

Changes in postoperative long-term nutritional status and quality of life after total pancreatectomy

Moon Young Oh*, Eun Joo Kim*, Hongbeom Kim*, Yoonhyeong Byun, Youngmin Han, Yoo Jin Choi, Jae Seung Kang, Wooil Kwon, Jin-Young Jang

Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Seoul National University College of Medicine, Seoul, Korea

Purpose: Quality of life (QoL) is widely known to be poor after total pancreatectomy (TP) due to the loss of pancreatic function and poor nutritional status, but prospective studies on changes in QoL over time are lacking. The aim of this study was to prospectively evaluate the short- and long-term consequences of pancreatic exocrine insufficiency, changes in nutritional status, and their associated effects on QoL after TP.

Methods: Prospective data were collected from patients who underwent TP between 2008 and 2018. Validated questionnaires (European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire [EORTC QLQ] Core 30, EORTC QLQ-pancreatic cancer module, and the Mini Nutritional Assessment), measured frequency of bowel movement, relative body weight (RBW), triceps skinfold thickness (TSFT), and serum levels of protein, albumin, transferrin, and hemoglobin A1c were collected serially for 1 year.

Results: Thirty patients who underwent TP were eligible for the study. Bowel movement frequency increased over time, and the RBW and TSFT were lowest by 1 year. The global health status score showed no significant difference over time. At 3 months, physical and role function scores as well as symptoms of fatigue, constipation, and digestive difficulties worsened significantly. Most indices recovered after 1 year, but poorer physical function scores, digestive difficulties, and altered bowel habits persisted.

Conclusion: Because some symptoms do not recover over time, careful follow-up and supportive postoperative management are needed for TP patients, including nutritional support with pancreatic enzyme replacement and education about medication adherence and diet.

[Ann Surg Treat Res 2021;100(4):200-208]

Key Words: Exocrine pancreatic insufficiency, Nutritional status, Pancreatic diseases, Pancreatectomy, Quality of life

INTRODUCTION

Total pancreatectomy (TP) is a rare surgical procedure performed only when the disease involves the entire pancreas and no other surgical options are available [1,2]. Recent studies have reported that mortality and morbidity after TP are comparable to those after partial pancreatectomy [3,4], and increasing evidence has confirmed its safety [5,6]. Moreover,

TP eliminates postoperative pancreatic fistula, among the most severe complications of partial pancreatectomy [7]. Despite these optimistic findings, surgeons are reluctant to perform TP because of the challenges of postoperative care caused by the complete loss of exocrine and endocrine functions [5,8,9] and the poor nutritional status and poor quality of life (QoL) that follow [10-13].

It is well known that lifelong medical treatment and self-

Received September 9, 2020, Revised November 14, 2020,
Accepted December 1, 2020

Corresponding Author: Jin-Young Jang

Division of Hepatobiliary and Pancreatic Surgery, Department of Surgery, Seoul National University Hospital, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Korea

Tel: +82-2-2072-2194, Fax: +82-2-766-3975

E-mail: jangjy4@snu.ac.kr

ORCID: <https://orcid.org/0000-0003-3312-0503>

*Moon Young Oh, Eun Joo Kim, and Hongbeom Kim contributed equally to this work as co-first authors.

Copyright © 2021, the Korean Surgical Society

© Annals of Surgical Treatment and Research is an Open Access Journal. All articles are distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

management of pancreatic insufficiency are required in TP patients, leading to a substantial impact on QoL [14,15]. Advancements in high-dose pancreatic enzyme replacement therapies and education on dietary changes have improved the management of pancreatic exocrine insufficiencies [16,17]. Diabetes mellitus (DM) caused by endocrine function insufficiency has been explored to a great extent, and endocrinologists have presented optimal glycemic control treatment strategies with evidence of new insulin formulations, antihyperglycemic medications, and glucose monitoring methods [18]. However, compared to the numerous studies on endocrine function insufficiency, prospective studies are lacking on the consequences of exocrine insufficiency and changes in patient-based QoL and nutritional status that results after TP.

Therefore, this study aimed to prospectively evaluate the short- and long-term consequences of pancreatic exocrine insufficiency after TP as well as nutritional status changes and their associated effects on QoL.

METHODS

Study design

Patients who underwent elective single-stage TP at Seoul National University Hospital between 2008 and 2018 were selected for the study, and those with at least a 1-year follow-up were considered eligible. Excluded were those who underwent remnant TP and those who expired within 1 year after surgery. All patients were prescribed a pancreatic enzyme dose of 40,000–80,000 units and given nutritional education prior to discharge. Insulin dose was determined and titrated with the help of endocrinologists, and after 1-month follow-up or until the dose stabilized, most of the patients continued DM or glycemic control management at clinical centers near their place of residence. The Institutional Review Board at Seoul National University Hospital granted approval of the data collection, storage, and analysis procedures (SNUH 1305-016-486). Written informed consent was obtained.

Data sources and questionnaires

Data were collected prospectively, once preoperatively and at 3 and 12 months postoperatively. Exocrine function, endocrine function, and nutritional status were assessed by the following measurements. Bowel movement frequency was measured to assess exocrine pancreatic function. Nutritional status was evaluated using the Mini Nutritional Assessment (MNA) questionnaire [19] and by measuring relative body weight (RBW), triceps skinfold thickness (TSFT), and serum levels of protein, albumin, and transferrin. The endocrine function was assessed by hemoglobin A1c (HbA1c).

