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Nationwide validation of the ISGPS risk classification for postoperative pancreatic fistula after pancreatoduodenectomy: "Less is more"

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ABSTRACT

Background: The International Study Group of Pancreatic Surgery 4-tier (ie, A–D) risk classification for postoperative pancreatic fistula grade B/C is based on pancreatic texture and pancreatic duct size: A (not-soft texture and pancreatic duct >3 mm), B (not-soft texture and pancreatic duct ≤3 mm), C (soft texture and pancreatic duct >3 mm), and D (soft texture and pancreatic duct ≤3 mm). This study aimed to validate the International Study Group of Pancreatic Surgery risk classification for postoperative pancreatic fistula after pancreatoduodenectomy.

Methods: Consecutive patients after pancreatoduodenectomy for all indications (2014–2021) were included from the nationwide, mandatory Dutch Pancreatic Cancer Audit. The rate of postoperative pancreatic fistula grade B/C (according to the International Study Group of Pancreatic Surgery 2016 definition) was calculated per risk category. Model performance was assessed using the area under the receiver operating curve (discrimination) and calibration plots.

Results: Overall, 3,900 patients were included in risk categories: A ($n = 1,046$), B ($n = 498$), C ($n = 963$), and D ($n = 1,393$) with corresponding postoperative pancreatic fistula grade B/C rates of 3.8%, 12.2%, 15.6%, and 29.6%. Per category, the in-hospital mortality rates were 1.3%, 3.4%, 2.9%, and 4.1%, $P = .001$. There was no difference in the rate of postoperative pancreatic fistula between risk categories B and C (12.2% vs 15.6%, $P = .101$). When simplifying the classification system to a 3-tier classification system (based on 0, 1, and 2 risk factors), the discrimination was not significantly different (area under the receiver operating curve 0.697 vs area under the receiver operating curve 0.701, $P = .077$).

Conclusion: This validation of the 4-tier International Study Group of Pancreatic Surgery risk classification for postoperative pancreatic fistula after pancreatoduodenectomy confirmed its predictive value. However, as the 2 middle risk categories provide no added predictive value, a simplified 3-tier classification with comparable predictive value is proposed and should be validated in future prospective studies.

Introduction

Postoperative pancreatic fistula (POPF) is a relatively common and potentially life-threatening complication after pancreatoduodenectomy.[1–4] As defined by the International Study

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Group of Pancreatic Surgery (ISGPS), a POPF grade B/C involves all fistulas with clinically relevant consequences in the presence of elevated drain fluid amylase.[5] In a recent comparison of four transatlantic registries of pancreatic surgery, the rate of POPF grade B/C varied from 10.9% to 15.8%.[6] Despite improved outcomes for pancreatic surgery in recent years, the rate of POPF has not decreased. For instance, the recent nationwide PORSCH trial improved postoperative complication management after pancreatic surgery and almost halved the postoperative mortality rate but did not reduce the rate of POPF.[7] Predicting the risk of POPF after pancreatoduodenectomy may be useful for tailored patient treatment such as drain placement, external pancreatic stents, and somatostatin.[7–9] Moreover, a simple and accurate risk classification may enhance comparability between studies, standardization, and for stratification in randomized trials.[10]

Since the publication of the landmark Fistula Risk Score in 2013[11], others have followed.[12–14] Recently, the ISGPS proposed a categorical 4-tier classification system to predict POPF and enhance comparison between studies. This system is based on intraoperative measurements of pancreatic texture (soft or not soft) and pancreatic duct size (≤3 mm or >3 mm).[15] This classification distinguishes 4 groups with increasing risks of POPF grade B/C, based on a cohort of 5,533 patients: type A (3.5% risk), type B (6.2% risk), type C (16.6% risk), and type D (23.3% risk).

However, validation of this novel ISGPS risk classification is lacking. Therefore, this study aimed to validate the ISGPS classification for predicting POPF grade B/C after pancreatoduodenectomy in a nationwide, observational cohort study.

