

**The feasibility, proficiency, and mastery learning curves in 635 robotic pancreatoduodenectomies following a multicenter training program: ‘standing on the shoulders of giants’**

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## ABSTRACT

**Objective:** To assess the feasibility, proficiency, and mastery learning curves for RPD in ‘second generation’ RPD centers following a multicenter training program adhering to the IDEAL framework.

**Background:** The long learning curves for robotic pancreatoduodenectomy (RPD) reported from ‘pioneering’ expert centers may discourage centers interested in starting a RPD program. However, the feasibility, proficiency, and mastery learning curves may be shorter in ‘second generation’ centers who participated in dedicated RPD training programs, although data are lacking. We report on the learning curves for RPD in ‘second generation’ centers trained in a dedicated nationwide program.

**Methods:** Post-hoc analysis of all consecutive patients undergoing RPD in seven centers that participated in the LAELAPS-3 training program, each with a minimum annual volume of 50 pancreatoduodenectomies, using the mandatory Dutch Pancreatic Cancer Audit (March 2016-December 2021). Cumulative sum (CUSUM) analysis determined cut-offs for the three learning curves: operative time for the feasibility (1), risk-adjusted major complication (Clavien-Dindo grade  $\geq$ III) for the proficiency (2), and textbook outcome for the mastery (3) learning curve. Outcomes before and after the cut-offs were compared for the proficiency and mastery learning curves. A survey was used to assess changes in practice and the most valued ‘lessons learned’.

**Results:** Overall, 635 RPD were performed by 17 trained surgeons, with a conversion rate of 6.6% (n=42). The median annual volume of RPD per center was 22.5±6.8. From 2016-2021, the nationwide annual use of RPD increased from 0% to 23% whereas the use of laparoscopic PD decreased from 15% to 0%. The rate of major complications was 36.9% (n=234), surgical site infection (SSI) 6.3% (n=40), postoperative pancreatic fistula (grade B/C) 26.9% (n=171), and 30-day/in-hospital mortality 3.5% (n=22). Cut-offs for the feasibility, proficiency, and mastery learning curves were reached at 15, 62, and 84 RPD. Major morbidity and 30-day/in-hospital mortality did not differ significantly before and after the cut-offs for the proficiency and mastery learning curves. Previous experience in laparoscopic pancreatoduodenectomy shortened the feasibility (-12 RPDs, -44%), proficiency (-32 RPDs, -34%), and mastery phase learning curve (-34 RPDs, -23%), but did not improve clinical outcome.

**Conclusions:** The feasibility, proficiency, and mastery learning curves for RPD at 15, 62, and 84 procedures in 'second generation' centers after a multicenter training program were considerably shorter as previously reported from 'pioneering' expert centers. The learning curve cut-offs and prior laparoscopic experience did not impact major morbidity and mortality. These findings demonstrate the safety and value of a nationwide training program for RPD in centers with sufficient volume.

ACCEPTED

## INTRODUCTION

Several ‘pioneering’ high-volume centers have described excellent outcomes for robotic pancreatoduodenectomy (RPD).<sup>1-8</sup> Some centers reported a shorter hospital stay and even a lower risk of postoperative pancreatic fistula after RPD, as compared to open pancreatoduodenectomy (OPD).<sup>9,10</sup> Based on these reports there is a growing interest in high-volume centers to start with RPD. However, concerns exist regarding the long learning curves reported from these ‘pioneering’ expert centers. The University of Pittsburgh Medical Center (UPMC) group reported a feasibility learning curve of 80 RPDs and mastery obtained at 240 RPDs.<sup>7,11</sup>

The recent international evidence-based Miami guidelines strongly advise participation in a structured training program for minimally invasive pancreatoduodenectomy.<sup>12</sup> In 2020, the Dutch Pancreatic Cancer Group (DPCG) reported on the LAELAPS-3 training (2016-2019) for RPD which was developed together with three surgeons from the UPMC group.<sup>13-15</sup> When the early results were reported from this training program only four centers had completed more than 20 RPDs. Recently, two other types of learning curve have been reported.<sup>16,17</sup> The ‘proficiency’ learning curve using risk-adjusted complications, and the ‘mastery’ learning curve, using risk-adjusted textbook outcome. The latter may require experience up to 30-80 and 160-250 RPD procedures based on data from a systematic review by Müller et al. and single center reports.<sup>7,17-19</sup> Furthermore, it is unclear to what extent previous experience with laparoscopic pancreatoduodenectomy (LPD) may shorten these learning curves of robotic pancreatic procedures.

Data on these three learning curves from ‘second generation’ centers which followed a dedicated RPD training program are lacking. This is relevant to inform new centers who may be discouraged by the long learning curves reported by the ‘pioneering’ centers. We hypothesize that the learning curves for RPD are shorter in trained ‘second generation’ centers as compared to ‘pioneering’ centers. Now, two years

after our initial report,<sup>20</sup> we report on the feasibility, proficiency, and mastery learning curves for RPD including the clinical impact of these learning curves and previous experience with LPD.

## **METHODS**

### **Patients and design**

This is a post-hoc analysis of outcomes of all consecutive RPD during and following the Dutch LAELAPS-3 multicenter training program in RPD, including the first RPD in every participating center. The study was designed and performed in collaboration with the UPMC group (MH, HZ, AZ).<sup>13</sup> Data were retrieved from the mandatory Dutch Pancreatic Cancer Audit (March 2016 to December 2021).<sup>21</sup> Data on RPD procedures from one center which did not participate in the nationwide training program were excluded. In addition, nationwide trends on the use of RPD and LPD were obtained via the Dutch Pancreatic Cancer Audit to assess practice shifts over time. This study followed the guidelines for Strengthening the Reporting of Observational Studies in Epidemiology (STROBE).<sup>22</sup> The scientific committee of the Dutch Pancreatic Cancer Group approved this project<sup>23</sup> and the medical ethics review committee of Amsterdam UMC waived the need for informed consent due to the observational nature of this study (W17\_129#17.149). This study was registered at the International Clinical Trials Registry Platform (identification number: NL8073).

### **Three learning curves**

The feasibility learning curve was based on operative time. The proficiency learning curve was based on risk-adjusted major complications (Clavien–Dindo grade 3 or higher)<sup>24</sup>. The mastery learning curve was based on textbook outcome defined according to Müller *et al.*:<sup>17</sup> hospital stay shorter inside the 75<sup>th</sup> percentile, (*i.e.*, <20 days); no mortality; no complication requiring (medium) intensive care unit admission; and no reoperation.<sup>17</sup>

## Outcomes

Surgical and postoperative outcomes were assessed in both phases (*i.e.*, before vs after the cut-off) of the three learning curves of RPD. Herein, the safety outcomes were conversion, major complications, and textbook outcome. Other outcomes included blood loss, delayed gastric emptying, wound infection, postoperative pancreatic fistula, postpancreatectomy hemorrhage, bile leakage, chyle leakage, readmission, in-hospital/30-day mortality, length of stay, and reoperations.

