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Palliative Partial Pancreaticoduodenectomy Impairs Quality of Life Compared to Bypass Surgery in Patients with Advanced Adenocarcinoma of the Pancreatic Head

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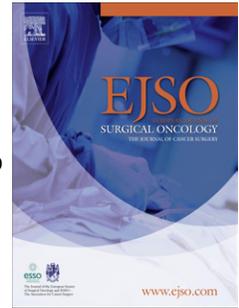
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Authors: J. Walter, A. Nier, T. Rose, J.H. Egberts, C. Schafmayer, T. Kuechler, D.C. Broering, B. Schniewind



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Palliative Partial Pancreaticoduodenectomy Impairs Quality of Life Compared to Bypass Surgery in Patients with Advanced Adenocarcinoma of the Pancreatic

Head

J. Walter, A. Nier, T. Rose, J.H. Egberts, C. Schafmayer, T. Kuechler, D.C. Broering, B.

Schniewind

Clinic for General and Thoracic Surgery, University Clinic of Schleswig-Holstein, Campus Kiel,
Arnold-Heller-Str. 3 (Haus 18), 24105 Kiel

Corresponding Author:

Dr. Jessica Walter

Clinic for General and Thoracic Surgery,
University Clinic of Schleswig-Holstein, Campus Kiel,
Arnold-Heller-Str. 3,
24105 Kiel, Germany

e-mail: Jessica.Walter@uksh-kiel.de

phone: ++49431-597-4301

fax: ++49431-597-1995

Original Article

Abstract

Background: Some surgical centres consider palliative resection (PR) to be superior to double loop bypass (DLB) as treatment for advanced carcinoma of the pancreatic head. We performed a retrospective study with prospectively collected data at a single centre to compare PR and DLB in regard to quality of life (QoL).

Methods: From January 1996 to September 2008, 196 patients were given palliative surgery for advanced pancreatic cancer at the University Hospital of Kiel. Forty-two patients underwent PR and 154 underwent DLB. These groups were compared with regard to survival, postoperative morbidity, and QoL. The EORTC QLQ-C30 was used to assess QoL before surgery, at discharge, three months after surgery, and six months after surgery.

Results: The median survival time after PR was 7.5 months (95% CI: 4.95-10.05) and after DLB was 6 months (95% CI: 4.98-7.02; log rank test: $p = 0.066$). There were no significant differences in mortality and morbidity rates (7.1% and 45.2% for PR; 3.9% and 38.3% for DLB, respectively). Assessment of QoL indicated that patients who underwent PR had more impairment of some functional metrics and increased symptoms compared to those who underwent DLB.

Conclusion: There was no significant difference in survival or morbidity after PR and DLB, but patients who underwent DLB had better QoL than patients who underwent PR. Therefore, clinicians may want to reconsider the use of PR for patients with advanced pancreatic cancer.

Keywords: quality of life, pancreatic cancer, palliative surgery

Abbreviations: palliative resection, PR; double loop bypass, DLB; quality of life, QoL; European Organization for Research and Treatment of Cancer quality of life questionnaire core 30, EORTC QLQ-C30; confidence interval, CI; pylorus-preserving pancreaticoduodenectomy, PPPD

Introduction

Pancreatic cancer is the fourth leading cause of cancer death in men and women in Western countries and has a 5-year survival rate of 5% regardless of stage¹. Most patients present with advanced disease, and only about 10-20% of patients are eligible for resection with curative intent². Up to 40% of patients who are considered to have resectable disease preoperatively are reclassified as having unresectable disease during surgical exploration³⁻⁵. Therefore, palliative treatment is widely used for patients with advanced pancreatic cancer.

The purpose of palliative care is to provide the best possible quality of life (QoL) for the short duration of a patient's remaining life. Palliation for unresectable pancreatic cancer with obstruction of the biliary and/or the intestinal tract can be treated by endoscopic or surgical approaches. Previous research indicated that the surgical option of biliary and gastric bypass was superior to endoscopic intervention in terms of QoL, and rates of re-interventions and re-hospitalization^{6, 7}. Palliative pancreaticoduodenectomy has been considered an acceptable alternative to bypass surgery⁸. Studies have shown that palliative resection (PR), which leaves microscopic or macroscopic residual tumour in situ, results in similar or even better survival rates than bypass surgery⁸⁻¹⁰. However, the definitive value of PR remains unclear. Our group found no survival benefit for patients given palliative resection relative to those who given double loop bypass (DLB) surgery¹¹. Moreover, only a few studies have assessed postoperative QoL following palliative surgical procedures^{11, 12}.

The present study compared the QoL of patients with advanced pancreatic cancer who were given PR or DLB.

Patients and Methods

From January 1996 to September 2008, a total of 196 patients with advanced adenocarcinoma of the pancreatic head were given palliative surgical procedures at the University

Hospital of Kiel. Patients with other types of pancreatic cancers or with adenocarcinomas in other regions of the pancreas were not included.

Preoperative examination indicated that 154 patients had unresectable tumours due to either extra-pancreatic metastases or locally advanced growth with involvement of the large blood vessels or retroperitoneum. Irrespective of any evident biliary or intestinal obstruction, DLB with retrocolic gastrojejunostomy, hepaticojejunostomy and reconstruction of the intestinal passage by Roux-en-Y anastomosis was performed in these patients (DLB-group, n = 154). The other 42 patients were treated by palliative resection (PR-group). These 42 patients were initially surgically explored with curative intention by the classical Whipple operation or by pylorus-preserving pancreaticoduodenectomy (PPPD), but all had intraoperative findings of locally advanced tumour growth with microscopic or macroscopic residual tumour after resection. A total of 117 patients in the DLB-group received postoperative chemotherapy (76%) and 30 patients in the PR-group were given adjuvant treatment (71.4%).

