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Metabolic and surgical factors affecting postoperative quality of life in patients with total pancreatectomy with or without splenectomy: Single center results

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ABSTRACT

Objective: Pancreatic resection may be required in the treatment of patients with pathologies of the pancreas. Total pancreatectomy is a major surgical procedure with serious risk of mortality and morbidity, and patient selection is important for prognosis. The endocrine and exocrine pancreatic insufficiency that develops in patients after total pancreatectomy can lead to a serious decrease in the quality of life of the patients due to pain, diarrhea, vomiting etc. Our aim was to evaluate the effect of total pancreatectomy with spleen preservation as well as splenectomy on the quality of life of the patients.

Material and Methods: In our study, we retrospectively analyzed the data of patients diagnosed with pancreatic cancer, intrapapillary mucinous neoplasia, pancreatic neuroendocrine tumors, and chronic pancreatitis undergoing from partial to total pancreatic resections in our clinic between 12/2017 and 12/2022. Quality of life was compared using the EORTC QLQ-C30 scale.

Results: A total of 47 total pancreatectomy patients, 30 (63.8%) males and 17 (36.2%) females, were included in the study. Mean age of the patients was 61.38 (39-83) years. Five (35.7%) patients underwent perioperative total pancreatectomy because of high risk of pancreatic fistula development due to hard parenchyma and narrow pancreatic duct. Patients had a perioperative blood loss of 500 mL or more, and there was a statistically significant increase in perioperative blood loss compared to patients without vascular resection ($p< 0.001$). Forty (85.1%) patients used enzyme preparations to replace pancreatic enzymes.

Conclusion: After total pancreatectomy, quality of life of the patients is reduced both by surgical factors and by metabolic factors due to endocrine and exocrine insufficiency in the postoperative period.

Keywords: Total pancreatectomy, pancreatic insufficiency, splenectomy, quality of life

INTRODUCTION

The pancreas is a vital organ in the regulation of metabolism with both endocrine and exocrine functions (1). Pancreatic resection may be required in the treatment of patients with pathologies such as solid or cystic tumors of the pancreas, pancreatic trauma, chronic hereditary pancreatitis (2-4). The resection of the pancreas can be partial or total, depending on the pathology.

After the first successful total pancreatectomy was performed by the Viennese surgeon Theodor Billroth in 1884, there have been many developments in pancreatic surgery over the last century, but the high mortality and morbidity rates have made surgeons hesitant about pancreatic surgery (5). However, there has been an increase in the number of pancreatic surgeries and total pancreatectomies in the last 2-3 decades due to new treatment modalities, surgical techniques, surgeons' experience and knowledge, and the increase in the number of health care institutions with high technology and facilities.

Total pancreatectomy is a major surgical procedure with serious risk of mortality and morbidity, and patient selection is important for prognosis. Patient's age, performance status, and comorbidities are the determinants of perioperative and postoperative mortality and morbidity, and it is important to operate on the patient with the correct indication (6). Common indications for elective total pancreatectomy include chronic pancreatitis that is refractory to medical management, premalignant lesions (intraductal papillary mucinous neoplasms) where partial resection is not sufficient, pancreatic neuroendocrine tumors, and

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malignant tumors of the pancreas (2-4). In addition, conversion total pancreatectomy is performed in patients who are scheduled for partial pancreatectomy but considered to be at high risk of developing pancreatic fistula in the postoperative period, and completion total pancreatectomy is also performed after complications such as postoperative bleeding and abscess development after partial pancreatectomy (7-9).

Another reason for the high mortality and morbidity rates in pancreatic surgery is the anatomical location of the pancreas and the multiple gastrointestinal system (GIS) reconstructions after resection. The retroperitoneal location of the pancreas, its close proximity to the duodenum, its proximity to major vascular structures, and its proximity to almost all organs in the upper abdomen make the operation technically difficult (10,11). GI resections and anastomoses, biliary anastomosis and vascular resections performed together with pancreatic resection increase the possibility of complications in the postoperative period and thus prolong the follow-up process (10,12). Splenectomy is also performed together with pancreatectomy in some patients due to the close proximity of the spleen and its vascular structures. Patients who undergo splenectomy are at risk for infectious diseases, such as encapsulated bacterial infections, in which the spleen plays a protective role in the postoperative period (13).

The exocrine pancreas is one of the most important organs in the absorption of nutrients with the digestive enzymes it produces. As a result, patients who undergo total pancreatectomy develop exocrine pancreatic insufficiency and may experience malnutrition, weight loss, persistent diarrhea and vomiting, which can reduce quality of life and even lead to serious morbidity and mortality (14,15). The endocrine pancreas is responsible for the production and release of hormones that regulate metabolism, and after total pancreatectomy, patients will not produce insulin and will develop diabetes. Endocrine pancreatic insufficiency leads to increased comorbidities, continuous diet and medication use, and serious morbidities in uncontrolled diabetes (16).

The endocrine and exocrine pancreatic insufficiency that develops in patients after total pancreatectomy can lead to a serious decrease in the quality of life of the patients due to these reasons. Therefore, frequent follow-up, pain relief, appropriate pancreatic enzyme replacement, and diabetic treatment plans should be established in the postoperative period to reduce mortality and morbidity and prevent decreased quality of life (17-19).

