Surgical complications in a multicenter randomized trial comparing preoperative chemoradiotherapy and immediate surgery in patients with resectable and borderline resectable pancreatic cancer (PREOPANC trial)

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Surgical Complications in a Multicenter Randomized Trial Comparing Preoperative Chemoradiotherapy and Immediate Surgery in Patients With Resectable and Borderline Resectable Pancreatic Cancer (PREOPANC Trial)

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Objectives: To investigate the effect of preoperative chemoradiotherapy on surgical complications in patients after pancreatic resection for (borderline-) resectable pancreatic cancer.

Summary of Background Data: Preoperative chemoradiotherapy is increasingly used in patients with (borderline-)resectable pancreatic cancer. concerns have been raised about the potential harmful effect of any preoperative therapy on the surgical complication rate after pancreatic resection.

Methods: An observational analysis was performed within the multicenter randomized controlled PREOPANC trial (April 2013–July 2017). The trial randomly assigned (1:1) patients to preoperative chemoradiotherapy followed by surgery and the remaining adjuvant chemotherapy or to immediate surgery, followed by adjuvant chemotherapy. The main analysis consisted of a per-protocol approach. The endpoints of the present analyses were the rate of postoperative complications.

Results: This study included 246 patients from 16 centers, of whom 66 patients underwent resection after preoperative therapy and 98 patients after immediate surgery. No differences were found regarding major complications (37.9% vs 30.6%, P=0.400), postpancreatectomy hemorrhage (9.1% vs 5.1%, P=0.352), delayed gastric emptying (21.2% vs 22.4%, P=0.930), bile leakage (4.5% vs 3.1%, P=0.686), intra-abdominal infections (12.1% vs 10.2%, P=0.800), and mortality (3.0% vs 4.1%, P=1.000). There was a significant lower incidence of postoperative pancreatic fistula in patients who received preoperative chemoradiotherapy (0% vs 9.2%, P=0.011).

Conclusions: Preoperative chemoradiotherapy did not increase the incidence of surgical complications or mortality and reduced the rate of postoperative

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pancreatic fistula after resection in patients with (borderline-)resectable pancreatic cancer.

Keywords: neoadjuvant therapy, pancreas, pancreatic cancer, pancreatic neoplasm, postoperative complications, postoperative morbidity, postoperative mortality, postoperative pancreatic fistula, preoperative chemoradiotherapy, preoperative therapy, surgical complications

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The 5-year survival rate of patients with pancreatic cancer is approximately 9%.[1] Pancreatic resection combined with systemic therapy offer the best overall survival but remains burdened with high postoperative morbidity.[2] A recent systematic review concluded that preoperative chemo(radio)therapy may improve overall survival.[3] Little is known about the effect of preoperative therapy on surgical complications. Retrospective studies have demonstrated a similar or decreased risk of surgical complications after neoadjuvant therapy as compared to immediate surgery.[4–13] Interestingly, especially a lower rate of postoperative pancreatic fistula (POPF) has been reported,[7–13] which might be attributable to pancreatic fibrosis and loss of acinar function after chemoradiotherapy.[14,15] However, studies reporting on the effect of preoperative therapy on postoperative outcomes are limited by their nonrandomized, retrospective study design.

The recently published Dutch Pancreatic Cancer Group (DPCG) PREOPANC trial randomized 246 eligible patients with resectable or borderline resectable pancreatic cancer between preoperative chemoradiotherapy and immediate surgery.[16] Median overall survival was 16.0 months after preoperative chemoradiotherapy versus 14.3 months after immediate surgery (HR 0.78, P=0.096). The disease-free survival after preoperative chemoradiotherapy was 8.1 months versus 7.7 months after immediate surgery (HR 0.73, P=0.032). In addition, the microscopically complete (R0) rate was 72% with preoperative chemoradiotherapy versus 40% with immediate surgery (P<0.001). The subset of patients who had a resection and started adjuvant therapy the median overall survival was 35.2 months in the preoperative chemoradiotherapy arm versus 19.8 months after immediate surgery (HR 0.58; P=0.029).

In the current study, we aimed to investigate the effect of preoperative chemoradiotherapy on pancreatic surgery-specific postoperative complications, major morbidity, and mortality in patients with resectable and borderline-resectable pancreatic cancer in the multicenter, randomized controlled PREOPANC trial.

