predictive mean matching for categorical and continuous variables. A pooled logistic regression analysis was performed using the Rubin rule to combine the results from each dataset. Predictor variables were defined based on clinical relevance and results from the univariable analyses. The cutoff for inclusion in the latter was a 2-sided P value <.20. To receive more clinically meaningful parameters, continuous variables were dichotomized based on clinically meaningful cutoffs. To assess information loss, the regression was first done using the continuous variable. There was no change in outcome direction or statistical significance. The dependent variables were major complication and mortality.

All statistical analysis were performed using R Statistical Software, version 4.2.3 (R Foundation for Statistical Computing).

Results

From January 2017 to December 2023, 994 patients underwent TP at 25 expert centers. Of these, a total of 333 patients (33.5%; median [IQR] age, 66 [58-72] years; 162 female [48.6%]; 171 male [51.4%]) qualified as LR-TP. Median (IQR) follow-up was 35.4 (28.5-45.4) months. The surgical indication was PDAC in the majority of patients (679 [68.3%]), followed by multifocal intraductal papillary mucinous neoplasm in 118 [11.9%]). Median (IQR) tumor size was 28 (20-38) mm. In one-half of the patients (408 [51.1%]), the decision to proceed with TP was made intraoperatively, most commonly due to tumor-related factors (307 [68.1%]) and only in a minority to avoid a high-risk pancreatic anastomosis (46 [4.6%]). Preoperatively in patients with PDAC, the tumor was classified as upfront resectable in 287 patients (44.8%), borderline resectable in 172 patients (26.9%), and locally advanced in 181 patients (28.3%). In patients with PDAC, median (IQR) preoperative carbohydrate antigen 19-9 level was 63 (20-240) U/mL, and 184 patients (35.4%) were treated with neoadjuvant therapy.

Overall, 449 patients (45.1%) underwent vascular resection. A venous resection was performed in 429 patients (43.2%) and arterial resections in 100 patients (10.1%). Of patients undergoing vascular resections, 20 (4.5%) underwent arterial resection only, 349 (77.8%) venous resections only, and 80 (17.8%) underwent combined resections. Baseline characteristics of the overall and LR-TP cohort can be found in **Table 1**.

Reference Values

Twenty reference values were defined in accordance with prior studies.[7,19] Reference values included blood loss (≤1000 mL), major complications (≤37%), 3-month postoperative mortality (<6%), retrieved lymph nodes (≥29), reoperation rate (≤26.3%), and 90-day mortality (≤6.3%). For patients with PDAC, the cutoff for combined R1 and positive CRM rate was ≤41.7% and the cutoff for 1-year overall survival was ≥68.4% (**Table 2**).

Postoperative Hypoglycemic Events

In the first 6 months after TP, 61 of 301 patients (21%) reported hypoglycemia episodes occurring weekly to monthly. Most patients had asymptomatic hypoglycemia or moderate symptoms, and only 2 patients experienced severe hypoglycemia requiring help from others. At 12 months, 39 of 244 patients (16%) reported hypoglycemia without changes in frequency or severity compared with 6 months (**Table 3**).