MATERIAL and METHODS

Patient Selection and Data Collection

In our study, we retrospectively analyzed the data of patients diagnosed with pancreatic cancer, intrapapillary mucinous neoplasia, pancreatic neuroendocrine tumors, and chronic pancreatitis undergoing from partial to total pancreatic resections in our clinic between 12/2017 and 12/2022. Demographic data, preoperative, perioperative and postoperative data, pathological data, current complaints if any, insulin use and prognosis of the patients were evaluated, and performance status was determined by the Eastern Cooperative Oncology Group (ECOG) performance status scale, and comorbidities were determined by the American Society of Anesthesiologists (ASA) physical status score (20,21). Postoperative complications were determined according to the Clavien-Dindo classification (22). Quality of life was compared using the EORTC QLQ-C30 scale (23). Emergency total pancreatectomies were not included in the study. Patients were called and asked about severe diarrhea, persistent vomiting, symptoms of weight loss suggesting exocrine pancreatic insufficiency, use of pancreatic enzymes, and use of insulin to assess endocrine insufficiency status. Early postoperative period was defined as the first 30 days. Relatives of the patients with late excitus were also called and asked about the pre-excitus period. Quality of life scale was administered to the surviving patients to assess both the preoperative period and the postoperative period.

Perioperative Data

All operations were performed by the same team of surgeons with a high level of experience in hepatobiliary surgery. Perioperative blood loss was assessed in all patients, and there were patients in which vascular resections were performed. Patients with adhesions to the spleen and splenic vascular structures or tumors invading the spleen underwent concomitant splenectomy. Patients who underwent partial resection and had a high risk of pancreatic fistula underwent total pancreatectomy at the discretion of the surgeon.

Statistical Analysis

Microsoft Office Excel 2023 was used for data collection, and SPSS version 26 (IBM, Armonk, New York, USA) was used for analysis. Independent samples t-test (for normally distributed data) and Mann-Whitney U test (for abnormally distributed data) were used to compare continuous variables between the study groups. Chi-square test was used for categorical variables. $p< 0.05$ was considered statistically significant.

The study was conducted in accordance with the tenets of the Declaration of Helsinki, and ethical approval was granted by the Ethics Committee of Ege University Hospital with document number 23-9.1T/26.

RESULTS

A total of 47 total pancreatectomy patients, 30 (63.8%) males and 17 (36.2%) females, were included in the study. Mean age of the patients was 61.38 (39-83) years. According to performance status, 16 (34%) patients were ECOG1, 24 (51.1%)

patients were ECOG2, seven (14.9%) patients were ECOG3. Four (8.5%) patients were ASA1, 24 (51%) patients were ASA2, 18 (38.3%) patients were ASA3, and one (2.1%) patient was ASA4. While 14 (29.8%) patients had no comorbidity, several patients had multiple comorbidities as follows: 19 (40.1%) patients had diabetes mellitus (DM), 19 (40.1%) patients had hypertension, three (6.4%) patients had cerebrovascular disease, three (6.4%) patients had coronary artery disease, and one (2.1%) patient had liver cirrhosis in the preoperative period (Table 1). Mean preoperative body mass index was 23.7. Forty-four (90.7%) patients were operated for pancreatic mass, while three (9.3%) patients were operated for chronic pancreatitis. Localization of the tumor in the pancreas was in the head of the pancreas in 32 (68.1%) patients. Thirty-five (74.5%) patients underwent simultaneous splenectomy.

When the median survival of patients who underwent splenectomy was evaluated according to their performance, 10 (28.6%) patients were ECOG1, 19 (54.3%) patients were ECOG2 and six (17.1%) patients were ECOG3, and it was found that there was no significant effect on the median survival (p= 0.717). The same subgroup analysis for patients with splenectomy was made according to ASA scores, and it was found that three (8.6%) patients were ASA1, 18 (51.4%) patients were ASA2, 13 (37.1%) patients were ASA3 and one (2.1%) patient was ASA4, and there was no significant effect on median survival (p= 0.973) (Figure 1).

Table 1. Characteristics and outcomes of the study group

	n= 47
Sex	
Male	30 (63.8%)
Female	17 (36.2%)
Age (mean)	61.38 (39-83)
ECOG	
1	16 (34%)
2	24 (51.1%)
3	7 (14.9%)
ASA	
1	4 (8.5%)
2	24 (51.1%)
3	18 (38.3%)
4	1 (2.1%)
Comorbidity	
HT	19 (40.1%)
DM	19 (40.1%)
CVD	3 (6.4%)
CAD	3 (6.4%)
CIRR	1 (2.1%)
Alcohol abuse	18 (38.2%)
Tobacco abuse	27 (57.4%)
Pancreas pathology	
Malignancy	37 (78.7%)
IPMN	4 (8.5%)
Pancreas NET	3 (6.4%)
CP	3 (6.4%)
Overall survival (month)	36.61 (0-57)
Exitus	35 (74.4%)

HT: Hypertension, DM: Diabetes mellitus, CVD: Cerebrovascular disease, CP: Chronic pancreatitis CAD: Coronary artery disease, CIRR: Cirrhosis.

Perioperative blood loss of 500 mL or more was observed in 18 (51.5%) patients who underwent splenectomy and no significant difference was found compared to the non-splenectomy group (p= 0.549). According to the Clavien-Dindo classification of patients who underwent splenectomy, the patients were stratified as follows: twenty-three (65.7%) of them as stage 2, four (11.4%) of them as stage 3, three (8.6%) of them as stage 4 and finally three (8.6%) of them as stage 5. Complications that developed in these patients were intraabdominal abscess in three (8.6%) patients, bleeding in two (5.7%) patients, sepsis in three (8.6%) patients, and early mortality in one (2.9%) patient; no significant difference was found compared to the non-splenectomized group. Mean length of hospital stay was 24.89 days in patients who underwent splenectomy and 21.42 days in those who did not. No significant difference was observed between the two groups (p= 0.449). Mean survival time was 23.3 months in patients who underwent splenectomy and 26.25 months in patients who did not undergo splenectomy; no significant difference was found between the two groups (p= 0.509).

Fourteen (29.7%) patients underwent partial resection prior to total pancreatectomy. Nine (64.2%) of these patients underwent perioperative total pancreatectomy because of positive surgical margin after frozen section and five (35.7%) patients underwent perioperative total pancreatectomy because of high risk of pancreatic fistula development due to hard parenchyma and narrow pancreatic duct.