METHODS

Study Design

This study is an observational analysis within the PREOPANC trial. This randomized controlled trial was conducted in 16 pancreatic cancer centers in the Netherlands. The protocol was centrally approved by the Erasmus MC Medical Ethics Committee (MEC-2012-249; December 11, 2012).[17]

Patients

The study population included patients enrolled in the PREOPANC trial between April 23, 2013, and July 25, 2017.[16] Patients were eligible for inclusion in the PREOPANC trial if they had pathologically confirmed resectable or borderline resectable pancreatic adenocarcinoma, without distant metastases on imaging. Resectability was determined according to DPCG definitions. Resectable disease was defined as no contact with the superior mesenteric artery, celiac axis or common hepatic artery and < 90 degrees contact with the superior mesenteric vein or portal vein; borderline resectable disease was defined <90 degrees contact with the superior mesenteric artery, celiac axis or common hepatic artery and <270 degrees contact with the superior mesenteric vein or portal vein without occlusion. Patients who underwent resection with curative intention were included in this analysis.

Procedures

Briefly, patients were randomized between staging laparoscopy followed by preoperative chemotherapy (3 cycles gemcitabine) combined with radiotherapy (15 fractions of 2.4 Gy in 3 weeks during the second cycle), followed by resection of the tumor and adjuvant chemotherapy (4 cycles gemcitabine) or patients underwent immediate explorative laparotomy, with intention to resection of the tumor and adjuvant chemotherapy (6 cycles gemcitabine). Written informed consent was obtained from all patients before entering the trial.

Data Collection

All data were collected in a prospectively maintained database and included age, sex, weight at time of surgery, length, comorbidities, diameter of the pancreatic duct, vascular involvement, pancreatic texture, information on preoperative and adjuvant therapy, details on surgical procedure, pathology, postoperative morbidity and mortality, length of hospital stay and readmission rate. The diameter of the pancreatic duct was measured on the preoperative computed tomography-scan at the line of pancreatic transection.

Surgical complications were retrospectively collected using the most recent International Study Group of Pancreatic Surgery definitions. The endpoints were the rate of major complications, mortality, POPF,[18] delayed gastric emptying (DGE),[19] postpan-createctomy hemorrhage (PPH),[20] bile leakage,[21] and intra-abdom-inal infections after pancreatic resection. Major complications were defined as grade ≥3 conform Clavien-Dindo Classification.[22] Intra-abdominal infections were defined as drained fluid collections with a positive culture or purulent output. Other endpoints included intraoperative blood loss, length of hospital stay, and the readmission rate.

Statistical Analysis

The main analysis consisted of a per-protocol comparison of the patients in both treatment groups. Continuous variables were expressed as a mean with standard deviation or as a median with interquartile range, depending on their distribution. For univariable analysis, continuous variables were compared using a T-test (parametric) or Mann-Whitney U-test (nonparametric). Categorical variables were compared using a Fisher exact test. Risk differences between the preoperative chemoradiotherapy group and immediate surgery group were calculated. A sensitivity analysis was performed using an intention-to-treat approach. P-values < 0.05 were considered statistically significant. R statistical software (version 3.4.3.; www.r-project.org) was used for all statistical analyses.

RESULTS

Study Population

Between April 23, 2013, and July 25, 2017, 246 patients were enrolled in the PREOPANC trial. Two patients withdrew informed consent. In the preoperative chemoradiotherapy group (n=119), no resection of the tumor was performed in 47 patients (41 patients had locally advanced or metastatic pancreatic cancer, 5 patients died before resection and 1 patient had a severe complication). In the immediate surgery group (n=127), no resection of the tumor was performed in 35 patients (33 patients had locally advanced or metastatic pancreatic cancer, 1 patient refused surgery and 1 patient died before resection). Six patients assigned to preoperative

TABLE 1. Baseline Characteristics of Patients Whom Underwent Resection for Pancreatic Cancer in the DPCG Multicenter Randomized PREOPANC Trial