Methods

Study design

This observational cohort study included consecutive patients after pancreatoduodenectomy for all indications (Jan 2014 to Dec 2021). Data were retrieved from the nationwide Dutch Pancreatic Cancer Audit (DPCA), a mandatory audit in which all (ie, 100%) patients after elective pancreatic resection in the Netherlands are included. Patient and tumor characteristics, treatment, and postoperative outcomes were collected prospectively by health care professionals. Follow-up data are collected up to 30 days after the pancreatic resection or, if a patient is still admitted after these 30 days, until discharge. The DPCA database was verified and demonstrated data completeness of 90% (case ascertainment) and data accuracy of more than 95%.[16] The study protocol was approved by the scientific committee of the Dutch Pancreatic Cancer Group (DPCG).[17] All data are anonymized and coded; therefore, no informed consent or ethical approval was required.[18] Data were reported according to the STROBE Statement checklist.[19]

Risk categories and variables

Patients after pancreatoduodenectomy for all indications with known pancreatic texture and duct size were included and stratified by the ISGPS risk categories A–D (Table I).[15] The surgeon subjectively evaluated pancreatic texture during surgery. The main pancreatic duct diameter was estimated intraoperatively at the transection point of the pancreas.

Endpoint

The primary endpoint was postoperative pancreatic fistula grade B/C, according to the ISGPS 2016 definition.[5] The secondary endpoint was in-hospital mortality.

Statistical analysis

Baseline characteristics were shown for the ISGPS risk categories (A–D). Continuous data were expressed as medians with interquartile ranges (IQRs) and tested using the Mann-Whitney *U* test. Categorical data were presented as frequencies with percentages and analyzed using the χ^2 test or Fisher exact test, as appropriate. Missing data were analyzed by comparing differences in predictors for POPF (sex, body mass index, ASA score, and diagnosis), POPF, and in-hospital mortality between the included and excluded (due to missing data on pancreatic texture and duct size) patients.

Rates of clinically relevant POPF (grade B/C), according to the ISGPS 2016 definition, were calculated for the 4 ISGPS risk categories and compared to the original ISGPS cohort using the χ^2 test. In addition, the median updated-alternative Fistula Risk Score (ua-FRS) was calculated for each risk category.[13] Based on the observation of a highly similar rate of POPF in the 2 middle ISGPS categories (i.e., B and C), a 3-tier system was proposed and assessed.

Model performance of the ISGPS 4-tier system and the proposed 3-tier system were assessed according to the area under the receiver operating curve (AUC; discrimination) and calibration plots. The calibration plots present the predicted versus the observed POPF risk per risk category. The DeLong's test was used to assess differences between the AUC curves of the ISGPS 4-tier system and the proposed 3-tier system. R-studio version 4.0.2 was used for all analyses.

Results

Patient and treatment characteristics

During the study period, 5,808 patients underwent pancreatoduodenectomy, of whom 3,900 patients had complete data regarding the pancreatic texture, pancreatic duct diameter, and the primary outcome, and could be included for analysis. No clinically relevant differences were found between the included and excluded patients (Supplementary Table S1). Patient distribution over the 4 categories was as follows: 1,046 patients (26.8%) type A; 498 patients (12.8%) type B; 963 patients (24.7%) type C; and 1,402 patients (35.7%) type D. Baseline characteristics per ISGPS risk category are shown in Table I. The rates of pancreatic ductal adenocarcinoma (PDAC) were: type A: 65%, type B: 56%, type C: 40%, and type D: 24%. Preoperative therapy in patients with PDAC was given in 23%, 32%, 13%, and 23%, respectively. The use of robot-assisted surgery was the highest in the highest fistula risk category, type D (20%), type C (14%), type B (13%), and lowest in type A (9.3%). Perioperative octreotide was most frequently used in the highest fistula risk category, type D (67%), compared to type C (62%), type B (44%), and type A (51%).

