



Universiteit  
Leiden  
The Netherlands

## **Outcome of pancreatic surgery during the first 6 years of a mandatory audit within the Dutch Pancreatic Cancer Group**

Suurmeijer, J.A.; Henry, A.C.; Bonsing, B.A.; Bosscha, K.; Dam, R.M. van; Eijck, C.H. van; ...  
; Dutch Pancreat Canc Grp

### **Citation**

Suurmeijer, J. A., Henry, A. C., Bonsing, B. A., Bosscha, K., Dam, R. M. van, Eijck, C. H. van, ... Besselink, M. G. (2023). Outcome of pancreatic surgery during the first 6 years of a mandatory audit within the Dutch Pancreatic Cancer Group. *Annals Of Surgery*, 278(2), 260-266. doi:10.1097/SLA.0000000000005628

Version: Publisher's Version  
License: [Creative Commons CC BY-NC-ND 4.0 license](#)  
Downloaded from: <https://hdl.handle.net/1887/3762341>

**Note:** To cite this publication please use the final published version (if applicable).

# Outcome of Pancreatic Surgery During the First 6 Years of a Mandatory Audit Within the Dutch Pancreatic Cancer Group

J. Annelie Suurmeijer, MD,\*† Anne Claire Henry, MD,‡ Bert A. Bonsing, MD, PhD,§  
 Koop Bosscha, MD, PhD,|| Ronald M. van Dam, MD, PhD,¶#  
 Casper H. van Eijck, MD, PhD,\*\* Michael F. Gerhards, MD, PhD,††  
 Erwin van der Harst, MD, PhD,‡‡ Ignace H. de Hingh, MD, PhD,§§  
 Martijn P. Intven, MD, PhD,|||| Geert Kazemier, MD, PhD,†¶¶  
 Johanna W. Wilmink, MD, PhD,†### Daan J. Lips, MD, PhD,\*\*\*  
 Fennie Wit, MD, PhD,††† Vincent E. de Meijer, MD, PhD,‡‡‡  
 I. Quintus Molenaar, MD, PhD,‡ Gijs A. Patijn, MD, PhD,§§§  
 George P. van der Schelling, MD, PhD,||||| Martijn W.J. Stommel, MD, PhD,¶¶¶  
 Olivier R. Busch, MD, PhD,\*† Bas Groot Koerkamp, MD, PhD,§  
 Hjalmar C. van Santvoort, MD, PhD,‡ Marc G. Besselink, MD, MSc, PhD,\*†✉  
 for the Dutch Pancreatic Cancer Group

From the \*Amsterdam UMC, Department of Surgery, University of Amsterdam, Amsterdam, the Netherlands; †Cancer Center Amsterdam, Amsterdam, the Netherlands; ‡Department of Surgery, Regional Academic Cancer Center Utrecht, St. Antonius Hospital and University Medical Center Utrecht, Utrecht, the Netherlands; §Department of Surgery, Leiden University Medical Center, Leiden, the Netherlands; ||Department of Surgery, Jeroen Bosch Ziekenhuis, Den Bosch, the Netherlands; ¶Department of Surgery, Maastricht University Medical Center, Maastricht, the Netherlands; \*\*University Hospital RWTH Aachen, Aachen, Germany; \*\*\*Department of Surgery, Erasmus MC Cancer Institute, Rotterdam, the Netherlands; ††Department of Surgery, OLVG, Amsterdam, the Netherlands; ‡‡Department of Surgery, Maastrichtziekenhuis, Rotterdam, the Netherlands; §§Department of Surgery, Catharina Cancer Institute, Eindhoven, the Netherlands; ||||Department of Radiation Oncology, University Medical Center Utrecht, Utrecht, the Netherlands; ¶¶Department of Surgery, Amsterdam UMC, Vrije Universiteit, Amsterdam, the Netherlands; ##Department of Medical Oncology, Amsterdam UMC, University of Amsterdam, Amsterdam, the Netherlands; \*\*\*Department of Surgery, Medisch Spectrum Twente, Enschede, the Netherlands; †††Department of Surgery, Tjongerschans hospital, Heerenveen, the Netherlands; ‡‡‡Department of Surgery, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands; §§§Department of Surgery, Isala Clinics, Zwolle, the Netherlands; |||||Department of Surgery, Amphia Hospital, Breda, the Netherlands; and ¶¶¶Department of Surgery, Radboud University Medical Center Nijmegen, the Netherlands.

✉m.g.besselink@amsterdamUMC.nl

J.A.S. and A.C.H. shared first authorship.

B.G.K., H.C. v.S., and M.G.B. shared senior authorship.

J.A.S. and A.C.H. were involved in conception and design of the study, acquisition of data, analysis and interpretation of data, in drafting and revising critically for important intellectual content of all versions of the article, and gave final approval of this version of the manuscript to be published. B.A.B., K.B., R.M.D., C.H.E., M.F.G., E.H., I.H.H., M.P.I., G.K., J.W.W., D.J.L., G.P.S., and M.W.S. were involved in conception and design of the study, interpretation of data, in revising critically for important intellectual content of the article, and gave final approval of this version of the manuscript to be published. B.K.G., H.C.S., and M.H.B. were involved in conception and design of the study, acquisition of data, interpretation of data, in drafting and revising critically for important intellectual content of all versions of the article, and gave final approval of this version of the manuscript to be published.

This work was supported by Deltaplan Alveesklierkanker and the Dutch Institute for Clinical Auditing.

The authors report no conflicts of interest.

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

Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

ISSN: 0003-4932/23/27802-0260

DOI: 10.1097/SLA.0000000000005628

**Objective:** To describe outcome after pancreatic surgery in the first 6 years of a mandatory nationwide audit.

**Background:** Within the Dutch Pancreatic Cancer Group, efforts have been made to improve outcome after pancreatic surgery. These include collaborative projects, clinical auditing, and implementation of an algorithm for early recognition and management of postoperative complications. However, nationwide changes in outcome over time have not yet been described.