Patient records concerning postoperative outcome and QoL prior to and after surgery were prospectively examined following informed consent. The local Ethics Committee approved this study.

Definition of complications

Delayed gastric emptying was defined as recurrent vomiting within 5 days after surgery or a drainage volume (via nasogastric tube) of more than 500 mL/day. A pancreatic fistula was defined by the presence of amylase activity in the drainage fluid that was three-fold greater than that in serum at three days after surgery. Pneumonia was diagnosed if there were new infiltrates on the chest radiograph, fever, and elevated white blood cell account.

Assessment of health-related quality of life

The questionnaires for assessing QoL were administered to all patients before surgery (baseline), at discharge, and at 3, 6, 12 and 24 months after surgery. Due to the short life-

expectancy of these patients, the 12-month and 24-month results were not used in our analysis. Analyses of inter-individual changes in QoL were calculated as changes of each item score over time and the mean differences of the DLB-group and the PR group were compared. Inter-individual differences were calculated to identify individual changes and dynamics that might be obscured by simple comparison of total values. Furthermore, the range of inter-individual health related QoL scores is well known to be extensive, leading to difficulties in identification of averaged differences¹³.

The health-related QoL was assessed with the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 core questionnaire. The EORTC QLQ-C30 is a cancer-specific 30-item questionnaire¹⁴ with five functional scales (physical, role, cognitive, emotional, social), three symptom scales (fatigue, pain, nausea/vomiting), a global health QoL scale, a number of individual items that assess additional symptoms commonly reported by patients with cancer (dyspnoea, appetite loss, insomnia, constipation, diarrhoea), and perceived financial impact. All EORTC QLQ-C30 items have response categories with four levels (“not at all” to “very much”) except the two items for overall physical condition and overall QoL, which had seven-point response categories (“very poor” to “excellent”). High scores indicate high response levels, high functional scale scores represent high/healthy levels of functioning, and high symptom scores represent high levels of symptoms/problems.

Statistical analysis

Data were analysed using WinSTAT^R. All distributions and frequencies were compared using the Chi-Square test. Scoring of the EORTC QLQ-C30 core questionnaire was performed according to the EORTC-QLQ-C30 Scoring Manual, with linear transformation of the raw scores to give ranges of 0 to 100¹⁵. Due to the non-normal distribution of the QoL data, non-parametric methods were used. Comparison of changes in QoL over time between the two groups was performed with the Mann-Whitney *U* test. Patient survival was calculated by the Kaplan-Meier

method and differences in survival were analysed with the log rank test. A p -value less than 0.05 was considered statistically significant.

Results

Patients and surgical data

Table 1 shows the demographic characteristics, operative data, post-operative complications, and use of chemotherapy of the 196 enrolled patients. There were no significant differences in median age and gender distribution between the DLB and PR groups. Seventy of 154 patients of the DLB group had extrapancreatic metastases and 84 patients had locally advanced tumours with infiltration of the mesenteric root or the retroperitoneum (data not shown). The PR patients were given the “classical” Whipple operation ($n = 24, 57\%$) or a pylorus-preserving pancreaticoduodenectomy ($n = 18, 43\%$). All patients in the PR-group had locally advanced tumours with either microscopic or macroscopic residual tumour mass in the mesenteric root or the retroperitoneum. As expected, the mean surgery time and mean hospitalisation time were significantly longer in the PR group (Table 1). Overall, postoperative complications tended to be more common in the PR group, but this was not statistically significant ($p = 0.084$). Patients given PR were more likely to develop pancreatic fistulas ($p = 0.002$) and gastrointestinal leakages ($p = 0.03$) than patients given DLB (Table 1).

Survival

The median survival time was 6 months for the DLB group (95% confidence interval [CI]: 4.98-7.02) and 7.5 months for the PR group (95% CI: 4.95-10.05). A log rank test indicated that this difference was not significant ($p = 0.066$) (Figure 1). In comparison, during the same study time, 114 pancreatic cancer patients at our institution underwent complete (R0) resection of the pancreatic head and this group had a median survival time of 23 months (95% CI: 12-34) and a 5-year survival rate of 21% (data not shown).

Quality of life

Questionnaires were administered to 61 patients of the DLB group and 25 patients of the PR group prior to surgery. Table 2 shows the response rates of completed questionnaires before surgery, at discharge, 3 months after surgery, and 6 months after surgery.

Analysis of QoL scales prior to surgery indicated that the DLB group had significantly higher symptom scores in five of eight scales (nausea/vomiting, dyspnea, insomnia, appetite loss, constipation) and a higher financial difficulties score. There were no significant differences in the functional scales or the global health status prior to surgery (Table 3).

Individual postoperative scores were subtracted from the individual preoperative scores to identify intra-individual changes of QoL after surgery. Table 4 shows the complete mean scale score differences, standard deviations, and *p*-values for all three time-points after surgery. Based on the five functional scales, patients given DLB had a significantly greater decrease of physical function at 6 months after surgery than those given PR. However, impairment of social and cognitive function at discharge and cognitive and emotional functioning at 3 months after surgery was greater in the PR group. Recovery of global health status was not significantly different between the two groups, with near normalisation at 3 months after surgery. Based on the eight symptom scales, patients given PR had significantly increased dyspnoea at discharge, increased nausea, dyspnoea, constipation, and diarrhoea at 3 months after surgery. However, appetite loss was more aggravated in DLB patients at 6 months after surgery .