Outcome ISGPS classification

Overall, POPF grade B/C was observed in 663 (17%) patients (Table II). The rates of POPF in patients classified as type A, B, C, and D were 3.8%, 12.2%, 15.6%, and 29.6%, respectively ($P < .001$). The POPF rates in categories B and C did not differ significantly ($P = .101$). The ua-FRS score in types A, B, C, and D were 11 (7–14), 24 (18–31), 24 (17–29), and 47 (38–55), respectively. Mortality rates in risk types A, B, C, and D were 1.3%, 3.4%, 2.9%, and 4.1%, $P = .001$, again showing no difference between type B and C ($P = .716$). Model discrimination of the 4-tier ISGPS classification had moderate discrimination (AUC: 0.701; 95% CI: 0.682–0.719; see Figure 1) and good calibration (Supplementary Figure S1).

Table I
Baseline characteristics for 3,900 patients after pancreatoduodenectomy, stratified according to the ISGPS risk categories

	Overall N = 3,900	Type A* N = 1,046	Type B* N = 498	Type C* N = 963	Type D* N = 1,393	P value†
Sex (female)	1,745 (45%)	477 (46%)	194 (39%)	450 (47%)	624 (45%)	.033
Missing	4	1	0	1	2	
Age	69 (61–75)	69 (60–75)	67 (59–73)	71 (64–76)	68 (61–74)	<.001
Missing	4	2	0	2	0	
Age (>75 years)	857 (22%)	226 (22%)	98 (20%)	251 (26%)	282 (20%)	.003
Missing	4	2	0	2	0	
CCI (≥2)	1,256 (32%)	308 (29%)	151 (30%)	325 (34%)	472 (34%)	.062
BMI	24 (22–27)	24 (22–27)	25 (22–27)	24 (21–26)	25 (22–28)	<.001
Missing	77	23	9	20	25	
ASA score (≥3)	1,133 (30%)	301 (30%)	161 (33%)	275 (29%)	396 (30%)	.419
Missing	133	29	15	27	62	
Diagnosis						<.001
PDAC	1,675 (43%)	678 (65%)	278 (56%)	385 (40%)	334 (24%)	
Periampullary carcinoma	1,239 (32%)	199 (19%)	126 (25%)	312 (33%)	602 (43%)	
NET	159 (4.1%)	18 (1.7%)	9 (1.8%)	34 (3.5%)	98 (7.1%)	
Premalignant lesions‡	457 (12%)	80 (7.7%)	32 (6.5%)	151 (16%)	194 (14%)	
Chronic pancreatitis	118 (3.0%)	39 (3.7%)	30 (6.0%)	20 (2.1%)	29 (2.1%)	
Other/unknown	237 (6.1%)	28 (2.7%)	21 (4.2%)	57 (5.9%)	131 (9.4%)	
Missing	15	4	2	4	5	
Preoperative therapy§						<.001
Chemotherapy	218 (13%)	76 (12%)	54 (20%)	34 (9.0%)	54 (17%)	
Chemoradiotherapy	148 (9.0%)	79 (12%)	34 (12%)	15 (4.0%)	20 (6.1%)	
Missing	39	18	4	9	8	
Surgical approach						<.001
Open	3,046 (79%)	876 (85%)	398 (81%)	745 (79%)	1,027 (75%)	
Laparoscopic	221 (5.8%)	56 (5.5%)	28 (5.7%)	66 (7.0%)	71 (5.2%)	
Robot-assisted	569 (15%)	95 (9.3%)	63 (13%)	133 (14%)	278 (20%)	
Missing	64	19	9	19	17	
Somatostatin analog	2,259 (59%)	527 (51%)	218 (44%)	594 (62%)	920 (67%)	<.001
Missing	36	12	4	11	9	
Vascular resection	634 (16%)	270 (26%)	131 (26%)	112 (12%)	121 (8.7%)	<.001
Missing	18	5	1	6	6	

ASA, American Society of Anesthesiologists score; *CCI*, Charlson Comorbidity Index; *NET*, neuroendocrine tumor; *PDAC*, pancreatic ductal adenocarcinoma; *POPF*, postoperative pancreatic fistula according to the ISGPS 2016 criteria.