Vascular resection with pancreatectomy was performed in 17 (36.2%) patients. According to the Clavien Dindo classification, 12 (25.5%) patients were stage 2, two (4.2%) patients were stage 3, one (2.1%) patient was stage 4, and one (2.1%) patient was stage 5. All of these patients had a perioperative blood loss of 500 mL or more, and there was a statistically significant increase in perioperative blood loss compared to patients without vascular resection (p< 0.001). Intraabdominal bleeding was observed in two (11.7%) patients who underwent vascular resection in the postoperative period. The duration of postoperative hospital stay was 23.4 (6-60) days in patients who underwent vascular resection and 18.23 (4-61) days in those who did not; there was no statistically significant difference in the duration of hospital stay (p= 0.086). Overall survival was 26.3 (17-35) months in patients who underwent vascular resection. Vascular resection had a statistically significant effect on overall survival (p= 0.019).

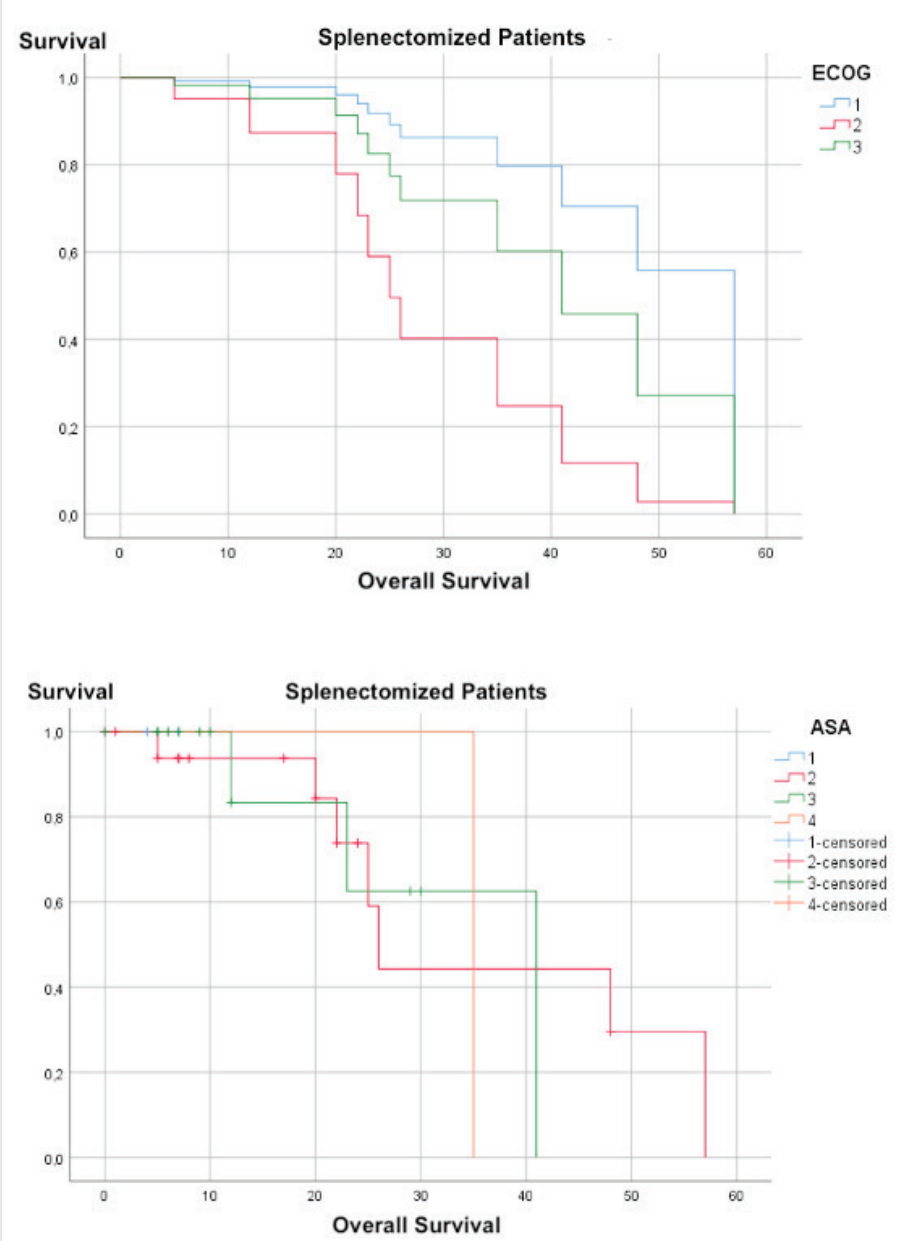

Figure 1. Survival analysis according to the ASA and ECOG scores.

Of the 17 patients who underwent vascular resection, one (5.8%) had arterial and 16 (94.2%) had venous vascular resection. Among the patients who underwent venous vascular resection, 12 (70.6%) patients underwent portal vein resection and four (29.4%) patients underwent superior mesenteric vein resection. The patient who underwent arterial resection underwent right hepatic artery resection. In this patient, the right hepatic artery originated from the superior mesenteric artery and reconstruction was performed by end-to-end anastomosis of the superior mesenteric artery and the gastroduodenal artery.

In three (75%) patients who underwent superior mesenteric vein resection, reconstruction was performed with end-to-end anastomosis, and in one (25%) falciform ligament was used as graft. In patients who underwent portal vein resection, eight (66.6%) underwent end-to-end anastomosis, one (8.35%) underwent primary repair, one (8.35%) underwent reconstruction with round ligament graft, one (8.35%) with splenic vein graft, and one (8.35%) with internal jugular vein graft.

