REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

Title:
Prehabilitation in patients undergoing pancreaticoduodenectomy: a randomized controlled trial

Authors:
Fabio Ausania, Paula Senra, Reyes Meléndez, Regina Caballeiro, Rubén Ouviña, Enrique Casal-Núñez

DOI: 10.17235/reed.2019.6182/2019
Link: PubMed (Epub ahead of print)

Please cite this article as:
Ausania Fabio, Senra Paula , Meléndez Reyes, Caballeiro Regina, Ouviña Rubén, Casal-Núñez Enrique. Prehabilitation in patients undergoing pancreaticoduodenectomy: a randomized controlled trial. Rev Esp Enferm Dig 2019. doi: 10.17235/reed.2019.6182/2019.

REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

OR 6182

Prehabilitation in patients undergoing pancreaticoduodenectomy: a randomized controlled trial

Fabio Ausania[1], Paula Senra[2], Reyes Meléndez[2], Regina Caballeiro[3], Rubén Ouviña[4] and Enrique Casal-Núñez[2]

[1]HPB and Transplant Surgery Department. Hospital Clínic. Barcelona, Spain. [2]HPB Surgery, [3]Endocrine and [4]Physiotherapy Departments. Complejo Hospitalario Universitario de Vigo. Vigo, Spain

Received: 02/02/2019

Accepted: 26/02/2019

Correspondence: Fabio Ausania. HPB and Transplant Surgery Department. Hospital Clinic. C/ Villarroel, 170. 08036 Barcelona, Spain

e-mail: f.ausania@googlemail.com

ABSTRACT

Introduction: prehabilitation has been proposed as an effective tool to prevent postoperative complications in patients undergoing major abdominal surgery. However, no studies have demonstrated its effectiveness in pancreatic surgical patients. The aim of this study was to assess the impact of prehabilitation on postoperative complications in patients undergoing a pancreaticoduodenectomy (PD).

Methods: this was a randomized controlled trial. Eligible candidates who accepted to participate were randomized to the control (standard care) or intervention (standard care + prehabilitation) group. All patients with pancreatic or periampullary tumors who were candidates for pancreaticoduodenectomy were included. Patients who received neoadjuvant treatment were excluded. Prehabilitation covered three actions: a) nutritional support; b) control of diabetes and exocrine pancreatic insufficiency; and c) physical and respiratory training. The main study outcome was the proportion of patients who suffered postoperative complications. Secondary

outcomes included the occurrence of specific complications (pancreatic leak and delayed gastric emptying) and hospital stay.

Results: forty patients were included in the analysis. Twenty-two patients were randomized to the control arm and 18, to the intervention group. No statistically significant differences were observed in terms of overall and major complications between the prehabilitation and standard care groups. Pancreatic leak was not statistically different between the groups (11% *vs* 27%, p = 0.204). However, DGE was significantly lower in the prehabilitation group (5.6% *vs* 40.9% in the standard care group, p = 0.01).

Conclusion: prehabilitation did not reduce postoperative complications following a pancreaticoduodenectomy. However, a reduction in DGE was observed. Further studies are needed to validate the role and the timing of prehabilitation in high-risk patients.

Key words: Pancreatectomy. Complications. Pancreatic surgery.

INTRODUCTION

Pancreaticoduodenectomy (PD) is associated with a high morbidity (40-50%) and relatively high mortality (2-5%), even in highly specialized centers (1,2). The complication rate remains high and several risk factors have been identified, such as the presence of malignancy, the severity of jaundice, impaired renal function, nutritional status and infection (3).

Cardiorespiratory functional reserve is associated with complications in pancreatic surgery (4,5) and prehabilitation is associated with a decrease in postoperative complications in several types of abdominal surgery (6,7). However, no randomized controlled trials have previously demonstrated the feasibility and the clinical impact of a prehabilitation program in pancreatic surgery.

The aim of this study was to assess whether a prehabilitation strategy could reduce postoperative complications compared to the standard care following a pancreaticoduodenectomy in patients with pancreatic or periampullary tumors.

METHODS

The study was designed as a randomized controlled trial. A consecutive sample of patients who were candidates for pancreaticoduodenectomy were recruited. All eligible patients fulfilled the following inclusion criteria: elective surgery, radiological diagnosis of pancreatic or peripancreatic malignancy, ASA score I-III and resectable or borderline resectable pancreatic or periampullary tumor according to NCCN 2014 definition (8). Only patients with a suspected malignant tumor were included as patients with other diseases tend to be more fit, which could bias the results. Patients with well-differentiated neuroendocrine tumors or IPMN without suspected malignancy were excluded. Only patients with elective surgery that allowed at least seven days of prehabilitation were evaluated for inclusion in the study. The exclusion criteria were as follows: a) unstable cardiac or respiratory disease; b) locomotor or cognitive limitations impeding adherence to the program; and c) previous neoadjuvant treatment.