Table 1. Patient Characteristics

Characteristic	Total cohort (N = 994)	Low-risk total pancreatectomy (n = 333)	Higher-risk total pancreatectomy (n = 212)	Total pancreatectomy high-risk anastomosis (n = 46)	Total pancreatectomy vascular resection (n = 449)
Age, median (IQR), y	66 (58-73)	66 (58-72)	67 (57-74)	70 (63-75)	66 (58-73)
Sex, No. (%)					
Female	476 (47.9)	162 (48.6)	93 (43.9)	12 (26.1)	221 (49.2)
Male	518 (52.1)	171 (51.4)	119 (56.1)	34 (73.9)	228 (50.8)
Body mass index, median (IQR)[a]	25.23 (4.97)	25.18 (3.76)	26.21 (6.44)	26.59 (3.85)	24.81 (4.90)
Comorbidities, No. (%)					
Diabetes	347 (34.9)	109 (32.7)	98 (46.2)	20 (43.5)	140 (31.2)
Chronic obstructive pulmonary disease	67 (6.7)	0	43 (20.3)	6 (13.0)	24 (5.3)
Chronic kidney failure	35 (3.5)	0	22 (10.4)	1 (2.2)	13 (2.9)
Cardiac disease	95 (9.6)	0	60 (28.3)	5 (10.9)	35 (7.8)
Histological diagnosis, No. (%)					
Pancreatic ductal adenocarcinoma	679 (69.1)	181 (55.7)	95 (45.2)	24 (52.2)	403 (90.0)
Neuroendocrine tumor	48 (4.9)	20 (6.2)	18 (8.6)	3 (6.5)	10 (2.2)
Intraductal papillary mucinous neoplasm	118 (12)	66 (20.3)	43 (20.5)	5 (10.9)	9 (2.0)
Other benign lesions	10 (1.0)	3 (0.9)	8 (3.9)	2 (4.3)	9 (2.0)
Chronic pancreatitis	67 (6.8)	24 (7.4)	37 (17.6)	0	6 (1.3)
Other malignant	8 (0.8)	5 (1.5)	9 (4.3)	5 (10.9)	11 (2.4)
Size of lesion, median (IQR), mm	28 (20-38)	26 (20-35)	26 (20-39)	24 (18-30)	30 (23-39)
Intraoperative gastrectomy due to venous congestion, No. (%)	21 (25.9)	9 (45)	3 (25)	1 (25)	7 (18.4)
Bile leak, No. (%)	65 (6.5)	21 (6.3)	17 (8.0)	6 (13.9)	27 (6.0)
Chyle leak, No. (%)	77 (7.8)	21 (6.3)	13 (6.2)	3 (6.7)	43 (9.7)
Postoperative gastric ischemia, No. (%)	15 (1.6)	6 (1.8)	3 (1.5)	2 (4.5)	6 (1.4)

[a] Calculated as weight in kilograms divided by height in meters squared.

Outcome Comparison

Outcomes for higher-risk TP were mostly comparable with results of the LR-TP cohort. Only readmission (23% vs LR-TP ≤20%) and mortality rate (6.6% vs LR-TP ≤6.3%) were slightly above the cutoffs for LR-TP.

For patients undergoing TP with vascular resection, several reference cutoffs were above the ones for LR-TP. For example, operative time (496 minutes vs LR-TP ≤456 minutes), major complications (51% vs LR-TP ≤37%,) and 90-day mortality (11% vs LR-TP ≤6%) were above the LR-TP cutoff. However, all oncologic reference values were similar in patients with TP undergoing vascular resection.

In patients with TP due to a potential high-risk pancreatic anastomosis, the 2 most relevant differences were a high failure to rescue rate (38% vs LR-TP ≤6%) and a mortality rate (11% vs LR-TP ≤6%) exceeding LR-TPs cutoffs. Importantly, the 90-day mortality of TP for high-risk anastomosis was almost double that of LR-TP and comparable with TP with vascular resection, whereas the failure to rescue rate was by far the highest in the high-risk anastomosis group.

Comparing the cutoffs for LR-TP with similarly defined low-risk pancreatoduodenectomy revealed several clinically relevant differences. Although cutoffs for operation time (456 minutes vs LR-TP ≤447 minutes) and major complications (≤37% vs LR-TP ≤33%) were comparable, postoperative mortality (≤2% vs LR-TP ≤6%) was 3 times higher for LR-TP. The reference values for number of resected lymph nodes (≥16 vs LR-TP ≥29) was higher after LR-TP, but the cutoff for combined R1 and positive CRM resections was similar for low-risk pancreatoduodenectomy (≤39% vs LR-TP ≤42%) (**Figure** and **Table 4**).

Predictors of Major Complications and Mortality

In the multivariable analysis of the overall cohort, operative time (odds ratio [OR], 1.86; 95% CI, 1.38-2.51; *P* <.001) and the intraoperative decision to perform TP (OR, 1.61; 95% CI, 1.13-2.30; *P* <.001) were the only predictors of major complications. Predictors for 90-day mortality were age (OR, 1.06; 95% CI, 1.03-1.09; *P* <.001), the intraoperative decision to perform TP (OR, 2.96; 95% CI, 1.61-5.43; *P* <.001), and intraoperative transfusion (OR, 1.02; 95% CI, 1.00-1.04; *P* = .01) (eTables 1 and 2 in Supplement 1).