**Methods:** This nationwide cohort study included consecutive patients after pancreatoduodenectomy (PD) and distal pancreatectomy from the mandatory Dutch Pancreatic Cancer Audit (January 2014–December 2019). Patient, tumor, and treatment characteristics were compared between 3 time periods (2014–2015, 2016–2017, and 2018–2019). Short-term surgical outcome was investigated using multilevel multivariable logistic regression analyses. Primary endpoints were failure to rescue (FTR) and in-hospital mortality.

**Results:** Overall, 5345 patients were included, of whom 4227 after PD and 1118 after distal pancreatectomy. After PD, FTR improved from 13% to 7.4% [odds ratio (OR) 0.64, 95% confidence interval (CI) 0.50–0.80,  $P < 0.001$ ] and in-hospital mortality decreased from 4.1% to 2.4% (OR 0.68, 95% CI 0.54–0.86,  $P = 0.001$ ), despite operating on more patients with age  $> 75$  years (18%–22%,  $P = 0.006$ ), American Society of Anesthesiologists score  $\geq 3$  (19%–31%,  $P < 0.001$ ) and Charlson comorbidity score  $\geq 2$  (24%–34%,  $P < 0.001$ ). The rates of textbook outcome (57%–55%,  $P = 0.283$ ) and major complications remained stable (31%–33%,  $P = 0.207$ ), whereas complication-related intensive care admission decreased (13%–9%,  $P = 0.002$ ). After distal pancreatectomy, improvements in FTR from 8.8% to 5.9% (OR 0.65, 95% CI 0.30–1.37,  $P = 0.253$ ) and in-hospital mortality from 1.6% to 1.3% (OR 0.88, 95% CI 0.45–1.72,  $P = 0.711$ ) were not statistically significant.

**Conclusions:** During the first 6 years of a nationwide audit, in-hospital mortality and FTR after PD improved despite operating on more high-risk patients. Several collaborative efforts may have contributed to these improvements.

**Keywords:** auditing, distal pancreatectomy, pancreatoduodenectomy, surgical outcome, trends

(*Ann Surg* 2023;278:260–266)

Improving the quality of surgery and patient outcome is especially relevant for pancreatic surgery, with its high risk of major complications (26%–40%) and mortality (2%–12%).<sup>1–3</sup> Previous studies reported that mortality after pancreatic resection is mostly attributed to “failure to rescue” (FTR), defined as the mortality rate among patients with major complications.<sup>4,5</sup> In the Netherlands, in-hospital mortality after pancreatoduodenectomy (PD) varied from 1% to 8% between hospitals (2014–2015).<sup>6</sup> This variation was found to be largely explained by differences in the rate of FTR, rather than differences in major complications.

Since then, numerous efforts to improve nationwide outcomes have been made by the Dutch Pancreatic Cancer Group (DPCG), which is a nationwide collaboration of medical specialists, researchers, nurses, and patient associations.<sup>7</sup> Among these efforts were multicenter randomized trials, clinical auditing, and ongoing centralization.<sup>8,9</sup> It is well established that increased surgical volume is associated with reduced postoperative mortality.<sup>10,11</sup> In addition, a nationwide algorithm for early recognition and minimally invasive management of complications after pancreatic surgery was implemented in the Netherlands in 2018 in the stepped-wedge randomized PORSCH trial.<sup>12</sup>

Several audits in pancreatic surgery have been introduced aiming to improve quality through transparency in health care outcomes between hospitals.<sup>13–17</sup> The mandatory, nationwide Dutch Pancreatic Cancer Audit (DPCA) was implemented by the DPCG in 2014 and includes patients after pancreatic surgery for all indications.<sup>7,18</sup> Although auditing in pancreatic surgery aims to improve quality of care, multicenter studies describing changes in outcome over time are scarce.<sup>19</sup> Therefore, this study aimed to investigate the nationwide evolution of FTR and mortality after pancreatic resection, during the first 6 years of the nationwide mandatory DPCA.

## METHODS

### Study Design and Patient Selection

Data for this observational cohort study were retrieved from the DPCA, the mandatory, nationwide audit in which all patients after pancreatic resection are included from all 16 Dutch centers performing pancreatic surgery. The study protocol was approved by the scientific committee of the DPCG.<sup>7</sup> Patient, tumor, and treatment characteristics are collected prospectively by health care professionals. Follow-up covers 30 days after index pancreatic resection or, if patients were still admitted after 30 days, until discharge. No patients were lost to follow-up. As data are registered anonymously, informed consent or ethical approval for this study was not required.<sup>20</sup> The DPCA database was verified and demonstrated data completeness over 90% (case ascertainment) and data accuracy over 95%.<sup>18</sup> For the current study, all consecutive patients after PD or distal pancreatectomy for all indications from the initiation of the DPCA (January 1, 2014–December 31st, 2019) were included. Data were reported according to the STROBE Statement checklist.<sup>21</sup>

### Data Collection and Definitions

Baseline characteristics consisted of sex, age at time of surgery, body mass index, the Charlson comorbidity index, American Society of Anesthesiologists (ASA) score, and histopathologic diagnosis. Treatment characteristics included use of neoadjuvant therapy, type of pancreatic resection, minimally invasive or open surgery, venous or arterial resection, and intraoperative drain placement. During the study period,

neoadjuvant therapy for pancreatic cancer was mostly administered in clinical trials.<sup>22,23</sup> Outcome parameters included FTR,<sup>6</sup> in-hospital mortality, major complications (Clavien-Dindo grade  $\geq$  III),<sup>24</sup> textbook outcome,<sup>25</sup> pancreatic surgery-related complications, postoperative interventions (surgical, endoscopic, and radiologic), complication-related intensive care admission, hospital stay (days), and readmission within 30 days after discharge. Pancreatic surgery-related complications included postoperative pancreatic fistula (POPF),<sup>26</sup> postpancreatectomy hemorrhage,<sup>27</sup> bile leakage<sup>28</sup> and delayed gastric emptying,<sup>29</sup> all grade B or grade C according to the International Study Group of Pancreatic Surgery (ISGPS), or International Study Group of Liver Surgery criteria. FTR was defined as in-hospital mortality in patients with a major complication.<sup>6</sup> Textbook outcome was defined as the absence of POPF, postpancreatectomy hemorrhage, bile leakage, major complications, readmission, and in-hospital mortality.<sup>25</sup> Hospital volume was based on the annual volume of PD and categorized according to the previous PORSCH trial, as high ( $>45$  pancreatoduodenectomies annually) versus low/medium volume (17–45/year). Hospital volume (high vs low/medium) was calculated for each period separately and could therefore vary for individual hospitals between periods.