Discussion

The life expectancy of a patient with locally advanced or metastatic pancreatic cancer is very short, thus underlining the importance of identifying the best palliation therapy so that the patients has the best possible QoL. The advantage of palliative surgery over interventional procedures seems to be evident⁶, but it is uncertain whether bypass surgery or palliative resection provides better QoL. Previous research has indicated that DLB and PR provide long-term relief of

the main symptoms associated with pancreatic cancer (biliary and gastroduodenal obstruction) and have similar morbidity and mortality rates in specialized centers^{10, 16, 17}.

Differences in survival

Survival after palliative resection was noted to be superior by some authors^{4, 9, 10, 16}, leading to a general preference for PR as palliative treatment for advanced pancreatic cancer. In our study cohort, median survival after PR (7.5 months) was slightly longer than that after DLB (6 months), but this difference was not statistically significant. Any survival benefit of PR might have arisen because these patients had less advanced disease and were initially operated with curative intent. Our PR group did not include patients with metastatic disease; in general, DLB is preferred in patients with metastatic pancreatic cancer. Previous research that compared the outcomes of patients who simultaneously underwent pancreaticoduodenectomy and hepatic resection for metastases indicated a survival rate similar to that of patients receiving only bypass surgery, thus questioning the need for a procedure with higher morbidity and mortality¹⁸.

Previous research indicated that the mean survival time after DLB was worse for pancreatic cancer patients who had liver metastases (5.8 months) than for those with no metastases (9.7 months)¹⁷. In the present study, there was no significant difference in the mean survival time between patients with and without liver metastases (5 months vs. 6 months respectively; log rank: $p = 0.196$).

Quality of life after PR and DLB

Knowledge of QoL after surgical palliation for pancreatic cancer is limited^{19, 20}, there are limited number of direct comparisons of QoL after PR and DLB^{9, 11, 12}, and investigation of QoL has not been standardised. Kuhlmann et al. previously reported comparable palliation rates by PR and DLB in terms of QoL as determined by readmission rate⁹.

A Polish group published an analysis of QoL after DLB vs. PR¹² using the same tool (EORTC QLQ-C30) as used in the present study and in our previous study that examined part of the

same study population¹¹. Kostro et al.¹² reported an improvement in emotional and physical status after PR relative to DLB and more gastro-intestinal problems after DLB (without showing scores on individual scales), and recommended PR over DLB for palliative care. Results from our previous study¹¹ and the current study are contrary to those observations. In our former study, we found superior scores in emotional and cognitive function after DLB and higher individual scale scores for diarrhoea after PR. Besides the differences in time period when these studies were performed, the present study analysed scores at several times after surgery, which allowed us to analyse intra-individual changes of QoL over time. Thus, we noted significantly lower levels of cognitive and social functioning soon after PR relative to DLB and higher impairment of emotional and cognitive functioning at 3 months after PR, but that those changes eventually normalized in both groups.

PR patients might have had worse QoL scores soon after surgery because they were initially told that their surgeries would be curative, but were suddenly given a new diagnosis of the presence of residual tumour, the non-curative nature of the surgery, and poor prognosis. The DLB patients were initially informed of the advanced nature of their disease and that they would be given palliative (not curative) surgery. The advanced stage of disease in the DLB group was indicated by their significantly higher symptom levels in almost every item prior to surgery. After the bypass operation, the DLB patients developed an amelioration of symptoms, whereas PR patients were more likely to report nausea, dyspnoea, diarrhoea, and constipation. Normalisation to almost baseline levels of symptoms in both groups might be due to a “response-shift”, that is, an adjustment to the prognosis with adaption of perceptions relative to expectations²¹. However, based on our study design, it is unclear if the differences between the groups depended on the time at which patients received knowledge of the terminal nature of the disease or depended on the surgical procedure itself.

In conclusion, survival after PR is not significantly different from survival after DLB, but PR is associated with increased morbidity. In particular, the QoL of the PR group relative to the DLB group is more impaired soon after surgery in the functional and symptom scales, although the

symptoms of DLB are less severe at 6 months after surgery, at which time both groups nearly returned to preoperative levels. Altogether, these data indicate that PR should be used more restrictively, because it provides no significant survival advantages, and is associated with worse QoL and elevated morbidity. We suggest that bypass surgery should be considered if complete resection of the tumour seems unachievable, and provides better quality of life during the palliative care of pancreatic cancer patients.

Conflict of interest statement: All authors state that there are no conflicts of interest regarding any financial or personal relationships.

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Legends

Table 1: Patient characteristics, operative data, postoperative complications, and postoperative chemotherapy of patients in the double loop bypass (DLB) group and the palliative pancreaticoduodenectomy (PR) group.

Table 2: Questionnaire response rates of patients in the double loop bypass (DLB) group and the palliative pancreaticoduodenectomy (PR) group before surgery, at discharge, 3 months after surgery, and 6 months after surgery.

Table 3: Comparison of mean scale scores (+/- SD) prior to surgery of the double loop bypass (DLB) group and the palliative resection (PR) group.

Table 4: Changes of mean intra-individual differences (+/- SD) of scores for the double loop bypass (DLB) group and the palliative resection (PR) group relative to scores before surgery.

Figure 1: Kaplan-Meier analysis of cumulative survival of patients given double loop bypass (DLB) surgery or palliative pancreaticoduodenectomy (PR).

Figure 2: Comparison of mean intra-individual changes in quality of life in the four functional scales at discharge, 3 months after surgery, and 6 months after surgery (DLB: double loop bypass, PR: palliative pancreaticoduodenectomy). * $p < 0.05$ (Mann-Whitney U test).