Table 2. Reference Values After Total Pancreatectomy in 333 Low-Risk Cases

Characteristic	Reference value	Median (IQR)
Estimated blood loss, mL	≤1000	639 (53-2021)
Operative time, min	≤456	400 (295-649)
Intensive care unit stay, d	≤5	3 (0-20)
Length of stay, d	≤23	17 (6-38)
Postoperative morbidity at 3 mo, %		
Any complication	≤85.6	78 (0-100)
Clavien-Dindo grade ≥3a	≤37	23 (0-100)
Reoperation rate	≤26.3	8.8 (0-57.1)
Mortality	≤6.3	0 (0-28.6)
Delayed gastric emptying grade B/C	≤33.3	14.3 (0-100)
Postpancreatectomy hemorrhage grade B/C	≤6.3	0 (0-50)
Comprehensive complication index	≤26.3	18.9 (0-100)
HbA_{1c} level, %	≤7.9	7.5 (6.4-8.5)
Readmission rate	≤24.4	15.4 (0-50)
Failure to rescue rate	≤6.2	0 (0-28.6)
Textbook outcome	≥54.2	67.7 (0-100)
Pancreatic surgery composite end point	≤30.8	17.6 (0-100)
Pancreatic ductal adenocarcinoma, % (n = 237)		
R1 rate[b]	≤41.7	16.7 (0-100)
No. of resected lymph nodes	≥29	30 (7-51)
1-y OS	≥68.4	78.8 (46-100)
3-y OS	≥28.9	50.0 (0-86)
Receiving adjuvant therapy	≥63.8	80.0 (45-100)

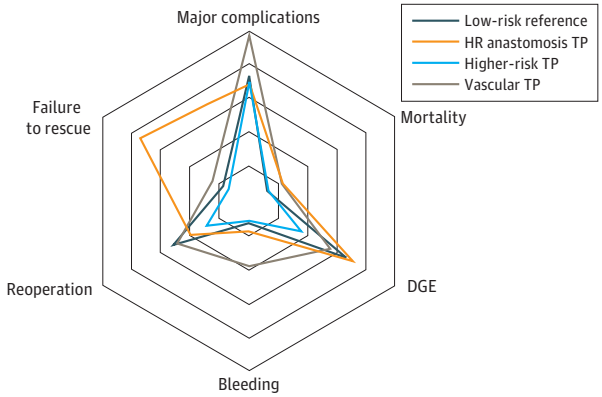
Abbreviations: HbA_{1c}, hemoglobin A_{1c}; OS, overall survival.

SI conversion factor: To convert HbA_{1c} to proportion of total hemoglobin, multiply by 0.01.

Table 3. Incidence and Severity of Postoperative Hypoglycemic Events

Event, No. (%)	6 mo (n = 301)	12 mo (n = 244)
Hypoglycemia episodes	61 (21)	39 (16)
Frequency		
Daily	2 (3)	1 (3)
Weekly	33 (54)	21 (54)
Monthly	26 (43)	17 (44)
Severity		
Asymptomatic	27 (44)	18 (46)
Moderate symptoms	1 (51)	20 (51)
Severe symptoms	2 (3)	3 (8)

Figure. Comparison of Total Pancreatectomy (TP) Reference Values in 4 Independent Cohorts



DGE indicates delayed gastric emptying; HR, high risk.