## Definitions

Conversion was defined as an urgent or non-urgent switch to open laparotomy to complete the procedure, other than specimen extraction.<sup>25</sup> An extracorporeal gastric anastomosis performed through the extraction site was not considered conversion. Operative time was defined as the time between first incision and final closure of incisions. Postoperative complications were classified using the Clavien–Dindo classification of surgical complications with grade 3 or higher defined as major morbidity.<sup>24</sup> The definitions of the International Study Group on Pancreatic Surgery were used to score postoperative pancreatic fistula, delayed gastric emptying, postpancreatectomy hemorrhage, bile leakage, and chyle leakage.<sup>26–30</sup> Only the clinically relevant grade B and C complications were included. Wound infection (surgical site infection) required at least opening, flushing and covering of the wound with gauze.<sup>21,31</sup> Resection margins were categorized according to the Royal College of Pathologists definition and classified into R0 (distance margin to tumor  $\geq$  1mm), R1 (distance margin to tumor  $<$  1mm) and R2 (macroscopically positive margin).<sup>32</sup> Complications requiring readmission and/or reoperation were recorded up to 30-days postoperatively. The Miami guideline volume cut-off of 20 RPDs/year was assessed per center for each individual full calendar year. Additional resection was defined according to the International Study Group on Pancreatic Surgery.<sup>33</sup> Vascular resection was classified according to resections of the portomesenteric-, splenic- or inferior mesenteric vein. Arterial resections were classified according to resection of the hepatic artery, superior mesenteric artery or

celiac trunk. Risk-categories for pancreatic anastomosis were defined according to ISGPS classification: A) not-soft (hard) texture and MPD >3 mm; B) hard texture and MPD ≤3 mm; C) soft texture and MPD >3 mm; and D) soft texture and MPD ≤3 mm.<sup>34</sup> The pancreatoduodenectomy difficulty score was defined according to Büchler et al: I) no additional resection; II) venous resection; III) additional resection; IV) arterial resection.<sup>34</sup>

## Survey

A short survey was developed using Google Forms Survey® (Google; Mountain View, CA, USA) and was disseminated by email to all surgeons performing RPD (Supplemental Material 1, Supplemental Digital Content 1, <http://links.lww.com/SLA/E628>). The survey included questions with regards to surgical experience, case selection, training, surgical experience, case selection for robotic pancreatectomy, and lessons learned during the training program and thereafter.

## Data collection

Data were prospectively collected in the DPCA database during hospital stay and after discharge up to 30 days postoperatively. Collected baseline characteristics were sex, age (years), body mass index (kg/m<sup>2</sup>), comorbidity and medical history, American Society of Anesthesiologist physical status (ASA score), pancreatic duct diameter (mm), and pancreatic texture (soft or firm). Collected outcomes were conversion, operative time (min), measured intraoperative blood loss (mL, combining blood in the suction canister and in gauzes), histopathological diagnosis, tumor size (mm), resection margins and lymph node retrieval. Collected postoperative outcomes were post-operative pancreatic fistula, bile leakage, delayed gastric emptying, post-pancreatectomy hemorrhage, chyle leakage, wound infections, intensive care unit admission, complications (Clavien-Dindo classification), length of hospital stay (days), readmission, neoadjuvant chemo(radio)therapy, in-hospital-, and 30-day mortality.

## Statistical analyses

Data were analyzed using IBM SPSS Statistics for Windows version 28 (IBM Corp., Orchard Road Armonk, New York, US). Student's t, Mann Whitney U, Chi-square, or Fisher's exact tests used as suitable. Categorical data were presented as proportions, continuous data were presented as either mean and standard deviation (SD) or median- and interquartile-range [IQR] as applicable. Alpha was set at a  $P$  value  $< 0.05$ , all analyses were two-sided. Missing data were resolved by multiple imputation wherever appropriate.

### *Subgroup analyses*

Subgroup analyses compared a) outcomes of centers in the years wherein the Miami guidelines volume advice<sup>35</sup> was met versus others, and b) surgical teams with and without LPD experience.

### *Learning curve CUSUM analysis*

The learning effects were assessed with cumulative sum (CUSUM) analyses. First, patients were ranked consecutively according to the date of their procedure and the difference of the data to the mean per center was calculated per case. Hereafter, data was aggregated for all centers and hereafter a cumulative sum the data was presented on the Y-axis with the ranked consecutive case numbers presented on the X-axis. The magnitude by which the line ascends or descends is determined by the difference between the observed and expected outcome. For example, the line ascends when operative time in that case was above average for that center by an amount relative to the standard deviation, and for a case with operative time below average, the line descends. The top of the CUSUM graph thus represented the total operative expressed in standard deviations above average up to that case. When interpreting the CUSUM graph, 'slope' is the informative part, wherein an uphill slope indicates an outcome above average and a downhill slope indicates an outcome below average for that consecutive case number. The turning point of curvature indicate the point at which the centers transition from one phase to another and overcomes



the specific learning curve (Indicated by #n=turningpoint case number). The turning point determined cut-offs for the feasibility and proficiency learning curves were then used to compare operative outcomes. CUSUM analyses assessed the feasibility learning curves comprised of operative time. RA-CUSUM analysis assessed the proficiency learning curve (major complications) and mastery learning curve (text book outcome). For risk-adjusting, a regression analysis was performed with variables identified from the I-MIPS RPD cohort (Age; BMI; ASA; center),<sup>36</sup> pancreatic anastomosis classification, and pancreatoduodenectomy difficulty score.

## RESULTS

### Implementation

Between 2016 and 2021, the nationwide use of RPD increased from 0% to 23% (269/1166). In 2016, three centers started with RPD, in 2017 one additional center followed, and in 2018 three more centers. For more details on implementation see Figure 1. In the study period, the use of laparoscopic pancreatoduodenectomy decreased from 15% to 0%.