	Preoperative Chemoradiotherapy Group (n=66)	Immediate Surgery Group (n=98)	*P*-value
Age in years, median (interquartile range)	66 (58–72)	66 (58–72)	0.910
Male sex, no. (%)	36 (54.5)	54 (54.6)	1.000
Body mass index, median (interquartile range)	25.1 (21.8–26.7)	24.4 (23.0–27.8)	0.726
ASA status 3–4, no. (%)	14 (22.2)	11 (11.8)	0.130
Diabetes mellitus, no. (%)	19 (28.8)	34 (34.7)	0.504
Smoking, no. (%)	14 (23.3)	18 (21.2)	1.000
Preoperative biliary drainage, no. (%)	38 (59.4)	56 (62.2)	0.850
Diameter pancreatic duct in mm, median (interquartile range)	4 (2–7)	4 (2.5–7)	0.401
Hard/fibrotic pancreatic texture, no. (%)	35 (77.8)	44 (69.8)	0.486
Borderline resectable pancreatic cancer, no. (%)	26 (39.4)	34 (34.7)	0.635
Type of resection			0.147
Classical Whipple	33 (50.0)	46 (46.9)	—
Pylorus preservering pancreatoduodenectomy	20 (30.3)	40 (40.8)	—
Distal pancreatectomy	12 (18.2)	8 (8.2)	—
Total pancreatectomy	1 (1.5)	4 (4.1)	—
Minimally invasive resection, no. (%)	6 (9.4)	7 (7.5)	0.880
Time to resection after diagnosis in days, median (IQR)	131 (120–146)	31 (22–39.5)	<0.001
Vascular resection, no. (%)	25 (39.1)	32 (35.2)	0.744

DPCG indicates Dutch Pancreatic Cancer Group; IQR, interquartile range.

chemoradiotherapy crossed over to immediate resection of the tumor (3 patients crossed over due to a medical decision and 3 patients were, after randomization, diagnosed with a different histological diagnosis than pancreatic adenocarci-noma). Finally, 66 patients underwent resection after preoperative chemoradiotherapy compared to 98 patients that underwent immediate resection (per-protocol).

In univariate analysis of baseline characteristics, time to resection after diagnosis was the only significant difference between the preoperative chemoradiotherapy group and the immediate surgery group (Table 1).

Surgical Outcomes

Table 2 displays the surgical outcomes of the 2 treatment groups. In the preoperative chemoradiotherapy group, 25 patients (37.9%) experienced a major complication compared to 30 patients (30.6%) in the immediate surgery group (P=0.400). Among patients with a major complication, the preoperative chemoradiotherapy group demonstrated a shorter length of hospital stay compared to the immediate surgery group (13.5 days vs 20.5 days, P<0.001). No differences were found regarding length of hospital stay, intraoperative blood loss, postoperative blood transfusions, antibiotic treatment, or the readmission rate.

A detailed overview of the invasive postoperative interventions is shown in Table 3. The most frequent intervention was radiological drainage of fluid collections (19.7% in the preoperative chemoradiotherapy group vs 14.3% in the immediate surgery group, P=0.395). There were no patients with POPF in the preoperative chemoradiotherapy group and 8 patients with POPF grade B and 1

TABLE 2. Surgical Outcomes of Patients Whom Underwent Resection for Pancreatic Cancer in the DPCG Multicenter Randomized PREOPANC Trial

	Preoperative Chemoradiotherapy Group (N=66)	Immediate Surgery Group (N=98)	Risk Difference (95% CI)	*P*-value
Major complication, no. (%)*	25 (37.9)	30 (30.6)	7.2 (−7.6 to 22.1)	0.400
Mortality, no. (%)	2 (3.0)	4 (4.1)	−1.1 (−6.8 to 4.7)	1.000
Postoperative pancreatic fistula grade B/C, no. (%)†	0 (0)	9 (9.2)	−9.2 (−15.3 to −3.0)	0.011
Postpancreatectomy hemorrhage B/C, no. (%)‡	6 (9.1)	5 (5.1)	4.0 (−4.2 to 12.2)	0.352
Delayed gastric emptying grade B/C, no. (%)§	14 (21.2)	22 (22.4)	−1.2 (−14.1 to 11.6)	0.930
Bile leakage grade B/C, no. (%)¶	3 (4.5)	3 (3.1)	1.5 (−4.6 to 7.6)	0.686
Intra-abdominal infection, no. (%)	8 (12.1)	10 (10.2)	1.9 (−8.0 to 11.8)	0.800
Intra-operative blood loss in ml, median (IQR)	900 (400–1500)	900 (500–1300)	NA	0.695
Length of stay in days, median (IQR)	10 (8–15)	11 (8–15)	NA	0.476
Length of ICU stay in days, median (IQR)	5 (2–5)	3.5 (2–8)	NA	0.885
Postoperative blood transfusion, no. (%)	13 (21.3)	14 (16.5)	4.8 (−8.1 to 17.8)	0.519
Readmission, no. (%)	16 (24.2)	16 (16.3)	7.9 (−5.7 to 21.0)	0.313
No adjuvant therapy due to surgical complications, no. (%)	8 (12.7)	17 (20.7)	−8.0 (−4.0 to 20.6)	0.204