Validated questionnaires were also administered once preoperatively and at 3 and 12 months postoperative. The

European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30, ver. 3.0) [20], a multidimensional measure containing 30 questions investigating global health status (GHS) and functional symptoms, was employed to assess QoL. The additional pancreatic cancer module (EORTC QLQ-PAN26) [21] was used to assess pancreatic cancer-specific symptoms. Raw scores, the mean of the component items, on the EORTC QLQ-C30 and PAN26 underwent a linear transformation for standardization. Higher scores on the GHS and functioning scales represent better QoL, whereas higher scores on the symptom scale represent more serious symptoms or poorer QoL.

Statistical analysis

Changes in the different values over time were evaluated using repeated-measures analysis of variance. The results are presented as mean \pm standard deviation. Two-tailed values of $P < 0.050$ were considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics for Windows, ver. 25.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Patient characteristics

Between 2008 and 2018, a total of 39 patients underwent

Table 1. Patient demographics

Variable	Value
Sex, male:female	17:13
Age (yr)	64.3 \pm 12.32
Height (cm)	161.5 \pm 7.37
Weight (kg)	58.5 \pm 10.54
Body mass index (kg/m ²)	22.3 \pm 3.25
Alcohol	8 (26.7)
Smoking	4 (13.3)
Operation history	12 (40)
Preoperative DM	13 (43.3)
Diagnosis	
AoV cancer	2 (6.6)
CBD cancer	1 (3.3)
Pancreatic cancer	13 (43.3)
IPMN	10 (33.3)
Others ^{a)}	4 (13.3)
Hospitalization (day)	20.7 \pm 8.6
Postoperative complications	4 (13.3)
Stool elastase (μ g/g)	130.6 \pm 128
<200	8/12 (66.7)
Adjuvant chemotherapy (in 16 cancer patients)	10/16 (62.5)

DM, diabetes mellitus; AoV, ampulla of Vater; CBD, common bile duct; IPMN, intraductal papillary mucinous neoplasm.

^{a)}Serous cystic neoplasm, mucinous cystic neoplasm, and neuroendocrine tumor.

TP at Seoul National University Hospital. Of them, 4 who underwent remnant TP and 5 who expired within 1 year after surgery were excluded. Three of the 5 patients expired due to disease progression within 1 year after surgery, and the remaining 2 patients died from surgery-related septic shock and liver failure, respectively. Thus, 30 patients who underwent TP were eligible for the study.

The mean patient age was 64.3 years and 17 (56.7%) were male. The mean body weight immediately before surgery was 58.5 kg, while the mean body mass index was 22.3 kg/m². Of the total 30 patients, 13 (43.3%) had preoperative DM. A stool elastase level < 200 µg/g, which indicates pancreatic exocrine insufficiency, was apparent in 8 of the 12 patients (66.7%) in whom it was determined before surgery; the mean preoperative stool elastase level was 130.6 µg/g. The final pathological diagnosis consisted of 13 pancreatic cancers, 10 intraductal papillary mucinous neoplasms (IPMN), 2 ampullae of Vater (AoV) cancers, 1 common bile duct (CBD) cancer, and 4 non-cancerous lesions. Of the 2 patients diagnosed with AoV cancer: 1 underwent TP because of concomitant IPMN, while the other did so because cancer had spread along the main pancreatic

duct. The patient diagnosed with CBD cancer underwent TP due to severe pancreatitis that was considered too high risk for pancreatojejunostomy leakage. The other lesions consisted of one mucinous cystic neoplasm, 2 serous cystic neoplasms, and 1 grade-2 neuroendocrine tumor (NET). The patient with NET underwent TP due to positive margins on a frozen section biopsy, and the rest due to huge masses. Postoperative complications occurred in 4 of 30 patients (13.3%), including 2 surgical wound problems; 1 bleeding ulcer, and 1 marginal ulcer. Ten out of 16 cancer patients underwent adjuvant chemotherapy. Patient demographics are shown in Table 1.

Changes in exocrine function

Changes in parameters associated with exocrine function over time are shown in Fig. 1. The RBW was highest preoperatively and decreased significantly over time after surgery ($P < 0.001$) (Fig 1A). Bowel movement frequency increased over time from 1.96 times per day preoperatively to 3.05 times per day at 1 year after surgery, which meets the definition of diarrhea (Fig. 1B). The mean MNA score was lowest preoperatively, peaked at 3 months of follow-up, and then

