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*Original Research*

# Factors affecting mortality, morbidity and survival in pylorus-preserving pancreaticoduodenectomy

Results of pylorus preserving pancreaticoduodenectomy

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**Abstract**
Aim: Pancreatic tumors are considered highly mortal cancers worldwide, and surgical resection is considered the only curative method. Because of the efficacy of surgery as the gold standard treatment, finding the most accurate technique has been always important in the literature and clinical practice. Herein, we aimed to report our results in patients with periampullary tumors in whom we performed pylorus-preserving pancreaticoduodenectomy.
Material and Methods: We analyzed our results in patients who had been operated with pylorus-preserving pancreaticoduodenectomy for periampullary malignancy in a single tertiary center for 5 years, in terms of operative features, postoperative complications and survival.
Results: A total of 48 patients were involved in the study, and 37 of them had been operated with pylorus-preserving pancreaticoduodenectomy for periampullary malignancy. In 48 patients, 33 were males with a mean age of 60.73 years and 15 were females with a mean age of 56.9 years. The most common localization was pancreatic head (25 patients, 52%). We did not find any converse effects of pylorus-preserving technique on postoperative complications or survival. Although not significant, survival was longer in the group with extended lymph node resection.
Discussion: Although there is still a lack of standardized and randomized prospective studies with large study groups, pylorus preserving technique is accepted as an advantageous option in means of complications and hospital stay. We think that our results are consistent with the literature and may contribute to larger review studies.

**Keywords**
Pancreatic Cancer, Periampullary Tumors, Pylorus-Preserving Pancreaticoduodenectomy, Whipple Procedure

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## Introduction

### *Incidence, history and surgical technique*

Pancreatic cancer is considered as one of the most mortal gastrointestinal tract cancers with a 5-year overall survival rate of 5% to 13% [1]. By 2018, it is the fourth leading cause of cancer deaths in the Western World [1]. The tumor is usually found at the head of the organ (60-70%), while 25% are in the body or tail [2]. Pancreatic ductal adenocarcinoma represents most of all pancreatic neoplasms (85-90%) [3].

The gold standard curative treatment of tumors of the periampullary region, including pancreatic head is surgical resection. There are mainly two options of performing the surgery including standard or pylorus resection pancreaticoduodenectomy (prPD) and pylorus- preserving pancreaticoduodenectomy (ppPD). In prPD, resection involves the head of the pancreas with distal stomach, duodenum, distal common bile duct. The standard technique was first introduced by Whipple and Trimble in 1941 [4]. Shortly after following the first surgeons, Watson showed a modified technique preserving the distal stomach and pylorus mainly to decrease operative time and complications due to resected stomach [5]. In prPD, distal stomach and pylorus are resected and a gastrojejunostomy is performed to complete the gastrointestinal tract, while these parts are preserved and a duodenojejunostomy is created in ppPD [4]. Following the introduction of ppPD, the two techniques were compared for many times in various publications, indicating that they were similar in means of operative time, number of transfusions, and blood loss, but ppPD could cause a higher incidence of delayed gastric emptying (DGE) [6]. Although studies concerning the results of the two techniques usually focus on DGE, R0 tumor resection, recurrence rates and disease-free survival have been other important matters about the safety of ppPD [7].

### *Concerns about ppPD*

The main concerns regarding the oncologic safety of ppPD are usually influenced by the fact that this technique was initially introduced for the treatment of benign disorders such as chronic pancreatitis, and later republished for the treatment of periampullary malignancies [5]. Besides these controversies, most of the studies showed that ppPD decreases the operational time, blood loss, need for transfusions with no overall increase in tumor recurrence or survival [7]. Following the doubts of the surgeons about ppPD in terms of insufficient oncologic resection, negative-margins, and nodal dissection [8], none of the randomized controlled trials or meta-analyses have shown statistically significant differences [7].