Figure 3: Comparison of mean intra-individual changes in quality of life in four symptom scales at discharge, 3 months after surgery, and 6 months after surgery (DLB: double loop bypass, PR: palliative pancreaticoduodenectomy). * $p < 0.05$ (Mann-Whitney U test).

Tables

Table 1

	Double loop bypass <i>n = 154</i>	palliative pancreaticoduodenectomy <i>n = 42</i>	<i>p</i> value
Patient characteristics			
Median age, years (range)	65 (35-87)	63.5 (47-81)	0.71
Female	73	22	0.57
Male	81	20	0.57
Operative data			
Mean operation time, min	261 +/- 72	439 +/- 127	<0.00001
Mean hospitalisation, days	17 +/- 9	32 +/-21	<0.00001
Postoperative complications			
Overall morbidity, n (%)	59 (38.3)	19 (45.2)	0.42
Delayed gastric emptying, n (%)	22 (14.3)	7 (16.3)	0.7
Pancreatic fistula, n (%)	4 (2.6)	6 (14.3)	0.002
Biliary fistula, n (%)	8 (5.2)	3 (7)	0.63
Haemorrhage, n (%)	6 (3.9)	2 (4.7)	0.8
Cholangitis, n (%)	6 (3.9)	1 (2.4)	0.64
Gastrointestinal leakage, n (%)	2 (1.3)	3 (7)	0.03
Wound infections, n (%)	6 (3.9)	1 (2.4)	0.64
Cardiac complications, n (%)	6 (3.9)	1 (2.4)	0.64
Pneumonia, n (%)	3 (1.9)	3 (7)	0.08
Renal failure, n (%)	1 (1.5)	2 (4.7)	0.055
Others, n (%)	10 (6.5)	3 (7)	0.88
None, n (%)	95 (61.7)	23 (54.8)	0.42
Hospital mortality, n (%)	6 (3.9)	3 (7.1)	0.37
Postoperative chemotherapy, n (%)	117 (76)	30 (71.4)	0.641

Table 2

	DLB	PR	total
Pre-operative	61 (39.6%)	25 (59.5%)	86 (43.9%)
At discharge	61 (39.6%)	17 (40.5%)	78 (39.8%)
3 months after surgery	43 (27.9%)	15 (35.7%)	58 (29.6%)
6 months after surgery	34 (22.1%)	7 (16.7%)	41 (20.9%)

Table 3

	DLB	PR	P-value
Physical functioning	77 (+/-17)	72 (+/-30)	0.63
Role functioning	77 (+/-29)	75 (+/-32)	0.65
Emotional functioning	67 (+/-23)	60 (+/-23)	0.24
Cognitive functioning	83 (+/-23)	87 (+/-15)	0.87
Social functioning	67 (+/-25)	77 (+/-28)	0.08
Global health status	48 (+/-17)	47 (+/-22)	0.73
Fatigue	57 (+/-25)	48 (+/-39)	0.42
Nausea/Vomiting	37 (+/-20)	11 (+/-25)	0.0003
Pain	57 (+/-29)	58 (+/-37)	0.5
Dyspnoea	55 (+/-22)	30 (+/-38)	0.0002
Insomnia	63 (+/-29)	43 (+/-35)	0.02
Appetite loss	71 (+/-28)	49 (+/-33)	0.0006
Constipation	51 (+/-29)	16 (+/-36)	<0.0001
Diarrhoea	43 (+/-22)	32 (+/-39)	0.21
Financial difficulties	52 (+/-25)	10 (+/-30)	0.0007

Table 4

	Difference after discharge			Difference after 3 months			Difference after 6 months		
	DLB	PR	p-value	DLB	PR	p-value	DLB	PR	p-value
Physical functioning	-28 (+/-23)	-38 (+/-21)	0.15	-26 (+/-16)	-44 (+/-38)	0.56	-22 (+/-22)	0 (+/-0)	0.007
Role functioning	-36 (+/-29)	-55 (+/-22)	0.14	-38 (+/-40)	-46 (+/-29)	0.93	-29 (+/-48)	-7 (+/-9)	0.18
Emotional functioning	-15 (+/-20)	-9 (+/-12)	0.57	-4 (+/-20)	-12 (+/-18)	0.03	-1 (+/-24)	-7 (+/-9)	0.1
Cognitive functioning	-12 (+/-20)	-33 (+/-37)	0.04	3 (+/-28)	-20 (+/-13)	<0.0001	3 (+/-33)	-7 (+/-9)	0.12
Social functioning	-12 (+/-31)	-39 (+/-21)	0.002	-23 (+/-40)	-46 (+/-28)	0.28	-4 (+/-30)	-14 (+/-18)	0.6
Global health status	-11 (+/-23)	-17 (+/-25)	0.57	-5 (+/-22)	-4 (+/-19)	0.46	3 (+/-28)	14 (+/-13)	0.36
Fatigue	15 (+/-21)	33 (+/-33)	0.07	14 (+/-32)	28 (+/-21)	0.21	-7 (+/-26)	0 (+/-0)	0.07
Nausea/Vomiting	3 (+/-35)	6 (+/-8)	0.88	-15 (+/-27)	22 (+/-30)	0.0008	-19 (+/-28)	0 (+/-0)	0.06
Pain	8 (+/-18)	6 (+/-16)	1	-4 (+/-33)	5 (+/-14)	0.19	-12 (+/-33)	7 (+/-9)	0.16
Dyspnoea	-3 (+/-18)	22 (+/-16)	0.0007	-17 (+/-46)	19 (+/-21)	0.007	-10 (+/-30)	14 (+/-18)	0.12
Insomnia	14 (+/-31)	22 (+/-33)	0.32	-8 (+/-34)	12 (+/-21)	0.051	-21 (+/-33)	0 (+/-0)	0.06
Appetite loss	14 (+/-27)	22 (+/-66)	0.07	-10 (+/-52)	12 (+/-48)	0.09	-39 (+/-41)	-33 (+/-0)	0.01
Constipation	0 (+/-37)	0 (+/-0)	0.5	-27 (+/-43)	5 (+/-18)	0.01	-29 (+/-57)	0 (+/-0)	0.09
Diarrhoea	33 (+/-20)	55 (+/-45)	0.17	-25 (+/-45)	28 (+/-63)	0.02	-33 (+/-35)	-10 (+/-53)	0.3
Financial difficulties	22 (+/-26)	9 (+/-16)	0.09	-6 (+/-37)	21 (+/-43)	0.3	-11 (+/-46)	14 (+/-18)	0.65