Discussion

This case-control study presents the first, to our knowledge, international reference values for surgical and oncologic outcomes for TP in a low-risk patient cohort without vascular resections. Even in specialized centers, TP was associated with significant postoperative morbidity and mortality, and the oncologic outcomes for patients with PDAC were similar to the reference values of other formal pancreatic resections. Although major complications in LR-TP were comparable with low-risk pancreatoduodenectomy, mortality in LR-TP was 3 times higher than after low-risk pancreatoduodenectomy. Interestingly, in TP with vascular resection and TP due to high-risk pancreatic anastomosis, a relevant increase in morbidity, mortality, and failure to rescue rate was observed. These findings confirm the increased risk of vascular resections on outcomes in TP, in line with other prior studies on TP but also other formal pancreatic resections.[4,20] Furthermore, the higher complication and mortality risk of TP is in line with findings from recent nationwide analyses and other studies reporting mortality rates between 5% and 22%.[21-23] However, absolute complications and mortality rates are lower in this cohort compared with the recently published Germany-wide data analysis.[24]

Concomitant vascular resections are known to increase major complications and mortality in any pancreatic surgery.[4,25] In pancreatoduodenectomy, postoperative mortality doubled from 2% to 4% with portal-venous resections.[7,26] In case of TP with vascular resection, a similar doubling of the 90-day mortality to 11% was observed in this cohort.

More surprising, however, is the finding that TP for high-risk pancreatic anastomosis carries a similar mortality and failure to rescue rate as TP with vascular resection. This is of high clinical significance because TP has been suggested as an alternative to pancreatoduodenectomy for patients with a high risk for POPF and relevant comorbidities.[2] Although counterintuitive, TP for high-risk anastomosis had a 90-day mortality of 11%, almost 5-fold the mortality of low-risk pancreatoduodenectomy. These results need further investigation but strongly advise against a liberal use of completion pancreatectomy due to a high-risk pancreatic anastomosis. Although pancreatoduodenectomy with high-risk anastomoses (ISGPS type C-D) is associated with a 20% to 40% risk of POPF and an 11% rate of rescue completion pancreatectomies, the mortality in this series was still lower at 6%.[2,16] Furthermore, modern, algorithm-based complication management can halve mortality after pancreatoduodenectomy from 5% to below 3%.[27]

Although the cause of mortality after pancreatoduodenectomy is often POPF associated, the mortality of LR-TP in

Table 4. Comparison of Reference Values for Total Pancreatectomy With Higher-Risk Patients and Pancreatoduodenectomy

Characteristic	Higher-risk total pancreatectomy (n = 212)	Total pancreatectomy vascular resection (n = 449)	Total pancreatectomy high risk anastomosis (n = 46)	Reference values	
				Pancreato-duode-nectomy (n = 2375)	Low-risk total pancre-atectomy
Estimated blood loss, median (IQR), mL	380 (150-900)	1000 (500-2000)	500 (300-1000)	NA	≤1000
Operative time, median (IQR), min	402 (329-521)	496 (385-601)	440 (370-532)	<450	≤456
Intensive care unit stay, median (IQR), d	1 (0-3)	2 (0-4)	1 (0-3)	NA	≤5
Length of stay, median (IQR), d	13 (8-21)	17 (11-28)	16 (12-25)	≤15	≤23
Postoperative morbidity at 3 mo					
Any complication, No. (%)	161 (75.9)	358 (79.7)	36 (78.3)	≤73	≤86
Clavien-Dindo grade ≥3a, No. (%)	74 (34.9)	228 (50.8)	16 (34.8)	≤30	≤37
Reoperation rate, No. (%)	31 (14.7)	111 (24.7)	9 (20.0)	NA	≤26.3
Mortality, No. (%)	14 (6.6)	49 (10.9)	4 (11.1)	≤1.6[a]	≤6.3
Delayed gastric emptying grade B/C, No. (%)	17 (8.1)	44 (9.9)	8 (17.8)	NA	≤33.3
Postpancreatectomy hemorrhage grade B/C, No. (%)	10 (4.4)	34 (7.6)	4 (8.9)	≤7	≤6.3
Comprehensive complication index, median (IQR)	20.9 (8.7-35)	27.6 (20.9-43.4)	20.9 (8.7-42.3)	≤20.9	≤26.3
HbA_{1c} level, median (IQR), %	7.9 (7.2-8.9)	7.3 (6.9-8.3)	7.9 (7.4-8.5)	NA	≤7.8
Readmission rate, No. (%)	153 (23.4)	113 (25.2)	10 (21.7)	≤21[b]	≤20
Failure to rescue rate, %	7.1	12.5	37.5	≤9	≤6.2
Textbook outcome, No. (%)	118 (55.7)	188 (41.9)	24 (52.2)	NA	≥54.2
Pancreatic surgery composite end point, No. (%)	53 (25.1)	205 (45.7)	12 (26.7)	NA	≤30.8
Pancreatic ductal adenocarcinoma					
R1 rate, No. (%)	19 (22.6)	132 (32.8)	10 (25.0)	≤39	≤41.7
No. of resected lymph nodes, median (IQR)	26.5 (17-36)	31 (22-43)	22 (12-33)	≥16	≥29
1-y OS, median (IQR), %	71.5 (61-81)	73.5 (68-79)	68.8 (52-91)	≥68	≥68.4
3-y OS, median (IQR), %	30.9 (22-45)	38.9 (33-46)	14.4 (5-47)	≥21	≥28.9
Adjuvant therapy, No. (%)	42 (58.3)	139 (55.4)	14 (63.6)	NA	≥63.9