### *Delayed gastric emptying, definition, incidence*

Not only oncologic results, but also the risk of ppPD-related DGE is still studied and discussed today in various studies [9]. DGE is mainly thought to be caused by the functional defect of the propulsive action, the most important parts of which are the stomach and pylorus [10], and the incidence is reported as very wide in different studies varying between 4.5% and 45% [11]. Unfortunately, the underlying mechanism of DGE is thought to be multifactorial and has not been defined clearly, yet. Publications before 2007 defined DGE as the need for a nasogastric tube still on a postoperative day 7 to 10, while the International Study Group of Pancreatic Surgery (ISGPS) classified and graded DGE in 2007 [12]. Today, researchers focus on interrupted neural connections, local ischemia and partial or complete impairment of hormonal production in the mechanism of DGE [13]. Although DGE is a serious complication, it is not life-threatening itself. But more importantly, it has been shown to be related with other postoperative complications such as fistula and intraabdominal abscesses [14]. DGE impairs and prevents early oral intake, resulting in extended length of hospital stay and delay in postoperative adjuvant chemotherapy, which has a negative impact on survival [10].

In the German prospective single-center PROPP trial, prPD was not shown to be related with decreased incidence or severity of DGE, but conversely tended to have a higher incidence of DGE [15]. On the other hand, there are other published meta-analyses showing ppPD with increased rates of DGE [9]. The controversies are also similar in randomized trials. One of these studies including 33 patients showed 43% DGE in ppPD and zero percent in prPD [16], while another randomized trial did not show any differences between the two techniques [17].

Up to date, there are no high-quality multicentred randomized controlled trials proving the superiority of one of the techniques in means of survival or DGE and other major complications.

### *Aim of this study*

Published studies up to date defined the concerns about ppPD in means of oncologic results and causing DGE, which also decreases the quality of life and survival because of its chronic nature. The results are controversial, and there are no proven facts showing the disadvantages of ppPD. We aimed to show our postoperative results in ppPD patients to investigate and hypothesize that the technique is not disadvantageous in means of oncological results, survival, and DGE as a postoperative complication.

## Material and Methods

Following approval of the local ethics committee, the records were analyzed retrospectively. A total of 48 patients were involved in the study, and 37 of them had been operated with pylorus-preserving pancreaticoduodenectomy for a periampullary malignancy in a single tertiary center over a 5-year period. Demographics of the patients, symptoms, comorbid diseases, biochemical tests, tumor features, operational technique, postoperative complications, survival rates were retrospectively analyzed. For statistical analysis, the Mann-Whitney U, Wilcoxon W, Chi-square and Mantel-Cox tests were used. The survival analysis in groups was performed with the Kaplan-Meier method, and the survival comparison between groups and subgroups were performed with the Logrank (Mantel-Cox) test. Statistical significance was accepted as $p < 0,05$.

## Results

Thirty-seven of 48 patients were operated with ppPD for a periampullary tumor over a period of 5 years. Of the 48 patients, 33 were males (68,7%) with a mean age of 60.73 years and 15 were females (31,2%) with a mean age of 56,9 years. The most common localization was the pancreatic head (25 patients, 52%). Demographics were not found to be statistically significant with the chi-square test.

Jaundice was the most common preoperative symptom, seen in 40 patients (83,3%), abdominal pain (24 patients, 50%) and pruritus (16 patients, 33,3%) were other common symptoms. Hypertension was the most common comorbid disease which was seen in 13 patients (27,8%), followed by type II diabetes mellitus (n:13) and ischemic heart disease (n:3). Neither symptoms nor comorbidity were found to be statistically significant using the Wilcoxon W and Mann-Whitney U tests.

The mean operation time was 330 minutes (300-360). The mean number of peroperative blood transfusions was 1.2 units (0-3). While ppPD was performed in 37 patients (77,1%), 11 of the patients were accepted as inoperable during the operation.