Figures

Figure 1:

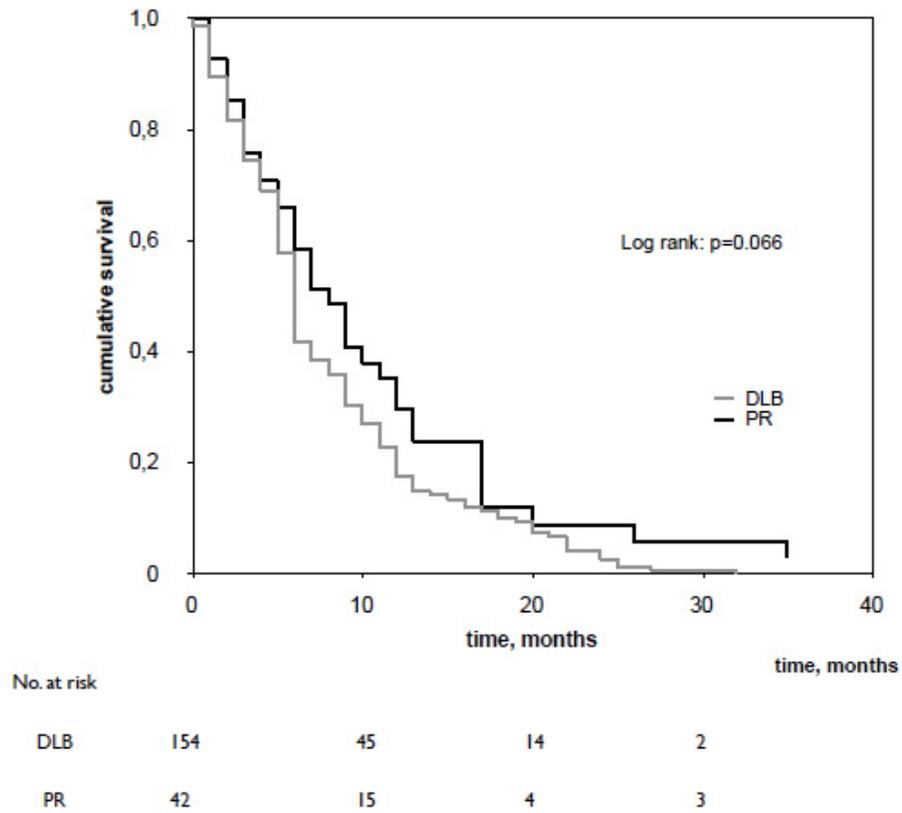


Figure 2:

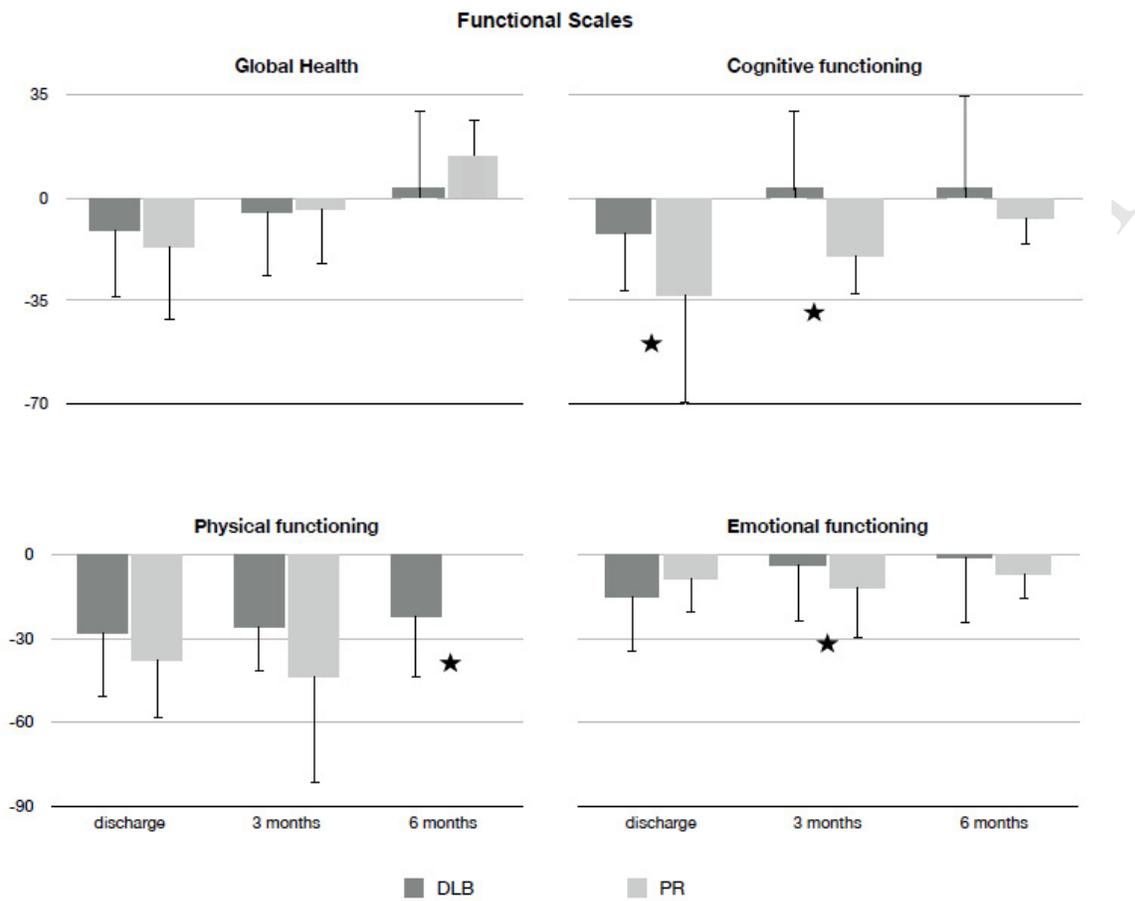
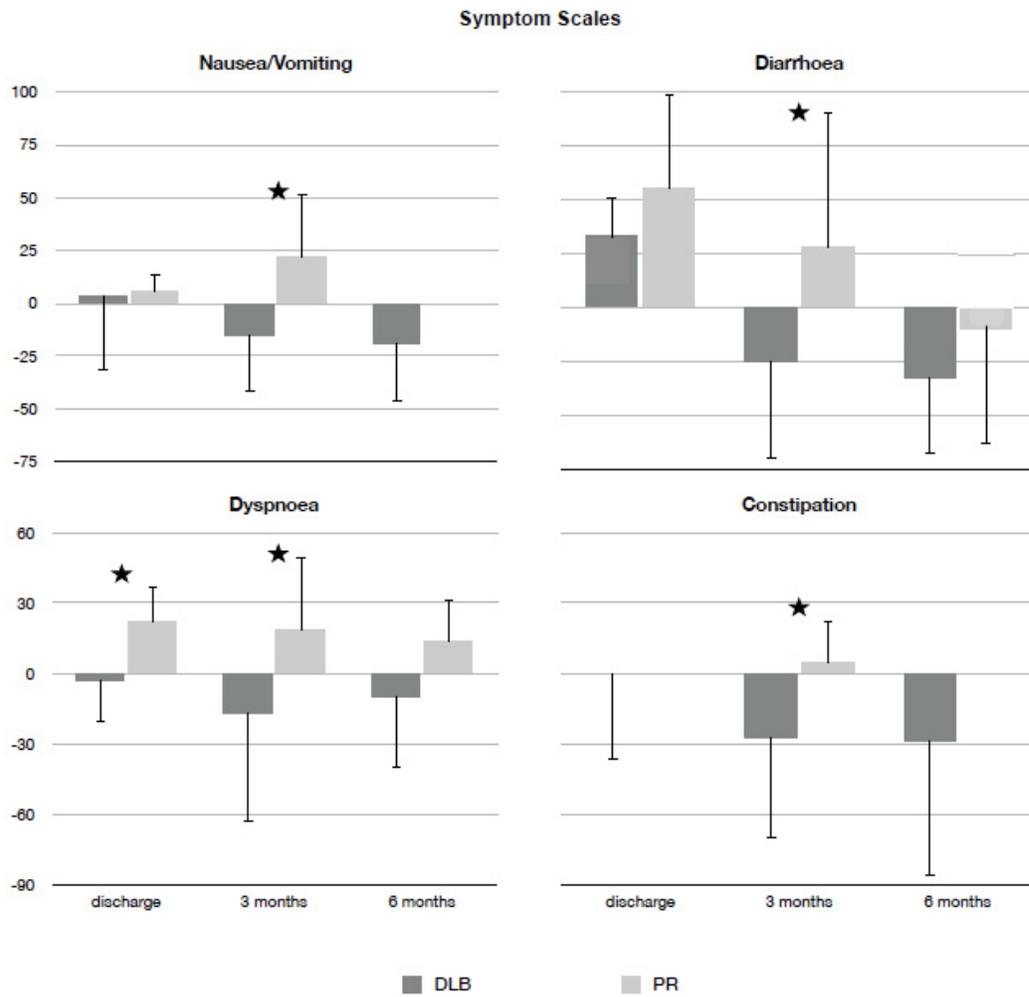


Figure 3:



Tables

Table 1

	Double loop bypass <i>n = 154</i>	palliative pancreaticoduodenectomy <i>n = 42</i>	<i>p</i> value
Patient characteristics			
Median age, years (range)	65 (35-87)	63.5 (47-81)	0.71
Female	73	22	0.57
Male	81	20	0.57
Operative data			
Mean operation time, min	261 +/- 72	439 +/- 127	<0.00001
Mean hospitalisation, days	17 +/- 9	32 +/-21	<0.00001
Postoperative complications			
Overall morbidity, n (%)	59 (38.3)	19 (45.2)	0.42
Delayed gastric emptying, n (%)	22 (14.3)	7 (16.3)	0.7
Pancreatic fistula, n (%)	4 (2.6)	6 (14.3)	0.002
Biliary fistula, n (%)	8 (5.2)	3 (7)	0.63
Haemorrhage, n (%)	6 (3.9)	2 (4.7)	0.8
Cholangitis, n (%)	6 (3.9)	1 (2.4)	0.64
Gastrointestinal leakage, n (%)	2 (1.3)	3 (7)	0.03
Wound infections, n (%)	6 (3.9)	1 (2.4)	0.64
Cardiac complications, n (%)	6 (3.9)	1 (2.4)	0.64
Pneumonia, n (%)	3 (1.9)	3 (7)	0.08
Renal failure, n (%)	1 (1.5)	2 (4.7)	0.055
Others, n (%)	10 (6.5)	3 (7)	0.88
None, n (%)	95 (61.7)	23 (54.8)	0.42
Hospital mortality, n (%)	6 (3.9)	3 (7.1)	0.37
Postoperative chemotherapy, n (%)	117 (76)	30 (71.4)	0.641