### Endpoints

The primary endpoints were FTR and in-hospital mortality. Secondary endpoints included major complications, pancreatic surgery-related complications, postoperative interventions, intensive care admission, textbook outcome, length of hospital stay, and readmission rates.

### Statistical Analysis

Results were stratified by type of surgery (PD and distal pancreatectomy) and analyzed in three time periods (2014–2015, 2016–2017, and 2018–2019). Differences in patient, tumor, and treatment characteristics were assessed using  $\chi^2$  tests. The changes over time of all aforementioned short-term surgical outcomes was investigated using multilevel multivariable logistic regression analysis, taking all 3 time periods (i.e. of 2 years each) into account. To correct for unmeasured hospital differences, a 2-level random effect was used. The following case mix factors were added to the multivariable models: sex (male/female), age ( $<75$ ,  $\geq 75$  years), Charlson comorbidity index ( $<2$ ,  $\geq 2$ ), body mass index ( $<20$ , 20–25, 26–30,  $>30$  kg/m<sup>2</sup>), ASA score ( $<3$ ,  $\geq 3$ ), diagnosis (pancreatic cancer yes, no), and vascular resection (yes, no). For outcomes with  $<10$  (non) events per category, relevant confounders were selected with backward selection to prevent overfitting of the model. Intercorrelations among 2 or more independent variables in the model (multicollinearity) was determined by a variance inflation factor  $>2.5$ . *P* values were based on complete case analysis, unless unknown is displayed. A 2-sided *P* value  $<0.05$  was considered statistically significant. A subgroup analysis was performed for trends in FTR and mortality rates, stratified for high versus low/medium annual center volume of PD ( $>45$  and 17–45), using univariable regression analysis. R-studio version 4.0.2 was used for all analyses.

## RESULTS

### Patient and Treatment Characteristics

Overall, 5345 patients were included, of whom 4227 after PD and 1118 after distal pancreatectomy. Baseline and treatment characteristics stratified for type of surgery are given in Table 1 and Supplementary Table 1, Supplemental Digital Content 1, <http://links.lww.com/SLA/E76>. Over time, patients undergoing PD more often

were aged >75 years (18%–20% and 22%,  $P=0.006$ ), had an ASA score  $\geq 3$  (19%–26% and 31%,  $P<0.001$ ) and a Charlson comorbidity index  $\geq 2$  (24%–26% and 34%,  $P<0.001$ ). In the subgroup of patients with pancreatic ductal adenocarcinoma, the use of neoadjuvant chemoradiotherapy increased ( $P<0.001$ ). The use of laparoscopic PD increased before it essentially stopped (7%–13% and 1%,  $P<0.001$ ), whereas the use of robot-assisted PD increased (0%–7% and 20%,  $P<0.001$ ). For distal pancreatectomy, the use of the laparoscopic approach decreased (40%–36% and 32%,  $P<0.001$ ) whereas the robot-assisted approach increased (7.3%–10% and 32%,  $P<0.001$ ).

**Outcome after PD**

Trends in postoperative outcome are given in Tables 2 and 3. Improved rates of FTR (13%–11% and 7.4%,  $P=0.004$ ) and in-hospital mortality (4.1%–3.2% and 2.4%,  $P=0.012$ ) were observed after PD (Fig. 1). The rates of textbook outcome (57%–57% and 55%,  $P=0.283$ ) and major complications remained stable (31%–31% and 33%,  $P=0.207$ ) over time, whereas complication-related intensive care admission decreased (13%–23% and 9%,  $P=0.002$ ). The rates of POPF (13%–15% and 19%,  $P<0.001$ ) and delayed gastric emptying (17%–17% and 21%,  $P=0.013$ ) increased, whereas the rates of bile leakage and postpancreatectomy hemorrhage did not change significantly over time. The rates of postoperative radiologic interventions (17%–19% and 25%,  $P<0.001$ ) and endoscopic interventions (5.8%–4.7% and 8.4%,  $P<0.001$ ) increased. The median (interquartile range) length of stay after PD was 12 days for all time periods. Readmission rates (16%–17% and 15%,  $P=0.433$ ) did not change significantly over time.

**Outcome after Distal Pancreatectomy**

After distal pancreatectomy, the improvements seen in the rates of FTR (8.8%–7.1% and 5.9%,  $P=0.513$ ) and in-hospital mortality (1.6%–1.5% and 1.3%,  $P=0.744$ ) were not statistically significant, see Table 2. Although the rates of POPF increased (16%–20% and 22%,  $P=0.031$ ), the rates of complication-related intensive care admission decreased (7.6%–6.5% and 3.7%,  $P=0.027$ ). The rate of postoperative radiologic interventions increased (8.3%–14% and 17%,  $P=0.003$ ). Other pancreatic-surgery-related complications did not change significantly over time.

**Hospital Volume**

The median (interquartile range) annual hospital volume for PD was 34 (24–45). The total number of pancreatoduodenectomies per 2-year time period were 1362, 1421, and 1444. The total number of distal pancreatectomies per time period were 318, 410, and 390. At the start of the DPCA, 18 centers in the Netherlands performed pancreatic surgery. Two centers stopped performing pancreatic surgery during the study period.

Figure 2 shows the trends for FTR and mortality rates after PD in high and low/medium volume centers. In high-volume centers, FTR improved from 13% to 10% and 5.7% [odds ratio (OR) 0.63, 95% confidence interval (CI) 0.44–0.89,  $P=0.010$ ] whereas mortality improved from 4.4% to 3.5% and 2.1% (OR 0.67, 95% CI 0.48–0.94,  $P=0.021$ ). In low/medium volume centers, the improvements seen in FTR (13%–11% and 10%, OR, 95% CI,  $P=0.300$ ) and mortality (4.0%–3.1% and 2.9%, OR 0.84, 95% CI 0.63–1.10,  $P=0.208$ ) were not statistically significant.

**TABLE 1. Baseline Characteristics of Patients after Pancreatoduodenectomy and Distal Pancreatectomy**

	Pancreatoduodenectomy				Distal Pancreatectomy			
	2014–2015	2016–2017	2018–2019	<i>P</i> *	2014–2015	2016–2017	2018–2019	<i>P</i> *
Total N	1362	1421	1444		318	410	390	
Sex (female)	584 (43%)	631 (44%)	682 (47%)	0.064	181 (57%)	209 (51%)	227 (58%)	0.092
Missing	1	0	0		0	0	0	
Age (> 75 yr)	248 (18%)	285 (20%)	318 (22%)	<b>0.044</b>	34 (11%)	56 (14%)	51 (13%)	0.448
Missing	4	0	2		0	2	1	
Charlson comorbidity index ( $\geq 2$ )	327 (24%)	372 (26%)	496 (34%)	<b>&lt;0.001</b>	88 (28%)	132 (32%)	146 (37%)	<b>0.022</b>
Body mass index	24 (22–27)	24 (22–27)	24 (22–27)	0.537	25 (22–28)	26 (23–29)	25 (22–29)	0.249
Missing	69	47	17		12	33	8	
ASA score ( $\geq 3$ )	258 (19%)	368 (26%)	450 (31%)	<b>&lt;0.001</b>	62 (20%)	92 (23%)	101 (27%)	0.099
Missing	30	8	13		3	2	9	
Diagnosis				NA				NA
Pancreatic ductal adenocarcinoma	567 (42%)	613 (43%)	573 (40%)		91 (29%)	111 (27%)	111 (29%)	
Cholangiocarcinoma	175 (13%)	185 (13%)	186 (13%)		—	—	—	
Ampullary cancer	188 (14%)	155 (11%)	207 (14%)		—	—	—	
Duodenal cancer	74 (5.5%)	93 (6.6%)	97 (6.7%)		—	—	—	
Neuroendocrine tumor	74 (5.5%)	64 (4.5%)	59 (4.1%)		65 (21%)	95 (23%)	76 (20%)	
IPMN, SPN, MCN	97 (7.2%)	114 (8.1%)	112 (7.8%)		73 (23%)	88 (22%)	107 (28%)	
Other/unknown	175 (13%)	189 (13%)	206 (14%)		87 (28%)	114 (28%)	95 (24%)	
Missing	27	20	14		2	2	1	
Pancreatic texture (soft/normal)	769 (63%)	802 (61%)	825 (63%)	0.479	170 (83%)	248 (84%)	211 (79%)	0.321
Missing	135	105	137		113	115	124	
Pancreatic duct size (mm)	5 (2–8)	4 (2–7)	3 (2–5)	<b>&lt;0.001</b>	2 (1–5)	2 (1–3)	2 (1–5)	0.322
Missing	619	556	193		168	232	247	

*P* < 0.05 values are in bold.

\* $\chi^2$  test based on complete case analysis.

IPMN indicates intraductal papillary mucinous neoplasm (all types, including invasive IPMN); MCN, mucinous cystic neoplasm; N, number of patients; NA, not applicable; SPN, solid-pseudopapillary neoplasm.

Downloaded from http://journals.lww.com/annalsurgery by BHDIM55PHKX1Z5Eom11QIN44+KJLHEZGbsiHo4Xm on 06/12/2024

TABLE 2. Postoperative Outcome in Patients After Pancreatoduodenectomy and Distal Pancreatectomy

	Pancreatoduodenectomy				Distal Pancreatectomy			
	2014–2015	2016–2017	2018–2019	<i>P</i> *	2014–2015	2016–2017	2018–2019	<i>P</i> *
Total (N)	1362	1421	1444		318	410	390	
In-hospital mortality	56 (4.1%)	46 (3.2%)	35 (2.4%)	<b>0.012</b>	5 (1.6%)	6 (1.5%)	5 (1.3%)	0.744
Missing	5	3	3		0	0	0	
Failure to rescue§	54 (13%)	46 (11%)	34 (7.4%)	<b>0.004</b>	5 (8.8%)	6 (7.1%)	5 (5.9%)	0.513
Missing	1	1	2		0	0	0	
Major complications	404 (31%)	426 (31%)	462 (33%)	0.207	57 (19%)	84 (21%)	85 (22%)	0.246
Missing	47	45	42		15	13	12	
Textbook outcome¶	740 (57%)	774 (57%)	766 (55%)	0.283	202 (66%)	259 (66%)	248 (65%)	0.750
Missing	64	72	51		14	15	10	
POPF, grade B/C#	181 (13%)	205 (15%)	277 (19%)	< <b>0.001</b>	49 (16%)	82 (20%)	86 (22%)	<b>0.031</b>
Missing	7	12	6		2	0	0	
PPH, grade B/C#	102 (7.6%)	128 (9.2%)	110 (7.7%)	0.918	11 (3.5%)	20 (4.9%)	17 (4.4%)	0.619
Missing	13	30	15		5	3	0	
DGE, grade B/C#	228 (17%)	297 (21%)	295 (21%)	<b>0.013</b>	NA	NA	NA	NA
Missing	15	13	21					
Bile leakage, grade B/C#	63 (4.7%)	81 (5.8%)	91 (6.4%)	0.054	NA	NA	NA	NA
Missing	14	24	15					
Reoperations	130 (9.9%)	109 (7.9%)	116 (8.3%)	0.171	18 (5.9%)	22 (5.6%)	14 (3.7%)	0.348
Missing	45	48	49		15	15	14	
Radiologic interventions	226 (17%)	262 (19%)	349 (25%)	< <b>0.001</b>	25 (8.3%)	57 (14%)	64 (17%)	<b>0.003</b>
Missing	45	36	39		15	12	14	
Endoscopic interventions	77 (5.8%)	65 (4.7%)	117 (8.4%)	< <b>0.001</b>	11 (3.6%)	13 (3.3%)	13 (3.5%)	0.962
Missing	44	39	46		16	11	16	
Intensive care admission	171 (13%)	172 (12%)	132 (9%)	<b>0.002</b>	23 (7.6%)	26 (6.5%)	14 (3.7%)	<b>0.027</b>
Missing	35	23	10		15	10	7	
Median hospital stay (IQR)	12 (9–18)	12 (8–19)	12 (8–19)	0.546	8 (6–11)	8 (6–10)	7 (6–10)	0.139
Missing	24	17	10		6	6	1	
Readmission rates	221 (16%)	242 (17%)	219 (15%)	0.433	49 (15%)	66 (16%)	76 (20%)	0.126
Missing	19	28	20		0	5	4	

*P* < 0.05 values are in bold.