* Type A: not-soft pancreatic texture and main pancreatic duct >3 mm; Type B: not-soft pancreatic texture and main pancreatic duct size ≤3 mm; Type C: soft pancreatic texture and main pancreatic duct size >3 mm; Type D: soft pancreatic texture and main pancreatic duct size ≤3 mm.

† χ^2 test based on complete case analysis.

‡ Intraductal papillary mucinous neoplasm, mucinous cystic neoplasm, solid pseudopapillary neoplasm, adenoma.

§ In patients with pancreatic ductal adenocarcinoma. Continuous data presented as median (IQR).

Table II
Postoperative pancreatic fistula rates grade B/C in the present cohort (n = 3,900) versus the original ISGPS (n = 5,533) cohort

	Present validation cohort				Original ISGPS cohort[15]		
	POPF	No POPF	Rate	ua-FRS score	POPF	No POPF	Rate
Type A	40	1,006	3.8%	11 (7–14)	56	1,533	3.5%
Type B	61	437	12.2%	24 (18–31)	56	854	6.2%
Type C	150	813	15.6%	24 (17–29)	169	847	16.6%
Type D	412	981	29.6%	47 (38–55)	471	1547	23.3%

POPF, postoperative pancreatic fistula according to the ISGPS 2016 criteria; *ua-FRS*, updated-alternative fistula risk score.[13]

Outcome simplified 3-tier ISGPS classification

In the proposed simplified 3-tier ISGPS classification, patients are scored as A, B, and C based on 0, 1, and 2 risk factors. The rates of POPF in patients classified as type A, B, and C were 3.8%, 14.4%, and 29.6%, respectively ($P < .001$). In-hospital mortality rates in types A, B, and C were 1.3%, 3.1%, and 4.1% ($P < .001$). Model discrimination of the 3-tier ISGPS classification had moderate discrimination (AUC: 0.697; 95% CI: 0.679–0.715; see Figure 2) and good calibration (Supplementary Figure S2). The discrimination did not differ significantly ($P = .077$) between the 4-tier and 3-tier classification systems. The ISGPS risk classification for POPF grade B/C after pancreatoduodenectomy and modified ISGPS system with corresponding POPF rates are shown in Table III. The proposed modified ISGPS risk classification system is shown in Figure 3.

Discussion

This first nationwide validation of the ISGPS risk classification for the prediction of POPF grade B/C in 3,900 patients after pancreatoduodenectomy confirmed its predictive value. However, no clinically relevant difference was observed between type B and C for fistula risk (12.2% vs 15.6%, $P = .101$) and between type B and C for in-hospital mortality (3.4% vs 2.9%, $P = .716$). A simplified 3-tier ISGPS risk classification (based on 0, 1, and 2 risk factors; type A

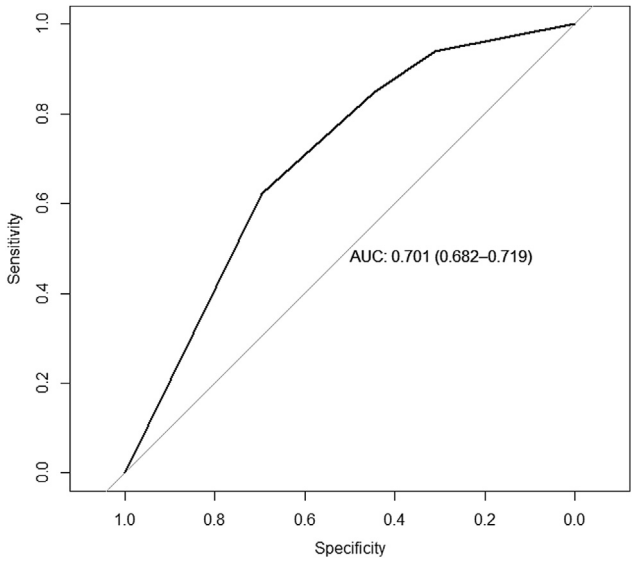

Figure 1. Correlation of the 4-tier ISGPS risk classification and fistula risk.

