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# Quality of life in patients with pancreatic ductal adenocarcinoma undergoing pancreaticoduodenectomy

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ABSTRACT

*Introduction:* Survival for pancreatic ductal adenocarcinoma (PDAC) is relatively short even after complete resection. Pancreaticoduodenectomy (PD) carries a high risk for postoperative morbidity, and the effect on quality of life (QoL) is unclear. We aimed to study QoL in PDAC patients undergoing PD.
*Patients and methods:* Sixty patients with suspected PDAC and planned PD were asked to complete EORTC QoL questionnaires QLQ-C30 and QLQ-PAN26 preoperatively and at 3-6-12-18-24 months postoperatively.
*Results:* 47 PDAC patients who underwent PD (66 (21–84) years, 53% men) were included. Follow-up was completed by 81% (6 months) and 45% (24 months) post-PD. Compared to preoperative level, QoL tended to improve or remained the same in 63% during the follow-up. At three months after PD patients had less hepatic symptoms (decreased by 100%; $p < 0.001$), pancreatic pain and sexuality symptoms tended to decrease by 33% and global and functional QoL tended to slightly improve. These parameters remained at the achieved level during the longer follow-up. A temporary rising tendency was seen in digestive symptoms at three months but this later reverted to the preoperative level. More altered bowel movements and sexuality symptoms tended to arise during the longer follow-up. A negative correlation was found between reported financial difficulties and length of survival.
*Conclusions:* PD does not worsen the QoL in most of the patients with PDAC. The potentially beneficial effect on QoL is apparent already at three months after surgery. This information may be helpful for the clinician and patient, when deciding on the treatment for PDAC.


## 1. Introduction

Survival for pancreatic ductal adenocarcinoma (PDAC) is relatively short, the 5-year survival rates being 22% for localized, 9% for regional and 2% for metastasized disease [1]. The only treatment with a curative potential is surgical resection, usually combined with chemotherapy [2]. When the tumour is located in the head of the pancreas, the surgical treatment is pancreaticoduodenectomy (PD). PD carries a high risk for postoperative morbidity [3] and also considerable mortality, even though it may be minimal in experienced centers. It would be of great importance not to further impair the quality of life (QoL) with surgery for the fairly short life expectancy after the operation. It is not known, however, whether there is any beneficial effect on QoL from surgery, even though this information would be helpful for clinicians and patients when discussing and deciding on the operative treatment for PDAC.

In earlier studies the reported effect of PD on QoL has been somewhat controversial. A retrospective case-control study showed that patients undergoing PD either for PDAC or chronic pancreatitis had slightly poorer QoL postoperatively than patients undergoing laparoscopic cholecystectomy [4]. A prospective study with patients undergoing pancreatic resections (PD in 77%, the remainder subtotal pancreatectomy or distal pancreatectomy) for various reasons (PDAC in 68%) showed that initially during the first two to three weeks after surgery QoL decreased compared to the preoperative level, but improved back to the preoperative level at six weeks and remained stable during the six months follow up [5]. A recent prospective, longitudinal study [6] reported QoL on 68 patients undergoing resection (Pylorus-preserving pancreaticoduodenectomy (PPPD) or Whipple) in 53/68 patients for

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various pathologies (41/68 PDAC) with a one year follow-up. To our knowledge, no studies with a longer follow-up have so far been presented on QoL in PDAC patients undergoing PD.

## 2. Aim

We aimed to study preoperative and postoperative QoL in PDAC patients undergoing PD with a prospective follow-up for up to two years.

## 3. Patients and methods

QoL was assessed using the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30) together with disease-specific pancreatic module QLQ-PAN26 [7–9]. QLQ-C30 is a validated 30-item instrument containing five functional scales (physical, role, emotional, cognitive and social functioning), three symptom scales (fatigue, nausea and vomiting and pain), a global health scale and six single items (dyspnea, insomnia, appetite loss, constipation, diarrhoea, and financial difficulties). QLQ-PAN26 is a 26 item questionnaire developed specifically to assess symptoms related to pancreatic cancer. There are seven multiple item scales (pain, digestive symptoms, altered bowel habits, hepatic, body image, satisfaction with health care and sexuality). During our analysis, we discovered that there had been a mistake in translating question 46 from the original English PAN-26 to Finnish version, significantly distorting the meaning of the original question. As a result, question 46 was excluded from analysis, and altered bowel movements were analysed by scaling question 47 only.