Eligible candidates were invited to participate in the study and those who agreed to participate were enrolled in the trial and randomized, either to standard preoperative care (control group) or standard preoperative care with prehabilitation (intervention group). Surgeons and nurses who followed the patients during perioperative period were blind to the patient group allocation. This study was designed as a non-inferiority trial. The calculation of the sample size was performed considering a reduction in the postoperative complications rate as the main outcome. Based on data from a similar group of patients undergoing pancreatic surgery in our hospital with a complication rate of 50%, a 30% complication rate was expected in the prehabilitation group. Assuming an α error of 0.1, a statistical power of 80% and anticipating a 20% drop-out rate, a total of 48 patients were included in the study. Comparisons were performed using the Chi-square or Fisher's exact tests for categorical variables and the Student or Wilcoxon tests for numerical variables depending on the distribution of the variables. Two-sided p values were used. All p values were considered as statistically significant if $p < 0.05$. Statistical analysis was performed using the SPSS Statistics software, version 19.0 (SPSS, Chicago, IL, USA).

The Ethics Committee of our hospital approved the study. Prehabilitation was initiated

in the intervention group immediately after the baseline assessment. Moreover, all participants were reassessed within 1-3 days before the surgical procedure.

Standard care consisted of nutritional counselling, physical activity recommendation and advices on smoking cessation. Patients suffering from steatorrhea received pancreatic enzyme supplementation. Patients at high-risk of malnutrition were referred to a dietician. Preoperative biliary drainage was indicated in patients with a bilirubin level > 15 mg/dl and the inability to schedule the operation within seven days.

The intervention group underwent a personalized prehabilitation program based on their individual needs following a multidisciplinary assessment. The physical and respiratory intervention consisted of five daily sessions of supervised exercise in the outpatient clinic during 60 minutes. During this time, the patients underwent a high-intensity endurance training performed on a cycle-ergometer stationary bicycle, which was personalized to the subject. Each session included ten minutes of warm-up cycling followed by 20 minutes of muscle toning exercise, 20 minutes of aerobic exercise and ten minutes of cool-down. Following the five day supervised program, patients were trained to perform unsupervised home-based functional exercises. Breathing exercises were also scheduled. Patients were asked to report the exercises during the entire prehabilitation period. Nutritional assessment was carried out by an endocrinology specialist, as shown in table 1. The patient-generated subjective global assessment (PG-SGA) was used as a nutrition assessment tool (9).

The type of nutritional support was decided accordingly using liquid oral nutrition supplements and vitamin supplements. Pancreatic enzyme replacement therapy was administered empirically to all patients. Patients were treated with oral antidiabetic therapy or insulin when required and were trained to check their blood glucose levels at home before surgery. Prehabilitation assessment and the tests used are explained in table 1. Physical and respiratory assessments were repeated before surgery to assess the impact of the exercise program. The Enhanced Recovery After Surgery (ERAS) Guidelines for perioperative care of pancreaticoduodenectomy were followed after surgery (10).

Outcomes

The primary outcome variable of the study was the number of patients with postoperative complications defined as any deviation from the normal postoperative course and were classified according to the Dindo-Clavien classification (11).

Other outcome variables included the occurrence of clinically relevant pancreatic fistula (type B and C), delayed gastric emptying defined according to ISGPS and postoperative hospital stay (12,13).

No funding was obtained for this study.

RESULTS

Sixty-two patients with suspected pancreatic or periampullary malignant tumor were evaluated for pancreaticoduodenectomy at our hospital from 2015 to 2017. All potential candidates were considered for the study. However, 14 patients did not meet inclusion criteria, ten patients had previously received neoadjuvant treatment, two patients refused to participate and two patients did not meet the histologic criteria. Therefore, 48 patients were finally included. Five patients were unresectable at the time of laparotomy and three patients were unable to comply with the preoperative program for logistic or social reasons. Patient characteristics are shown in table 2. Of 40 patients, 18 patients were randomized to the prehabilitation group and 22 to the standard care group. The median duration of prehabilitation was 12.6 days.