### Patient demographics

Overall, 635 patients undergoing RPD were included from seven trained centers (mean n=91 per center, range 47-166). The Miami annual volume recommendation of 20 RPDs was met in 16 (62%) of 26 study years (cumulative full years). In the final study year all but one center met the Miami annual volume advice. This one center did not meet this criterium in any year but performed at least 10 annual RPDs and performed at least 20 robotic pancreatic resections annually and other robotic procedures. Median patient age was 69 years [IQR: 61-75] and mean BMI 25 kg/m<sup>2</sup> [IQR: 23-28]. Patient demographics are presented in Table 1. The ISGPS A-D risk pancreatic anastomosis classification was available for 499 patients: A, n=108 (21.6%); B n=64 (12.9%); C, n=93 (18.7%); D, n=234 (46.9%). On preoperative imaging, vascular involvement was observed in 81 patients (12.4%) (90-180 degrees in 5.4% (n=35) and

<90 degrees in 7.0% (n = 46) which led to a vascular resection in 47/81 58% (performed robotically in 37 patients).

### **Surgeon and center demographics**

The number of surgeons performing RPD per center ranged from 1-4. Six of the seven centers performed RPD with two senior surgeons, consisting of a 'console surgeon' and a 'table side surgeon'. The remaining center used a one surgeon approach with two dedicated assistants. In four of the six centers, surgeons switched roles after the resection phase. Median surgical experience was 19 [11-24] years, with current focus (93%) on pancreatic surgery. Median minimally invasive experience was 15 [10-24] years. At the end of the study, the median individual surgeon experience was 45 [30-60] RPDs.

### **Intraoperative outcome and pathology**

Median operative time was 395 minutes [341-465] and median blood loss 200 mL [100-450]. Conversion to an open approach was performed in 42 patients (6.6%). Median tumor size was 25 mm [17-35], of which 67.1% malignant. Pancreatic cancer was the final diagnosis in 165 patients (26.0%). In patients with malignant disease, the median lymph node harvest was 15 [12-19], free resection margins rate was in 80.8% (n=426) and the R0 resection rate ( $\geq 1$ mm definition) 70.9% (n=302). Intraoperative outcomes are presented in Table 2.

### **Postoperative outcome**

The rate of major postoperative complications was 36.9% (n=234), of which 61 (9.6%) required reoperation. The rate of postoperative pancreatic fistula was 26.9% (n=171), bile leakage 8.0% (n=51), chyle leakage 2.7% (n=17), postpancreatectomy hemorrhage 12.1% (n=77), delayed gastric emptying 23.5% (n=149), and wound infection 6.5% (n=41). In patients with PDAC as histological diagnosis

compared to other diagnoses, the rate of postoperative pancreatic fistula was 9.7% (16/165) vs 33.0% (155/470)  $P < 0.001$ , respectively. Median length of hospital stay was 11 days [7-19]. The 30-day readmission rate was 22.8% (n=145). The in-hospital/30-day mortality rate was 3.5% (n=22), all of which as a cause of major morbidity (failure to rescue rate 9.4%).

## **The feasibility, proficiency, and mastery learning curves**

### *Feasibility*

The CUSUM analysis of operative time revealed a cut-off for the feasibility learning curve at 15 RPD procedures. The rates of conversion, major complications, and textbook outcome did not differ significantly between the two phases of the feasibility learning curve. Operative time decreased from 437 minutes to 386 minutes ( $P < 0.001$ ) and operative time below 360 minutes was attained in 18.9% versus 29.7% of patients ( $P = 0.005$ ). Length of initial hospital stay decreased (median 13 [9-21] to 11 days [7-19],  $P = 0.029$ ) and the rate of hospital stay  $< 7$  days, increased (6.7%, n=7 vs 17.2%, n=91,  $P = 0.002$ ). For more details, see Figure 2. For the outcome analysis, see Supplementary material 2, Supplemental Digital Content 2, <http://links.lww.com/SLA/E629>.

### *Proficiency*

Risk-adjusted CUSUM analysis of major morbidity revealed a cut-off for the proficiency learning curve at 62 RPD procedures (Figure 3). The rates of conversion (7.8% vs 4.4%,  $P = 0.069$ ), major complications (35.4% vs 39.6%,  $P = 0.295$ ), and textbook outcome (70.2% vs 64.9%,  $P = 0.165$ ) did not differ significantly between the two phases of the proficiency learning curve. The rates of delayed gastric emptying (25.7% to 16.0%,  $P < 0.001$ ), wound infections (8.8% to 1.8%,  $P < 0.001$ ), and reoperations (12.0% to 4.9%,  $P = 0.004$ ) all decreased, as did median blood loss (200mL [100-500] mL to 200mL [136-400],  $P = 0.004$ ). The rates of postpancreatectomy hemorrhage, bile leakage, chyle leakage, readmission, mortality, and length of stay remained stable. Although the rate of postoperative

pancreatic fistula increased (from 23.2% to 33.8%), the rate of grade C pancreatic fistula decreased (from 2.4% to 0.4%),  $P = 0.004$  (Table 3).

### *Mastery*

Risk-adjusted CUSUM analysis of textbook outcome revealed a cut-off for the mastery learning curve at 84 RPD procedures (see Figure 4). The rates of conversion (6.9% vs 6.2%,  $P = 0.400$ ), major complications (36.0% to 39.4%,  $P = 0.543$ ), and textbook outcome (70.0% to 67.0%,  $P = 0.238$ ) did not differ significantly between the two phases of the mastery learning curve. The rates of delayed gastric emptying (25.8% to 16.1%,  $P = 0.008$ ) and wound infections (8.1% to 0.6%,  $P < 0.001$ ) decreased. The rate of reoperations was significantly less after the turning point: 11.0% to 5.2%,  $P = 0.018$ . Whereas the rate of clinically relevant postoperative pancreatic fistula did not change, the rate of fistula grade C decreased (2.3% to 0%,  $P < 0.001$ ). The rates of postpancreatectomy hemorrhage, bile leakage, chyle leakage, readmission, mortality, and length of stay remained stable between the two phases. For more details, see Table 3.

### **Survey on the impact of training and experience**

The survey results are presented in Supplemental Material 3, Supplemental Digital Content 3, <http://links.lww.com/SLA/E630>. Most surgeons would strongly recommend LAELAPS-3 to be repeated in other countries (median strength 9 [8.5-10]). The most mentioned added value of LAELAPS-3 was the structured approach combined with written material, biotissue with feedback, videos, on-site proctoring all focusing on the same operative approach. The three most mentioned 'valuable technical aspects' taken from LAELAPS-3 were: 1) Structured methods for the anastomosis; 2) Strict adherence to procedural steps; 3) Feedback by peers. Main changes made to the procedure by participating surgeons after full training were: 1) Interrupted sutures for the hepatico-jejunostomy anastomosis regardless of bile duct size and wall thickness in five center aiming to reduce biliary leak rates; 2) Mobilization of the first jejunal loop from the right side in four centers, aiming to reduce the need for 're-docking' and

instrument collision; 3) Gastric anastomosis through the extraction site in two centers, as an attempt to mitigate delayed gastric emptying and reduce operating time.