Sixty patients with suspected PDAC and planned PD during 2006–2008 were asked to complete QLQ-C30 and QLQ-PAN26 preoperatively. Out of those 60 patients three tumours were discovered to be unresectable, on one patient a total pancreatectomy was performed, and two patients withdrew from the study after surgery. In addition, patients were excluded if the final pathological analysis of surgical specimens revealed any pathology other than PDAC. The 47 patients with a final diagnosis of PDAC completed QoL questionnaires preoperatively and at 3, 6, 12, 18 and 24 months postoperatively. Postoperative pancreas-related morbidity was graded according to the International Study Group of Pancreatic Surgery (ISGPS) guidelines for post-operative pancreatic fistulae (POPF), post-pancreatectomy hemorrhage (PPH) and delayed gastric emptying (DGE) [11–13], and overall morbidity according to the Clavien-Dindo classification [14]. In-hospital, 30-day and 90-day mortality was recorded. Chemotherapy was administered according to normal treatment protocols in our hospital, and taken into consideration during analysis.

Focus of our study was in longitudinal comparison within the study group. In addition, we aimed to compare our findings in general population. No Finnish data reporting QoL on general population was found. To compare our results to those of general population, a study reporting normative data on a Dutch population [10] was used instead. This study reported the results from a QLQ-C30 questionnaire with 1.731 respondents (78%, 935 men and 796 women, median age 54.7 and 50.8 years, respectively). Of these, 651 (38%) reported that they did not have any chronic health problem. 128 (7%) had ever been diagnosed with cancer. Men had heart disease more often than women (11% vs. 4%, $p < 0.0001$). Other chronic diseases reported were asthma/COPD, depression, joint conditions, diabetes, hypertension, diseases of the stomach, kidneys or liver and thyroid conditions [10].

## 4. Statistical analysis

The data acquired with the QLQ-C30 and QLQ- PAN26 questionnaires was scaled on a scale from 0 to 100 according to the instructions from the EORTC scoring manual taking into account that in positive parameters (functional QoL, global QoL) a high score means good QoL, and in symptom parameters (hepatic symptoms, pancreatic pain, etc.) a high score means numerous symptoms and poorer QoL. Changes in the results during follow-up were compared to preoperative values using Wilcoxon's signed rank test. Spearman's correlations were calculated to observe possible correlations between QoL variables and length of survival. The group of patients receiving postoperative chemotherapy was compared to the patients not receiving chemotherapy with Mann-Whitney test.

## 5. Ethical aspects

The study protocol was duly inspected and approved by the ethics committee of Pirkanmaa Hospital District. The participants received a letter informing them about the study protocol and requesting their written consent. The participants were asked to complete EORTC QoL questionnaires QLQ-C30 and QLQ-PAN26 preoperatively and at 3, 6, 12, 18 and 24 months thereafter.

## 6. Results

Median age of the 47 patients included was 66 years (range 21–84, 53% men). After three to six months 81% of the patients were still retained in follow-up, after 12 months 62%, after 18 months 49% and at 24 months 45%. Survival and follow-up statistics are highlighted in Table 1. Overall median survival was 26 months (2–107 months). Out of 47 patients eight were still alive in August 2015 with a survival time of 79–107 months. 41 out of 47 patients received chemotherapy postoperatively.

### 6.1. Morbidity and mortality

Postoperative morbidity is shown in Table 2. Clinically relevant grade B-C complications were 10% for POPF, 12% for PPH and 19% for DGE. Clavien-Dindo grade 3–4 overall complications were seen in 30% of the patients. In-hospital mortality and 30-day mortality were zero, and 90-day mortality 4% (2/47).

### 6.2. QLQ-C30 functional quality of life

In QLQ-C30, Functional QoL (Fig. 1) was reported to be 82 (35.7–100.0) (median; range) preoperatively. At three months postoperatively, it was at the preoperative level 82 (24.4–100.0) and remained at that level during longer follow-up.

Physical functioning was reported to be 80 (26.67–100.00) preoperatively. At three months postoperatively, it was 73 (0.0–100.0) and from six months to 18 months it was constantly 80. At 24 months physical functioning was reported to be 67 (20.0–100.0). There were no statistically significant changes during follow-up.

Role functioning was reported to be 83 (0.0–100.0)

**Table 1**
Number of patients responding to the questionnaire and number of patients alive at the different time points.

| | Baseline | 3 months | 6 months | 12 months | 18 months | 24 months |
|---|---|---|---|---|---|---|
| Patients, n responding/ alive | 47/47 | 38/45 | 38/42 | 30/33 | 23/25 | 20/23 |

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