Reconstruction following pancreaticoduodenectomy consisted of an isolated pancreatic anastomosis technique with a Roux-en-Y limb. A 40-cm jejunal loop was left for the biliary reconstruction. This biliary loop was brought through another opening in the mesocolon. A side-to-side gastrojejunal anastomosis was performed 40 cm downstream from the hepaticoyeyunostomy in an antecolic fashion. Finally, an end-to-side jejunostomy was performed to join the pancreatic loop with the biliary/gastric loop.

Six patients underwent a resection of the superior mesenteric vein, three in each group. In two cases, an end-to-end venous anastomosis was performed without any graft interposition. A left renal vein graft interposition was necessary in one case. In the remaining three cases, a bovine pericardial patch was used to close lateral venous resections. Finally, an end-to end venous anastomosis was combined with end-to-end

superior mesenteric artery resection in one case.

Surgical drains were routinely used and drain amylase was performed at day 3 and the drains were removed if normal levels were detected. A nasogastric tube was routinely placed during the surgery and removed at postoperative day 2, unless abdominal distension as a sign of intraabdominal complications was detected. Oral feeding was introduced at day 3. Parenteral nutrition was used for patients unable to tolerate oral feeding at postoperative day 6. Pancreatic enzymes replacement therapy (PERT) was administrated to all patients (14).

Malnutrition according to Patient Generated Subjective Global Assessment was detected in all patients. Exocrine pancreatic insufficiency was detected in six (33.2%) patients, three patients were clinically diagnosed with steatorrhea and a low level of fecal elastase was detected in three patients. Median levels of vitamin A and D were below the normal values. Reassessment of the physical and respiratory function showed a 16-21% improvement in all tests. These data are shown in table 3.

There were no postoperative deaths. Postoperative complication occurred in 18 cases (45%). There was no statistically significant difference between the standard care and the prehabilitation group (54.5% *vs* 33.3%, respectively; p = 0.18). Pancreatic fistulas occurred in eight patients and the leak rate was lower in the prehabilitation group, 11.1% *vs* 27.3% in the standard care group. However, this difference was not statistically significant (p= 0.204). Four patients were treated with antibiotics and total parenteral nutrition (grade B). A grade C pancreatic leak occurred in four patients and a percutaneous drainage of infected peripancreatic collection was performed in three cases. One patient required arterial embolization due to a pseudoaneurysm of the gastroduodenal artery and a laparotomy.

DGE occurred in ten patients and was significantly lower in the prehabilitation group, 5.6% *vs* 40.9% in the standard care group (p = 0.01). This was associated with a pancreatic fistula in six patients and no specific treatment for DGE was administered. Two patients were unable to tolerate solid food and required naso-gastric tube reinsertion and total parenteral nutrition after postoperative day 7. Domperidone and metoclopramide were also administered in these two cases. There were no biliary complications. Major complications occurred in eight patients and there were no

differences between the groups.

Four patients experienced grade C pancreatic fistula and three patients required ICU admission, two had central venous catether-related sepsis and one had a chest infection. One patient required arterial embolization of the inferior pancreaticoduodenal artery stump due to early postoperative bleeding. Three patients were readmitted with suspected intrabdominal collections that were successfully treated with antibiotics. The readmission rate and postoperative hospital stay were similar between the groups. These data are shown in table 4.

DISCUSSION

This is the first randomized clinical trial in the literature that assesses the feasibility and the potential benefit of preoperative rehabilitation for patients undergoing PD. In our study, prehabilitation was not associated with a lower incidence of postoperative complications. We also observed a significantly lower DGE rate and a lower clinically relevant pancreatic fistula rate (not significant) in the prehabilitation group, with no difference in hospital stay. Since there is a strong association between DGE and pancreatic fistula (15), the lower incidence of DGE in the prehabilitation group could be explained by the lower pancreatic leak rate. However, specific complications were evaluated as secondary outcome variables and therefore, these results should be cautiously interpreted. We also observed an improvement in physical and respiratory function in patients undergoing preoperative exercise, although this did not impact on the postoperative complication rate. Some preliminary studies have already reported the feasibility of a preoperative rehabilitation program in patients who are candidates for upfront surgery (16) or following neoadjuvant treatment (17) for pancreatic tumors. Running a prehabilitation program is feasible, as we demonstrated in our study. However, we noticed several issues that could have led to different results in our study. Firstly, a minimum number of days should be offered to patients for the prehabilitation to work effectively. In our study, we only considered patients with a minimum prehabilitation time of seven days. This decision was made during the study design, as it is very difficult to improve physical or nutrition status in a very short time and currently, there are no criteria to justify a delay of the surgery. Oncologic patients

who are candidates for PD tend to deteriorate very quickly and this could mean that they are unable to successfully comply with physical exercise or even nutrition schedules. However, improvement may be a very subjective factor, meaning that some patients could obtain good results in a short time and others will never experience an improvement in their functional status due to several factors. From the logistic point of view, it was very challenging to organize a correct time schedule for the preoperative program, since most of the participants were inpatients with jaundice and sometimes fasting whilst waiting for scans or endoscopic procedures. Secondly, many patients in the "standard of care" group received some sort of prehabilitation. However, no pancreatic surgeon would operate on a patient without a basic preoperative optimization such as diabetes control, oral supplements in case of noticeable malnutrition, PERT supplementation when symptoms of malabsorption are detected and advice for physical exercise before surgery. We estimated that half of patients in the "standard of care" group in our study were "partially prehabilitated" and this might have biased the results.

Some questions remain open with regard to the design of a proper study to validate prehabilitation in cancer patients who are PD candidates. Should all patients be prehabilitated regardless of the diagnosis? Is a randomized controlled study the way forward and is it ethical to avoid prehabilitation in the standard care control arm? Is delaying surgery for prehabilitation justified?

Another limitation of our study is related to the test chosen for the assessment. Cardiopulmonary exercise testing was not available in our hospital at the time of the study, so we decided to use a 10 m walk test that has never been validated for abdominal surgery. However, similar tests have shown that it is equivalent to a 10 m walk test (18,19).

Despite this, we did not demonstrate a benefit of a prehabilitation program in patients with cancer who are candidates for PD. Therefore, we think that further research is needed in this area. Some patients would clearly benefit from a prehabilitation program such as those who are denied surgery due to a high risk, or those who undergo neoadjuvant treatment and therefore do not have sufficient time to allow a proper program. There is recent evidence that suggests that resectable patients may

benefit from neoadjuvant treatment and therefore prehabilitation may play an important role (20). Patients who undergo biliary preoperative biliary drainage also are potential candidates for prehabilitation, since recent studies suggest that delaying surgery by four weeks could reduce perioperative complications (21). Specific complications of pancreatic surgery should be used as the main outcome measure in order to validate our findings, which means that a larger number of patients should be enrolled.

In conclusion, prehabilitation did not seem to reduce overall complications after PD for pancreatic cancer. However, an improved patient selection and evaluation of specific complications needs to be assessed in differently designed studies.

REFERENCES

1. Muscari F, Suc B, Kirzin S, et al. Risk factors for mortality and intraabdominal complications after pancreatoduodenectomy: multivariate analysis in 300 patients. Surgery 2006;139:591-8. DOI: 10.1016/j.surg.2005.08.012

2. Winter JM, Cameron JL, Campbell KA, et al. 1423 pancreaticoduodenectomies for pancreatic cancer: a single-institution experience. J Gastrointest Surg 2006;10:1199-211. DOI: 10.1016/j.gassur.2006.08.018

3. Pitt HA, Cameron JL, Postier RG, et al. Factors affecting mortality in biliary tract surgery. Am J Surg 1981;141:66-71. DOI: 10.1016/0002-9610(81)90014-3

4. Ausania F, Snowden CP, Prentis JM, et al. Effects of low cardiopulmonary reserve on pancreatic leak following pancreaticoduodenectomy. Br J Surg 2012;99(9):1290-4. DOI: 10.1002/bjs.8859

5. Ausania F, Vallance AE, Manas DM, et al. Double bypass for inoperable pancreatic malignancy at laparotomy: postoperative complications and long-term outcome. Ann R Coll Surg Engl 2012;94(8):563-8. DOI: 10.1308/003588412X13373405386934

6. Barberán-García A, Ubré M, Roca J, et al. Personalised prehabilitation in high-risk patients undergoing elective major abdominal surgery: a randomized blinded controlled trial. Ann Surg 2018;267(1):50-6. DOI: 10.1097/SLA.0000000000002293

7. Moran J, Guinan E, McCormick P, et al. The ability of prehabilitation to influence postoperative outcome after intra-abdominal operation: a systematic review and meta-analysis. Surgery 2016;160(5):1189-201. DOI: 10.1016/j.surg.2016.05.014

8. Tempero MA, Malafa MP, Behrman SW, et al. Pancreatic adenocarcinoma, version 2.2014: featured updates to the NCCN guidelines. J Natl Compr Canc Netw 2014;12(8):1083-93.