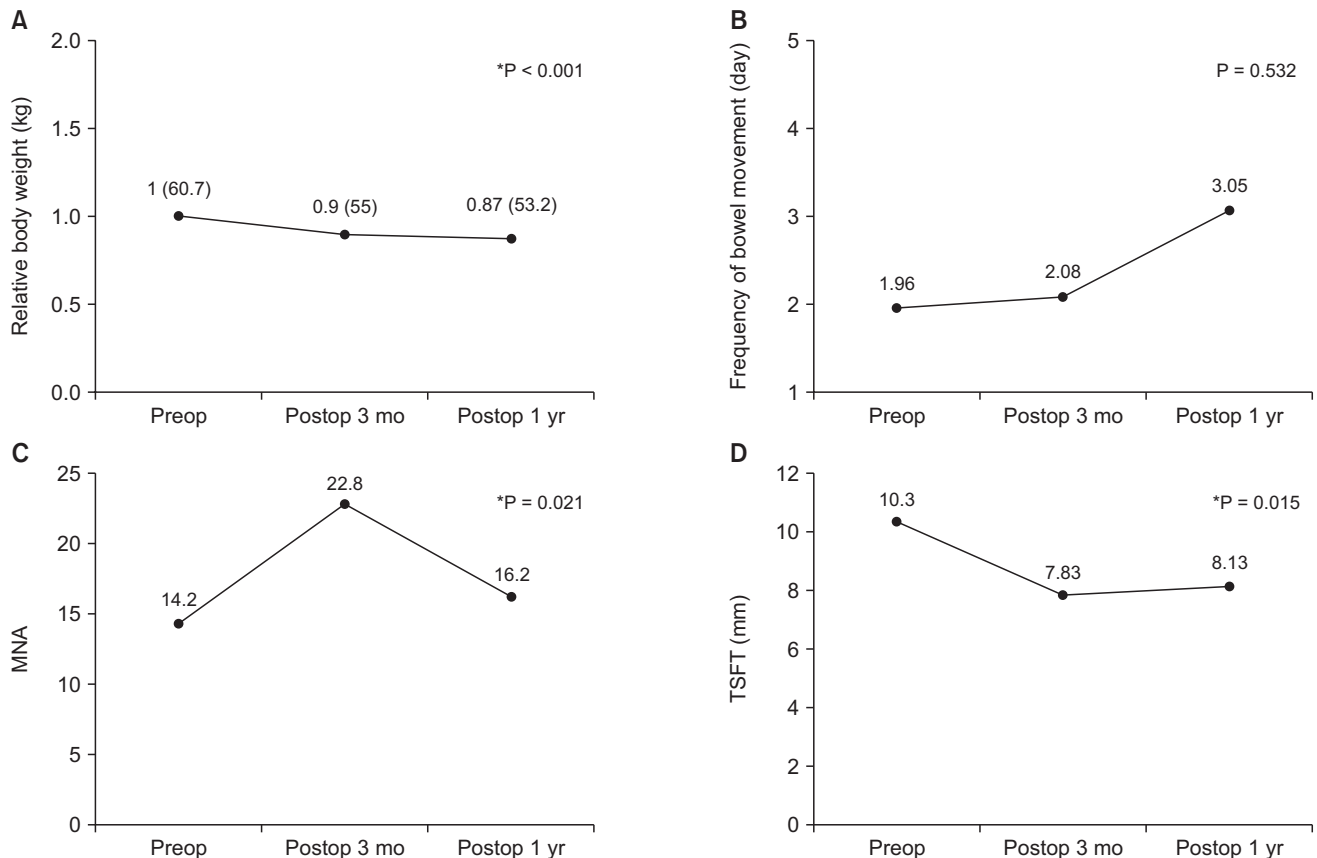


Fig. 1. Changes in exocrine function. (A) Relative body weight was highest preoperatively and continued to decrease over time. (B) Bowel movement frequency increased over time. (C) Mini Nutritional Assessment (MNA) score was lowest preoperatively, peaked at 3 months of follow-up, and then decreased almost to the preoperative state by 1 year of follow-up. (D) Triceps skinfold thickness (TSFT) decreased significantly after surgery. Preop, preoperative; Postop, postoperative. * $P < 0.050$.