\**P* value based on complete case analysis of the period of surgery variable (continuous) in univariable logistic regression analyses for dichotomous outcomes and in linear regression analyses for continuous outcomes.

§In-hospital mortality of patients with Clavien-Dindo grade III or higher.

||Clavien-Dindo grade III or higher.

¶Textbook outcome: the absence of pancreatic fistula, bile leak, postpancreatectomy hemorrhage (all grade B/C according to ISGPS or ISGLS), major complications (Clavien-Dindo grade III), readmission within 30 days after discharge, and in-hospital mortality.<sup>25</sup>

#Complications according to the ISGPS or ISGLS criteria.

DGE indicates delayed gastric emptying; IQR, interquartile range; N, number of patients; NA, not applicable; PPH, postpancreatectomy hemorrhage.

## DISCUSSION

In the first 6 years of a mandatory nationwide audit for pancreatic surgery established by the DPCG, despite operating on more high-risk patients and stable rates of textbook outcome and major complications, the rates of FTR and mortality after PD improved significantly. These improvements were mostly seen in high volume centers. FTR and mortality also improved after distal pancreatectomy but these changes were not statistically significant.

Nationwide studies on trends in short-term surgical outcome in audits of pancreatic surgery are scarce. Trends in outcome of pancreatic surgery were assessed in the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP; 2013–2017).<sup>19</sup> In this study, improvement in the primary outcome “optimal pancreatic surgery” (defined as: the absence of postoperative mortality, serious morbidity, percutaneous drainage, reoperations, postoperative length of stay <75th percentile, and readmission) was seen in 16,222 patients after PD from 53.7% to 56.9% (OR 1.06 96% CI 1.02–1.092, *P*<0.001) and in 7946 patients after distal pancreatectomy from 53.3% to 58.8% (OR 1.09; 95% CI 1.04–1.14, *P*<0.001). Furthermore, a decline in 30-day mortality from 2.1% to 1.6% (*P*=0.047) after PD was reported without relevant difference after distal pancreatectomy (0.4%–0.5%, *P*=0.977). This

NSQIP-based study did not report outcomes on FTR. In comparison, the current study found higher mortality rates (from 4.1% to 2.4% after PD and from 1.6% to 1.3% after distal pancreatectomy) as compared with the NSQIP-based study, but a greater decline was observed. However, the current study included in-hospital mortality, which could also include death after 30 days. When the “optimal pancreatic surgery” criteria were applied in the current study, no significant differences after PD (53% in all time periods, *P*=0.941) and distal pancreatectomy (59%–61%, and 61%, *P*=0.732) were observed, similar as reported for textbook outcome.

The current study showed an improvement in FTR after PD from 13% to 7.4%. This is actually better than compared with a recently published international benchmark study from high volume centers, defined as ≥ 50 complex pancreas interventions per year. They reported a FTR cutoff value of 9%, based on an international cohort of 2375 low-risk patients after PD.<sup>1</sup> Furthermore, FTR rates found in the current study were also better when compared with the GAPASURG study: 13.3% (the Netherlands), 10.9% (Sweden), and 10.2% (Germany), but still worse as compared with the 5.4% reported for the United States/Canada.<sup>5</sup> After distal pancreatectomy, FTR (8.8%–7.1% and 5.9%) and mortality rates (1.6%–1.5% and 1.3%) in the current study were lower in all time periods compared with a recent nationwide French administrative database that reported FTR

**TABLE 3.** Multilevel Multivariable Logistic Regression Analyses on the Trend of Short-term Surgical Outcomes Over All 3 Time Periods After Pancreatoduodenectomy and Distal Pancreatectomy

	Pancreatoduodenectomy					Distal Pancreatectomy				
	N/Total N	OR	CI 2.5%	CI 97.5%	P*	N/Total N	OR	CI 2.5%	CI 97.5%	P*
Failure to rescue <sup>§</sup>	1190/1292	0.64	0.50	0.82	< 0.001	222/226	0.65	0.30	1.37	0.253
Mortality <sup>  </sup>	3932/4227	0.68	0.54	0.86	0.001	1089/1118	0.88	0.45	1.72	0.711
Major complications <sup>¶</sup>	3816/4227	1.07	0.98	1.17	0.147	996/1118	1.10	0.90	1.35	0.332
Textbook outcome <sup>#</sup>	3769/4227	0.95	0.87	1.03	0.229	998/1118	0.99	0.83	1.17	0.869
POPF, grade B/C**	3917/4227	1.25	1.11	1.40	< 0.001	1029/1118	1.28	1.04	1.58	0.020
PPH, grade B/C**	3886/4227	0.94	0.82	1.09	0.423	1024/1118	1.03	0.69	1.54	0.891
DGE, grade BC**	3895/4227	1.16	1.05	1.29	0.005	—	—	—	—	—
Bile leakage, grade B/C**	3893/4227	1.19	0.99	1.42	0.059	—	—	—	—	—
Reoperations	3812/4227	0.84	0.73	0.97	0.019	994/1118	0.76	0.53	1.09	0.137
Radiologic interventions	3834/4227	1.25	1.13	1.39	< 0.001	995/1118	1.50	1.17	1.92	0.002
Endoscopic interventions	3824/4227	1.34	1.13	1.60	0.001	993/1118	0.97	0.63	1.50	0.889
Intensive care admission	3882/4227	0.81	0.71	0.92	0.001	1104/1118	0.66	0.47	0.93	0.017
Length of stay	3896/4227	0.98	0.55	1.76	0.959	1019/1118	0.59	0.29	1.22	0.156
Readmission	3877/4227	0.98	0.88	1.09	0.682	1022/1118	1.14	0.93	1.41	0.206

P < 0.05 values are in bold.

\*P value based on complete case analysis of the period of surgery variable (continuous) in multilevel multivariable logistic regression analyses. All outcomes were corrected for sex, age, Charlson comorbidity index, body mass index, ASA score, diagnosis (PDAC y/n), vascular resection, and hospital identification number as random effect factor.

§In-hospital mortality of patients with Clavien-Dindo grade III or higher. For distal pancreatectomy corrected for age and ASA score.

||For distal pancreatectomy corrected for: ASA score and vascular resection.

¶Clavien-Dindo grade III or higher.

#Textbook outcome: the absence of pancreatic fistula, bile leak, postpancreatectomy hemorrhage (all grade B/C according to ISGPS or ISGLS), major complications (Clavien-Dindo grade III), readmission within 30 days after discharge, and in-hospital mortality.<sup>25</sup>

\*\*Complications according to the ISGPS or ISGLS criteria.

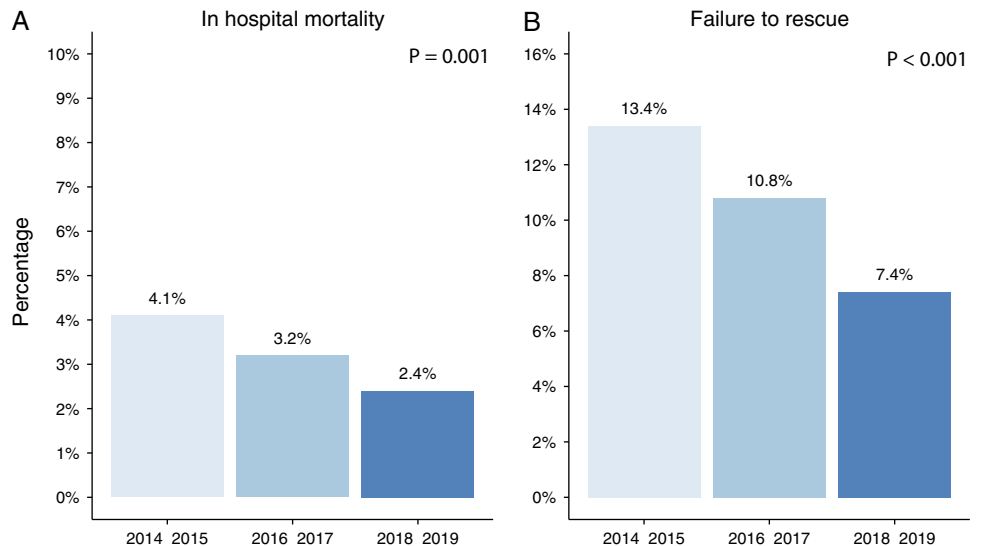
DGE indicates delayed gastric emptying; N, number of patients assessed in the multilevel multivariable analysis; PPH, postpancreatectomy hemorrhage.

(11.2%) and mortality (3.9%) rates of 10,632 patients.<sup>30</sup> However, the French analysis reported 90-day mortality, rather than in-hospital mortality in the present study. A recent study presented the first results from the Swedish National Pancreatic and Periampullary Cancer Registry.<sup>15</sup> However, no trends in the rates of FTR, mortality, or pancreatic surgery-related complications were reported.

Before introduction of the DPCA, nationwide mortality after PD in the Netherlands was 9.8% in 2004.<sup>9</sup> The current study shows a substantial reduction in mortality after PD to 2.4%. Recently, the Global Audits on Pancreatic Surgery

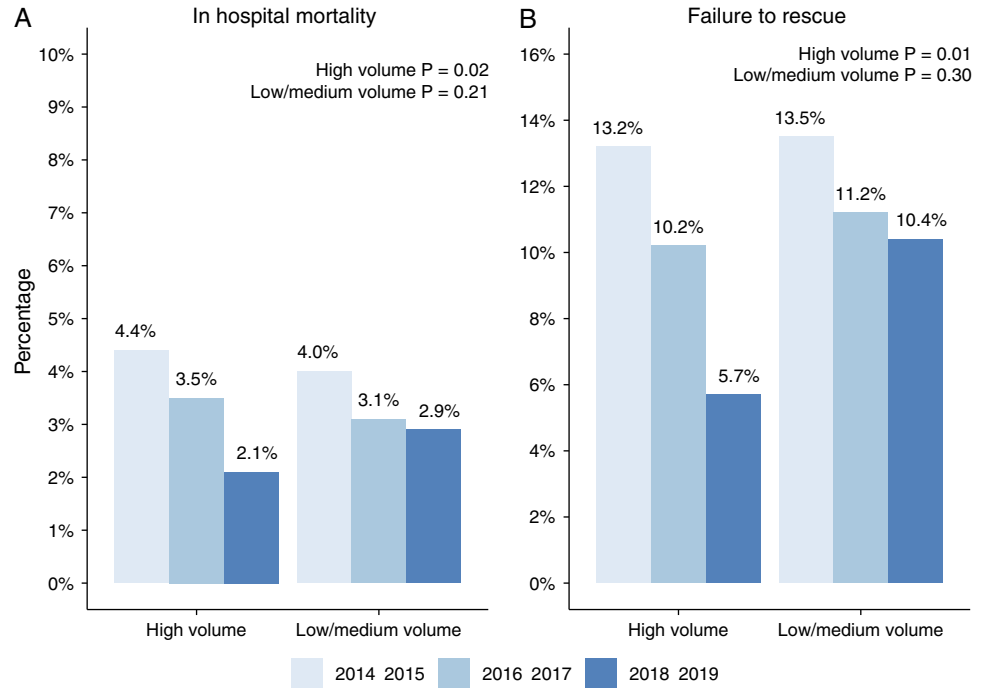
(GAPASURG) consortium compared surgical outcome after PD in 4 registries, including the DPCA.<sup>31</sup> In that study, including data from 2014 to 2017, the in-hospital mortality rate in the DPCA (3.6%) was lower as compared with the German StuDoQ (4.7%) audit, but higher as compared with the Swedish SNPPCR (2.7%), and the NSQIP (1.3%) audits.