Table 2. Consequences of pancreatic insufficiency

	n= 45
Persistent nausea and vomiting	23 (48.9%)
Diarrhea	17 (36.2%)
Weight loss	33 (70.2%)
Diabetes	45 (100%)
Pancreatic enzyme usage	40 (85.1%)
Insulin dependency	44 (97.7%)

In 24 (51.1%) patients, perioperative blood loss was less than 500 mL, in 20 (42.6%) patients, it was 500 to 1000 mL, and in three (6.4%) patients, it was more than 1000 mL. Perioperative blood loss of 500 mL or more was observed in 16 (48.4%) patients with comorbidities; there was no statistically significant difference between them and patients without comorbidities (p= 0.98). Mean length of postoperative hospital stay was 20.69 (4-60) days in patients with perioperative blood loss of 500 mL or more and 18.23 (4-61) days in patients without perioperative blood loss. There was no statistically significant difference (p= 0.42).

According to Clavien-Dindo classification, 32 (68.1%) patients developed stage 2, five (10.6%) stage 3, three (6.4%) stage 4 and four (8.5%) stage 5 complications in the postoperative period. Five (10.6%) patients had postoperative intraabdominal abscess, two (4.3%) patients had bleeding during follow-up and two (4.2%) patients had early postoperative mortality. Percutaneous drainage catheter was placed in two patients with intraabdominal abscess. Sepsis due to nosocomial infection was the cause of death in both patients. Surgical and percutaneous drainage catheters were removed before discharge in all patients, and no patient was discharged with a drain.

Mean postoperative hospital stay was 20.1 days. When the pathology results of the patients were analyzed, 37 (84.09%) of the 44 patients operated for pancreatic mass were operated for pancreatic adenocarcinoma. Fourteen (37.8%) patients had T3 stage tumors and 21 (56.7%) patients had T4 stage tumors. Seventeen (45.9%) patients had positive retroperitoneal surgical margins. Three (6.8%) patients were operated for pancreatic neuroendocrine tumor and four (9%) patients for IPMN.

In the postoperative follow-up period, all of the surviving 45 patients developed endocrine pancreatic insufficiency, and two exitus patients were not evaluated. Out of 45 patients, 23 (48.9%) patients had persistent attacks of nausea and vomiting, and 17 (36.2%) patients had persistent diarrhea. Weight loss of 15 kg or more was observed in 33 (70.2%) patients in the postoperative period. Forty (85.1%) patients used enzyme preparations to replace pancreatic enzymes. Mean age of the patients without symptoms due to loss of exocrine function was 63.9 (40-83) years, while mean age of the patients with symptoms was 60.47 (39-79) years, and there was no significant difference (p= 0.33). In the classification of patients with symptoms according to performance, there were 14 (38.9%) ECOG1, 15 (41.7%) ECOG2, seven (19.4%) ECOG3 patients. There was no significant effect of performance on the development of symptoms (p= 0.053). Again, three (8.3%) ASA1, 19 (52.8%) ASA2, 13 (36.1%) ASA3, one (2.8%) ASA4 patients were observed, and no significant difference was observed between patients according to ASA score (p= 0.898). Mean age of the patients not using pancreatic enzymes was 65.3 (59-68) years, while mean age of the patients using pancreatic enzymes was 60.5 (39-83) years, and this difference was statistically significant (p= 0.035) (Table 2).

While all patients developed DM following total pancreatectomy, one (2.2%) of the 45 patients who were discharged had adequate oral antidiabetic therapy without requiring insulin. Of the 44 (97.8%) patients who were on insulin, four (9%) had an increase in the dose of insulin compared to the early postoperative period. Mean age of the patients whose insulin dose was increased in the late postoperative period was 69.2 (58-83) years, and mean age of the patients whose insulin dose was not increased was 60.3 (39-79) years; no significant difference was observed between these two groups (p= 0.104). ASA and ECOG scores were not associated with increased insulin dose (p= 0.504, p= 0.738). One (2.5%) patient with preoperative DM had an increase in insulin dose. This was not statistically significant (p= 0.915) (Table 2).

Preoperative and postoperative quality of life data were analyzed using the EORTC QLQ-C30 scale. The scale was applied to the living patients, one (7.1%) patient did not want to complete the scale. In 11 patients, preoperative and postoperative EORTC QLQ-C30 scores showed a significant decrease in physical function, role function, social function, and emotional function. There was also a statistically significant decrease in general health. Among the symptom scales, fatigue, pain, dyspnea showed a statistically significant increase, while nausea and vomiting, insomnia, loss of appetite, constipation and diarrhea showed no significant change (Table 3).

All splenectomized patients were vaccinated after the 14th postoperative day. No postplenectomy infection was observed in any of the splenectomized patients.

When patients were divided into two groups according to their symptoms in the follow-up period as those who were symptomatic, and those who were not symptomatic, overall survival was calculated as 25.29 months (± 7.28) in non-symptomatic group, 40.57 months (± 4.14) in symptomatic group. The difference between groups in overall survival was found to be significant (p= 0.003).

Table 3. EORTC QLQ-C30 quality of life scale scores

	Preoperative	Postoperative	p
Global health status	84.7 (75-100)	71.6 (58-83)	0.007
Physical functioning	87.2 (54-100)	70.5 (27-100)	0.005
Role functioning	85.1 (50-100)	73.5 (17-100)	0.042
Emotional functioning	79.5 (50-100)	56.1 (0-100)	0.007
Cognitive functioning	88.1 (50-100)	72.9 (34-100)	0.139
Social functioning	83.8 (50-100)	65.4 (0-100)	0.010
Fatigue	31 (0-66)	57 (0-100)	0.008
Nausea and vomiting	1.45 (0-16)	2.9 (0-16)	0.317
Pain	22.45 (0-50)	37.6 (0-83)	0.027
Dyspnea	6 (0-33)	39.2 (0-10)	0.031
Insomnia	21 (0-66)	33 (0-100)	0.102
Constipation	6 (0-33)	9 (0-66)	0.317
Appetite loss	21 (0-66)	24 (0-100)	0.661
Diarrhea	9 (0-100)	9 (0-100)	1.000

DISCUSSION

In recent years, the frequency of total pancreatectomy has increased. As a result, patients with exocrine and endocrine pancreatic insufficiency develop pathologies that increase the frequency of hospitalization in the postoperative period, which decreases the patients' standard of living and quality of life. For this reason, many studies and research are being carried out in order to reduce the discomfort of the patients after total pancreatectomy and to increase the success of the treatment, as well as to reduce the surgical complications (24). Our study is the only study to investigate the quality of life after pancreatectomy in Türkiye.