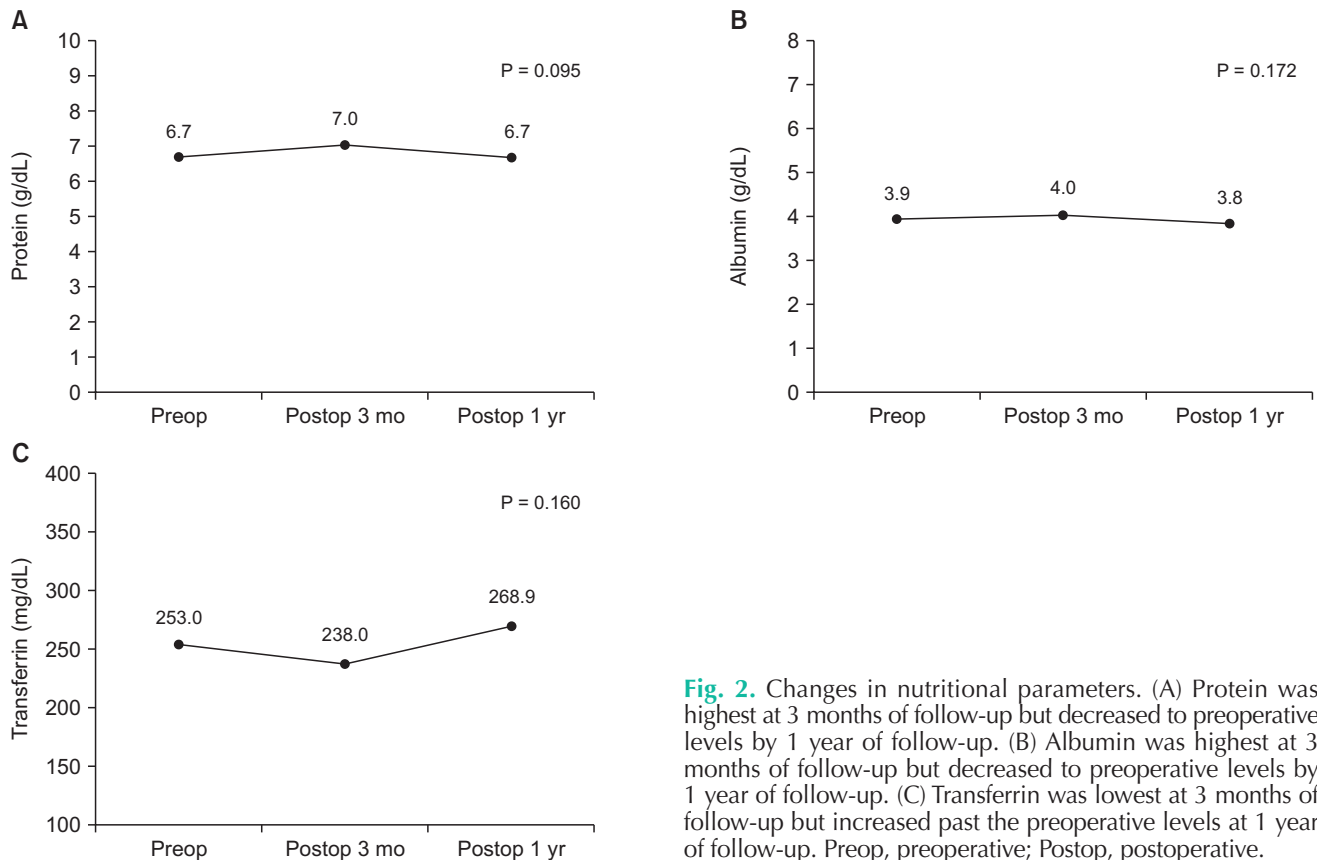


Fig. 2. Changes in nutritional parameters. (A) Protein was highest at 3 months of follow-up but decreased to preoperative levels by 1 year of follow-up. (B) Albumin was highest at 3 months of follow-up but decreased to preoperative levels by 1 year of follow-up. (C) Transferrin was lowest at 3 months of follow-up but increased past the preoperative levels at 1 year of follow-up. Preop, preoperative; Postop, postoperative.

decreased almost to the preoperative state by 1 year of follow-up (Fig. 1C). The mean TSFT started at 11.1 mm before surgery but decreased to 7.83 mm and 8.13 mm at 3 months and 1 year of follow-up, respectively (Fig. 1D).

Changes in nutritional parameters

Changes in the nutritional parameters over time are shown in Fig. 2. Protein, albumin, and transferrin levels did not differ significantly over time. Although the difference was very small, protein and albumin levels were highest at 3 months of follow-up but decreased to preoperative levels by 1 year of follow-up (Fig. 2A, B). Transferrin levels, on the other hand, was lowest at 3 months of follow-up but increased past the preoperative level at 1 year of follow-up (Fig. 2C).

Changes in endocrine function

The change in endocrine function, represented by the HbA1c over time, is shown in Fig. 2. The mean HbA1c was 7.2% before TP, and although not statistically different, it increased slightly to 7.9% at 3 months of follow-up and remained at this level until 1 year of follow-up.

Changes in quality of life

The GHS score and each of the QoL categories, measured by

the EORTC QLQ-C30 and PAN26, are summarized in Table 2, while the changes over time are shown in Fig. 3.

At 3 months after undergoing TP, the GHS showed no significant difference (preoperative, 57.0 vs. 3 months postoperative, 68.3; $P = 0.119$). The physical function score (79.2 vs. 73.1, $P = 0.040$) and role function score (84.0 vs. 65.3, $P = 0.001$) decreased with statistical significance. Patients also presented with worsened symptoms of fatigue (30.7 vs. 41.8, $P = 0.047$), constipation (21.3 vs. 9.0, $P = 0.009$), and digestive difficulties (14.9 vs. 32.7, $P = 0.022$) (Table 2).

By 1 year postoperative, the GHS still showed no significant difference (preoperatively, 57 vs. 1 year postoperatively, 52.4; $P = 0.200$), and no statistically significant differences were seen in most of the QoL categories. However, poor physical function (79.2 vs. 67.6; $P = 0.010$) continued even 1 year after surgery. All of the symptoms in the EORTC QLQ-C30 that were significant at 3 months were resolved 1 year after surgery, and the only statistically significant symptoms that persisted on the pancreatic cancer-specific PAN26 module were digestive difficulties (14.9 vs. 36.9; $P = 0.030$) and altered bowel habits (9.2 vs. 25.6; $P = 0.030$) (Table 2).

Most of the QoL scores that had decreased at 3 months postoperative significantly improved to postoperative levels by 1 year postoperative. However, symptoms that did not improve

Table 2. Change in patient quality of life

Variable		Preoperative	Postoperative			
			3 Months	P-value ^{a)}	1 Year	P-value ^{b)}
EORTC QLQ-C30						
Global health score		57.0 ± 28.30	68.3 ± 20.57	0.119	52.4 ± 21.78	0.200
Functional	Physical	79.2 ± 17.46	73.1 ± 14.59	0.040*	67.6 ± 19.54	0.010*
	Role	84.0 ± 20.68	65.3 ± 24.01	0.001*	70.2 ± 22.81	0.093
	Emotional	77.7 ± 28.43	85.3 ± 13.45	0.061	80.4 ± 27.07	0.248
	Cognitive	82.7 ± 14.01	84.0 ± 13.54	0.590	83.3 ± 14.61	>0.999
	Social	77.3 ± 28.81	69.6 ± 21.82	0.522	76.9 ± 12.79	0.780
Symptom	Fatigue	30.7 ± 17.65	41.8 ± 19.31	0.047*	39.7 ± 15.53	0.206
	Nausea and vomiting	7.6 ± 17.7	4.0 ± 7.26	0.267	5.13 ± 14.24	0.394
	Pain	12.0 ± 23.3	22.0 ± 23.43	0.212	19.0 ± 17.11	0.311
	Dyspnea	13.3 ± 19.24	8.3 ± 14.74	0.258	12.8 ± 16.87	>0.999
	Insomnia	28.0 ± 38.10	22.7 ± 28.41	0.629	16.7 ± 28.49	>0.999
	Appetite loss	20.0 ± 30.42	22.7 ± 26.73	0.358	14.3 ± 28.38	0.724
	Constipation	21.3 ± 30.24	9.0 ± 22.11	0.009*	10.3 ± 21.01	0.279
	Diarrhea	14.7 ± 21.68	10.7 ± 18.55	0.545	12.8 ± 25.59	0.509
	Financial difficulties	25.0 ± 28.23	27.5 ± 28.8	>0.999	28.6 ± 31.64	0.267
	EORTC QLQ-PAN26					
Functional	Health care satisfaction	60.7 ± 27.16	64.1 ± 30.07	0.803	65.4 ± 23.03	0.485
	Sexuality	61.7 ± 26.54	52.6 ± 37.78	0.630	39.6 ± 39.77	0.109
Symptom	Pancreatic pain	17.1 ± 19.05	20.0 ± 13.33	0.236	13.8 ± 13.73	0.534
	Digestive	14.9 ± 35.45	32.7 ± 31.35	0.022*	36.9 ± 25.46	0.030*
	Altered bowel habits	9.2 ± 28.72	23.3 ± 29.65	0.096	25.6 ± 33.06	0.030*
	Hepatic	10.0 ± 19.24	8.7 ± 15.30	0.550	14.3 ± 26.84	0.192
	Body image	21.3 ± 29.86	32.0 ± 35.65	0.171	41.7 ± 32.52	0.079