### **Impact of laparoscopic experience**

In three centers with previous experience in LPD, the feasibility learning curve was shorter, 10 vs 22 RPDs, difference -12 RPDs (-44%). Similarly, the operative time was median 88 minutes shorter in these centers: 342 [302-385] min vs 430 [380-508],  $P < 0.001$ . Prior experience did not reduce the rate of major complications (39.4% vs 35.5%,  $P = 0.337$ ), textbook outcome (76.7% vs 68.9%,  $P = 0.081$ ), and in-hospital/30-day mortality (3.6% vs 3.4%,  $P = 0.876$ ). In centers with experience in LPD, the proficiency learning curve was also shorter, 62 vs 94 RPDs, difference -32 RPDs (-34%). Finally, in these centers, the mastery learning curve was also shorter. This reduction was seen in two phases: phase I: 65 vs 21 RPDs; phase II: 110 vs 87 RPDs; average difference: -34 RPDs (-23%) (Supplemental Material 4, Supplemental Digital Content 4, <http://links.lww.com/SLA/E631>).

### **Impact of volume**

In centers meeting the Miami guidelines volume advice,<sup>35</sup> the rate of conversion (5.3% vs 11.3%,  $P = 0.010$ ) was less as compared to other centers. Operative time (415 vs 408 min,  $P = 0.982$ ), blood loss (368 mL vs 449 mL,  $P = 0.252$ ), major morbidity (32.6% vs 38.1%,  $P = 0.238$ ), and 30-day/in-hospital mortality (2.8% vs 5.7%,  $P = 0.085$ ) did not differ significantly between centers meeting the Miami guideline volume advice and those who did not (Supplemental Material 5, Supplemental Digital Content 5, <http://links.lww.com/SLA/E632>).

## **DISCUSSION**

This first multicenter study reporting on the feasibility, proficiency, and mastery learning curves in seven 'second generation' centers, specifically trained in RPD, found learning curve cut-offs at 15, 62, and 84 RPDs in 635 RPD procedures. These cut-offs did not affect the conversion rate and had no

negative impact on major complications, textbook outcome, and in-hospital/30-day mortality. Previous experience in laparoscopic pancreatoduodenectomy was associated with shorter learning curves (range -23% to -44%). Altogether, this experience shows markedly shorter learning curves as previously reported from RPD 'pioneering' centers.

Previous studies have reported on the feasibility<sup>11,37-45</sup>, proficiency<sup>7,11,36</sup>, and mastery<sup>7,36</sup> learning curves of RPD. For the feasibility learning curve (*i.e.*, operative time), a meta-analysis reported an average cut-off of 25 RPD.<sup>17</sup> Thus, the cut-off of 15 RPDs in the present study is considerably earlier, including the cut-off of 22 RPDs in centers without LPD experience. Second, a systematic review found a proficiency learning curve (*i.e.*, risk-adjusted major complications decreased by 46%, of which POPF decreased 48%) cut-off of 100 RPDs.<sup>17,36,40</sup> Again, the cut-off of 62 RPD in this present study is considerably earlier and showed no negative impact on outcome in patients who were included before the learning curve cut-off. Third, this is the first multicenter study to report a CUSUM analysis learning curve for the mastery learning curve (*i.e.*, textbook outcome).<sup>17</sup> Zureikat *et al.* reported that operating times plateaued after 240 procedures and considered this the 'mastery' cut-off.<sup>7</sup> Again, the cut-off of 84 RPDs in the present study was considerably earlier.

The largest single center series of 500 RPD procedures in the Western world is from the UPMC group, who were the proctors of the LAELAPS-3 training program.<sup>7</sup> We compared outcomes from our multicenter study (seven centers) to their monocenter study, the present results regarding operative time, blood loss, and conversion were similar. However, the term 'proficiency' in the current study should be nuanced by the UPMC data, with lower rates of postoperative pancreatic fistula (7.8% vs 27%), major morbidity (24.8% vs 37%), and 30-day mortality (1.4% vs 3.5%).<sup>7</sup> For more details, see Supplemental Material 6, Supplemental Digital Content 6, <http://links.lww.com/SLA/E633>. As the RPD data are comparable to that of the OPD in the Netherlands,<sup>46</sup> these data also demonstrate that outcomes in the

Dutch centers may further improve with increasing experience. We will continue to monitoring our outcomes, especially since only a limited number of centers had performed >100 RPDs in the current cohort. Some differences may also exist in patient selection, volume, and postoperative management. For example, a difference in risk factors for POPF exists between the UPMC study (46% PDAC) and the current study (26% PDAC).

We will also continue to collaborate with the three US based proctors and other international surgeons to learn from each other with the aim to improve the outcomes of RPD in the Netherlands. Especially regarding the 8% biliary leak rate, 26.9% POPF rate, and the 3.5% in-hospital mortality rate. Although part of these results could be related to patient selection for RPD it will be interesting to see whether these outcomes improve with increasing experience. We aim to further investigate these hypotheses when all centers have performed >100 RPDs and compare these outcomes to international expert centers. Some evidence points to patient selection as partial explanation for the higher biliary leak rate. Patients for minimally invasive PD in this series were typically selected on the basis of absence of vascular involvement which is often accompanied by a non-dilated bile duct and pancreatic duct and hence higher leak rates. Notably, in the four available RCTs on laparoscopic versus open PD, the bile leak rates were on average 7.4% and 7.6%, respectively.<sup>47-49</sup>