Abbreviations: HbA_{1c}, hemoglobin A_{1c}; NA, not applicable; OS, overall survival.

SI conversion factor: To convert HbA_{1c} to proportion of total hemoglobin, multiply by 0.01.

[a] In-hospital.

[b] 1-year Readmission rate.

this series[21] was due to septic shock (42%), postoperative bleeding (29%), and visceral ischemia (14%). This finding is of relevance because no POPFs can occur after TP, which is generally considered the main driver of postpancreatectomy complications and mortality.[28] In TP, postoperative bleeding and gastric venous congestion (GVC) have been identified as strong mortality-driving factors.[29] However, it is possible that pancreatic surgeons likely underestimate GVC after TP as highlighted by the need of a more extensive gastrectomy in 26% of patients due to GVC intraoperatively. Furthermore, delayed relaparotomy with gastrectomy for GVC was found to be an independent predictor for 90-day mortality.[29]

Another drawback of TP compared with partial pancreatectomy is the subsequent diabetes. Despite postoperative patient education, specialized diabetes teams, and the introduction of the insulin pumps, glycemic control after TP is particularly challenging.[30,31] The current study revealed symptomatic hypoglycemic episodes in 1 of 5 patients with no reduction up to 12 months postoperatively. Endocrine insufficiency is a rarely reported outcome after TP, however, approximately 25% of patients are readmitted due to endocrine-related morbidity, and 2% die of hypoglycemia and ketoacidosis in the long term.[32] In patients undergoing pancreatoduodenectomy with preoperative diabetes, only 40% were insulin dependent postoperatively, showing the importance of pancreas preservation, whenever possible. Also, the quality of life in the same study was significantly better compared with patients undergoing TP.[3]

In patients with PDAC, oncologic survival cutoffs after TP were comparable with those after pancreatoduodenectomy, even though the lymph node retrieval rate was higher after TP. In fact, TP with concomitant vascular resections might be considered as the most radical pancreatic resection, emphasized by the excellent long-term survival of 39 months. Although modern resection strategies such as the triangle operation might sometimes be impeded in patients undergoing pancreatoduodenectomy, TP allows for an excellent clearance around the vascular structures such as the celiac trunk or the superior mesenteric artery. Currently, little is known about the potentially more radical oncologic effect of TP, and further studies should aim at comparing similar tumors regarding anatomical and biological factors undergoing either TP or pancreatoduodenectomy. However, whether the level of radicality justifies the postoperative morbidity after TP requires a case by case assessment and individualized decision-making.

Limitations

This study has some limitations. The inclusion of patients by center resulted in an unequal patient distribution, which could lead to a bias in volume-outcome associations. Furthermore, with only 1 Asian center, this cohort was underrepresented. As a third limitation, we contextualized the reference cutoffs of the 75th and 25th percentile. However, there is criticism as these cutoffs may not represent the best possible outcome realistically.[5]

Conclusions

In conclusion, this was the first, to our knowledge, international multicentric outcome analysis to set novel reference values comparing 4 clinically common scenarios for TP, indicating several relevant differences compared with pancreatoduodenectomy. Due to the increased mortality after TP, its indication as a POPF mitigation strategy should be carefully balanced, and the potential risk of TP is likely underestimated. TP with vascular resection is a high-risk operation with relevant perioperative mortality and should only be performed in specialized centers with a high expertise in complex pancreatic resections.

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Author Affiliations: Department of Surgery, University Digestive Health Care Center—Clarunis, Basel, Switzerland (P. C. Müller, Berchtold, Kuemmerli, Eden, Cecchetto, Dutkowski, Billeter, B. P. Müller); Department of Surgery and Transplantation, University Hospital Zurich, Zurich, Switzerland (Breuer); Department of Surgery, Mayo Clinic, Rochester, Minnesota (Li, Gudmundsdottir, Kendrick, Starlinger, Truty); Pancreatic Surgery, Pancreas Translational and Clinical Research Center, IRCCS San Raffaele Scientific Institute, Vita-Salute University, Milan, Italy (Vallorani, Pecorelli, Guarneri, Falconi); Department of Surgery and Transplantation, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark (Hansen, Farooqui, Tschuor, Burgdorf); Oncological HPB and Liver Transplant Unit, University of Modena and Reggio Emilia, Modena, Italy (Guidetti, Di Benedetto); Division of Hepatobiliary and Pancreatic Surgery, Johns Hopkins University School of Medicine, Baltimore, Maryland (Campbell, Wu, He); Department of Surgery, Cantonal Hospital of Lucerne, Lucerne, Switzerland (Mühlhäusser, Gass); Department of Health Sciences and Medicine, University of Lucerne, Lucerne, Switzerland (Mühlhäusser, Gass); Department of Hepatopancreatobiliary and Transplant Surgery, Singapore General Hospital and National Cancer Centre Singapore, Singapore (Goh, Koh); Department of Visceral, Vascular and Endocrine Surgery, Martin Luther University Halle Wittenberg, Halle, Germany (Rebelo, Kleeff); Hepato-Pancreato-Biliary Surgery Section and Liver Transplant Unit, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina (Seip, Santibanes); Hepato Biliary Pancreatic and Liver Transplant Surgery, Department of Surgery, Oncology and Gastroenterology (DiSCOG), Padova University Hospital, Italy (Todeschini, Marchegiani); Department of HPB Surgery & Liver Transplantation, Beaujon Hospital, University of Paris Cité, Clichy, France (Belfil, Lesurtel); Department of Surgery, Nove de Julho Hospital, São Paulo, Brazil (Machado); Division of General and Transplant Surgery, University of Pisa, Pisa, Italy (Boggi, Kauffmann); Department of Surgery, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands (Cappelle, Koerkamp); Hepatobiliary and Pancreatic Surgery Unit, Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom (Roberts); Department of Surgery, Thomas Jefferson University Hospital, Philadelphia, Pennsylvania (Nevler, Lavu); Department of General, Visceral and Thoracic Surgery, University Medical Center Hamburg-Eppendorf, Hamburg, Germany (Nickel, Hackert).

Outcomes for Total Pancreatectomy Group: James Halle-Smith, MD; Valentina Valle, MD; Pier Giulianotti, MD; Fabio Giannone, MD; Patrick Pessaux, MD; Patricia Sánchez-Velázquez, MD, PhD; Prabin Bikram Thapa, MD; Dhiresh Maharjan, MD; Orlando Torres, MD; Matta Kuzman, MD; Sanjay Pandanaboyana, MD.