Values are presented as mean ± standard deviation.

EORTC QLQ-C30, European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EORTC QLQ-PAN26, EORTC QLQ pancreatic cancer module.

^{a)}Comparison of perioperative patients and 3 months postoperative patients; ^{b)}comparison of perioperative patients and 1 year postoperative patients.

*P < 0.050 (paired t-test).

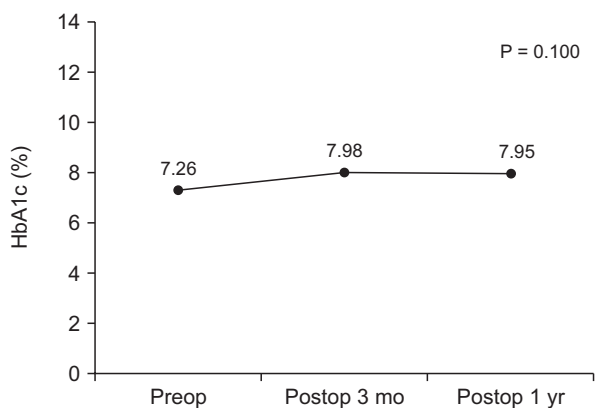


Fig. 3. Changes in endocrine function. Hemoglobin A1c (HbA1c) increased slightly at 3 months and was maintained at this level until 1 year of follow-up. Preop, preoperative; Postop, postoperative.

even after 1 year postoperative, including digestive difficulties and altered bowel habits, were attributed to pancreatic exocrine

function insufficiency (Fig. 4).

DISCUSSION

Many studies have already shown that postoperative outcomes after TP and pancreatoduodenectomy are comparable [3,4]. Hence, the chief concern in extending resection to the entire pancreas is associated with the inevitable consequences brought about by the apancreatic state. QoL is becoming increasingly important to clinical decision-making in even the most aggressive diseases and in settings in which life expectancy is short. Moreover, studies have shown that QoL is a significant predictor of cancer survival above and beyond demographic and medical factors [22,23]. This study assessed which factors affect QoL after TP and to which extent they impact patient QoL over time. Many of the symptoms after TP worsen significantly after 3 months postoperative but then improve to a comparable level at 1 year postoperative. However, poorer physical function and nutrition and symptoms