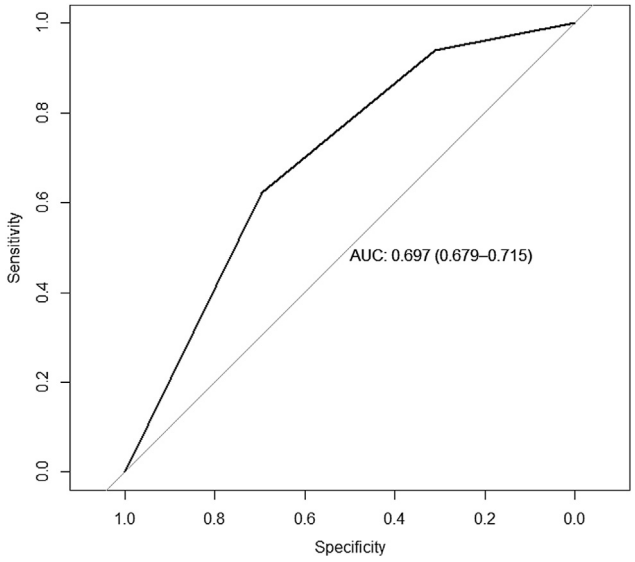

Figure 2. Correlation of the proposed 3-tier ISGPS risk classification system and fistula risk.

3.8% risk, type B 14.4% risk, type C 29.6% risk) would be as predictive and lead to a more balanced patient distribution per risk category.

A few retrospective single-center studies have looked at the patient distribution across the ISGPS risk types, although the actual rates of POPF grade B/C per risk type were not presented.[20,21] In both studies, the 2 smallest patient groups were in risk category type B and C. In recent years, multiple prediction models for POPF after pancreatoduodenectomy (eg, FRS, a-FRS, ua-FRS) have been published.[11,13,22] These models provide a precise estimate of the individual patient's risk of POPF. Although online calculation tools have been made available to calculate these exact risks, surgeons typically translate these risks back to discrete risk categories. Of note, the ua-FRS translates and assigns the risk predictions into 3 risk categories,[13] and a 3-tier POPF prediction model based on the preoperative variables main pancreatic duct diameter ($\geq$ or <5 mm) and BMI ($\geq$ or <25 kg/m^2) was recently presented by the Verona group.[14]

The ISGPS risk classification could aid in perioperative decision-making, such as drain placement, the use of preoperative somatostatin analogs and hydrocortisone, although the value of both latter agents in the prevention of POPF remains debated.[23,24] Recently, even total pancreatectomy has been advocated as an alternative to pancreatoduodenectomy in high-risk (type D) patients.[25,26] Although this remains a topic for discussion, clearly a cutoff value for a clinical decision rule for the application of different methods and agents is preferred. However, evaluating this classification system in large, prospective studies is needed before treating patients differently based on a risk score. Ultimately, good postoperative complication management in all patients after pancreatic surgery remains essential.