Clearly, the shorter learning curves in the seven centers were a tribute to and result of the combination of close collaboration with the UPMC group in the structured LAELAPS-3 training program and the previous experience of intermediate-volume surgeons in our group. Previous training programs (LAELAPS-1 and -2) were performed in the Netherlands for laparoscopic distal pancreatectomy and laparoscopic pancreatoduodenectomy.<sup>50,51</sup> The seemingly short feasibility learning curve (*i.e.*, 15 RPDs), should be viewed in the light of the previous training of the participating surgeons and structured training program including group reflection meetings with ongoing proctoring/mentoring

during the proficiency and mastery learning curve. This is reflected by the later turning points in the learning curves for conversion (37 RPDs) and blood loss (43 RPDs). Furthermore, volume criteria might apply, therefore, the European Consortium on Minimally Invasive Pancreatic Surgery is performing the LEARNBOT training program for RPD, endorsed by the E-AHPBA, ~~again~~ only in centers performing at least 50 pancreatoduodenectomies per year, either in dual- or single surgeon approach. Although the dual-surgeon approach demonstrated the longest learning curve in the current study, the relevance of this is unclear as only one center used the single surgeon approach. Naturally, there are other high-value trainings courses available, such as the ‘Robotic Whipple Surgery Course’ by Giulianotti *et al.* and the ‘Surgical training model’ by Takagi *et al.*<sup>52</sup> The need for training and support during the safe implementation of minimally invasive pancreatoduodenectomy is further reflected by a worldwide survey with over 400 HPB surgeons from 50 countries, of which 44% stated they did not perform minimally invasive pancreatoduodenectomy due to the lack of adequate training opportunities.<sup>53</sup>

It is of interest to compare outcomes before and after the cut-offs of the learning curves. If these outcomes do not differ one could conclude that patients had no negative impact based on the learning curve process. For all three learning curves, the rate of conversion, major complications, textbook outcome, and in-hospital/30-day mortality did not differ between the periods before and after the cut-offs. However, our learning curve analysis did reveal a significant decrease in reoperation rates, mitigation of postoperative pancreatic fistula severity, bile leakage, postpancreatectomy hemorrhage, wound infections, and delayed gastric emptying. It is therefore likely that the progression of the experience came with a mitigation of the severity of the complications. During the LAELAPS-3 program, the Dutch PORSCHE trial investigated whether implementation of an algorithm for early detection and management of pancreatic fistula may improve outcomes after pancreatic resection and subsequently halved mortality after pancreatic surgery.<sup>54</sup> This intervention might have increased rate of



postoperative fistula, due to increased use of percutaneous drainage, but may also have played a role in the decrease in grade C postoperative pancreatic fistula to 0% after the ‘mastery’ cut-off.

In the current study, the median number of 15 retrieved lymph nodes was similar to the 16 nodes retrieved in a recent Dutch multicenter randomized trial on pancreatoduodenectomy specimen grossing.<sup>55</sup> Although this median number of 15 lymph nodes is<sup>54</sup> somewhat below a recent international benchmark cut-off (>16 nodes)<sup>56</sup> it is much lower than the >28 required lymph nodes reported in a recent study.<sup>57</sup> The rate of R0 resection (>0mm definition) was 81% in the current study, which conforms to textbook outcomes for pancreatic adenocarcinoma as identified from the National Cancer Database (>77.9%).<sup>58</sup> However, the R0 resection (>0mm definition) rate in patients with pancreatic adenocarcinoma of 71% has clear room for improvement. Furthermore, the 74% R0-rate ( $\geq 1$ mm definition) in malignancy was substantially higher than reported in the earlier experience of the LAELAPS-3 cohort (52.8%).<sup>20</sup>

The survey performed in the present study demonstrated that surgeons largely adhered to the previously determined (relative) contraindications for RPD, namely previous extensive abdominal surgery, history of chronic pancreatitis, central obesity with BMI  $>35$  kg/m<sup>2</sup> and segmental vascular resections during the early learning curve.<sup>59,60</sup> Several studies have suggested that robotic vascular resections were safe when performed in highly experienced centers by surgeons who have surpassed the RPD learning curve.<sup>60,61</sup> Additionally, we found that surgeons with experience in LPD had shorter operative time and shorter major morbidity learning curves compared to others, this could have resulted from a transfer of skill van laparoscopy to robotic, *e.g.*, trocar placements. Finally, centers with an annual volume of >20 RPD had reduced a conversion rate. Although center volume halved the rate of in-hospital/30-day mortality, this was not statistically significant, possibly because of a type II error.

Similar findings were reported from the E-MIPS group for minimally invasive pancreatoduodenectomy.<sup>62,63</sup>

The results of this study should be interpreted in light of some limitations. First, while the data used for this study were collected prospectively, the post-hoc nature of the study limits data collection such as for costs and 90-day mortality, which are not available in the Dutch Pancreatic Cancer Audit. Second, this study involved mainly (*i.e.*, in six of seven centers) a two-surgeon approach and may therefore not be generalizable to centers routinely using a one-surgeon approach, for example there was a median individual experience of 45 RPDs per surgeon, of which 4 surgeons completed the mastery learning curve (>84 RPDs). Third, variations in patient treatment over time might have impacted the learning curves. For example, the increased rate of grade B postoperative pancreatic fistula might be explained by both more drainage interventions as a result of the effort to limit the impact of postoperative pancreatic fistula in the PORSCHE trial by earlier detection and proactive drainage.<sup>54</sup> The major strength of this study is the homogeneous selection criteria for RPD and training provided in the seven participating centers in combination with the large sample size.

In conclusion, a structured multicenter training program for RPD in 'second generation' centers with sufficient surgical volume demonstrated shorter feasibility, proficiency, and mastery learning curves of 15, 62, and 84 RPDs as compared to previous reports from 'pioneering' centers. Prior laparoscopic experience shortened the learning curves but did not reduce major morbidity and mortality. In centers meeting the Miami guidelines volume advice the conversion rate halved as compared to other centers. Ultimately, randomized studies are needed in high-volume centers with high-volume surgeons who have surpassed the learning curves, to compare outcomes of RPD with the open approach, several of which are currently ongoing, such as the European DIPLOMA-2 trial and the Chinese PLOT trial, or have recently been completed.<sup>64,65</sup>