Although indications for total pancreatectomy are limited due to the associated potential morbidity and mortality, potential indications for total pancreatectomy include chronic pancreatitis unresponsive to conventional therapies, surgical removal of precancerous pancreatic lesions, surgical resection of locally advanced pancreatic cancer, and the care of patients with exceptionally high-risk pancreatic texture after pancreaticoduodenectomy (25).

Likewise, in our series, patients who underwent partial resection were determined at the discretion of the surgeon as high risk of pancreatic fistula with a high-risk pancreatic texture or had locally advanced disease. Fourteen (29.7%) patients underwent partial resection prior to total pancreatectomy. Nine (64.2%) of these patients underwent perioperative total pancreatectomy because of positive surgical margin after frozen section and five (35.7%) patients underwent perioperative total pancreatectomy because of high risk of pancreatic fistula development due to hard parenchyma and narrow pancreatic duct. Thirty-five (74.5%) patients underwent simultaneous splenectomy, 17 (36.2%) patients underwent vascular resection due to invasion. In patients who had vascular resection, 14 (82.3%) of them had splenectomy, and the remaining three of them (17.7%) were operated because of chronic pancreatitis.

Pancreatic anastomotic leakage is associated with postoperative complications such as intraabdominal collections, abscess formation, and pancreatic fistula formation after partial pancreatectomy. Perioperative evaluation of the pancreatic morphology and surgical technique can prevent the development of leakage. Pancreatic duct diameter, parenchymal tissue (hard, soft), pancreatic pathology (malignancy, pancreatitis, etc.) and perioperative blood loss, which are the parameters of pancreatic fistula risk scoring published by Callery et al., should be evaluated by the surgeon and the right decision should be made to achieve a good patient prognosis in patients with high fistula risk (7,8,26). In a single-center study conducted in Germany, the likelihood of leakage at the pancreatic duct anastomosis has been found higher in hard tissue than in soft tissue. The likelihood of leakage at the narrow duct anastomosis has also been reported to be higher (27). In an Italian study, it has been shown that deciding to perform total pancreatectomy in patients at high risk of developing pancreatic fistula reduces the risk of postoperative complications (9). In our study, five patients were decided to undergo perioperative total pancreatectomy due to high risk of developing pancreatic fistula, which was consistent with the literature.

In a meta-analysis by Ning Shi et al., it has been found that perioperative blood loss was higher in patients who underwent splenectomy with pancreatectomy than in patients who underwent spleen preserving surgery. In the same study, there was no significant difference between splenectomy and spleen-preserving pancreatectomy in terms of hospital stay and survival (28). However, a study by Lee et al. comparing patients who underwent distal pancreatectomy with splenectomy and with spleen preservation showed that longer operation time, increased perioperative blood loss, and more extensive surgical resection prolonged postoperative hospital stay and had a poor prognosis (29). According to our results, there was no significant difference in perioperative blood loss between splenectomy and spleen-preserving pancreatectomy groups, while the length of hospital stay and mean survival did not show a significant difference.

Some studies have shown that the spleen is the most effective organ for removing IgG-coated bacteria and is critical for clearance of encapsulated bacteria that are not opsonized by antibodies or complement (30). Therefore, vaccination is recommended for patients to prevent encapsulated bacterial infection after splenectomy. In our study, all patients were vaccinated after postoperative day 14, and no post-splenectomy infection was observed in any of the patients.

Another surgical factor that affects patient prognosis is vascular resection. Major arterial and venous structures are also included in the dissection margins in pancreatic surgery due to their proximity. In a study by Belfiori et al. that reviewed patients operated for pancreatic head malignancies, vascular resection has been shown to have no effect on survival (31). Similar results were found in a study by Marangoni et al. evaluating the outcomes of patients who underwent vascular resection during pancreatectomy (32). In our data, perioperative blood loss was higher in patients who underwent vascular resection compared to those who did not. However, this difference and the surgical technique did not have a significant effect on postoperative complications, prognosis, and median survival, similar to the literature.

It is known in the literature that endocrine failure can develop in 3-40% of the patients due to insulin deficiency after total pancreatectomy. Kusakabe et al. have reported the results of long-term follow-up of patients after pancreatectomy and found that 20.15% of patients developed postoperative endocrine insufficiency and 62.6% of these patients required insulin. While 19.7% of the patients included in the study used insulin in the preoperative period due to DM, it was observed that the need for insulin increased in the postoperative period (18). Stoop et al. have investigated the effect of exocrine and endocrine insufficiency on quality of life after total pancreatectomy and shown that patients had a very good quality of life with appropriate endocrine treatment (17). In our study, we found that all patients developed DM postoperatively, while only one of the discharged patients had no need for insulin. However, we found that the need for insulin increased in the postoperative period in a small proportion of patients, and only one of the patients who used insulin in the preoperative period because of DM increased the insulin dose in the postoperative period.