9. Bauer J, Capra S, Ferguson M. Use of the scored Patient-Generated Subjective Global Assessment (PG-SGA) as a nutrition assessment tool in patients with cancer. Eur J Clin Nutr 2002;56(8):779-85. DOI: 10.1038/sj.ejcn.1601412

10. Lassen K, Coolsen MM, Slim K, et al. Guidelines for perioperative care for pancreaticoduodenectomy: Enhanced Recovery After Surgery (ERAS®) Society recommendations. Clin Nutr 2012;31(6):817-30. DOI: 10.1016/j.clnu.2012.08.011

11. Clavien PA, Barkun J, De Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 2009;250(2):187-96. DOI: 10.1097/SLA.0b013e3181b13ca2

12. Bassi C, Marchegiani G, Dervenis C, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years after. Surgery 2017;161(3):584-91. DOI: 10.1016/j.surg.2016.11.014

13. 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(5):761-8. DOI: 10.1016/j.surg.2007.05.005

14. Sabater L, Ausania F, Bakker OJ, et al. Evidence-based guidelines for the management of exocrine pancreatic insufficiency after pancreatic surgery. Ann Surg 2016;264(6):949-58. DOI: 10.1097/SLA.0000000000001732

15. Parmar AD, Sheffield KM, Vargas GM, et al. Factors associated with delayed gastric emptying after pancreaticoduodenectomy. HPB (Oxford) 2013;15(10):763-72. DOI: 10.1111/hpb.12129

16. Jones C, Kelliher L, Dickinson M, et al. Impact of a prehabilitation program on functional status and length of stay following major pancreatic surgery with an ERAS pathway. Clin Nutr ESPEN 2017;19:91. DOI: 10.1016/j.clnesp.2017.04.059

17. Ngo-Huang A, Parker N, Martínez V, et al. Feasibility of a prehabilitation program for patients with potentially resectable pancreatic cancer: pilot study. PM&R 2016;8(9S):S183. DOI: 10.1016/j.pmrj.2016.07.111

18. Pecorelli N, Fiore JF Jr, Gillis C, et al. The six-minute walk test as a measure of postoperative recovery after colorectal resection: further examination of its measurement properties. Surg Endosc 2016;30(6):2199-206. DOI: 10.1007/s00464-015-4478-1

19. Dalgas U, Severinsen K, Overgaard K. Relations between 6 minute walking distance and 10 meter walking speed in patients with multiple sclerosis and stroke. Arch Phys Med Rehabil 2012;93(7):1167-72. DOI: 10.1016/j.apmr.2012.02.026

20. Van Tienhoven, Versteijne E, Suker M, et al. Preoperative chemoradiotherapy versus immediate surgery for resectable and borderline resectable pancreatic cancer (PREOPANC-1): a randomized, controlled, multicenter phase III trial. J Clin Oncol 2018;36:18(suppl):LBA4002. DOI: 10.1200/JCO.2018.36.18_suppl.LBA4002

21. Sandini M, Honselmann KC, Birnbaum DJ, et al. Preoperative biliary stenting and major morbidity after pancreatoduodenectomy: does elapsed time matter? The FRAGERITA Study Group. Ann Surg 2018;268(5):808-14. DOI: 10.1097/SLA.0000000000002838

22. Tilson JK, Sullivan KJ, Cen SY, et al. Meaningful gait speed improvement during the first 60 days poststroke: minimal clinically important difference. Phys Ther 2010;90(2):196-208. DOI: 10.2522/ptj.20090079

23. Mahoney FI, Barthel DW. Functional evaluation: the Barthel index. Md State Med J 1965;14:61-5.

Table 1. Pre-treatment assessment and type of prehabilitation

	Pre-treatment assessment	Type of prehabilitation
Physiotherapy	– Spirometry and pulse oximetry – 10-meters walk test (22) – Barthel index (23)	– 5 days training in outpatient clinic (60 min) – Daily training at home
Nutrition	– Patient Generated Subjective Global Assessment – Anthropometric measurements – Estimation of the last 24 hours intake – Bioimpedanciometry – Serum albumin and pre-albumin	– Nutritional support (oral supplement) – Total parenteral nutrition if required – Follow-up in outpatient clinic
Endocrine	– Family history of diabetes mellitus – Physical examination – Blood glucose, HbA1C	– Metformin if fasting and repeated blood glucose < 180 mg/dl or HbA1C < 8.5% – Insulin 0.2 UI/kg if glucose ≥ 180 mg/dl or HbA1C ≥ 8.5% – Blood glucose monitor to check glucose level at home
Exocrine	– Symptoms of steatorrhea – Weight loss – Fecal elastase 1 (cut-off < 200 µg/g) – Vitamin A, D, E	– Pancreatic enzymes replacement therapy (PERT) (40,000 UI/8 h with main meals) – Vitamin oral support