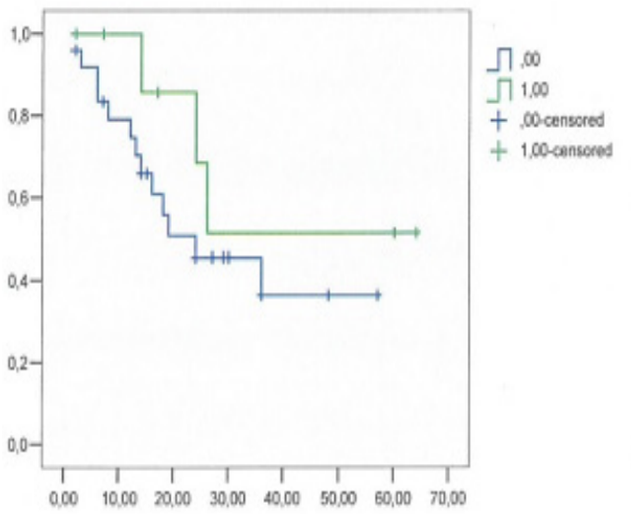


**Figure 1.** Cumulative survival probability (in months)

**Table 1.** Survival rates of patients (Survival in 'months')

| | Medial | | | | Median | | | |
|---|---|---|---|---|---|---|---|---|
| | Survival | Std Dev | 95% Confidence | | Survival | Std Dev | 95% Confidence | |
| | | | Min | Max | | | Min | Max |
| Operable | 36,26 | 4,71 | 27,03 | 45,49 | 26 | 9,05 | 8,26 | 43,74 |
| Inoperable | 13,67 | 3,7 | 6,41 | 20,93 | 12 | 2,8 | 6,52 | 17,48 |
| Total | 31,82 | 4,1 | 23,79 | 39,85 | 24 | 3,66 | 16,83 | 31,17 |
| | Chi-square | df | Significance | | | | | |
| Log Rank (Mantel-Cox) | 6,34 | 1 | 0,012 | | | | | |

**Table 2.** Extended lymph node dissection and survival (Survival in 'months')

| | Medial | | | | Median | | | |
|---|---|---|---|---|---|---|---|---|
| | Survival | Std Dev | 95% Confidence | | Survival | Std Dev | 95% Confidence | |
| | | | Min | Max | | | Min | Max |
| - | 30,73 | 4,76 | 21,39 | 40,06 | 24 | 10,13 | 4,15 | 43,85 |
| + | 43,49 | 8,63 | 26,58 | 60,39 | - | - | - | - |
| Overall | 36,26 | 4,71 | 27,03 | 45,49 | 26 | 9,05 | 8,26 | 43,74 |
| | Chi-square | df | Significance | | | | | |
| Log Rank (Mantel-Cox) | 1,12 | 1 | 0,29 | | | | | |

Hepaticojejunostomy could be performed in 9 of these patients, and only a tru-cut biopsy could be performed in the remaining 2 patients. In our operabl ppPD group duct-to-mucosa anastomosis was performed in 27 patients (72,9%) in whom the Wirsung duct was ≥3 mm, while Dunking-type anastomosis was performed in the remaining 10 patients with the Wirsung duct of <3mm. Extended lymph node dissection (LND) was performed in 12 patients (32,4%) increasing the operational time with a mean time period of 20 minutes. Operational features were not found to be significantly significant due to the chi-square test.

Local wound infection was the most common postoperative complication, encountered in 6 patients (12,5%). Other complications were pancreatic fistula, hemorrhage and delayed gastric emptying (DGE). There was no any significant relation between comorbid disease and postoperative complications. There was no any significant relation between biochemical results and postoperative complications. Similarly, the type of anastomosis was not found to be significantly effective in terms of postoperative complications rates. Postoperative hospital stay was 11.1 days in operable patients (8-44), while it was found to be 8.2 days (7-13) in inoperable ones. The significance was determined due to Mann-Whitney U and chi-square tests.