Although the rates of major complications in the current study remained similar over time, complication-related intensive care admissions decreased, and FTR rates improved. This may suggest that in the latest period complications were treated more



**FIGURE 1.** Trends in annual rates of all cause in-hospital mortality (A) and failure to rescue (B) among 4227 patients after pancreatoduodenectomy in the Netherlands. \*A best practice algorithm for early recognition and management of complications after pancreatic resection (PORSCH trial) was implemented in all 16 Dutch centers performing pancreatic surgery in 2018 to 2019.<sup>12</sup>

Downloaded from https://journals.lww.com/annalsurgery by BHM/MS/PH/Kav/1z/Eom/11Q/N/44-H/LHEZGbsH-10dXMM on 06/12/2024



**FIGURE 2.** Trends in annual rates of all cause in-hospital mortality (A) and failure to rescue (B) after pancreatoduodenectomy in high volume (>45 PDs annually) and low/medium volume ( $\leq$ 45 PDs annually) centers in 3 time periods in the Netherlands.

adequately. In 2018 and 2019, the nationwide stepped-wedge cluster-randomized PORSCH trial implemented an algorithm for early recognition and minimally invasive management of complications after pancreatic surgery in all pancreatic centers in the Netherlands.<sup>12</sup> Based on changes in vital signs, white blood cell count, and c-reactive protein, the algorithm dictated low-threshold use of abdominal computed tomography, radiologic catheter drainage, and antibiotic treatment. This lowered threshold for radiologic drainage will likely have contributed to the higher rates of POPF observed over time, as drainage was performed more frequently and is classified as Grade B according to the International Study Group of Pancreatic Surgery criteria.<sup>26</sup> Notably, the introduction of the algorithm resulted in a significant reduction of the composite endpoint of bleeding requiring invasive intervention, organ failure, and death within 90 days after resection (composite endpoint reached in 14% of the patients assigned to usual care vs 8.5% of patients assigned to PORSCH algorithm-centered care).<sup>32</sup> These results demonstrate that timely recognition and minimally invasive management of complications, such as POPF, considerably improve outcome and reduce mortality after pancreatic resection. This finding is supported by our study, which found an improved FTR rather than a decrease in major complications.

As for changes in treatment over time, the use of neoadjuvant chemotherapy and chemoradiotherapy increased for patients with pancreatic cancer from 5.5% in the first time period to 21% in the latest time period. A second major change was the introduction of robot-assisted PD. Both developments can be explained by the rise of neoadjuvant therapy use in clinical trial setting and the implementation of a training program for robotic PD in high volume Dutch centers.<sup>22,23,33,34</sup> The use of laparoscopic PD almost stopped completely, in line with earlier reported safety concerns in the Dutch LEOPARD-2 trial,<sup>35</sup> despite good results in 3 other randomized trials.<sup>36–38</sup>

Since 2011, clinicians from all Dutch hospitals performing pancreatic surgery have been collaborating in the DPCG.<sup>7</sup> The

benchmark results from the DPCA may help improve outcomes on a local, regional, and nationwide level.<sup>39</sup> Furthermore, transparency on hospital outcome during national DPCG meetings further evoked the discussion about best practices and improvement on a nationwide scale. In addition, centralization and regional multidisciplinary team meetings have been established to improve patient selection.<sup>11,40</sup> Patients benefit from centralization due to increased resection rates and reduced mortality, probably related to improved FTR.<sup>9,10</sup> As Dutch minimum hospital volume requirements were raised to 20 pancreatoduodenectomies annually, 2 out of 18 centers stopped pancreatic surgery during the study period. The current study showed a significant decrease in FTR and in-hospital mortality over the periods, which was only statistically significant in high volume (>45 pancreatoduodenectomies annually) centers. In the PORSCH trial, these improvements were also significant in the low/medium-volume centers, possibly because 90-day outcomes were available.

The findings of this study should be interpreted in light of several limitations. First, only short-term outcomes (during hospital stay and in case of earlier discharge until 30 days) are registered in the DPCA. Efforts are currently being made to combine data from the DPCA with the Netherlands Cancer Registry data, which may provide insight in 90-day and long-term cancer outcome. Second, most data are manually registered in the DPCA, thus introducing a risk for inaccuracies or incomplete data entry. Currently, several initiatives towards automatic data transfer from the electronic patient files to the audit registry have started. Third, due to the sample size and low number of events after distal pancreatectomy per time period, we cannot exclude a Type II error. Despite these limitations, the demonstrated nationwide improvement of FTR and in-hospital mortality after pancreatic surgery suggests that progress has been made in the Netherlands. The DPCG aims for continuous improvement of quality of care through auditing, collaborative research, and transparency on patient outcome in nationwide meetings.

## CONCLUSION

In the first 6 years of a mandatory nationwide audit for pancreatic surgery, despite operating on more high-risk patients, improvement of FTR rates and in-hospital mortality after PD was seen. Nationwide efforts including collaboration between the DPCG centers, clinical auditing, and implementation of an algorithm for early recognition and management of complications, have likely contributed to these improvements.