*Major complications defined as Clavien-Dindo grade ≥3a.
†Grade B/C postoperative pancreatic fistula according to the International Study Group for Pancreatic Surgery criteria.
‡Grade B/C postpancreatectomy hemorrhage according to the International Study Group for Pancreatic Surgery criteria.
§Grade B/C delayed gastric emptying according to the International Study Group for Pancreatic Surgery criteria.
¶Grade B/C/bile leakage according to the International Study Group for Liver Surgery definition.
CI indicates confidence interval; DPCG, Dutch Pancreatic Cancer Group; ICU, intensive care unit.

TABLE 3. Postoperative Interventions of Patients Whom Underwent Resection for Pancreatic Cancer in the DPCG Multicenter Randomized PREOPANC Trial

	Preoperative Chemoradiotherapy Group (N=66)	Immediate Surgery Group (N=98)	*P*-value
Antibiotic treatment, no. (%)	24 (36.3)	30 (30.6)	0.499
Percutaneous drainage of fluid collection, no. (%)	13 (19.7)	14 (14.3)	0.395
Endovascular stenting/coiling, no. (%)	0 (0)	5 (5.1)	0.083
Percutaneous transhepatic cholangiography drainage, no. (%)	2 (3.0)	3 (3.1)	1.000
Placement feeding tube, no. (%)	9 (13.6)	10 (10.2)	0.620
Gastroscopic treatment intra-luminal hemorrhage, no. (%)	2 (3.0)	0 (0)	0.166
Abdominal wall dehiscence correction, no. (%)	2 (3.0)	2 (2.0)	1.000
Relaparotomy, no. (%)	4 (6.1)	6 (6.1)	1.000
ICU admittance, no. (%)	10 (15.2)	12 (12.2)	0.644

DPCG indicates Dutch Pancreatic Cancer Group; ICU, intensive care unit.

with POPF grade C in the immediate surgery group (0% vs 9.2%, *P*=0.011). Intra-abdominal infections occurred in 8 patients (12.1%) in the preoperative therapy group, compared to 10 patients (10.2%) in the immediate surgery group *(P*=0.800).

In the preoperative chemoradiotherapy group 6 patients (9.1%) experienced PHH grade B/C, compared to 5 patients (5.1%) in the immediate surgery group (*P*=0.352); details on the type of bleeding are reported in Table 4. In the preoperative chemoradiotherapy group, 2 patients had an early PPH, 2 patients had a gastric bleeding and 2 patients had an bleeding after postoperative drain placement. In the immediate surgery group 4 patients had a bleeding from a peri-pancreatic vessel, compared with none in the preoperative chemoradiotherapy group (*P*=0.155).

DGE grade B/C occurred in 14 patients (21.2%) in the preoperative chemoradiotherapy group, 5 qualified as grade B and 9 as grade C. In 8 of these patients a nasojejunal feeding tube was placed, median day of placement was 7.5 days after surgery (range 6–44 days). In the immediate surgery group, DGE grade B/C was found in 22 patients (22.4%), 13 qualified as grade B and 9 as grade C. Nasojejunal feeding tubes were placed 9 of these patients, median day of placement was 7 days after surgery (range 5–18 days).

Two patients (3.0%) died within 90 days after resection in the preoperative chemoradiotherapy group; 1 patient of brain infarction caused by air embolisms and 1 patient of myocardial infarction. In the immediate surgery group 4 patients (4.1%) died within 90 days; 1 of respiratory insufficiency, 2 of sepsis due to intestinal necrosis and 1 due to late PPH and subsequent multi organ failure.

In the preoperative chemoradiotherapy group, 63 patients were eligible for adjuvant treatment after resection, 8 of these patients (12.7%) did not receive adjuvant treatment due to surgical complications. Of the 82 patients eligible for adjuvant treatment after immediate surgery, 17 patients (20.7%) did not receive it due to surgical complications.

The intention-to-treat analysis demonstrated similar complication rates compared to the per-protocol analysis (Supplementary Table 1, http://links.lww.com/SLA/C438).