Table 2

	DLB	PR	total
Pre-operative	61 (39.6%)	25 (59.5%)	86 (43.9%)
At discharge	61 (39.6%)	17 (40.5%)	78 (39.8%)
3 months after surgery	43 (27.9%)	15 (35.7%)	58 (29.6%)
6 months after surgery	34 (22.1%)	7 (16.7%)	41 (20.9%)

Table 3

	DLB	PR	P-value
Physical functioning	77 (+/-17)	72 (+/-30)	0.63
Role functioning	77 (+/-29)	75 (+/-32)	0.65
Emotional functioning	67 (+/-23)	60 (+/-23)	0.24
Cognitive functioning	83 (+/-23)	87 (+/-15)	0.87
Social functioning	67 (+/-25)	77 (+/-28)	0.08
Global health status	48 (+/-17)	47 (+/-22)	0.73
Fatigue	57 (+/-25)	48 (+/-39)	0.42
Nausea/Vomiting	37 (+/-20)	11 (+/-25)	0.0003
Pain	57 (+/-29)	58 (+/-37)	0.5
Dyspnoea	55 (+/-22)	30 (+/-38)	0.0002
Insomnia	63 (+/-29)	43 (+/-35)	0.02
Appetite loss	71 (+/-28)	49 (+/-33)	0.0006
Constipation	51 (+/-29)	16 (+/-36)	<0.0001
Diarrhoea	43 (+/-22)	32 (+/-39)	0.21
Financial difficulties	52 (+/-25)	10 (+/-30)	0.0007

Table 4

	Difference after discharge			Difference after 3 months			Difference after 6 months		
	DLB	PR	p-value	DLB	PR	p-value	DLB	PR	p-value
Physical functioning	-28 (+/-23)	-38 (+/-21)	0.15	-26 (+/-16)	-44 (+/-38)	0.56	-22 (+/-22)	0 (+/-0)	0.007
Role functioning	-36 (+/-29)	-55 (+/-22)	0.14	-38 (+/-40)	-46 (+/-29)	0.93	-29 (+/-48)	-7 (+/-9)	0.18
Emotional functioning	-15 (+/-20)	-9 (+/-12)	0.57	-4 (+/-20)	-12 (+/-18)	0.03	-1 (+/-24)	-7 (+/-9)	0.1
Cognitive functioning	-12 (+/-20)	-33 (+/-37)	0.04	3 (+/-28)	-20 (+/-13)	<0.0001	3 (+/-33)	-7 (+/-9)	0.12
Social functioning	-12 (+/-31)	-39 (+/-21)	0.002	-23 (+/-40)	-46 (+/-28)	0.28	-4 (+/-30)	-14 (+/-18)	0.6
Global health status	-11 (+/-23)	-17 (+/-25)	0.57	-5 (+/-22)	-4 (+/-19)	0.46	3 (+/-28)	14 (+/-13)	0.36
Fatigue	15 (+/-21)	33 (+/-33)	0.07	14 (+/-32)	28 (+/-21)	0.21	-7 (+/-26)	0 (+/-0)	0.07
Nausea/Vomiting	3 (+/-35)	6 (+/-8)	0.88	-15 (+/-27)	22 (+/-30)	0.0008	-19 (+/-28)	0 (+/-0)	0.06
Pain	8 (+/-18)	6 (+/-16)	1	-4 (+/-33)	5 (+/-14)	0.19	-12 (+/-33)	7 (+/-9)	0.16
Dyspnoea	-3 (+/-18)	22 (+/-16)	0.0007	-17 (+/-46)	19 (+/-21)	0.007	-10 (+/-30)	14 (+/-18)	0.12
Insomnia	14 (+/-31)	22 (+/-33)	0.32	-8 (+/-34)	12 (+/-21)	0.051	-21 (+/-33)	0 (+/-0)	0.06
Appetite loss	14 (+/-27)	22 (+/-66)	0.07	-10 (+/-52)	12 (+/-48)	0.09	-39 (+/-41)	-33 (+/-0)	0.01
Constipation	0 (+/-37)	0 (+/-0)	0.5	-27 (+/-43)	5 (+/-18)	0.01	-29 (+/-57)	0 (+/-0)	0.09
Diarrhoea	33 (+/-20)	55 (+/-45)	0.17	-25 (+/-45)	28 (+/-63)	0.02	-33 (+/-35)	-10 (+/-53)	0.3
Financial difficulties	22 (+/-26)	9 (+/-16)	0.09	-6 (+/-37)	21 (+/-43)	0.3	-11 (+/-46)	14 (+/-18)	0.65

Figures

Figure 1:

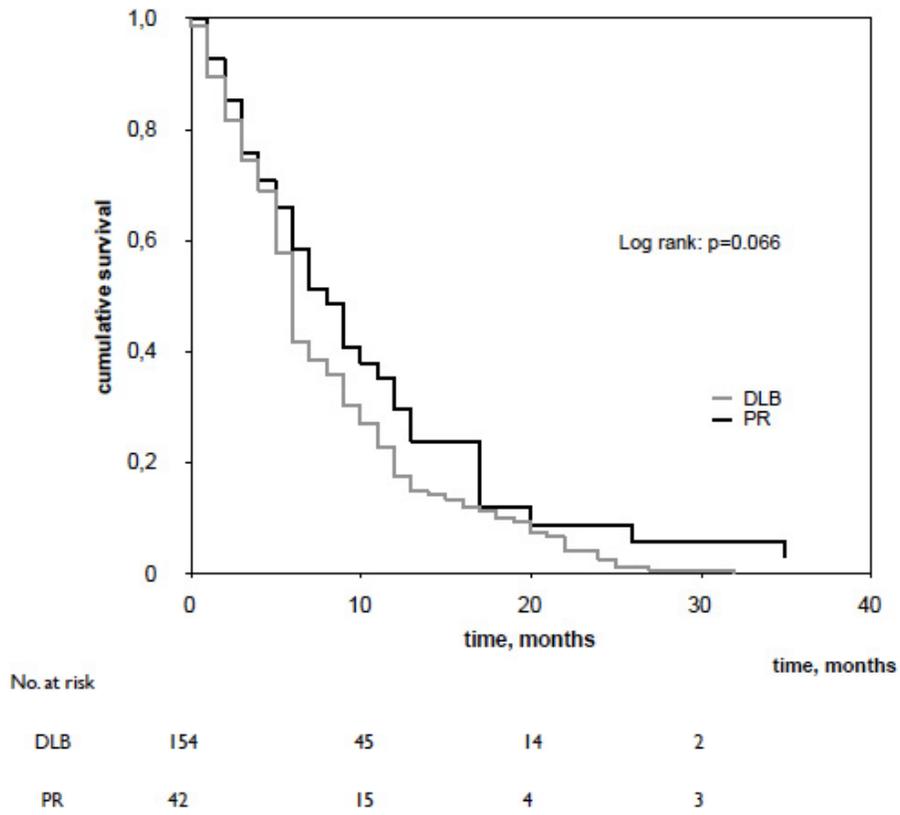


Figure 2:

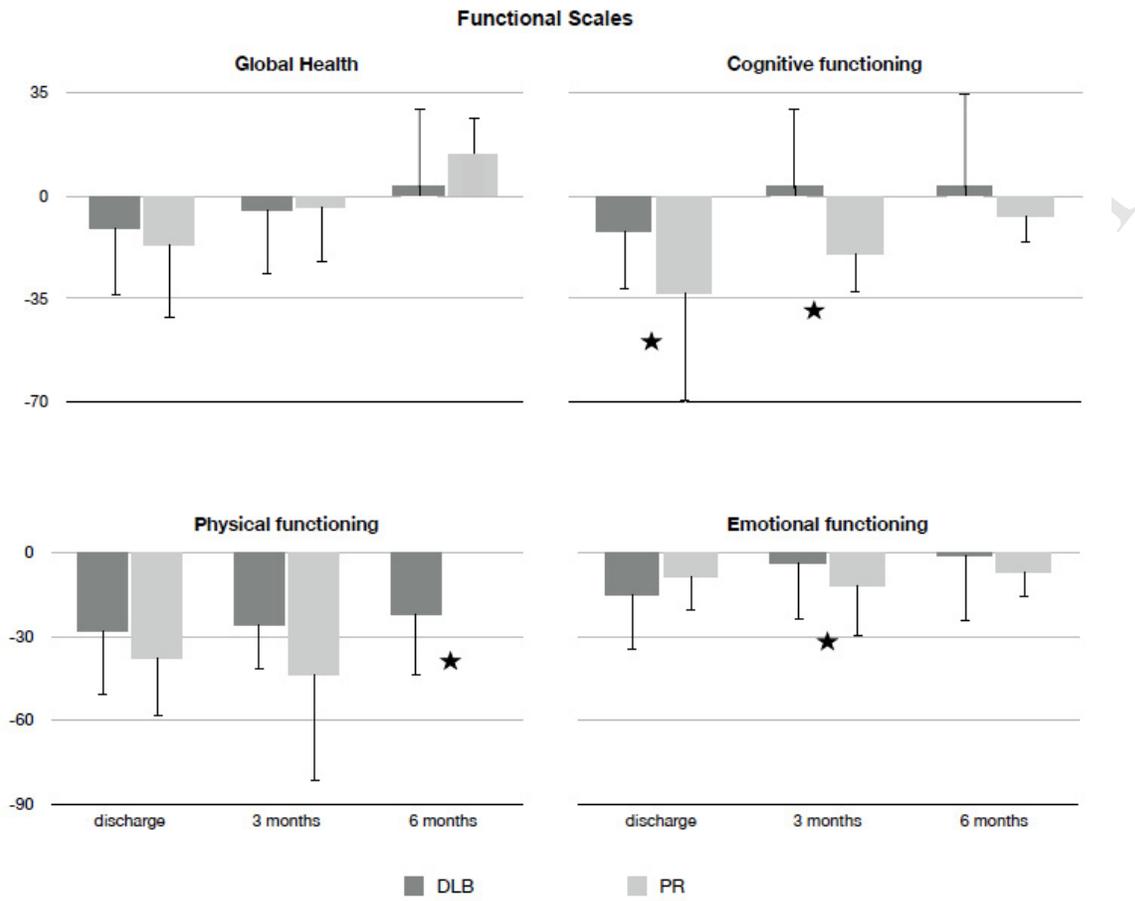


Figure 3:

