



A Nationwide Comparison of Laparoscopic and Open Distal Pancreatectomy for Benign and Malignant Disease

Thijs de Rooij, BSc, Anneke P Jilesen, MD, Djamila Boerma, MD, PhD, Bert A Bonsing, MD, PhD, Koop Bosscha, MD, PhD, Ronald M van Dam, MD, PhD, Susan van Dieren, PhD, Marcel G Dijkgraaf, PhD, Casper H van Eijck, MD, PhD, Michael F Gerhards, MD, PhD, Harry van Goor, MD, PhD, Erwin van der Harst, MD, PhD, Ignace H de Hingh, MD, PhD, Geert Kazemier, MD, PhD, Joost M Klaase, MD, PhD, I Quintus Molenaar, MD, PhD, Els J Nieveen van Dijkum, MD, PhD, Gijs A Patijn, MD, PhD, Hjalmar C van Santvoort, MD, PhD, Joris J Scheepers, MD, PhD, George P van der Schelling, MD, PhD, Egbert Sieders, MD, PhD, Jantien A Vogel, MD, Olivier R Busch, MD, PhD, Marc G Besselink, MD, MSc, PhD, for the Dutch Pancreatic Cancer Group

BACKGROUND: Cohort studies from expert centers suggest that laparoscopic distal pancreatectomy (LDP) is superior to open distal pancreatectomy (ODP) regarding postoperative morbidity and length of hospital stay. But the generalizability of these findings is unknown because nationwide data on LDP are lacking.

STUDY DESIGN: Adults who had undergone distal pancreatectomy in 17 centers between 2005 and 2013 were analyzed retrospectively. First, all LDPs were compared with all ODPs. Second, groups were matched using a propensity score. Third, the attitudes of pancreatic surgeons toward LDP were surveyed. The primary outcome was major complications (Clavien-Dindo grade \geq III).

RESULTS: Among 633 included patients, 64 patients (10%) had undergone LDP and 569 patients (90%) had undergone ODP. Baseline characteristics were comparable, except for previous abdominal surgery and mean tumor size. In the full cohort, LDP was associated with fewer major complications (16% vs 29%; $p = 0.02$) and a shorter median [interquartile range, IQR] hospital stay (8 days [7–12 days] vs 10 days [8–14 days]; $p = 0.03$). Of all LDPs, 33% were converted to ODP. Matching succeeded for 63 LDP patients. After matching, the differences in major complications (9 patients [14%] vs 19 patients [30%]; $p = 0.06$) and median [IQR] length of hospital stay (8 days [7–12 days] vs 10 days [8–14 days]; $p = 0.48$) were not statistically significant. The survey demonstrated that 85% of surgeons welcomed LDP training.

CONCLUSIONS: Despite nationwide underuse and an impact of selection bias, outcomes of LDP seemed to be at least noninferior to ODP. Specific training is welcomed and could improve both the use and outcomes of LDP. (J Am Coll Surg 2015;220:263–270. © 2015 by the American College of Surgeons)

Disclosure Information: Nothing to disclose.

Presented at the combined meeting of the International Association of Pancreatology / European Pancreatic Club, Southampton, UK, June 2014; the Dutch Surgical Society, Veldhoven, the Netherlands, May 2014; and the United European Gastroenterology Week, Vienna, Austria, October 2014.

Received September 17, 2014; Accepted November 13, 2014.

From the Department of Surgery (De Rooij, Jilesen, Nieveen van Dijkum, Van Santvoort, Vogel, Busch, Besselink) and the Clinical Research Unit (Dieren, Dijkgraaf), Academic Medical Center; the Department of Surgery, Onze Lieve Vrouwe Gasthuis (Gerhards); and the Department of Surgery, VU Medical Center (Kazemier), Amsterdam; and the Department of Surgery, St Antonius Hospital, Nieuwegein (Boerma); the Department of Surgery, Leiden University Medical Center, Leiden (Bonsing); the Department of Surgery, Jeroen Bosch Hospital, Den Bosch (Bosscha); the Department of Surgery, Maastricht University Medical

Center, Maastricht (Van Dam); the Department of Surgery, Erasmus Medical Center (van Eijck); the Department of Surgery, Maastad Hospital (Van der Harst), Rotterdam; the Department of Surgery, Radboud University Medical Center, Nijmegen (Van Goor); the Department of Surgery, Catharina Hospital, Eindhoven (De Hingh); the Department of Surgery, Medisch Spectrum Twente, Enschede (Klaase); the Department of Surgery, University Medical Center Utrecht, Utrecht (Molenaar); the Department of Surgery, Isala Clinics, Zwolle (Patijn); the Department of Surgery, Reinier de Graaf Gasthuis, Delft (Scheepers); the Department of Surgery, Amphia Hospital, Breda (Van der Schelling); and the Department of Surgery, University Medical Center Groningen, Groningen (Sieders), the Netherlands.