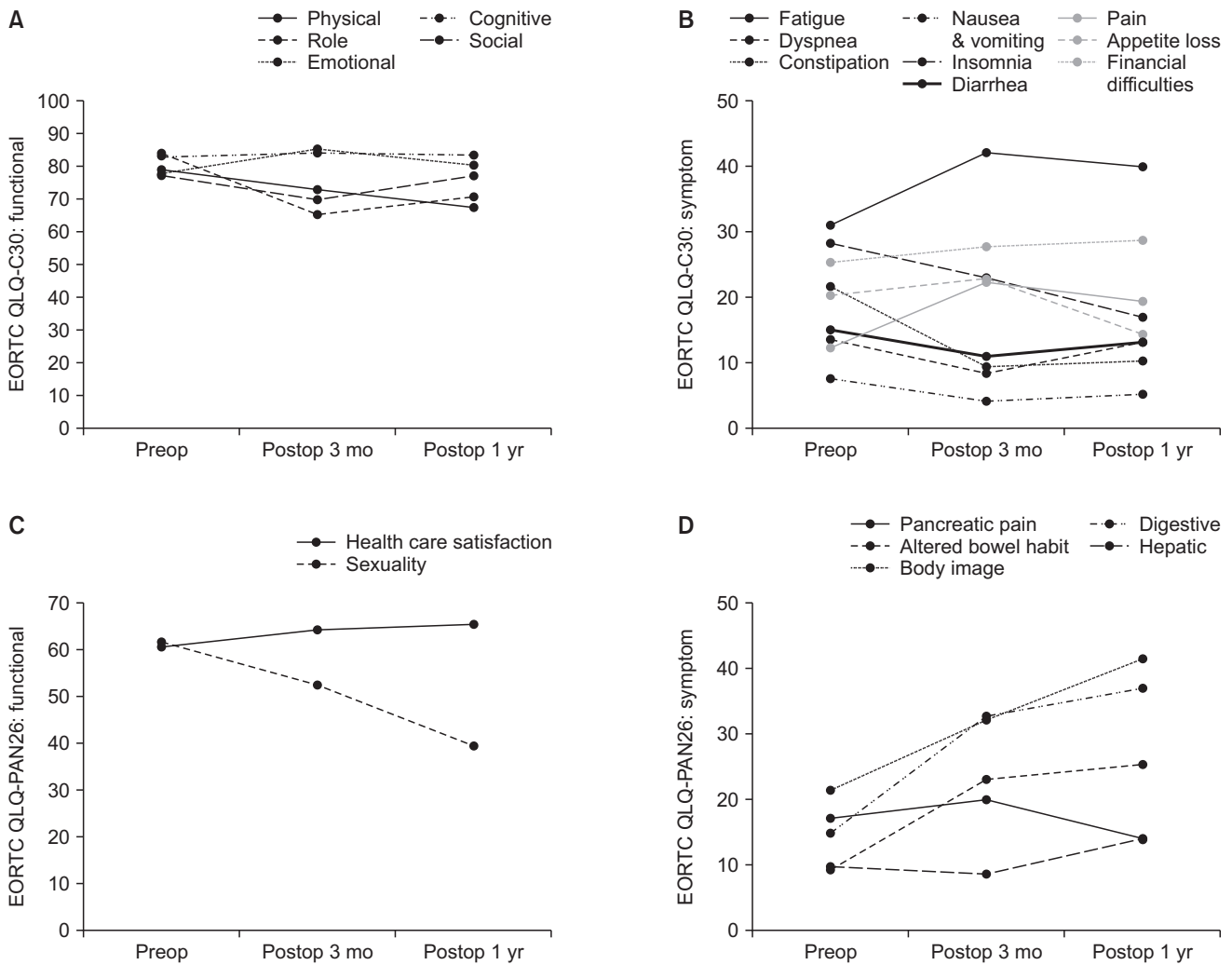


Fig. 4. Changes in quality of life. (A) EORTC QLQ-C30 functional scores showed that the physical function and role function scores decreased at 3 months of follow-up, whereas the role function score recovered after 1 year of follow-up while the physical function score worsened. (B) EORTC QLQ-C30 symptom scores showed that fatigue and constipation worsened at 3 months of follow-up but recovered at 1 year of follow-up. (C) EORTC QLQ-PAN26 functional scores showed no significant differences, but the trend of the sexuality scores seemed to decrease over time. (D) EORTC QLQ-PAN26 symptom scores showed that digestive and altered bowel habit symptoms continued to worsen over time. EORTC QLQ-C30, European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EORTC QLQ-PAN26, EORTC QLQ pancreatic cancer module; Preop, preoperative; Postop, postoperative.

associated with pancreatic exocrine function such as digestive difficulties and altered bowel habits persisted even after 1 year had passed.

Of the existing studies, many reported worse general health perception and physical status of patients who underwent TP versus the matched general population [2,10,11]. A systematic review of 21 studies published between 2005 and 2018 revealed that overall QoL after TP is adversely affected, possibly due to the impact of diarrhea- and DM-related morbidity [13]. A recent nationwide multicenter retrospective cohort study in the Netherlands reported that long-term QoL was lower in patients than in the general population, although the difference was small [12]. On the other hand, studies demonstrate the

comparability of QoL before and after TP or with matched healthy control groups. Hartwig et al. [1] found, in a large single-center study, no relevant change in global QoL over time between patients who underwent TP and a matched general population. Stoop et al. [24] demonstrated that overall QoL after surgery was reduced to some extent compared with the general population but did not differ with the self-matched preoperative QoL. Accordingly, the QoL after TP stays worse throughout the postoperative period.

In this study, the GHS scores of the patients in the follow-up period did not differ significantly from the preoperative scores. However, the GHS is based on the results of the EORTC QLQ-C30, a QoL questionnaire for cancer patients in general.

The limitation of the GHS score in this study is that it does not reflect factors specific to pancreatic disease or patients who underwent pancreatic resection. Studies are exploring ways to overcome this limitation. Rijssen et al. [25] established a core set of patient-reported outcomes (PROs) in pancreatic cancer selected by both patients and healthcare providers internationally through a Delphi process. The identified 8 core PROs highlight the priorities of patients and healthcare providers in the treatment of pancreatic cancer and are expected to help facilitate the design of future research and prospective studies. Likewise, more studies on pancreas-specific parameters are needed to fully evaluate the QoL of patients with pancreatic disease.

Previous studies have observed that fatigue and gastrointestinal (GI) symptoms, including diarrhea and altered bowel habits, are the most frequently reported symptoms after TP [8,12,13]. Our study also showed that digestive difficulties and altered bowel habits persisted even 1 year after surgery, and bowel movement frequency continued to increase over time, eventually causing diarrhea. Because these symptoms associated with exocrine function persisted even over time, careful management of pancreatic enzyme replacement therapy (PERT) is important. Although the patients in this study were routinely prescribed PERT, the GI symptoms may have persisted or worsened due to the inadequate prescribed dosage or lack of patient compliance. To achieve optimal enzyme replacement therapy, clinicians should routinely prescribe pancreatic enzymes and refer patients to a dietician to help ensure the correct dosage. Dose titration ought to be individualized according to the types of food and medications ingested by each patient [26]. Because compliance is also a crucial factor in the maximal effect of PERT, extensive patient education is also needed [17]. Malabsorption of nutrients after TP is caused by various factors, such as pancreatic enzyme insufficiency, altered bowel habits, neural damage to the celiac and superior mesenteric ganglia, and altered homeostatic balance of GI hormones [27]. Because many factors may be involved, management using PERT alone may be insufficient; thus, further investigations are needed on this issue.