Exocrine pancreatic insufficiency causes malabsorption of nutrients due to a deficiency of pancreatic enzymes in the gastrointestinal tract, resulting in symptoms such as nausea and vomiting, bowel dysfunction, malnutrition, and weight loss (26). There are many studies in the literature on exocrine insufficiency and its treatment due to the increasing number of pancreatic diseases and pancreatic surgeries. In a prospective study by Halloran et al, 76.9% of the patients have developed exocrine insufficiency at six weeks and 86.9% at one year after pancreatectomy (33). The largest US-based study in the literature with 1165 patients has shown that 34.7% of patients developed exocrine insufficiency after pancreatectomy (34). In our study, approximately 50% of the patients developed symptoms due to exocrine pancreatic insufficiency. Age and comorbidities did not affect the development of exocrine insufficiency.

It has been well established that both exocrine and endocrine pancreas insufficiency have a negative impact on quality of life, including physical and role function (35). In a single-center study of 34 patients by Billings et al., it has been shown that patients who underwent total pancreatectomy had a decreased quality of life (36). In the study by Müller et al. comparing patients who underwent Whipple procedure and total pancreatectomy, acceptable quality of life results have been obtained after Whipple procedure, whereas quality of life has decreased after total pancreatectomy (37). In a study from New York, although the quality of life of patients after total pancreatectomy was acceptable, most of the patients included in the study were operated for benign reasons, and it was shown that the quality of life after pancreatectomy also depends on the pancreatic pathology (38). In our study, in which we utilized the EORTC QLQ-C30 scale scores for both pre- and postoperative periods, patients who underwent total pancreatectomy and survived had a significant decrease in postoperative quality of life.

Early recognition of exocrine pancreatic insufficiency and initiation of pancreatic enzyme replacement therapy is critical to prevent the development of malabsorption-related morbidities in patients (39). In addition, enzyme replacement plays an effective role in improving patients' quality of life by alleviating their symptoms. It is recommended to start taking pancreatic enzymes soon after starting oral intake following

total pancreatectomy. Large-scale studies have shown that weight loss and malabsorption-related symptoms decreased after the use of pancreatic enzyme preparations in patients with exocrine pancreatic insufficiency (35,40,41). Our data showed that most of the patients we operated on used pancreatic enzyme supplements. Although age had no effect on the development of exocrine insufficiency symptoms, the mean age of patients who used enzyme preparations was lower than that of those who did not.

CONCLUSION

After total pancreatectomy, patients are exposed to great stress in the postoperative period due to both surgical factors and metabolic factors related to endocrine and exocrine insufficiency, and these factors may lead to complications, morbidity, and mortality in the early and late postoperative period. In addition, the discomfort that develops especially in patients with exocrine insufficiency leads to a decrease in patients' quality of life. There are many studies in the literature evaluating both exocrine and endocrine insufficiency and quality of life after pancreatic resection. In the literature, many centers have reported a decrease in quality of life in the postoperative period in total pancreatectomy patients. In our study, we found that patients with endocrine and exocrine insufficiency showed similar results to the literature.

Limitations of our study were use of a single scale to assess quality of life, limited number of patients, and short duration of study. However, we believe that this study, which is the first in Türkiye to compare quality of life with preoperative and postoperative outcomes, will draw attention to the importance of follow-up and treatment planning for patients with total pancreatectomy. However, in our country, where the prevalence of pancreatic surgery is increasing, we believe that more meaningful results should be obtained by analyzing a larger number of patient data and by regulating the endocrinological and surgical follow-up and treatment of patients by conducting a multicenter study.

Ethics Committee Approval: This study was approved by Ege University Faculty of Medicine Medical Research Ethics Committee (Decision no: 23-9.1T/26, Date: 21.09.2023).

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REFERENCES

1. *Leung PS. Physiology of the pancreas. Adv Exp Med Biol 2010; 690: 13-27. https://doi.org/10.1007/978-90-481-9060-7_2*
2. *Wilson GC, Sutton JM, Smith MT, Schmulewitz N, Salehi M, Choe KA, et al. Completion pancreatectomy and islet cell autotransplantation as salvage therapy for patients failing previous operative interventions for chronic pancreatitis. Surgery 2015; 158(4): 872-8; discussion 879-80. https://doi.org/10.1016/j.surg.2015.04.045*
3. *Yamaguchi K, Konomi H, Kobayashi K, Ogura Y, Sonoda Y, Kawamoto M, et al. Total pancreatectomy for intraductal papillary-mucinous tumor of the pancreas: Reappraisal of total pancreatectomy. Hepatogastroenterology 2005; 52(65): 1585-90.*
4. *Johnston WC, Hoen HM, Cassera MA, Newell PH, Hammill CW, Hansen PD, et al. Total pancreatectomy for pancreatic ductal adenocarcinoma: Review of the National Cancer Database. HPB (Oxford) 2016; 18(1): 21-8. https://doi.org/10.1016/j.hpb.2015.07.009*
5. *Rockey EW. Total pancreatectomy for carcinoma: Case report. Ann Surg 1943; 118(4): 603-11. https://doi.org/10.1097/00000658-194310000-00008*
6. *Reddy S, Wolfgang CL, Cameron JL, Eckhauser F, Choti MA, Schulick RD, et al. Total pancreatectomy for pancreatic adenocarcinoma: Evaluation of morbidity and long-term survival. Ann Surg 2009; 250(2): 282-7. https://doi.org/10.1097/SLA.0b013e3181ae9f93*
7. *Büchler MW, Wagner M, Schmied BM, Uhl W, Friess H, Z'graggen K. Changes in morbidity after pancreatic resection: Toward the end of completion pancreatectomy. Arch Surg 2003; 138(12): 1310-4; discussion 1315. https://doi.org/10.1001/archsurg.138.12.1310*
8. *Salvia R, Lionetto G, Perri G, Malleo G, Marchegiani G. Total pancreatectomy and pancreatic fistula: Friend or foe? Updates Surg 2021; 73(4): 1231-6. https://doi.org/10.1007/s13304-021-01130-3*
9. *Capretti G, Donisi G, Gavazzi F, Nappo G, Pansa A, Piemonti L, et al. Total pancreatectomy as alternative to pancreatico-jejunal anastomosis in patients with high fistula risk score: The choice of the fearful or of the wise? Langenbecks Arch Surg 2021; 406(3): 713-9. https://doi.org/10.1007/s00423-021-02157-1*
10. *Casadei R, Monari F, Buscemi S, Laterza M, Ricci C, Rega D, et al. Total pancreatectomy: Indications, operative technique, and results: A single centre experience and review of literature. Updates Surg 2010; 62(1): 41-6. https://doi.org/10.1007/s13304-010-0005-z*
11. *Kulu Y, Schmied BM, Werner J, Muselli P, Büchler MW, Schmidt J. Total pancreatectomy for pancreatic cancer: Indications and operative technique. HPB (Oxford). 2009; 11(6): 469-75. https://doi.org/10.1111/j.1477-2574.2009.00085.x*
12. *Heidt DG, Burant C, Simeone DM. Total pancreatectomy: Indications, operative technique, and postoperative sequelae. J Gastrointest Surg 2007; 11(2): 209-16. https://doi.org/10.1007/s11605-006-0025-7*
13. *Aldridge MC, Williamson RC. Distal pancreatectomy with and without splenectomy. Br J Surg 1991; 78(8): 976-9. https://doi.org/10.1002/bjs.1800780827*
14. *Hue JJ, Ocuin LM, Kyasaram RK, Shanahan J, Rao G, Rothermel LD, et al. Weight tracking as a novel prognostic marker after pancreatectomy. Ann Surg Oncol 2022; 29(6): 3450-9. https://doi.org/10.1245/s10434-022-11325-6*
15. *Giuliano CA, Dehoorne-Smith ML, Kale-Pradhan PB. Pancreatic enzyme products: Digesting the changes. Ann Pharmacother 2011; 45(5): 658-66. https://doi.org/10.1345/aph.1P770*