The present study found a higher risk of POPF grade B/C in risk category B (12.2%) than the original ISGPS cohort (6.2%).[15] Since information on the baseline and perioperative variables of the ISGPS cohort is lacking, potential causes could not be assessed, and the reason for this difference remains unclear. Even though the histopathologic diagnosis and perioperative treatment strategies were not identical between the ISGPS categories, highly similar rates of POPF in ISGPS types B (12.2%) and C (15.6%) were observed in the present cohort. This is further underlined by the corresponding similar median (IQR) ua-FRS scores of 24 in both types B and C. Although the ISGPS type B (MPD $\leq$3 mm and non-soft texture) and type C (soft texture and MPD >3 mm) might differ from a technical point of view, the findings of the present study suggest that the ISGPS risk category can be simplified into a 3-tier (A, B, C) system. This simpler classification should be based on the presence of 0, 1, and 2 risk factors (Table III, Figure 2). There was no statistically significant difference in model performance between the original 4-tier (AUC 0.701) and the proposed 3-tier classification (AUC 0.697, $P = .077$), suggesting that the 3-tier classification would be an acceptable alternative, but this has to be validated and confirmed in future prospective studies.

A remarkable finding of this study is that 20% of the patients in type D (highest risk of POPF) underwent robotic pancreatoduodenectomy, compared to only 9.3% in type A. This is probably explained by the selection for the robotic approach, mostly excluding patients with larger pancreatic cancers with vascular involvement, who often present with a dilated pancreatic duct and non-soft pancreas.[27,28] Future studies on surgical technique in pancreatic surgery should take the ISGPS risk classification into account when interpreting the rates of POPF and surgical outcome.

Table III
ISGPS risk classification system for postoperative pancreatic fistula grade B/C after pancreatoduodenectomy and proposed simplified ISGPS system

ISGPS Risk categories	Risk factor	POPF B/C risk	Simplified ISGPS Risk categories	Risk factor	POPF B/C risk
A	Non-soft texture AND MPD >3 mm	3.8%	A	None	3.8%
B	Non-soft texture AND MPD $\leq$3 mm	12.2%	B	Soft texture	14.4%
C	Soft texture AND MPD >3 mm	15.6%		OR MPD $\leq$3 mm	
D	Soft texture AND MPD $\leq$3 mm	29.6%	C	Soft texture AND MPD $\leq$3 mm	29.6%

Risk factors: soft pancreatic texture, main pancreatic duct (MPD) $\leq$3 mm.

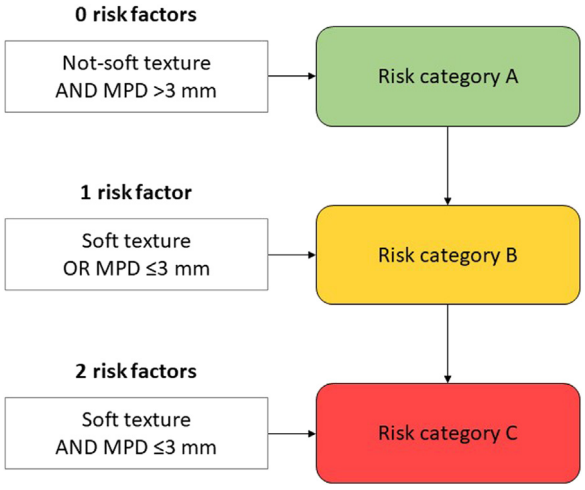

Figure 3. Simplified ISGPS risk classification system for pancreatic fistula after pancreatoduodenectomy

The findings of this study should be interpreted in light of certain limitations. First, the retrospective nature of this study introduces a risk of information bias, reflected by the 1,886 patients with missing data. However, analysis of excluded patients showed no difference in POPF rates compared to the included cohort (17.0% vs 17.6%). Second, the design and assessment of the 3-tier system was a post-hoc analysis; external validation should ideally compare the 3-tier and the 4-tier systems in a prospective study. Nevertheless, the 3-tier system performs as well as the 4-tier system, has a better patient distribution, and combines the 2 middle categories with little to no distinctive value. Third, the interactions between factors that protect against and those that predispose to POPF are considered in the ISGPS classification system. Therefore, large prospective multicenter studies are needed, ideally comparing model performance among all existing POPF risk prediction models. The strength of this study is that it is the first multicenter, nationwide study in which the ISGPS risk classification system was critically assessed.