GI symptoms such as diarrhea, altered bowel habits, and digestive difficulties worsen after TP due to altered GI anatomy and exocrine insufficiency, ultimately leading to malnutrition and poor QoL [27,28]. In this study, the RBW, TSFT, and MNA scores of the patients were all lower at 3 months and 1 year of follow-up than they were preoperatively. However, although the changes in RBW and TSFT reflect the deteriorating nutritional status of patients over time, the MNA scores showed that the nutritional status had improved by 3 months after surgery and then worsened after 1 year. This points to the limitation of the MNA to accurately reflect the actual nutritional status; thus, more assessment tools for nutritional status that include

objective parameters are needed. The MNA was originally designed to evaluate the nutritional status of the geriatric population, and nutritional assessment instruments appropriate for pancreatic resection patients are also needed. This study also showed that most of the patients were already at risk of malnutrition prior to surgery and that the postoperative nutritional status assessed by the MNA questionnaire was comparable. Considering that about half of the patients in this study were diagnosed with pancreatic cancer, it is feasible that their nutritional status was already poor preoperatively due to cancer-related cachexia and anorexia [28]. Because morbidity, mortality, and response to treatment improve with improving nutritional status, nutritional support before and after surgery is of vital importance [29].

Historically, the notion that TP could cause brittle DM was the main reason for the surgeon's reluctance to perform it. However, evidence has shown that DM distress in TP patients is not significantly greater than in patients with type 1 DM [30], and more recent studies have described marked improvement of treatment options for DM in patients after TP [18]. Studies have attributed the improvement of glucose control in TP patients to close monitoring and education for the management of appropriate insulin usage and diet [16,18]. In our center, the starting insulin dose and titration dose according to the changes in the patients' general condition and diet, were determined with the consultation of an endocrinologist. The patients were continued to be followed-up by an endocrinologist for a month even after discharge or until the insulin dose stabilized, then referred to clinical centers near the patients' place of residence. For effective glycemic management, consultation and close follow-up with specialized endocrinologists and dieticians, especially in the early period after surgery, are highly recommended.

One of the limitations of this study was that there were insufficient data since some of the patients did not complete the questionnaires or some tests were not performed during follow-up. There was a limitation in the statistical analysis due to the missing data and the consequent small sample size; thus, we could only show trends. Because this was a single-center study including only 30 patients, additional prospective studies with larger study populations or multiple centers are needed to thoroughly explore the QoL of TP patients. As mentioned earlier, another limitation of this study includes lack of parameters specific to pancreatic function. More pancreas-specific questionnaires and objective parameters reflecting pancreatic insufficiency are needed to fully evaluate QoL. Although all patients were prescribed PERT, some chose alternative drugs and others tended to skip doses over time. The PERT was not dose titrated according to each individual's food content and the degree of maldigestion. Emphasis on medication adherence and more research is needed on

individualized PERT dose titration depending on each patient's response and experience. And finally, we were unable to fully evaluate endocrine function before and after TP because our main focus was on symptoms associated with exocrine insufficiency and changes in QoL.

The overall GHS score after TP was comparable to the preoperative QoL score. Many of the symptoms significantly worsened after 3 months postoperatively but then improved to a comparable level after 1 year. However, poorer physical function and nutrition and symptoms associated with pancreatic exocrine function, such as digestive difficulties and altered bowel habits, persist even after 1 year. Because nutrition status, physical function, and symptoms produced by exocrine insufficiency continue to deteriorate over time, attention and supportive postoperative management are needed for patients receiving TP, including PERT with dose titration, nutritional support, and education on medication adherence and diet.

ACKNOWLEDGEMENTS

Fund/Grant Support

This study was supported by the grant (No. 04-2020-3130) from the SNUH Research Fund and by the National Research Foundation funded by the Ministry of Science and ICT (NRF-2017M3C9A5031591). The funding source has no role in the

design, practice, or analysis of this study.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