Table 2. Patient characteristics

	Total n.40	Standard care n.22	Prehabilitation n.18	p
Age (median, years)	65.9 (38-81)	65.7 (38-81)	66.1 (38-80)	0.928
BMI (median)	25.8 (18-33)	26.5	24.8	0.182
Male gender	22 (55)	13 (59.1)	9 (50)	0.565
ASA – II – III	 16 (40) 24 (60)	 9 (40.9) 13 (59.1)	 7 (38.9) 11 (61.1)	0.896
Preoperative biliary drainage (%)	15 (37.5)	9 (40.9)	6 (33.3)	0.622
Mortality risk score (P-POSSUM)	2.7 (0.3-19)	2.1 (0.4-9.3)	3.4 (0.3-19)	0.284
Morbidity risk score (P-POSSUM)	26.8 (0.4-82)	(0.4-58.9)	(0.8-82)	0.950
Time from baseline assessment to surgery (days)	18.2 (7-30)	19.2 (7-30)	17 (7-28)	0.399
Intraoperative bleeding (ml) – < 100 – 100-500 – > 500	 31 (77.5) 8 (20) 1 (2.5)	 16 (72.7) 5 (22.7) 1 (4.5)	 15 (83.3) 3 (16.7) -	0.564
Histology – Ductal carcinoma – Ampullary carcinoma – Cholangiocarcinoma – IPMN Carcinoma	 18 (45) 16 (40) 3 (7.5) 3 (7.5)	 13 1 5 3	 9 3 3 3	-
Wirsung duct size (mm, median)	2.4 (1-10)	2 (1-3)	3 (1-10)	0.175
Pancreatic consistency – Soft – Normal – Hard	 20 (50) 15(37.5) 5 (12.5)	 11 (50) 8 (36.4) 3 (13.6)	 9 (50) 7 (38.9) 2 (11.1)	0.967

BMI: body mass index; ASA: American Society of Anesthesiology score; PD: pancreaticoduodenectomy; P-POSSUM: Portsmouth Physiological and Operative Severity Score for the enumeration of mortality and morbidity.

Table 3. Baseline characteristics of the prehabilitation group and improvement following prehabilitation

	Before prehabilitation	*Before surgery*	*Improvement (%)*
Diabetes mellitus			
– IGT, n. pts	3/18, 16.6% (3 new-onset)		
– Diabetes, n. pts	6/18, 33.2% (3 new-onset)		
– HbA1c, median %	6.6 (4.4-9.6)		
Exocrine insufficiency			
– Steatorrhea n. pts	3/18 (16.6%)		
– Weight loss %, median	13 (5-21%)		
– Fecal elastase (NV > 200), median	103.5 (3 patients)		
– Vit D (NV > 20 ng/ml), median	16.1 0.48		
– Vit A (NV > 1.05 mmol/l), median	15.9		
Vit E (NV > 12 mmol/l), median			
Malnutrition, %	100		
Cardiopulmonary status			
– FEV 1 (l, median)	2.38	2.86	0.48 (20)
– FVC (l, median)	3.0	3.6	0.6 (20)
– O_2 sat %	98.2	98.5	
Dynamometer strength test			
– Left hand	27.9	33.83	5.9 (21)
– Right hand	29.3	34.1	4.8 (16)
10 m walk test (sec)	6.03	4.83	1.2 (19)

Table 4. Primary and secondary outcome measures

	Total (40 pts)	*Standard care (22 pts)*	*Prehabilitation (18 pts)*	*p*
Complications, number of patients (%)	18 (45)	12 (54.5)	6 (33.3)	0.18
Major complications (type III-IV)	8 (20)	4 (18.2)	4 (22.2)	0.751
Pancreatic leak (B + C)	8 (20)	6 (27.3)	2 (11.1)	0.204
DGE	10 (25)	9 (40.9)	1 (5.6)	0.01
Hospital stay	12.7 (7-60)	13.2 (7-60)	11.4 (7-46)	0.449
Readmission	3 (7.5)	2 (9.6)	1 (5.6)	0.673

DGE: delayed gastric emptying.