DISCUSSION

This analysis of the surgical postoperative morbidity in the multicenter randomized controlled PREOPANC trial demonstrated that preoperative chemoradiotherapy did not increase the risk of complications in patients with (borderline-)resectable pancreatic cancer. Conversely, preoperative chemoradiotherapy was associated with a decreased rate of POPF (0% vs 9.2%) compared to immediate surgery. In addition, major complications were associated with a

TABLE 4. Postpancreatectomy Hemorrhage in 11 Patients Whom Underwent Resection for Pancreatic Cancer in the DPCG Multicenter Randomized PREOPANC Trial

Grade PPH*	Type PPH	Intervention	POD	Description	POPF or Biochemical Leak†
Preoperative radiotherapy group					
Grade C	Extra-luminal	Relaparotomy	1	Diffuse bleeding at the site of resection	No
Grade C	Extra-luminal	Relaparotomy	2	Large intra-abdominal hematoma without an active leak upon surgical exploration	Biochemical leak
Grade C	Intra-luminal	Endoscopic adrenaline injection	13	Hemorrhage caused by a gastric ulcer at the gastro-jejunal anastomosis	Biochemical leak
Grade C	Intra-luminal	Endoscopic clipping	14	Hemorrhage caused by a gastric ulcer at the gastro-jejunal anastomosis	No
Grade B	Extra-luminal	ICU admittance	14	Hemorrhage after intra-abdominal drain placement	No
Grade B	Extra-luminal	Blood transfusions	45	Hemorrhage after PTC drain placement	No
Immediate surgery group					
Grade C	Extra-luminal	Endovascular coiling	5	Hemorrhage hepatic artery	POPF
Grade B	Extra-luminal	Endovascular stent	7	Hemorrhage hepatic artery	No
Grade B	Extra-luminal	Endovascular coiling	15	Hemorrhage vessel at gastro-jejunal anastomosis	No
Grade B	Extra-luminal	Endovascular coiling	25	Pseudo-aneurysm of the splenic artery	No
Grade B	Extra-luminal	Blood transfusions	7 and 56	Decreased hemoglobin levels	POPF

*According to the International Study Group of Pancreatic Surgery definition.
†According to the International Study Group for Pancreatic Fistula definition.
DPCG indicates Dutch Pancreatic Cancer Group; ICU, intensive care unit; POD, postoperative day; POPF, postoperative pancreatic fistula; PPH, postpancreatectomy hemorrhage.

shorter length of hospital stay in the preoperative chemoradiotherapy group compared to the immediate surgery group. These results imply that preoperative chemoradiotherapy is safe with respect to surgical complications after resection of pancreatic cancer.

Previous nonrandomized studies also reported a decreased rate of POPF after preoperative therapy in patients with pancreatic cancer.[7–13] In our trial, no patients experienced POPF after preoperative chemoradiotherapy. Similarly, Ferrone et al found a POPF rate of 0% in 40 patients with locally advanced/borderline pancreatic cancer after preoperative FOLFIRINOX treatment (0% vs 22%, $P<0.001$).[9] Also, Hank et al recently demonstrated a lower rate of POPF in 346 patients receiving preoperative chemoradiotherapy vs 407 patients undergoing immediate resection (3.8% vs 13.8%; $P<0.001$).[13] Marchegiani et al found a POPF rate of 9.1% in 99 patients treated with preoperative FOLFIRINOX or gemcitabine-based chemotherapy, compared to 15.6% in 206 patients after immediate surgery ($P=0.05$).[7] Several retrospective studies based on the National Surgical Quality Improvement Program data in the USA found POPF rates between 4.9% and 10.7% in patients who received preoperative chemo(radio)therapy, however, these studies lack details on the specific preoperative therapy administered.[8,10,12] Besides, all these studies are potentially limited by confounding by indication as patients generally received preoperative therapy in case of locally-advanced pancreatic cancer, suggesting more complex surgery, hence a higher chance of complications. Two previous randomized phase 2/3 trials found no difference in POPF rate after preoperative therapy compared to immediate surgery. Jang et al found 0 POPF in 17 patients treated with gemcitabine-based chemo-radiotherapy compared to 1 POPF (5.6%) in 18 patients after immediate resection ($P=1.000$).[23] Furthermore, Reni et al reported no decreased rate of POPF in 27 patients after preoperative PEGX chemotherapy compared to 2 groups after immediate resection (11% vs 11% and 14%).[24] However, both studies were limited by their sample size and the trial by Reni et al only concerned preoperative chemotherapy.