In conclusion, this external validation of the ISGPS classification for predicting POPF grade B/C after pancreatoduodenectomy confirmed its predictive value. However, no clinically relevant difference was found between the 2 middle risk categories (B and C). For this reason, we propose simplifying the ISGPS risk categories to a 3-tier system (type A, B, and C based on 0, 1, and 2 risk factors) with a similar model performance. Future prospective studies are required to validate this proposal.

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Conflict of interest/Disclosure

The authors have no relevant disclosures.

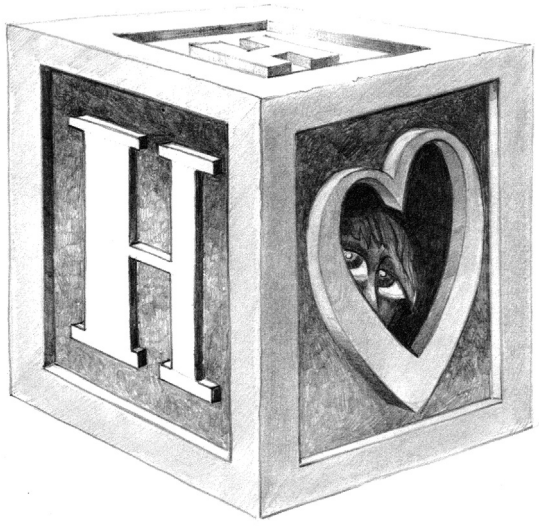
Supplementary materials

Supplementary materials associated with this article can be found in the online version, at https://doi.org/10.1016/j.surg.2023.01.004.