16. Shaw K, Thomas AS, Rosario V, Kwon W, Schrope BA, Sugahara K, et al. Long term quality of life amongst pancreatectomy patients with diabetes mellitus. Pancreatology 2021; 21(3): 501-8. https://doi.org/10.1016/j.pan.2021.01.012

17. Stoop TF, Ateeb Z, Ghorbani P, Scholten L, Arnelo U, Besselink MG, et al. Impact of endocrine and exocrine insufficiency on quality of life after total pancreatectomy. Ann Surg Oncol 2020; 27(2): 587-96. https://doi.org/10.1245/s10434-019-07853-3

18. Kusakabe J, Anderson B, Liu J, Williams GA, Chapman WC, Doyle MMB, et al. Long-term endocrine and exocrine insufficiency after pancreatectomy. J Gastrointest Surg 2019; 23(8): 1604-13. https://doi.org/10.1007/s11605-018-04084-x

19. Epelboym I, Winner M, DiNorcia J, Lee MK, Lee JA, Schrope B, et al. Quality of life in patients after total pancreatectomy is comparable with quality of life in patients who undergo a partial pancreatic resection. J Surg Res 2014; 187(1): 189-96. https://doi.org/10.1016/j.jss.2013.10.004

20. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 1982; 5(6): 649-55. https://doi.org/10.1097/00000421-198212000-00014

21. Owens WD, Felts JA, Spitznagel EL Jr. ASA physical status classifications: A study of consistency of ratings. Anesthesiology 1978; 49(4): 239-43. https://doi.org/10.1097/00000542-197810000-00003

22. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, et al. The Clavien-Dindo classification of surgical complications: Five-year experience. Ann Surg 2009; 250(2): 187-96. https://doi.org/10.1097/SLA.0b013e3181b13ca2

23. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 1993; 85(5): 365-76. https://doi.org/10.1093/jnci/85.5.365

24. Scholten L, Stoop TF, Del Chiaro M, Busch OR, van Eijck C, Molenaar IQ, et al; Dutch Pancreatic Cancer Group. Systematic review of functional outcome and quality of life after total pancreatectomy. Br J Surg 2019; 106(13): 1735-46. https://doi.org/10.1002/bjs.11296

25. Del Chiaro M, Rangelova E, Segersvärd R, Arnelo U. Are there still indications for total pancreatectomy? Updates Surg 2016; 68(3): 257-63. https://doi.org/10.1007/s13304-016-0388-6

26. Callery MP, Pratt WB, Kent TS, Chaikof EL, Vollmer CM Jr. A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatoduodenectomy. J Am Coll Surg 2013; 216(1): 1-14. https://doi.org/10.1016/j.jamcollsurg.2012.09.002

27. Luu AM, Olchanetski B, Herzog T, Tannapfel A, Uhl W, Belyaev O. Is primary total pancreatectomy in patients with high-risk pancreatic remnant justified and preferable to pancreaticoduodenectomy? A matched-pairs analysis of 200 patients. Gland Surg 2021; 10(2): 618-28. https://doi.org/10.21037/gs-20-670

28. Shi N, Liu SL, Li YT, You L, Dai MH, Zhao YP. Splenic preservation versus splenectomy during distal pancreatectomy: A systematic review and meta-analysis. Ann Surg Oncol 2016; 23(2): 365-74. https://doi.org/10.1245/s10434-015-4870-z

29. Lee KF, Chong CCN, Wong J, Cheung SYS, Fung AKY, Lok HT, et al. A retrospective comparative study of robotic distal pancreatectomy with or without splenic vessel and spleen preservation. Surgeon 2022; 20(3): 129-36. https://doi.org/10.1016/j.surge.2021.02.004

30. Brown EJ, Hosea SW, Frank MM. The role of the spleen in experimental pneumococcal bacteremia. J Clin Invest 1981; 67(4): 975-82. https://doi.org/10.1172/JCI110148