Correspondence address: Marc G Besselink, MD, MSc, PhD, Department of Surgery, Academic Medical Center, PO Box 22660, 1100 DD, Amsterdam, the Netherlands. email: m.g.besselink@amc.nl

Abbreviations and Acronyms

| | |
|-------|---|
| ASA | = American Society of Anesthesiologists |
| CDC | = Centers for Disease Control and Prevention |
| IQR | = interquartile range |
| ISGPS | = International Study Group of Pancreatic Surgery |
| LDP | = laparoscopic distal pancreatectomy |
| ODP | = open distal pancreatectomy |
| OR | = odds ratio |

Since the first reported laparoscopic distal pancreatectomy (LDP) in 1996,¹ its introduction into clinical practice has been relatively slow, especially when compared with other laparoscopic gastrointestinal procedures.²⁻⁴ This slow introduction may be related to the low volume and high-risk nature of pancreatic surgery, which hampers completion of the learning curve of approximately 10 to 17 LDPs.^{5,6} Considering an average of 3 to 6 distal pancreatectomies are performed per center per year in recent US⁷ and UK⁸ studies, completing the learning curve might take approximately 2 to 3 years. However, the ongoing centralization of pancreatic surgery^{9,10} may enhance completion of this learning curve within a reasonable time. An additional factor in the slow introduction of LDP may be the lack of specific LDP training.

In several recent systematic reviews, LDP was associated with less intraoperative blood loss (263 to 355 mL), more splenic preservation (odds ratio [OR] 2.98), lower postoperative morbidity (OR 0.7), and a shorter hospital stay (3 to 6 days).¹¹⁻¹⁶ Notably, 80% (24 of 30) of the studies included in these reviews originated from very high-volume expert pancreatic centers, and none of these studies was performed on a nationwide level. Therefore, it is unclear whether these promising results are generalizable to "real-world" clinical practice. Because most series were retrospective, selection bias might have played a relevant role in the perceived superiority of LDP. Propensity score matching could be used to reduce some of this bias in retrospective studies.^{17,18} Furthermore, it is unclear whether pancreatic surgeons consider nationwide introduction of LDP feasible and are willing to undergo specific training in LDP, if needed. We aimed to determine the use and outcomes of LDP vs ODP and surgeons' attitudes toward LDP, all on a nationwide level.

METHODS**Patients**

A nationwide retrospective study was performed on all consecutive adult patients who had undergone an elective distal pancreatectomy in 1 of 17 centers of the Dutch Pancreatic Cancer Group (DPCG)¹⁹ between January 1, 2005 and September 1, 2013. All 17 centers performed at

least 20 pancreatoduodenectomies annually. Patients were excluded if distal pancreatectomy was not the primary procedure or if essential data on the surgical procedure, such as the operative report or the postoperative course, were lacking. Patient categorization was done according to the applied method of surgery: laparoscopic or open. Analyses were performed according to intention-to-treat principles, meaning that the results of a converted LDP were analyzed in the LDP group. The Medical Ethics Review Committee of the Academic Medical Center (Amsterdam, the Netherlands) approved the study protocol.

Surgical technique

Laparoscopic distal pancreatectomy was performed using 3 to 4 trocars placed around an umbilical camera. The resected specimen was extracted by enlarging one of the trocar incisions or via a Pfannenstiel incision. During LDP, the patient was in a supine or right lateral decubitus position. Hand access ports were not used. Open distal pancreatectomy was performed using a bilateral subcostal incision or a midline laparotomy using standard techniques. In some cases, during either laparoscopic or open surgery, the pancreatic remnant was treated subsequently with additional sutures or with an absorbable fibrin sealant patch. In patients with benign disease, spleen preserving distal pancreatectomy with preservation of the splenic vessels (Kimura's technique²⁰) was attempted and if preservation of the splenic vessels was considered not feasible, a spleen preserving distal pancreatectomy with ligation of splenic vessels (Warshaw's technique²¹) or subsequent splenectomy was performed. In case of suspected or proven malignant disease, splenectomy and additional lymphadenectomy were performed. One or 2 drains were placed near the pancreatic remnant and left subphrenic space.

Definitions

Postoperative complications during hospital stay and 30 days thereafter were collected, dichotomously scored, and classified using the Clavien-Dindo classification of surgical complications.²² Major complications were defined as Clavien-Dindo grade III or higher. Postoperative pancreatic fistula, delayed gastric emptying and post-pancreatectomy hemorrhage were all scored using the recommended International Study Group of Pancreatic Surgery (ISGPS) definitions.²³⁻²⁵ Grade B/C complications were considered major, and only these grades were noted. Surgical site infection was defined using the Centers for Disease Control and Prevention (CDC) definition.²⁶ Resection margins, including transection and circumferential margins, were classified into R0 (distance margin to tumor ≥ 1 mm), R1 (distance margin to tumor < 1 mm) and R2 (macroscopically positive margin).²⁷

Readmissions within 30 days after discharge were recorded. Mortality was recorded during a patient's hospital stay or within 30 days after discharge.

Data collection

Data were collected from patient records. Baseline characteristics collected included sex, age, American Society of Anesthesiologists (ASA) physical status, body mass index, previous abdominal surgery, diabetes mellitus, tumor size on preoperative imaging, and tumor involvement in other organs besides the pancreas. Primary outcome was the occurrence of at least 1 major complication after the surgical procedure. Main secondary outcomes were operative time, intraoperative blood loss, splenectomy, conversion, histopathologic diagnosis, resection margin and lymph node retrieval (both exclusively in case of malignancy), postoperative pancreatic fistula, delayed gastric emptying, postpancreatectomy hemorrhage, surgical site infection, ICU admission, length of hospital stay, and mortality.

Survey

An online survey, consisting of 12 questions regarding experiences, opinions and expectations concerning LDP (see [Appendix](#), online only), was sent to 30 pancreatic surgeons (representing >95% of Dutch pancreatic surgeons). Non-responders received a maximum of 2 reminders.

Statistical analysis

This study was performed using Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.²⁸ Data were analyzed using IBM SPSS Statistics for Windows version 20.0 (SPSS Inc). For comparison of continuous variables, either the 2 independent samples *t*-test or the Mann-Whitney U test was used, and for categorical variables, either the chi-square or Fisher's exact test was used as appropriate. The size of the study control group (ODPs) was expected to be less than 100 times the size of the study intervention group (LDPs) and therefore, matching with random sampling and replacement was applied in order to obtain independent sample values. Patients who had undergone LDP were matched to patients who had undergone ODP, using a propensity score, on a 1:1 ratio, based on sex (identical), age (± 10 years), indication for surgery (pancreatic mass vs others), tumor size when tumor was the indication for surgery (± 17 mm), and ASA physical status (identical). Matching on a higher ratio was not expected to be feasible. For every case, the most homologous control was chosen. Patients were excluded when matching failed for at least 1 criterion. For comparison of matched data, paired tests were applied.²⁹ Matched continuous variables were compared using the paired samples *t*-test or Wilcoxon signed rank test and matched categorical variables were compared using the McNemar's test as appropriate. Univariable and

Table 1. Baseline Full Cohort

| Characteristic | LDP (n = 64) | ODP (n = 569) | p Value |
|--|--------------|---------------|---------|
| Male, n (%) | 34 (53) | 235 (41) | 0.07 |
| Age, y, mean (SD) | 56 (14) | 57 (14) | 0.59 |
| BMI, kg/m ² , mean (SD) | 26 (4) | 26 (5) | 0.65 |
| Previous abdominal surgery, n (%) | 19 (30) | 245 (43) | 0.04 |
| Diabetes mellitus, n (%) | 8 (13) | 96 (17) | 0.37 |
| ASA physical status, n (%) | — | — | 0.37 |
| 1 | 18 (28) | 123 (22) | — |
| 2 | 39 (61) | 361 (63) | — |
| 3 | 6 (9) | 82 (14) | — |
| 4 | 1 (2) | 3 (1) | — |
| Indication for surgery, n (%) | — | — | 0.46 |
| Neoplasm | 41 (64) | 312 (55) | — |
| Cyst | 16 (25) | 178 (31) | — |
| Pancreatitis | 4 (6) | 57 (10) | — |
| Other | 3 (5) | 22 (4) | — |
| Tumor size on CT/MRI, mm, mean (SD) | 20 (14) | 49 (9) | <0.001 |
| Other organs involved on CT/MRI, n (%) | 2 (3) | 59 (10) | 0.06 |
| Spleen | 1 (2) | 20 (4) | — |
| Stomach | 1 (2) | 16 (3) | — |
| Intestine | — | 6 (1) | — |
| Kidney | — | 6 (1) | — |
| Multiple organs | — | 10 (2) | — |

ASA, American Society of Anesthesiologists; BMI, body mass index; LDP, laparoscopic distal pancreatectomy; ODP, open distal pancreatectomy.

multivariable conditional logistic regression analyses were performed to identify predictors of experiencing at least 1 major complication. Parameters with a p value <0.1 in a univariable analysis were included in the multivariable analysis. Results were summarized using ORs and 95% confidence intervals (CI). A sensitivity analysis was performed to determine whether matching with or without replacement influenced the study outcomes, by excluding all replaced controls and their matched patients from the laparoscopic group. Subsequently, outcomes of univariable analyses before exclusion of replaced controls were compared with outcomes of univariable analyses after exclusion. A 2-tailed p value <0.05 was considered statistically significant.

RESULTS

Full cohort

Of 761 patients who had undergone elective distal pancreatectomy, 128 patients were excluded, because distal pancreatectomy was not the primary surgical procedure (n = 124) or because of missing essential data (n = 4). So, 633 patients were included, of whom 64 patients (10%) had undergone LDP and 569 patients (90%) ODP (Table 1). The annual volume of elective distal pancreatectomies increased by 130% throughout the 8-year study period in the 17 centers, but the proportion of laparoscopic procedures (10%) remained unchanged. LDP was performed in 10 and

Table 2. Outcomes Full Cohort

| Outcomes | LDP (n = 64) | ODP (n = 569) | p Value |
|---|--------------|----------------|---------|
| Primary | | | |
| Major complication, n (%) | 10 (16) | 166 (29) | 0.02 |
| Abdominal abscess | 5 (8) | 57 (10) | — |
| Feeding tube placement | 1 (2) | 72 (13) | — |
| Respiratory insufficiency | 2 (3) | 28 (5) | — |
| Bleeding | 1 (2) | 23 (4) | — |
| Perforated stomach | 0 (0) | 5 (1) | — |
| Other | 1 (2) | 26 (5) | — |
| Secondary | | | |
| Operative time, min, mean (SD) | 213 (111) | 208 (98) | 0.76 |
| Intraoperative blood loss, mL, median (IQR) | 275 (38–638) | 700 (350–1400) | <0.001 |
| Splenectomy, n (%) | 13 (20) | 389 (68) | <0.001 |
| Nonmalignancy | 6 (9) | 230 (40) | <0.001 |
| Conversion, n (%) | 21 (33) | — | — |
| Histopathologic diagnosis, n (%) | | | 0.01 |
| Neuroendocrine tumor | 24 (38) | 110 (19) | — |
| Pancreatic ductal adenocarcinoma | 7 (11) | 134 (24) | — |
| Chronic pancreatitis | 11 (17) | 97 (17) | — |
| Mucinous cystic neoplasm | 6 (9) | 75 (13) | — |
| Serous cystic neoplasm | 1 (2) | 44 (8) | — |
| Intraductal papillary mucinous neoplasm | 5 (8) | 36 (6) | — |
| Metastatic disease | 1 (2) | 16 (3) | — |
| Other | 9 (14) | 57 (10) | — |
| Malignancy, n (%) | 13 (20) | 183 (32) | 0.05 |
| R0 resection, n (% malignancies)* | 8 (62) | 93 (51) | 0.45 |
| Lymph nodes retrieved, mean (SD)* | 7 (7) | 9 (7) | 0.32 |
| Pancreatic fistula, n (%) [†] | 7 (11) | 101 (18) | 0.17 |
| Delayed gastric emptying, n (%) [†] | 3 (5) | 89 (16) | 0.02 |
| Postpancreatectomy hemorrhage, n (%) [†] | 1 (2) | 30 (5) | 0.19 |
| Surgical site infection, n (%) | 5 (8) | 61 (11) | 0.47 |
| ICU admission, n (%) | 10 (16) | 68 (12) | 0.40 |
| Length of hospital stay, d, median (IQR) | 8 (7–12) | 10 (8–14) | 0.03 |
| Readmission, n (%) | 7 (11) | 78 (14) | 0.54 |

*For malignancies only.

[†]International Study Group of Pancreatic Surgery grades B/C.

IQR, interquartile range; LDP, laparoscopic distal pancreatectomy; ODP, open distal pancreatectomy.

ODP in 17 centers. For both groups, male sex and mean age were comparable. In the laparoscopic group, fewer patients had a history of abdominal surgery (30% vs 43%; $p = 0.04$) and mean [SD] tumor size was smaller (20 mm [14 mm] vs 49 mm [9 mm]); $p < 0.001$) (Table 1).

Intraoperative outcomes

Median [IQR] intraoperative blood loss was less during laparoscopy (275 mL [38 to 638 mL] vs 700 mL [350 to 1,400 mL]; $p < 0.001$); mean [SD] operative times were similar (213 minutes [111 minutes] vs 208 minutes [98 minutes] respectively; $p = 0.76$). Conversion to open surgery occurred in 21 LDPs (33%), and this proportion did not change throughout the study period. Reasons for conversion were bleeding ($n = 8$), insufficient overview ($n = 7$), and problems with identifying the tumor ($n = 6$). A lower rate of splenectomy in patients with a nonmalignant lesion was found in the LDP group ($p < 0.001$, Table 2).

Postoperative outcomes

Laparoscopic distal pancreatectomy was associated with fewer major complications (10 patients [16%] vs 166 patients [29%]; $p = 0.02$), less delayed gastric emptying grades B/C (3 patients [5%] vs 89 patients [16%]; $p = 0.02$), and a shorter median [IQR] hospital stay (8 days [7 to 12 days] vs 10 days [8 to 14 days]; $p = 0.03$) compared with ODP (Table 2). Mortality during hospitalization or within 30 days after discharge was similar between groups (3% vs 2%; $p = 0.52$).

Results after propensity score matching

Adequate matching was obtained for all but 1 LDP patient who was subsequently excluded. Seven ODP patients were matched to more than 1 LDP patient. Matched groups were comparable for baseline characteristics (Table 3).

Intraoperative outcomes—after matching

Mean operative time and median intraoperative blood loss were similar for both groups. Laparoscopic distal pancreatectomy was associated with a lower rate of splenectomy among patients with nonmalignant disease (6 [10%] vs 16 [25%]; $p = 0.01$), as shown in Table 4.

Postoperative outcomes—after matching

A major complication occurred in 9 patients (14%) after LDP vs 19 patients (30%) after ODP ($p = 0.06$; Table 4). Outcomes after converted LDP ($n = 21$) were comparable to outcomes after primary ODP ($n = 21$); major complications (1 patient [5%] converted LDP vs 6 patients [29%] primary ODP; $p = 0.13$) and median [IQR] length of hospital stay (8 days [7 to 11 days] vs 10 days [9 to 15 days] respectively; $p = 0.13$).

Table 3. Baseline Matched Cohort

| Characteristic | LDP (n = 63) | ODP (n = 63) |
|--|-----------------|-----------------|
| Male, n (%) | 33 (52) | 33 (52) |
| Age, y, mean (SD) | 56 (13) | 56 (12) |
| BMI, kg/m ² , mean (SD) | 26 (4) | 25 (4) |
| Previous abdominal surgery, n (%) | 19 (30) | 25 (40) |
| Diabetes mellitus, n (%) | 7 (11) | 11 (17) |
| ASA physical status, n (%) | | |
| 1 | 18 (29) | 18 (29) |
| 2 | 39 (62) | 39 (62) |
| 3 | 6 (10) | 6 (10) |
| Indication for surgery, n (%) | | |
| Neoplasm | 41 (65) | 41 (65) |
| Cyst | 15 (24) | 17 (27) |
| Pancreatitis | 4 (6) | 1 (2) |
| Other | 3 (5) | 4 (6) |
| Tumor size on CT/MRI, mm, mean (SD) | 24 (12) | 26 (12) |
| Other organs involved on CT/MRI, n (%) | 2 (3) | 2 (3) |
| Spleen | 1 (2) | 1 (2) |
| Stomach | 1 (2) | 0 (0) |
| Intestine | 0 (0) | 1 (2) |

ASA, American Society of Anesthesiologists; BMI, body mass index; LDP, laparoscopic distal pancreatectomy; ODP, open distal pancreatectomy.

Univariable, multivariable, and sensitivity analyses—after matching

Laparoscopic distal pancreatectomy was a significant predictor of experiencing no major complication in the univariable analysis (OR 0.41 [95% CI 0.17 to 0.99]; $p = 0.048$), but not in the multivariable analysis (OR 0.47 [95% CI 0.18 to 1.20]; $p = 0.12$; Table 5). Excluding all replaced controls and coupled patients from the LDP group did not change the significance of the parameters chosen in the univariable analysis.

Survey among pancreatic surgeons

The response rate was 90% (27 of 30). Advanced laparoscopic gastrointestinal procedures had been performed by 70% of Dutch pancreatic surgeons for longer than 5 years, and 74% performed, on average, 10 or more advanced laparoscopic gastrointestinal procedures each year (see Appendix, online only). Despite this experience, 48% of pancreatic surgeons had no experience with LDP. Training would be welcomed by 85% and subsequently, participation in a randomized controlled trial on LDP vs ODP by 96%.

DISCUSSION

Despite underuse of LDP on a nationwide level and a clear impact of selection bias, LDP appeared to be at least noninferior to ODP. The benefits of LDP (lower rate of

Table 4. Outcomes Matched Cohort

| Outcome | LDP (n = 63) | ODP (n = 63) | p Value |
|---|--------------|---------------|---------|
| Primary | | | |
| Major complication, n (%) | 9 (14) | 19 (30) | 0.06 |
| Abdominal abscess | 4 (6) | 8 (13) | — |
| Feeding tube placement | 1 (2) | 5 (8) | — |
| Respiratory insufficiency | 2 (3) | 2 (3) | — |
| Bleeding | 1 (2) | 2 (3) | — |
| Other | 1 (2) | 4 (6) | — |
| Secondary | | | |
| Operative time, min, mean (SD) | 217 (109) | 192 (72) | 0.39 |
| Intraoperative blood loss, mL, median (IQR) | 275 (38–638) | 650 (250–975) | 0.06 |
| Splenectomy, n (%) | 13 (21) | 34 (54) | <0.001 |
| Nonmalignancy | 6 (10) | 16 (25) | 0.01 |
| Conversion, n (%) | 21 (33) | — | — |
| Histopathologic diagnosis, n (%) | — | — | 0.45 |
| Malignancy, n (%) | 12 (19) | 24 (38) | 0.02 |
| R0 resection, n (% malignancies)* | 7 (58) | 14 (58) | 0.63 |
| Lymph nodes retrieved, mean (SD)* | 7 (7) | 10 (8) | 0.29 |
| Pancreatic fistula, n (%) [†] | 7 (11) | 11 (17) | 0.45 |
| Delayed gastric emptying, n (%) [†] | 3 (5) | 8 (13) | 0.23 |
| Postpancreatectomy hemorrhage, n (%) [†] | 1 (2) | 6 (10) | 0.13 |
| Surgical site infection, n (%) | 5 (8) | 10 (16) | 0.30 |
| ICU admission, n (%) | 9 (14) | 17 (27) | 0.12 |
| Length of hospital stay, d, median (IQR) | 8 (7–12) | 10 (8–13) | 0.48 |
| Readmission, n (%) | 7 (11) | 8 (13) | >0.99 |

*For malignancies only.

[†]ISGPS, International Study Group of Pancreatic Surgery grades B/C.

LDP, laparoscopic distal pancreatectomy; ODP, open distal pancreatectomy.

major complications, less blood loss, and shorter hospital stay), as seen in the full cohort analysis, became nonsignificant after propensity score matching, highlighting the

importance of correcting for selection bias. The underuse of LDP, the high conversion rate and the large proportion (48%) of pancreatic surgeons without experience in LDP

Table 5. Matched Univariable and Multivariable Analyses for Predictors of Experiencing a Major Complication after Distal Pancreatectomy

| Characteristic | Univariable analysis | | Multivariable analysis | |
|------------------------------|----------------------|---------|------------------------|---------|
| | OR (95% CI) | p Value | OR (95% CI) | p Value |
| Laparoscopic approach | 0.41 (0.17–0.99) | 0.048 | 0.47 (0.18–1.20) | 0.12 |
| Histopathological diagnosis | — | — | — | — |
| NET | RC | RC | — | — |
| Pancreatic adenocarcinoma | 10.46 (0.85–128.60) | 0.07 | 5.70 (0.65–49.91) | 0.12 |
| Serous or mucinous neoplasm | 2.05 (0.09–46.22) | 0.65 | — | — |
| IPMN | 3.24 (0.10–106.70) | 0.51 | — | — |
| BMI (OR/kg/m ²) | 1.05 (0.89–1.23) | 0.56 | — | — |
| Diabetes mellitus | 1.05 (0.89–1.23) | 0.56 | — | — |
| Tumor size on CT/MRI (OR/mm) | 1.10 (0.88–1.37) | 0.42 | — | — |
| Operative time (OR/min) | 1.00 (0.99–1.01) | 0.90 | — | — |
| Blood loss (OR/mL) | 1.00 (1.00–1.00) | 0.13 | — | — |
| Splenectomy | 1.25 (0.34–4.66) | 0.74 | — | — |
| Combined procedure | 3.00 (0.61–14.86) | 0.18 | — | — |

BMI, body mass index; IPMN, intraductal papillary mucinous neoplasm; NET, neuroendocrine tumor; OR, odds ratio; RC, reference category.

emphasize the need for specific LDP training, which would be welcomed by the vast majority (85%) of Dutch pancreatic surgeons.

The results of this nationwide analysis largely support findings from earlier systematic reviews from mainly expert centers.^{11,14,16} Interestingly, in our study, after matching, no statistically significant differences were seen in complication rates, such as major complications, postoperative pancreatic fistula, delayed gastric emptying, postpancreatectomy hemorrhage, or surgical site infection. This might be explained by a type II error: a larger sample sizes could have shown an (potential) advantage of LDP. However, a recent systematic review that included only case-matched studies comparing LDP vs ODP (75% performed in a single expert center), similarly, did not find significant advantages of LDP concerning complication rates.¹⁵ Splenectomy rates were reported only in 1 case-matched study and were lower in the LDP group (70% after LDP vs 88% after ODP; $p < 0.001$).³⁰ It is unclear as to exactly why laparoscopy could prevent splenectomy. Nevertheless, preventing splenectomy whenever possible is important because splenectomy necessitates vaccinations and a supply of appropriate antibiotics for emergency use.³¹ Furthermore, most case-matched studies and several multivariable analyses^{30,32} demonstrated a significant reduced hospital stay after LDP. These findings require confirmation in a pragmatic randomized controlled multicenter trial performed by surgeons trained in LDP.

In this series, only 10% of distal pancreatectomies were started laparoscopically, but this still compares favorably to the 4% in a recent US nationwide series (1998 to 2009). Nonetheless, in the US, the proportion of distal pancreatectomies performed via a minimally invasive approach tripled over the study period, from 2% to 7%,³³ while the proportion in the Netherlands did not increase over the past 8 years. A clear explanation for this stagnation in the Netherlands is lacking, but it could be related to an absence of specific training in LDP combined with worries for a learning curve effect. In series from expert centers, up to 73% of distal pancreatectomies were performed laparoscopically.³⁴ This implies that the use of LDP varies widely between expert and nonexpert centers.

Failure to identify the tumor as an indication for conversion in 10% of all LDPs highlights the need for intraoperative ultrasound, which was not performed routinely. These factors could explain the high conversion rate (33%). Conversion rates as low as 0% have been reported⁸ and demonstrate which results can be obtained in high-volume expert centers.³⁵ The positive impact of centralization of pancreatic surgery is widely recognized,^{9,10,36} but the influence of centralization on outcomes of LDP is still under debate, because conversion rates of 25% to 30% are

also reported by some very high-volume expert centers.^{37,38} High-volume pancreatic surgery is apparently no guarantee for low conversion rates and good outcomes during attempted LDP. This is one of the reasons why specific training in LDP appears useful.

This study is the first to describe the use and outcomes of LDP on a nationwide level. Limitations of this study are its retrospective design with risk of selection bias and information bias. However, we attempted to reduce the impact of these biases by propensity score matching based on 5 relevant baseline characteristics and by adopting Clavien-Dindo, ISGPS, and CDC definitions.

CONCLUSIONS

Altogether, despite of an underuse, LDP seemed to be at least noninferior to ODP on a nationwide level. Because of the limited number of LDP (10%) and high conversion rate (33%) in “real-world” clinical practice, there is clearly room for improvement, which could be achieved by structured training. Such a training program has recently been implemented on a nationwide level by the Dutch Pancreatic Cancer Group. Pragmatic randomized controlled multicenter trials should determine whether outcomes after LDP are truly superior.

Author Contributions

Study conception and design: De Rooij, Busch, Besselink
Acquisition of data: De Rooij, Jilesen, Boerma, Bonsing, Bosscha, Van Dam, Van Eijck, Gerhards, Van Goor, Van der Harst, De Hingh, Kazemier, Klaase, Molenaar, Patijn, Van Santvoort, Scheepers, Van der Schelling, Sieders, Busch, Besselink

Analysis and interpretation of data: De Rooij, Jilesen, Van Dieren, Dijkgraaf, Van Santvoort, Vogel, Busch, Besselink

Drafting of manuscript: De Rooij, Jilesen, Boerma, Bonsing, Bosscha, Van Dam, Van Eijck, Gerhards, Van Goor, Van der Harst, De Hingh, Kazemier, Klaase, Molenaar, Nieveen van Dijkum, Patijn, Scheepers, Van der Schelling, Sieders, Vogel, Busch, Besselink

Critical revision: De Rooij, Jilesen, Boerma, Bonsing, Bosscha, Van Dam, Van Dieren, Dijkgraaf, Van Eijck, Gerhards, Van Goor, Van der Harst, De Hingh, Kazemier, Klaase, Molenaar, Nieveen van Dijkum, Patijn, Van Santvoort, Scheepers, Van der Schelling, Sieders, Vogel, Busch, Besselink

REFERENCES

1. Cuschieri A, Jakimowicz JJ, van Spruijvel J. Laparoscopic distal 70% pancreatectomy and splenectomy for chronic pancreatitis. *Ann Surg* 1996;223:280–285.

2. Winslow ER, Brunt LM. Perioperative outcomes of laparoscopic versus open splenectomy: A meta-analysis with an emphasis on complications. *Surgery* 2003;134:647–653.
3. Sain AH. Laparoscopic cholecystectomy is the current “gold standard” for the treatment of gallstone disease. *Ann Surg* 1996;224:689–690.
4. Smith CD, Weber CJ, Amerson JR. Laparoscopic adrenalectomy: new gold standard. *World J Surg* 1999;23:389–396.
5. Braga M, Ridolfi C, Balzano G, et al. Learning curve for laparoscopic distal pancreatectomy in a high-volume hospital. *Updates Surg* 2012;64:179–183.
6. Ricci C, Casadei R, Buscemi S, et al. Laparoscopic distal pancreatectomy: what factors are related to the learning curve? *Surg Today* 2014 Mar 9 [Epub ahead of print].
7. Cho CS, Kooby DA, Schmidt CM, et al. Laparoscopic versus open left pancreatectomy: can preoperative factors indicate the safer technique? *Ann Surg* 2011;253:975–980.
8. Abu Hilal M, Hamdan M, Di Fabio F, et al. Laparoscopic versus open distal pancreatectomy: a clinical and cost-effectiveness study. *Surg Endosc* 2012;26:1670–1674.
9. 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.
10. Topal B, Van de Sande S, Fieuws S, Penninckx F. Effect of centralization of pancreaticoduodenectomy on nationwide hospital mortality and length of stay. *Br J Surg* 2007;94:1377–1381.
11. Drymoussis P, Raptis DA, Spalding D, et al. Laparoscopic versus open pancreas resection for pancreatic neuroendocrine tumours: a systematic review and meta-analysis. *HPB (Oxford)* 2014;16:397–406.
12. Jin T, Altaf K, Xiong JJ, et al. A systematic review and meta-analysis of studies comparing laparoscopic and open distal pancreatectomy. *HPB (Oxford)* 2012;14:711–724.
13. Jusoh AC, Ammori BJ. Laparoscopic versus open distal pancreatectomy: a systematic review of comparative studies. *Surg Endosc* 2012;26:904–913.
14. Venkat R, Edil BH, Schulick RD, et al. Laparoscopic distal pancreatectomy is associated with significantly less overall morbidity compared to the open technique: a systematic review and meta-analysis. *Ann Surg* 2012;255:1048–1059.
15. Pericleous S, Middleton N, McKay SC, et al. Systematic review and meta-analysis of case-matched studies comparing open and laparoscopic distal pancreatectomy: is it a safe procedure? *Pancreas* 2012;41:993–1000.
16. Sui C-J, Li B, Yang J-M, et al. Laparoscopic versus open distal pancreatectomy: a meta-analysis. *Asian J Surg* 2012;35:1–8.
17. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika* 1981;70:41–55.
18. Parsons LS. Performing a 1: N case-control match on propensity score. Proceedings of the 26th SAS Users Group International Conference, Montreal, Canada 2004;1–11.
19. Dutch Pancreatic Cancer Group participating medical centers. Amsterdam, the Netherlands. Available at: <http://www.dpcg.nl/werkgroep/deelnemers.html>. Accessed June 1, 2014.
20. Kimura W, Inoue T, Futakawa N, et al. Spleen-preserving distal pancreatectomy with conservation of the splenic artery and vein. *Surgery* 1996;120:885–890.
21. Warshaw AL. Conservation of the spleen with distal pancreatectomy. *Arch Surg* 1988;123:550–553.
22. Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg* 2009;250:187–196.
23. Bassi C, Dervenis C, Butturini G, et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. *Surgery* 2005;138:8–13.
24. 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.
25. 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.
26. Mangram AJ, Horan TC, Pearson ML, et al. Guideline for prevention of surgical site infection, 1999. *Am J Infect Control* 1999;27:97–134.
27. The Royal College of Pathologists. Standards and Minimum Datasets for Reporting Cancers Minimum dataset for the histopathological reporting of pancreatic, ampulla of Vater and bile duct carcinoma. London R Coll Pathol 2002;(261035).
28. Vandembroucke JP, von Elm E, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): Explanation studies in epidemiology (STROBE): explanation and elaboration. *Int J Surg* 2014; July 18 [Epub ahead of print].
29. Austin PC. Comparing paired vs non-paired statistical methods of analyses when making inferences about absolute risk reductions in propensity-score matched samples. *Stat Med* 2011;30:1292–1301.
30. Kooby DA, Gillespie T, Bentrem D, et al. Left-sided pancreatectomy: a multicenter comparison of laparoscopic and open approaches. *Ann Surg* 2008;248:438–446.
31. Davies JM, Lewis MPN, Wimperis J, et al. Review of guidelines for the prevention and treatment of infection in patients with an absent or dysfunctional spleen: prepared on behalf of the British Committee for Standards in Haematology by a working party of the Haemato-Oncology task force. *Br J Haematol* 2011;155:308–317.
32. Vijan SS, Ahmed KA, Harmsen WS, et al. Laparoscopic vs open distal pancreatectomy: a single-institution comparative study. *Arch Surg* 2010;145:616–621.
33. Tran Cao HS, Lopez N, Chang DC, et al. Improved perioperative outcomes with minimally invasive distal pancreatectomy: results from a population-based analysis. *JAMA Surg* 2014;149:237–243.
34. Kim SC, Park KT, Hwang JW, et al. Comparative analysis of clinical outcomes for laparoscopic distal pancreatic resection and open distal pancreatic resection at a single institution. *Surg Endosc* 2008;22:2261–2268.
35. Abu Hilal M, Jain G, Kasasbeh F, et al. Laparoscopic distal pancreatectomy: critical analysis of preliminary experience from a tertiary referral centre. *Surg Endosc* 2009;23:2743–2747.
36. Balzano G, Zerbi A, Capretti G, et al. Effect of hospital volume on outcome of pancreaticoduodenectomy in Italy. *Br J Surg* 2008;95:357–362.
37. Jayaraman S, Gonen M, Brennan MF, et al. Laparoscopic distal pancreatectomy: evolution of a technique at a single institution. *J Am Coll Surg* 2010;211:503–509.
38. DiNorcia J, Schrope BA, Lee MK, et al. Laparoscopic distal pancreatectomy offers shorter hospital stays with fewer complications. *J Gastrointest Surg* 2010;14:1804–1812.

Appendix. Survey among Dutch Pancreatic Surgeons

| Question | Answers (n = 27) |
|---|------------------|
| 1. Working in an academic medical center, % | 48 |
| 2. >5 years' experience with advanced laparoscopic GI surgery, % | 70 |
| 3. >10 advanced laparoscopic GI surgical procedures per year, % | 74 |
| 4. No experience with laparoscopic pancreatic surgery, % | 48 |
| 5. Indication for a laparoscopic approach* | |
| Benign tumor, % | 100 |
| Premalignant tumor, % | 100 |
| Malignant tumor, % | 85 |
| 6. Reject a laparoscopic approach if* | |
| Other organs involved, % | 81 |
| Tumor >6 cm, % | 48 |
| Malignant tumor, % | 15 |
| Morbid adiposity, % | 19 |
| Never, % | 11 |
| 7. Willing to participate in LDP training, % | 85 |
| 8. Expected eventual percentage LDP of all distal pancreatectomies, % | 43 |
| 9. Barriers of starting with LDPs* | |
| None, % | 63 |
| Lack of specific training in LDP, % | 37 |
| Lack of time in operative schedules, % | 33 |
| 10. LDP with splenectomy is a technical problem, % | 26 |
| 11. Spleen preserving DP is a technical problem, % | 41 |
| 12. Willing to participate in a RCT on LDP vs ODP, % | 96 |

*Multiple answers possible.

DP, distal pancreatectomy; GI, gastrointestinal; LDP, laparoscopic distal pancreatectomy; ODP, open distal pancreatectomy; RCT, randomized controlled trial.