References

1. Sharon CE, Thaler AS, Straker III RJ, et al. Fourteen years of pancreatic surgery for malignancy among ACS-NSQIP centers: trends in major morbidity and mortality. *Surgery*. 2022;172:708–714.
2. Fuks D, Piessen G, Huet E, et al. Life-threatening postoperative pancreatic fistula (grade C) after pancreaticoduodenectomy: incidence, prognosis, and risk factors. *Am J Surg*. 2009;197:702–709.
3. Sánchez-Velázquez P, Muller X, Malleo G, et al. Benchmarks in pancreatic surgery: a novel tool for unbiased outcome comparisons. *Ann Surg*. 2019;270:211–218.
4. Swanson RS, Pezzi CM, Mallin K, et al. The 90-day mortality after pancreatectomy for cancer is double the 30-day mortality: more than 20,000 resections from the national cancer data base. *Ann Surg Oncol*. 2014;21:4059–4067.
5. 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;161:584–591.
6. Mackay TM, Gleeson EM, Wellner UF, et al. Transatlantic registries of pancreatic surgery in the United States of America, Germany, the Netherlands, and Sweden: comparing design, variables, patients, treatment strategies, and outcomes. *Surgery*. 2021;169:396–402.
7. Smits FJ, Henry AC, Besselink MG, et al. Algorithm-based care versus usual care for the early recognition and management of complications after pancreatic resection in the Netherlands: an open-label, nationwide, stepped-wedge cluster-randomised trial. *Lancet*. 2022;399:1867–1875.
8. McMillan MT, Malleo G, Bassi C, et al. Drain management after pancreatoduodenectomy: reappraisal of a prospective randomized trial using risk stratification. *J Am Coll Surg*. 2015;221:798–809.
9. Allen PJ, Gönen M, Brennan MF, et al. Pasireotide for postoperative pancreatic fistula. *N Engl J Med*. 2014;370:2014–2022.
10. Ecker BL, McMillan MT, Asbun HJ, et al. Characterization and optimal management of high-risk pancreatic anastomoses during pancreatoduodenectomy. *Ann Surg*. 2018;267:608–616.
11. Callery MP, Pratt WB, Kent TS, et al. A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatoduodenectomy. *J Am Coll Surg*. 2013;216:1–14.
12. Kantor O, Talamonti MS, Pitt HA, et al. Using the NSQIP Pancreatic Demonstration Project to derive a modified fistula risk score for preoperative risk stratification in patients undergoing pancreaticoduodenectomy. *J Am Coll Surg*. 2017;224:816–825.
13. Mungroop TH, Klompmaker S, Wellner UF, et al. Updated alternative fistula risk score (ua-FRS) to include minimally invasive pancreatoduodenectomy: pan-European validation. *Ann Surg*. 2021;273:334–340.
14. Perri G, Marchegiani G, Partelli S, et al. Preoperative risk stratification of postoperative pancreatic fistula: a risk-tree predictive model for pancreatoduodenectomy. *Surgery*. 2021;170:1596–1601.
15. 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 (ISGPS). *Ann Surg*. 2023;277:e597–e608.
16. van Rijssen LB, Koerkamp BG, Zwart MJ, et al. Nationwide prospective audit of pancreatic surgery: design, accuracy, and outcomes of the Dutch Pancreatic Cancer Audit. *HPB (Oxford)*. 2017;19:919–926.
17. Strijker M, Mackay TM, Bonsing BA, et al. Establishing and coordinating a nationwide multidisciplinary study group: lessons learned by the Dutch Pancreatic Cancer Group. *Ann Surg*. 2020;271:e102–e104.
18. RIVM. Handreiking ontsluiting patientgegevens voor wetenschappelijk onderzoek 2019-09-03. https://www.rivm.nl/documenten/handreiking-ontsluiting-patientgegevens-voor-wetenschappelijk-onderzoek. Accessed November 3, 2022.
19. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Int J Surg*. 2014;12:1495–1499.
20. Marino MV, Heng Chiow AK, Mirabella A, et al. Rate of post-operative pancreatic fistula after robotic-assisted pancreaticoduodenectomy with pancreato-jejunostomy versus pancreato-gastrostomy: a retrospective case matched comparative study. *J Clin Med*. 2021:10.
21. Bizzoca C, Fedele S, Lippolis AS, et al. Modified technique for Wirsung-pancreatogastric anastomosis after pancreatoduodenectomy: a single center experience and systematic review of the literature. *J Clin Med*. 2021:10.
22. Mungroop TH, van Rijssen LB, van Klaveren D, et al. Alternative fistula risk score for pancreatoduodenectomy (a-FRS): design and international external validation. *Ann Surg*. 2019;269:937–943.

23. Laaninen M, Sand J, Nordback I, et al. Perioperative hydrocortisone reduces major complications after pancreaticoduodenectomy: a randomized controlled trial. *Ann Surg*. 2016;264:696–702.
24. Tarvainen T, Sirén J, Kokkola A, et al. Effect of hydrocortisone vs pasireotide on pancreatic surgery complications in patients with high risk of pancreatic fistula: a randomized clinical trial. *JAMA Surg*. 2020;155:291–298.
25. Marchegiani G, Perri G, Burelli A, et al. High-risk pancreatic anastomosis vs. total pancreatectomy after pancreatoduodenectomy: postoperative outcomes and quality of life analysis. *Ann Surg*. 2022;276:e905–e913.
26. Stoop TF, Ghorbani P, Scholten L, et al. Total pancreatectomy as an alternative to high-risk pancreatojejunostomy after pancreatoduodenectomy: a propensity score analysis on surgical outcome and quality of life. *HPB (Oxford)*. 2022;24:1261–1270.
27. Asbun HJ, Moekotte AL, Vissers FL, et al. The Miami International Evidence-based Guidelines on minimally invasive pancreas resection. *Ann Surg*. 2020;271:1–14.
28. Jones LR, Zwart MJW, Molenaar IQ, et al. Robotic pancreatoduodenectomy: patient selection, volume criteria, and training programs. *Scand J Surg*. 2020;109:29–33.



A Heart Block