31. Belfiori G, Fiorentini G, Tamburrino D, Partelli S, Pagnanelli M, Gasparini G, et al. Vascular resection during pancreatectomy for pancreatic head cancer: A technical issue or a prognostic sign? Surgery 2021; 169(2): 403-10. https://doi.org/10.1016/j.surg.2020.08.002

32. Marangoni G, O'Sullivan A, Faraj W, Heaton N, Rela M. Pancreatectomy with synchronous vascular resection-an argument in favour. Surgeon 2012; 10(2): 102-6. https://doi.org/10.1016/j.surge.2011.12.001

33. Halloran CM, Cox TF, Chauhan S, Raraty MGT, Sutton R, Neoptolemos JP, et al. Partial pancreatic resection for pancreatic malignancy is associated with sustained pancreatic exocrine failure and reduced quality of life: A prospective study. Pancreatology (2011); 11(6): 535-45. https://doi.org/10.1159/000333308

34. Elliott IA, Epelboym I, Winner M, Allendorf JD, Haigh PI. Population-level incidence and predictors of surgically induced diabetes and exocrine insufficiency after partial pancreatic resection. Perm J 2017; 21: 16-095. https://doi.org/10.7812/TPP/16-095

35. Braga M, Cristallo M, De Franchis R, Mangiagalli A, Zerbi A, Agape D, et al. Pancreatic enzyme replacement therapy in post-pancreatectomy patients. Int J Pancreatol 1989; 5 Suppl: 37-44.

36. Billings BJ, Christein JD, Harmsen WS, Harrington JR, Chari ST, Que FG, et al. Quality-of-life after total pancreatectomy: Is it really that bad on long-term follow-up? J Gastrointest Surg 2005; 9(8): 1059-66; discussion 1066-7. https://doi.org/10.1016/j.gassur.2005.05.014

37. Müller MW, Friess H, Kleeff J, Dahmen R, Wagner M, Hinz U, et al. Is there still a role for total pancreatectomy? Ann Surg 2007; 246(6): 966-74; discussion 974-5. https://doi.org/10.1097/SLA.0b013e31815c2ca3

38. Epelboym I, Winner M, DiNorcia J, Lee MK, Lee JA, Schrope B, et al Quality of life in patients after total pancreatectomy is comparable with quality of life in patients who undergo a partial pancreatic resection. J Surg Res 2014; 187(1): 189-96. https://doi.org/10.1016/j.jss.2013.10.004

39. Hallac A, Aleassa EM, Rogers M, Falk GA, Morris-Stiff G. Exocrine pancreatic insufficiency in distal pancreatectomy: Incidence and risk factors. HPB (Oxford) 2020; 22(2): 275-81. https://doi.org/10.1016/j.hpb.2019.06.017

40. Gregořík M, Skalický P, Tesaříková J, Mohelníková-Duchoňová B, Klos D, Loveček M. Enzyme replacement following total pancreatectomy; population analysis. Rozhl Chir 2022; 101(11): 530-4.

41. Leung G, Buscaglia JM. Pancreatic enzyme replacement therapy in post-whipple patients: Optimizing the dose and maximizing compliance. Clin Gastroenterol Hepatol 2020; 18(4): 789-91. https://doi.org/10.1016/j.cgh.2019.10.020

ORİJİNAL ÇALIŞMA-ÖZET
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Splenektomili veya splenektomisiz total pankreatektomili hastalarda ameliyat sonrası yaşam kalitesini etkileyen metabolik ve cerrahi faktörler: Tek merkez sonuçlarımız

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ÖZET

Giriş ve Amaç: Total pankreatektomi, pankreas patolojileri hastalarda gerekebilen ciddi mortalite ve morbidite riski taşıyan majör bir cerrahi işlemdir ve hasta seçimi prognoz açısından önemlidir. Total pankreatektomi sonrası hastalarda gelişen endokrin ve ekzokrin pankreas yetmezliği ağrı, ishal, kusma vb. nedenlerle hastaların yaşam kalitesinde ciddi düşüşe neden olabilmektedir. Amacımız dalak korunarak yapılan total pankreatektomi ve splenektominin hastaların yaşam kalitesi üzerine etkisini değerlendirmektir.

Gereç ve Yöntem: Çalışmamızda, 12/2017 ile 12/2022 tarihleri arasında kliniğimizde pankreas kanseri, intrapapiller müsinöz neoplazi, pankreatik nöroendokrin tümörler ve kronik pankreatit tanısıyla total pankreas rezeksiyonu yapılan hastaların verileri retrospektif olarak analiz edilmiştir. Yaşam kalitesi EORTC QLQ-C30 ölçeği kullanılarak karşılaştırılmıştır.

Bulgular: Çalışmaya 30 (%63,8) erkek ve 17 (%36,2) kadın olmak üzere toplam 47 total pankreatektomi hastası dahil edildi. Hastaların yaş ortalaması 1,38 (39-83) yıl idi. Beş (%35.7) hastaya sert parankim ve dar pankreatik kanal nedeniyle pankreatik fistül gelişme riski yüksek olduğu için perioperatif total pankreatektomi uygulandı. Hastaların perioperatif kan kaybı 500 mL veya daha fazlaydı ve vasküler rezeksiyon yapılmayan hastalara kıyasla perioperatif kan kaybında istatistiksel olarak anlamlı bir artış vardı ($p< 0,001$). Kırk (%85,1) hasta pankreatik enzimlerin yerine enzim preparatları kullanmıştır.

Sonuç: Total pankreatektomi sonrasında hastaların yaşam kalitesi hem cerrahi faktörler hem de postoperatif dönemde endokrin ve ekzokrin yetmezliğe bağlı metabolik faktörler nedeniyle azalmaktadır.

Anahtar Kelimeler: Total pankreatektomi, pankreas yetmezliği, splenektomi, yaşam kalitesi

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