ORCID iD

Moon Young Oh: <https://orcid.org/0000-0002-8939-1735>

Eun Joo Kim: <https://orcid.org/0000-0002-9792-4546>

Hongbeom Kim: <https://orcid.org/0000-0002-1595-0135>

Yoonhyeong Byun: <https://orcid.org/0000-0002-4258-891X>

Youngmin Han: <https://orcid.org/0000-0003-0456-7824>

Yoo Jin Choi: <https://orcid.org/0000-0002-1142-1842>

Jae Seung Kang: <https://orcid.org/0000-0001-6587-9579>

Wooil Kwon: <https://orcid.org/0000-0002-4827-7805>

Jin-Young Jang: <https://orcid.org/0000-0003-3312-0503>

Author Contribution

Conceptualization: MYO, HK, JYJ

Formal Analysis: EJK

Investigation: MYO, EJK

Methodology: YB, YH, YJC, JSK, WK, JYJ

Project Administration: HK, JYJ

Writing – Original Draft: MYO, EJK, HK

Writing – Review & Editing: YB, YH, YJC, JSK, WK, JYJ

REFERENCES

- Hartwig W, Gluth A, Hinz U, Bergmann F, Spronk PE, Hackert T, et al. Total pancreatectomy for primary pancreatic neoplasms: renaissance of an unpopular operation. *Ann Surg* 2015;261:537-46.
- 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;246:966-74.
- 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;187:189-96.
- Suzuki S, Kajiyama H, Takemura A, Shimazaki J, Nishida K, Shimoda M. The clinical outcomes after total pancreatectomy. *Dig Surg* 2017;34:142-50.
- Datta J, Lewis RS Jr, Strasberg SM, Hall BL, Allendorf JD, Beane JD, et al. Quantifying the burden of complications following total pancreatectomy using the postoperative morbidity index: a multi-institutional perspective. *J Gastrointest Surg* 2015;19:506-15.
- Zakaria HM, Stauffer JA, Raimondo M, Woodward TA, Wallace MB, Asbun HJ. Total pancreatectomy: short- and long-term outcomes at a high-volume pancreas center. *World J Gastrointest Surg* 2016;8:634-42.
- Ryska M, Rudis J. Pancreatic fistula and postoperative pancreatitis after pancreatoduodenectomy for pancreatic cancer. *Hepatobiliary Surg Nutr* 2014;3:268-75.
- 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;23:1604-13.
- Watanabe Y, Ohtsuka T, Matsunaga T, Kimura H, Tamura K, Ideno N, et al. Long-term outcomes after total pancreatectomy: special reference to survivors' living conditions and quality of life. *World J Surg* 2015;39:1231-9.
- 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;9:1059-66.
- Pulvirenti A, Pea A, Rezaee N, Gasparini C, Malleo G, Weiss MJ, et al. Perioperative outcomes and long-term quality of life after total pancreatectomy. *Br J Surg* 2019;106:1819-28.
- Scholten L, Latenstein AE, van Eijck C, Erdmann J, van der Harst E, Mieog JS, et

- al. Outcome and long-term quality of life after total pancreatectomy (PANORAMA): a nationwide cohort study. *Surgery* 2019;166:1017-26.
13. Scholten L, Stoop TF, Del Chiaro M, Busch OR, van Eijck C, Molenaar IQ, et al. Systematic review of functional outcome and quality of life after total pancreatectomy. *Br J Surg* 2019;106:1735-46.
 14. Struyvenberg MR, Fong ZV, Martin CR, Tseng JF, Clancy TE, Fernández-Del Castillo C, et al. Impact of treatments on diabetic control and gastrointestinal symptoms after total pancreatectomy. *Pancreas* 2017;46:1188-95.
 15. Yang DJ, Xiong JJ, Liu XT, Li J, Dhanushka Layanthi Siriwardena KM, Hu WM. Total pancreatectomy compared with pancreaticoduodenectomy: a systematic review and meta-analysis. *Cancer Manag Res* 2019;11:3899-908.
 16. Suzuki S, Miura J, Shimizu K, Tokushige K, Uchigata Y, Yamamoto M. Clinicophysiological outcomes after total pancreatectomy. *Scand J Gastroenterol* 2016;51:1526-31.
 17. Kim H, Yoon YS, Han Y, Kwon W, Kim SW, Han HS, et al. Effects of pancreatic enzyme replacement therapy on body weight and nutritional assessments after pancreatoduodenectomy in a randomized trial. *Clin Gastroenterol Hepatol* 2020;18:926-34.
 18. Maker AV, Sheikh R, Bhagia V; Diabetes Control and Complications Trial (DCCT) Research Group. Perioperative management of endocrine insufficiency after total pancreatectomy for neoplasia. *Langenbecks Arch Surg* 2017;402:873-83.
 19. Guigoz Y. The Mini Nutritional Assessment (MNA) review of the literature: what does it tell us? *J Nutr Health Aging* 2006;10:466-85.
 20. 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;85:365-76.
 21. Fitzsimmons D, Johnson CD, George S, Payne S, Sandberg AA, Bassi C, et al. Development of a disease specific quality of life (QoL) questionnaire module to supplement the EORTC core cancer QoL questionnaire, the QLQ-C30 in patients with pancreatic cancer. EORTC Study Group on Quality of Life. *Eur J Cancer* 1999;35:939-41.
 22. Anwar S, Tan W, Yu J, Hutson A, Javle M, Iyer R. Quality-of-life (QoL) as a predictive biomarker in patients with advanced pancreatic cancer (APC) receiving chemotherapy: results from a prospective multicenter phase 2 trial. *J Gastrointest Oncol* 2014;5:433-9.
 23. Lis CG, Gupta D, Grutsch JF. Patient satisfaction with quality of life as a predictor of survival in pancreatic cancer. *Int J Gastrointest Cancer* 2006;37:35-44.
 24. 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;27:587-96.
 25. Rijssen LB, Gerritsen A, Henselmans I, Sprangers MA, Jacobs M, Bassi C, et al. Core set of outcomes in pancreatic cancer (COPRAC): an international Delphi study among patients and health care providers. *Ann Surg* 2019;270:158-64.
 26. Struyvenberg MR, Martin CR, Freedman SD. Practical guide to exocrine pancreatic insufficiency: breaking the myths. *BMC Med* 2017;15:29.
 27. Dresler CM, Fortner JG, McDermott K, Bajorunas DR. Metabolic consequences of (regional) total pancreatectomy. *Ann Surg* 1991;214:131-40.
 28. Gilliland TM, Villafane-Ferriol N, Shah KP, Shah RM, Tran Cao HS, Massarweh NN, et al. Nutritional and metabolic derangements in pancreatic cancer and pancreatic resection. *Nutrients* 2017;9:243.
 29. Nanashima A, Hiyoshi M, Imamura N, Yano K, Hamada T, Hamada R, et al. Clinical significance of preoperative nutritional parameter and patient outcomes after pancreatectomy: a retrospective study at two academic institute. *Ann Hepatobiliary Pancreat Surg* 2019;23:168-73.
 30. Roberts KJ, Blanco G, Webber J, Marudanayagam R, Sutcliffe RP, Muiesan P, et al. How severe is diabetes after total pancreatectomy? A case-matched analysis. *HPB (Oxford)* 2014;16:814-21.