Affiliations of Outcomes for Total Pancreatectomy Group: Hepatobiliary and Pancreatic Surgery Unit, Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom (Halle-Smith); Division of General, Minimally Invasive, and Robotic Surgery, Department of Surgery, University of Illinois at Chicago, Chicago (Valle, Giulianotti); Department of Visceral and Digestive Surgery, Unit of Hepato-Bilio-Pancreatic Surgery, Nouvel Hospital Civil, University Hospital of Strasbourg, Strasbourg, France (Giannone, Pessaux); Hepato-Biliary and Pancreatic Surgery Unit, Hospital del Mar, Universitat Pompeu Fabra, Barcelona, Spain (Sánchez-Velázquez); Department of HPB Surgery, Medical College Teaching Hospital and Nepal Cancer Hospital, Kathmandu, Nepal (Thapa, Maharjan); Department of Gastrointestinal Surgery, Hepatopancreatobiliary Unit, Universidade Federal do Maranhão, São Luís, Brazil (Torres); Hepatopancreatobiliary and Transplant Unit, Freeman Hospital, Newcastle Upon Tyne, United Kingdom (Kuzman, Pandanaboyana).

Author Contributions: Dr P. C. Müller had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs P. C. Müller, Berchtold, Kuemmerli shared first authorship. Drs Billeter and B. P. Müller shared last authorship.
Concept and design: P. C. Müller, Kuemmerli, Li, Cecchetto, Farooqui, Tschuor, de Santibañes, Marchegiani, Nickel, Hackert, Falconi, Truty, Billeter, B. P. Müller, Valle, Giulianotti.
Acquisition, analysis, or interpretation of data: P. C. Müller, Berchtold, Kuemmerli, Breuer, Li, Vallorani, Hansen, Guidetti, Eden, Campbell, Wu, Cecchetto, Gudmundsdottir, Kendrick, Starlinger, Pecorelli, Guarneri, Farooqui, Tschuor, Burgdorf, Mühlhäusser, Gass, Goh, Koh, Rebelo, Kleeff, Seip, de Santibañes, Todeschini, Marchegiani, Belfil, Lesurtel, Machado, Boggi, Kauffmann, Cappelle, Groot Koerkamp, Di Benedetto, Roberts, Nevler, Lavu, Dutkowski, Nickel, He, Falconi, Truty, Billeter, Halle-Smith, Giulianotti, Giannone, Pessaux, Sánchez-Velázquez, Thapa, Maharjan, Torres, Kuzman, Pandanaboyana.
Drafting of the manuscript: P. C. Müller, Berchtold, Li, Starlinger, Mühlhäusser, Rebelo, Marchegiani, Truty, Billeter, Torres.
Critical review of the manuscript for important intellectual content: P. C. Müller, Berchtold, Kuemmerli, Breuer, Li, Vallorani, Hansen, Guidetti, Eden, Campbell, Wu, Cecchetto, Gudmundsdottir, Kendrick, Starlinger, Pecorelli, Guarneri, Farooqui, Tschuor, Burgdorf, Mühlhäusser, Gass, Goh, Koh, Kleeff, Seip, de Santibañes, Todeschini, Belfil, Lesurtel, Machado, Boggi, Kauffmann, Cappelle, Groot Koerkamp, Di Benedetto, Roberts, Nevler, Lavu, Dutkowski, Nickel, Hackert, He, Falconi, Truty, Billeter, B. P. Müller, Halle-Smith, Valle, Giulianotti, Giannone, Pessaux, Sánchez-Velázquez, Thapa, Maharjan, Torres, Kuzman, Pandanaboyana.
Statistical analysis: Berchtold, Kuemmerli, Breuer, Burgdorf, Seip, Billeter.
Administrative, technical, or material support: P. C.

Müller, Berchtold, Kuemmerli, Breuer, Vallorani, Hansen, Campbell, Cecchetto, Gudmundsdottir, Kendrick, Starlinger, Farooqui, Tschuor, Mühlhäusser, Gass, Goh, Rebelo, de Santibañes, Machado, Di Benedetto, Nevler, He, Halle-Smith, Thapa, Maharjan, Torres, Pandanaboyana. *Supervision:* P. C. Müller, Hansen, Eden, Cecchetto, Starlinger, Pecorelli, Guarneri, Tschuor, Mühlhäusser, Gass, Goh, de Santibañes, Marchegiani, Lesurtel, Boggi, Kauffmann, Cappelle, Di Benedetto, Dutkowski, Nickel, Hackert, Falconi, Truty, Billeter, B. P. Müller, Giulianotti, Giannone, Pessaux, Sánchez-Velázquez, Torres.

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