## REFERENCES

- 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.
- 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.
- Polonski A, Izbicki JR, Uzunoglu FG. Centralization of pancreatic surgery in Europe. *J Gastrointest Surg.* 2019;23:2081–2092.
- Ghaferi AA, Birkmeyer JD, Dimick JB. Complications, failure to rescue, and mortality with major inpatient surgery in medicare patients. *Ann Surg.* 2009;250:1029–1034.
- Gleeson EM, Pitt HA, Mackay TM, et al. Failure to rescue after pancreatoduodenectomy: a transatlantic analysis. *Ann Surg.* 2021;274:459–466.
- van Rijssen LB, Zwart MJ, van Dieren S, et al. Variation in hospital mortality after pancreatoduodenectomy is related to failure to rescue rather than major complications: a nationwide audit. *HPB (Oxford).* 2018;20:759–767.
- 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.
- van der Geest LG, Besselink MG, Busch OR, et al. Elderly patients strongly benefit from centralization of pancreatic cancer surgery: a population-based study. *Ann Surg Oncol.* 2016;23:2002–2009.
- de Wilde RF, Besselink MG, van der Tweel I, et al. Impact of nationwide centralization of pancreaticoduodenectomy on hospital mortality. *Br J Surg.* 2012;99:404–410.
- Birkmeyer JD, Siewiers AE, Finlayson EV, et al. Hospital volume and surgical mortality in the United States. *N Engl J Med.* 2002;346:1128–1137.
- van der Geest LG, van Rijssen LB, Molenaar IQ, et al. Volume-outcome relationships in pancreatoduodenectomy for cancer. *HPB (Oxford).* 2016;18:317–324.
- Smits FJ, Henry AC, van Eijck CH, et al. Care after pancreatic resection according to an algorithm for early detection and minimally invasive management of pancreatic fistula versus current practice (PORSCH-trial): design and rationale of a nationwide stepped-wedge cluster-randomized trial. *Trials.* 2020;21:389.
- Pitt HA, Kilbane M, Strasberg SM, et al. ACS-NSQIP has the potential to create an HPB-NSQIP option. *HPB (Oxford).* 2009;11:405–413.
- Wellner UF, Klinger C, Lehmann K, et al. The pancreatic surgery registry (StuDoQIPancreas) of the German Society for General and Visceral Surgery (DGAV) – presentation and systematic quality evaluation. *Trials.* 2017;18:163.
- Tingstedt B, Andersson B, Jönsson C, et al. First results from the Swedish National Pancreatic and Periapillary Cancer Registry. *HPB (Oxford).* 2019;21:34–42.
- van der Heijde N, Vissers FL, Boggi U, et al. Designing the European registry on minimally invasive pancreatic surgery: a pan-European survey. *HPB (Oxford).* 2021;23:566–574.
- Maharaj AD, Holland JF, Scarborough RO, et al. The Upper Gastrointestinal Cancer Registry (UGICR): a clinical quality registry to monitor and improve care in upper gastrointestinal cancers. *BMJ Open.* 2019;9:e031434.
- 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.
- Beane JD, Borrebach JD, Zureikat AH, et al. Optimal pancreatic surgery: are we making progress in North America? *Ann Surg.* 2021;274:e355–e363.
- RIVM. Handreiking ontsluiting patientgegevens voor wetenschappelijk onderzoek 2019-09-03, 2019. Accessed December 27, 2021. <https://www.rivm.nl/documenten/handreiking-ontsluiting-patientgegevens-voor-wetenschappelijk-onderzoek>.
- von Elm E, Altman DG, Egger M, et al. The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol.* 2008;61:344–349.
- Versteijne E, Suker M, Groothuis K, et al. Preoperative chemoradiotherapy versus immediate surgery for resectable and borderline resectable pancreatic cancer: results of the Dutch Randomized Phase III PREOPANC Trial. *J Clin Oncol.* 2020;38:1763–1773.
- Janssen QP, van Dam JL, Bonsing BA, et al. Total neoadjuvant FOLFIRINOX versus neoadjuvant gemcitabine-based chemoradiotherapy and adjuvant gemcitabine for resectable and borderline resectable pancreatic cancer (PREOPANC-2 trial): study protocol for a nationwide multicenter randomized controlled trial. *BMC Cancer.* 2021;21:300.
- Clavien PA, Sanabria JR, Strasberg SM. Proposed classification of complications of surgery with examples of utility in cholecystectomy. *Surgery.* 1992;111:518–526.
- 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;271:155–162.
- Bassi C, Marchegiani G, Dervenis C, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of post-operative pancreatic fistula: 11 Years After. *Surgery.* 2017;161:584–591.
- Wente MN, Veit JA, Bassi C, et al. Postpancreatectomy hemorrhage (PPH): an International Study Group of Pancreatic Surgery (ISGPS) definition. *Surgery.* 2007;142:20–25.
- 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;149:680–688.
- Wente MN, Bassi C, Dervenis C, et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery.* 2007;142:761–768.
- Lequeu JB, Cottenet J, Facy O, et al. Failure to rescue in patients with distal pancreatectomy: a nationwide analysis of 10,632 patients. *HPB (Oxford).* 2021;23:1410–1417.
- 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.
- 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.
- Nota CL, Zwart MJ, Fong Y, et al. Developing a robotic pancreas program: the Dutch experience. *J Vis Surg.* 2017;3:106.
- Zwart MJW, Nota CLM, de Rooij T, et al. Outcomes of a multicenter training program in robotic pancreatoduodenectomy (LAELAPS-3). *Ann Surg.* 2022;276:e886–e895.
- van Hilst J, de Rooij T, Bosscha K, et al. Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours (LEOPARD-2): a multicentre, patient-blinded, randomised controlled phase 2/3 trial. *Lancet Gastroenterol Hepatol.* 2019;4:199–207.
- Palanivelu C, Senthilnathan P, Sabnis SC, et al. Randomized clinical trial of laparoscopic versus open pancreatoduodenectomy for periampullary tumours. *Br J Surg.* 2017;104:1443–1450.
- Poves I, Burdío F, Morató O, et al. Comparison of perioperative outcomes between laparoscopic and open approach for pancreatoduodenectomy: the PADULAP randomized controlled trial. *Ann Surg.* 2018;268:731–739.
- Wang M, Li D, Chen R, et al. Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours: a multicentre, open-label, randomised controlled trial. *Lancet Gastroenterol Hepatol.* 2021;6:438–447.
- Beck N, van Bommel AC, Eddes EH, et al. The Dutch Institute for clinical auditing: achieving Codman's Dream on a nationwide basis. *Ann Surg.* 2020;271:627–631.
- Augustin T, Burstein MD, Schneider EB, et al. Frailty predicts risk of life-threatening complications and mortality after pancreatic resections. *Surgery.* 2016;160:987–996.