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## DISCLOSURES

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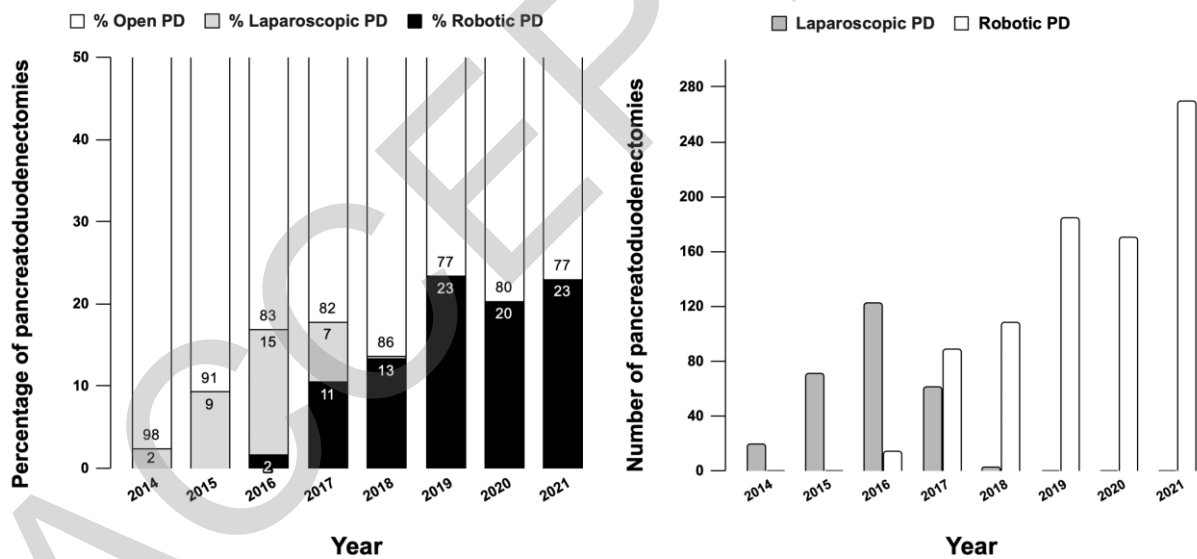
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# FIGURE 1.

**Caption:** Nationwide use of Laparoscopic and Robotic Pancreatoduodenectomy in the Netherlands

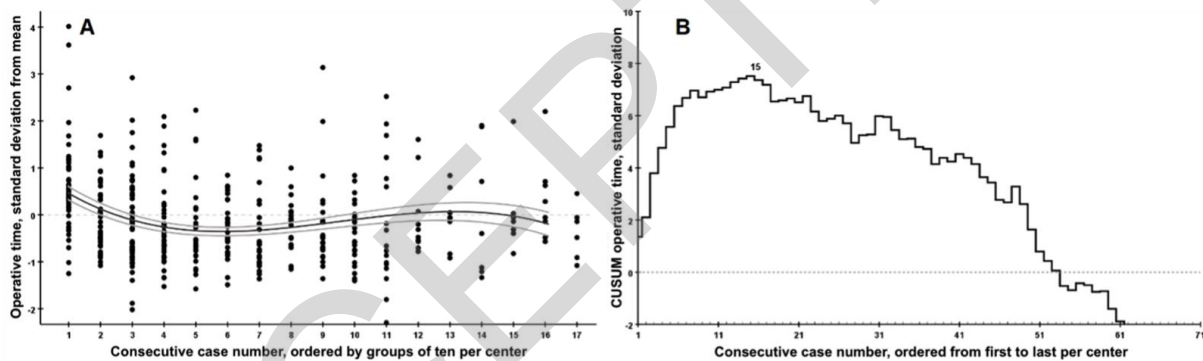
**Legend:** The left figure demonstrates the proportion of minimally invasive pancreatoduodenectomies per year. Grey indicates the laparoscopic pancreatoduodenectomies, black indicates the robotic pancreatoduodenectomies. The right figure demonstrates the absolute number of minimally invasive pancreatoduodenectomies per year. Grey indicates the laparoscopic pancreatoduodenectomies, white indicates the robotic pancreatoduodenectomies.



## FIGURE 2.

**Caption:** Figure 2. Feasibility Learning Curve of Operative Time for Robotic Pancreatoduodenectomy

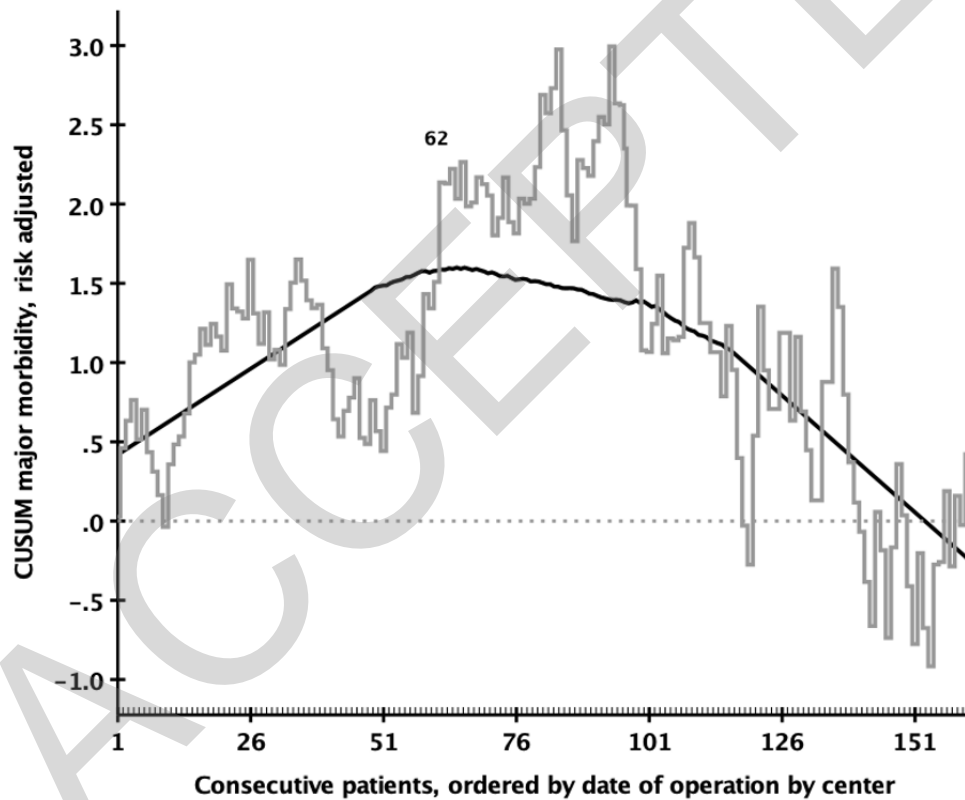
**Legend:** In figure A and B, the X-axis indicates groups of 10 consecutive RPDs ranked from first to last per center, and the Y-axis indicates the operative time in standard deviations from the mean. In figure B, the black line indicates cumulative sum analysis of operative time. The label [n=15] indicates the first top turning point of the learning curve, where after, a continuous downward slope occurs.