The average survival was found to be 36.3 months (med:26 months) in resected ppPD patients, while it was 13.6 months ( med:12 months) in inoperable patients. The difference was statistically significant (p:0.012) as shown in Table 1. Tumor localization or postoperative complications were not found to significantly affect survival. Survival rates were analyzed with the Kaplan-Meier method.

Although it was not statistically significant when compared to other operable patients, the average survival was 43.4 months (med:24 months) in the group with extended lymph node dissection ( Table 2 and Figure 1). Significance between these subgroups was performed with Logrank (Mantel-Cox) test.

## Discussion

Although pancreaticoduodenectomy has been curative gold standard treatment for periampullary tumors for many years, the efficacy and long-term results of ppPD compared to prPD still remain questionable. Besides numerous published studies, the choice of surgical technique often depends on the practice of the surgeon and the institution. In our study, we aimed to analyse and define our results after performing ppPD and report short- and long-term results. We used statistical methods to determine data in means of short-term complications such as DGE, oncological results such as LND and survival, and overall costs such as length of hospital stay.

Pylorus preserving technique has some advantages with regard to shorter operational time, lesser blood loss and fewer blood transfusions, similar to our results [18]. Patients undergoing ppPD had a lower mortality and shorter hospital stay when compared to prPD [19]. Although in a smaller group of patients, a Cochrane review showed opposite results [11]. In most of the studies, ppPD offers a significantly shorter hospital stay when compared to the standard technique [20]. Previous studies have reported higher rates of postoperative complications, including

DGE, which led to longer hospital stay [6]. There are also studies showing that even DGE occurrence did not increase the length of stay following ppPD technique [21]. Although we did not compare with the standard technique, both the rate of DGE was lower and the length of stay was shorter when compared to standard pancreaticoduodenectomy results in the literature. It is well known that DGE is not mortal itself, but it is a serious complication deteriorating quality of life, even decreasing survival by delaying the start of adjuvant chemotherapy. Underlying mechanisms are thought to be gastric atony following vagatomy, resection of duodenal neural tissues and ischemic injury of distal stomach, intraabdominal complications and decreased motilin levels [22]. There is a remarkable inconsistency in systematic reviews regarding the DGE incidence in terms of surgical technique [23]. The rate of DGE is reported to be between a large scale of percentage, occurring in 19-57% of the patients [12].

Our goal was not only to determine postoperative complications, but also to analyze the oncological outcomes of ppPD technique. The data are retrospective and we did not compare with a prPD group, which is open to bias naturally. Researchers state that long-term survival mostly depends on the extension of LND. Early studies analyzed ppPD technique for oncological concerns in relation tolymph node and margin status [8]. Yeo et al. reported that the standard prPD technique provides a higher number of dissected lymph nodes [24]. More recent studies showed similar results and no significant difference in means of oncological status [6,19]. Although not statistically significant, we provided adequate LND and acceptable survival even without causing a significant increase in the length of hospital stay. Both our survival rates were acceptable in the standard ppPD and the extended LD group, 36.3 and 43.4 months, respectively, which may be a sign of objection to concerns for the oncological results of the ppPD technique.

## *Conclusion*

Pylorus-preserving technique is performed less frequently than the standard resection in the world. Although there are published studies suggesting opposite results, none of the two techniques is significantly superior to another in means of oncological results or overall survival. But today, it is accepted that ppPD has advantages in terms of shorter hospital stay and short-term postoperative complications, which may indicate that the technique is a good choice when the tumor is not on the first part of the duodenum.

There is still a lack of standardized and randomized prospective studies with large study groups comparing the two techniques. In addition to all the published studies, the choice of the surgeon and traditions of a tertiary institute played roles in preferring the resections technique as well as literature findings. The limitations of our study are its retrospective design, the absence of comparison with the standard technique and single-center results, which may lead to statistical bias. Even so, we think that our result may show the advantages of ppPD technique in the literature, which can contribute to larger review studies.

***Scientific Responsibility Statement***

*The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.*

***Animal and human rights statement***

*All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.*

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***Conflict of interest***

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