The decreased POPF rate after preoperative chemoradiotherapy might be attributable to increased levels of fibrosis and loss of functional pancreatic tissue.[8,14,15] This histological benefit might be a direct result of the chemoradiotherapy. In addition, the delayed time to resection in case of preoperative therapy may cause morphological and functional changes due to prolonged pancreaticobiliary obstruction. Despite this, we did not find a difference in the proportion of hard/fibrotic pancreatic texture (77.8% vs 69.8%, $P=0.486$). However, this was a subjective measure and it included a significant proportion of missing values (34.1%). For a more objective analysis of pancreatic function and consistency, a frozen section analysis should be performed to assess the amount of functional acini.[25] Besides, other more objective characteristics generally used to determine the POPF risk profile (blood loss, pathology, and pancreatic duct diameter) did not differ between treatment groups.[26,27]

We found no decrease in radiologically drained fluid collections and intra-abdominal infections in the preoperative chemoradiotherapy group, despite the reduced rate of POPF. Noteworthy, in the preoperative chemoradiotherapy group none of these collections constituted a POPF (ie, none contained amylase-rich fluid), but mainly contained infected or purulent fluid. Whether the chemo (radio)therapy causes intestinal barrier dysfunction or still has an immunosuppressive effect at time of surgery is unknown.

PPH is also a major cause of severe morbidity after pancreatic resection.[28] In the current study, we did not find a difference in the rate of PPH, however, we observed a trend towards more late PPH from peripancreatic vessels in the immediate surgery group. The corrosive effect of pancreatic fluid in combination with bowel content in case of pancreatic leakage may damage vessels and cause late PPH. The primary approach of late PPH is often endovascular.[29] The introduction of preoperative chemoradiotherapy in clinical practice could, therefore, decrease the number of postoperative endovascular interventions. Interestingly, we also found a trend towards less endovascular interventions in the preoperative chemo-radiotherapy group. Yet, based on this study the cause of all PPH could not be established.

Preoperative oxaliplatin-based chemotherapy has been linked to an increase of nonorganic DGE after pancreatic surgery, perhaps as a result of chemotherapy-related neurotoxicity.[7] We found no increase of DGE after preoperative gemcitabine. Patients often experienced DGE simultaneously with major complications in both study arms. Hence, preoperative chemoradiotherapy with gemcitabine does not seem to cause neurotoxicity and subsequent DGE. In previous studies, preoperative therapy was also associated with more extensive node harvest, which might increase neural denervation and the DGE rate.[30,31]

This is the first study that compares surgical complications after preoperative chemoradiotherapy to immediate surgery in patients with pancreatic cancer within a phase 3 randomized controlled trial. The randomized study design minimizes the risk of bias and confounding. A limitation of the study is the sample size, as it was not powered for studying surgical complications. However, no oncological trial will ever be powered for such endpoints and despite this we still found a significant reduction of POPF after preoperative chemoradiotherapy. The sample size was also smaller because less patients underwent resection with curative intention than expected. Hereby, subtle risk differences possibly could not be demonstrated. However, we feel a sufficient number of patients was recruited to demonstrate clinically relevant differences in complication rates. In theory, the higher rate of disease progression and irresectable disease before resection in the preoperative chemoradiotherapy group could result in the selection of patients more fit for surgery, and subsequently a lower rate of complications. However, there were no differences in baseline characteristics between both treatment groups to support this assumption.

The PREOPANC-trial demonstrated that preoperative chemoradiotherapy is safe with respect to toxicity and side-effects.[16] The utilization of preoperative therapy in the prevention of POPF after pancreatic resection is an interesting topic for future research. Patients with pathological diagnoses other than pancreatic adenocar-cinoma have an increased risk of developing POPF due to a softer, well-functioning pancreas.[26] In these patients, preoperative radiotherapy potentially could be used to induce fibrosis and subsequently reduce postoperative morbidity and mortality. However, based on the current study, we were not able to investigate whether the decreased POPF rate was caused by radiotherapy, chemotherapy, chemoradio-therapy or the prolonged time to surgery. This should be investigated in future research.

CONCLUSIONS

This observational study in the DPCG multicenter PREOP-ANC trial of preoperative chemoradiotherapy versus immediate surgery showed that preoperative chemoradiotherapy is safe with regards to surgical complications after curative resection in patients with (borderline-)resectable pancreatic cancer. We found a significant reduction of POPF after preoperative chemoradiotherapy. No significant differences were observed with respect to overall major complications, PPH, DGE, intra-abdominal infections, bile leakage, and mortality.

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