### FIGURE 3.

**Caption:** Proficiency Learning Curve of Risk-adjusted Major Morbidity for Robotic Pancreatoduodenectomy

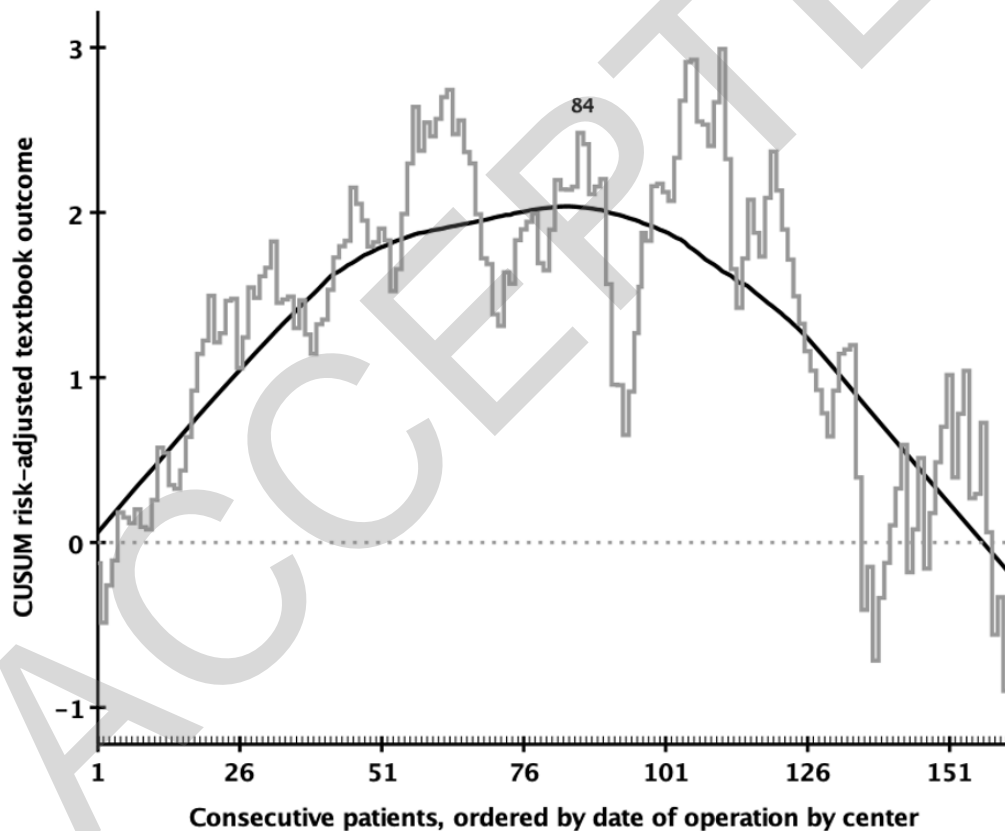
**Legend:** The X-axis indicates groups of consecutive RPDs ranked from first to last per center, and the black-line indicates the risk-adjusted cumulative sum analysis of major morbidity. The first label [n=84] indicates the first top turning point of the learning curve, where after, a continuous downward slope occurs.



## FIGURE 4.

**Caption:** Mastery Learning Curve of Risk-adjusted Textbook Outcome in Robotic Pancreatoduodenectomy

**Legend:** The X-axis indicates groups of consecutive RPDs ranked from first to last per center, and the black-line indicates the risk-adjusted cumulative sum analysis of textbook outcome. The first label [n=84] indicates the first top turning point of the learning curve, where after, a continuous downward slope occurs.



**Table 1. Baseline Characteristics**

	<b>n = 635</b>
<b>Patient characteristic</b>	
<b>Age, years, median (IQR)</b>	<b>69 (61-75)</b>
<b>Age <math>\geq</math> 75 years</b>	<b>139 (21.9)</b>
<b>BMI, kg/m<sup>2</sup>, median (IQR)</b>	<b>25 (23-28)</b>
<b>BMI <math>\geq</math> 30 kg/m<sup>2</sup> (%)</b>	<b>81 (12.8)</b>
<b>Male, n (%)</b>	<b>354 (55.7)</b>
<b>Comorbidity and medical history, any, n (%)</b>	<b>396 (62.4)</b>
<b>Diabetes</b>	<b>129 (20.3)</b>
<b>Pulmonary disease</b>	<b>93 (14.6)</b>
<b>Cardiovascular disease</b>	<b>90 (14.2)</b>
<b>Peripheral vascular disease</b>	<b>65 (10.2)</b>
<b>Oncologic disease &lt; 5 years prior</b>	<b>51 (8.0)</b>
<b>Pancreatitis</b>	<b>51 (8.0)</b>
<b>Cerebro-vascular attack</b>	<b>40 (6.3)</b>
<b>Kidney disease</b>	<b>28 (4.4)</b>
<b>Gastric ulcer disease</b>	<b>14 (2.2)</b>
<b>Liver disease</b>	<b>12 (1.9)</b>
<b>ASA physical status, n (%)</b>	
<b>I and II</b>	<b>431 (67.9)</b>
<b>III and IV</b>	<b>204 (32.1)</b>
<b>Neoadjuvant chemo(radio)therapy, n (%)</b>	<b>46 (7.2)</b>
<b>Pancreatic classification, available in n=499</b>	
<b>A) Not-soft (hard) texture and MPD <math>&gt;</math>3 mm</b>	<b>108 (21.6)</b>
<b>B) Not-soft (hard) texture and MPD <math>\leq</math>3 mm</b>	<b>64 (12.9)</b>
<b>C) Soft texture and MPD <math>&gt;</math>3 mm</b>	<b>93 (18.7)</b>
<b>D) Soft texture and MPD <math>\leq</math>3 mm</b>	<b>234 (46.9)</b>
<b>Disease characteristics</b>	
<b>Vascular involvement</b>	<b>81 (12.4)</b>
<b>Malignant disease, n (%)</b>	<b>426 (67.1)</b>
<b>Pancreatic cancer, n (%)</b>	<b>165 (26.0)</b>
<b>Distal cholangiocarcinoma, n (%)</b>	<b>88 (13.9)</b>
<b>Ampullary cancer, n (%)</b>	<b>110 (17.3)</b>
<b>Other, n (%)</b>	<b>63 (9.9)</b>
<b>Premalignant/Benign disease, n (%)</b>	<b>209 (32.9)</b>
<b>Intraductal papillary mucinous neoplasm, n (%)</b>	<b>88 (13.9)</b>
<b>Adenoma, n (%)</b>	<b>27 (4.3)</b>
<b>Auto-immune or IgG4 related disease, n (%)</b>	<b>15 (2.4)</b>
<b>Chronic pancreatitis</b>	<b>20 (3.1)</b>

**Other benign, n (%)**

**59 (9.3)**

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**ASA = American Society of Anesthesiologists**

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**Table 2. Operative Outcomes**

<b>Operative outcome</b>	<b>Total n = 635</b>
<b>Pylorus resecting PD, n (%)</b>	<b>488 (76.9)</b>
<b>Pylorus preserving PD, n (%)</b>	<b>147 (23.1)</b>
<b>Total operative time, min., median [IQR]</b>	<b>395 [341–465]</b>
Operative time < 360 min., n (%)	213 (33.5)
<b>Blood loss, mL, median [IQR]</b>	<b>200 [100–450]</b>
Blood loss >500 mL, n (%)	118 (18.6)
Blood loss >1000 mL, n (%)	34 (5.4)
<b>Conversion, n (%)</b>	<b>42 (6.6)</b>
<b>Vascular resection, n (%)</b>	<b>47 (7.4)</b>
<b>Venous resection, n (%)</b>	<b>43 (6.8)</b>
Wedge resection, n (%)	32 (5.1)
Segmental venous resection, n (%)	11 (1.7)
Arterial resection, n (%)	4 (0.6)
<b>Additional resection, n (%)</b>	<b>20 (3.6)</b>
<b>Extracorporeal gastric anastomosis, n (%)</b>	<b>147 (23.1)</b>

**PD = Pancreatoduodenectomy**



**Table 3. Outcomes in Learning Phases**

	Before proficiency cut-off ≤62 RPD (n = 410)	After proficiency cut-off >62 RPD (n = 225)	<i>p</i> =	Before mastery cut-off ≤84 RPD (n = 480)	After mastery cut-off >84 RPD (n = 155)	<i>p</i> =
<b>Safety outcomes</b>						
Conversion, n (%)	32 (7.8)	10 (4.4)	0.069	33 (6.9)	9 (6.2)	0.400
Clavien-Dindo complication ≥ III, n (%)	145 (35.4)	89 (39.6)	0.295	173 (36.0)	61 (39.4)	0.543
Requiring catheter drainage, n (%)	126 (30.7)	84 (37.3)	0.091	169 (33.1)	41 (32.8)	0.517
Reoperation, n (%)	50 (12.2)	11 (4.9)	0.004	53 (11.0)	8 (5.2)	0.018
Unplanned ICU admission, n (%)	55 (13.4)	16 (7.1)	0.010	56 (11.7)	15 (9.7)	0.494
Textbook outcome, n (%)	288 (70.2)	146 (64.9)	0.165	334 (69.6)	100 (64.5)	0.238
Type I <sup>34</sup> only (no additional resection), n (%)	250/346 (72.3)	145/216 (67.1)	0.053	293/410 (71.5)	92/145 (62.8)	0.072
<b>Other outcomes</b>						
Length of initial stay, median days (IQR)	11 [7-18]	11 [7-19]	0.654	11 [7- 19]	11 [7- 21]	0.488
Initial hospital stay < 7 days, n (%)	66 (16.1)	33 (14.7)	0.371	79 (16.5)	19 (12.3)	0.270
Readmission, n (%)	95 (23.1)	50 (22.2)	0.823	104 (21.7)	41 (26.4)	0.216
In-hospital/30-day mortality, n (%)	14 (3.4)	8 (3.5)	0.629	15 (3.1)	7 (4.5)	0.410
Postoperative pancreatic fistula (B/C), n (%)	95 (23.2)	76 (33.8)	0.004	131 (24.2)	40 (35.5)	<0.001
Of which grade C, n (%)	10 (2.4)	1 (0.4)		11 (2.3)	0 (0.0)	
Grade B/C in class	61/250	57/156	0.006	75/296	43/110	0.007

<b>A&amp;B (soft)</b>	<b>(24.4)</b>	<b>(36.5)</b>		<b>(25.3)</b>	<b>(39.1)</b>	
<b>Grade B/C in class</b>	<b>13/71</b>	<b>7/22 (31.8)</b>	<b>0.178</b>	<b>17/78</b>	<b>3/15</b>	<b>0.591</b>
<b>C&amp;D (hard)</b>	<b>(18.3)</b>			<b>(21.8)</b>	<b>(20.0)</b>	
<b>Bile leakage (B/C), n (%)</b>	<b>31 (7.6)</b>	<b>20 (8.9)</b>	<b>0.308</b>	<b>39 (8.1)</b>	<b>12 (7.7)</b>	<b>0.517</b>
<b>Delayed gastric emptying (B/C), n (%)</b>	<b>113 (27.6)</b>	<b>36 (16.0)</b>	<b>0.001</b>	<b>124 (25.8)</b>	<b>25 (16.1)</b>	<b>0.008</b>
<b>Postpancreatectomy hemorrhage (B/C), n (%)</b>	<b>53 (13.0)</b>	<b>24 (10.6)</b>	<b>0.228</b>	<b>56 (11.7)</b>	<b>21 (13.5)</b>	<b>0.400</b>
<b>Chyle leakage (B/C), n (%)</b>	<b>9 (2.2)</b>	<b>8 (3.6)</b>	<b>0.540</b>	<b>11 (2.3)</b>	<b>6 (3.9)</b>	<b>0.752</b>
<b>Wound infection*, n (%)</b>	<b>36 (8.8)</b>	<b>4 (1.8)</b>	<b>&lt;0.001</b>	<b>39 (8.1)</b>	<b>1 (0.6)</b>	<b>&lt;0.001</b>
<b>Oncologic outcome</b>						
<b>Tumor size, mm [IQR]</b>	<b>25 [18-33]</b>	<b>25 [15-35]</b>	<b>0.584</b>	<b>25 [18-35]</b>	<b>25 [15-35]</b>	<b>0.654</b>
<b>Lymph node harvest<sup>^</sup>, n [IQR]</b>	<b>15 [12-19]</b>	<b>14 [11-17]</b>	<b>0.024</b>	<b>15 [12-19]</b>	<b>14 [10-17]</b>	<b>0.013</b>
<b>R0 resection<sup>^</sup>, n (%)</b>	<b>216/294 (73.5)</b>	<b>97/132 (73.4)</b>	<b>0.377</b>	<b>253/345 (73.3)</b>	<b>60/81 (74.1)</b>	<b>0.813</b>
<b>R0 resection in pancreatic ductal adenocarcinoma</b>	<b>60/110 (54.5)</b>	<b>31/48 (64.6)</b>	<b>0.132</b>	<b>69/127 (54.3)</b>	<b>22/31 (71.0)</b>	<b>0.230</b>

\*= Wound infection (surgical site infection) required at least opening, flushing and covering of the wound with gauze. <sup>^</sup>= In patients with malignant disease.