의학석사 학위논문

The atrophy of remnant pancreas after pancreatoduodenectomy ; its risk factors and effects on quality of life, nutritional status and pancreatic function

췌십이지장절제술 후 잔존 췌장의 위축
; 위험 인자와 삶의 질, 영양 상태 및 췌장 기능에 미치는 영향

2015년 8월

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이 논문을 의학석사 학위논문으로 제출함

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Abstract

Background/Aim Remnant pancreas atrophy after pancreatoduodenectomy has been reported in previous studies. However, the factors aggravating atrophy and the effects of the atrophy were not studied well. The aim of this study was to evaluate the clinical factors to affect remnant pancreas atrophy and to assess effects of atrophy on quality of life, nutritional status and pancreatic exocrine/endocrine functions.

Methods Prospectively collected data of 122 patients who completed 12 months follow-up with CT and quality of life questionnaire after pancreaticoduodenectomy were analyzed. Preoperative, remnant and 12 months follow-up pancreas volume were measured using CT volumetry program. Patients were divided into 2 groups. Group I was the patients with pancreas volume decrease under 50% and group II was the patients with pancreas volume decrease over 50% at 12 months. The patients with preoperative diabetes were excluded in endocrine function analysis.

Results The volume of remnant pancreas decreased about 45% during 12 months after operation. Malignancy and adjuvant chemoradiotherapy were significantly associated with volume decrease over 50% in multivariate analysis.

Mostly of quality of life scores and nutritional indexes at 12 months were not significantly associated with the atrophy. However, stool elastase was significantly more decreased in group II (33.6 μg/g vs. 104.1 μg/g, p=0.003). In group I, 14.6% of patients showed no exocrine deficiency (stool elastase ≥ 200 μg/g) and 78.0% of patients showed severe exocrine deficiency (stool elastase < 100 μg/g). In group II, 92.0% of patients had severe exocrine

deficiency and there was no patient with normal exocrine function. Diabetes at 12 months were more frequently detected in group II (26.8% vs. 10.5%, p=0.057). Serum fasting blood glucose level was not different between 2 groups, but postprandial 2-hour blood glucose was significantly higher in group II (163.7 mg/dl vs. 133.6 mg/dl, p=0.035) and glycosylated hemoglobin level showed higher tendency in group II (6.0% vs. 5.7%, p=0.088).

Conclusions The atrophy of remnant pancreas after pancreatoduodenectomy was more severe in the patients with malignancy and who underwent adjuvant chemoradiotherapy. The quality of life and nutritional status were not significantly affected by the remnant pancreas atrophy, however, exocrine and endocrine function were associated with the atrophy.

More careful monitoring and active management of exocrine and endocrine deficiency will be needed in the patients who underwent pancreatoduodenectomy due to malignancy and who carried out adjuvant chemoradiotherapy.

Keyword : pancreatoduodenectomy, atrophy, quality of life, pancreatic function

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List of Abbreviations

PD	Pancreatoduodenectomy
QOL	Quality of life
CT	Computed tomography
PJ	Pancreaticojejunostomy
RPV	Remnant pancreas volume
12RPV	12-month after remnant pancreas volume
RBW	Relative body weight
BMI	Body mass index
POPF	Postoperative pancreatic fistula
ISGPF	International Study Group on Pancreatic Fistula
EORTC	European Organization for Research and Treatment of Cancer
FBS	Fasting blood sugar
PP2	Post prandial 2 hour blood glucose
HbA1c	Serum glycosylated hemoglobin
PG	Pancreatiogastrostomy

Contents

Introduction

Pancreatoduodenectomy (PD) is generally performed operation for periampullary tumors. As the postoperative mortality and major morbidity rates after PD have been remarkably decreased [1-4], the concerns about long-term outcomes after PD were more increased, such as quality of life (QOL), exocrine and endocrine functions.

In the follow-up course of patients underwent PD, the atrophy of remnant pancreas is not observed infrequently. Many previous studies already reported atrophic changes of remnant pancreas. [5-14] However, there were only limited results about volume decrease of remnant pancreas by specific measurement such computed tomography (CT) volumetry. Also, the volume decrease of remnant pancreas was observed to varying degrees and there could be associated clinicopathological factors with the severity of remnant pancreas atrophy. And, atrophy of pancreas could cause pancreatic exocrine/endocrine deficiency and result in decreased QOL. However, there were only a few small studies about these issues.

This study aimed to evaluate the clinicopathological factors to affect remnant pancreas atrophy and to assess effects of remnant pancreas atrophy on QOL, nutritional status and pancreatic exocrine/endocrine function through specific quantitative measurement of remnant pancreas atrophy after PD by CT volumetry.

Methods

Patients and operation

Between May 2007 and June 2012, 122 patients with benign or malignant periampullary diseases underwent pancreatoduodenectomy and completed postoperative 12-month follow-up with CT volumetry at Seoul National University Hospital. The patients with pancreatic atrophy in preoperative CT scan and recurrence-detected cases within first 12 months after operation were excluded. All data of 122 enrolled patients were collected prospectively. Operations were performed by 2 specialized biliary-pancreas surgeons and duct-to-mucosa pancreaticojejunostomy (PJ) was done in all cases.

Pancreas volumetry

Pancreas volumetry was performed using the images acquired from multidetector-row CT scanner with 3-mm slices on portal venous phase (Fig 1-a). Xelis 3D software (INFINITT Healthcare, Korea) of INFINITT picture archiving and communication system (PACS) was used for pancreas volumetry (Fig 1-b). Single surgeon performed all volumetry procedures of all included patients to avoid inter-observer variation. Preoperative total pancreas volume, remnant pancreas volume (RPV) and 12-month after remnant pancreas volume (12RPV) of each patient were measured. RPV was measured using preoperative CT images according to the surgical resection line of postoperative CT images (Fig 1-c).

Remnant pancreas atrophy definition

The degree of remnant pancreas atrophy after 12 months was presented as the percentage of decreased remnant pancreas volume (RPV-12RPV) to RPV. We divided the patients into 2 groups according to the percentage of atrophy such as patients with remnant pancreas atrophy < 50% (group I, n=72) and patients with remnant pancreas atrophy ≥ 50% (group II, n=50) to evaluate the risk factors and effects of remnant pancreas atrophy.

Risk factors for remnant pancreatic atrophy

Age, sex, relative body weight (RBW), body mass index (BMI), presence of preoperative diabetes, diagnosis, pancreas texture, pancreatic duct size at preoperation and 12 months after operation, operation type, methods of pancreatic drainage, postoperative pancreatic fistula (POPF) grade and performance of adjuvant chemoradiation therapy were checked to evaluate the possible risk factors for remnant pancreas atrophy. POPF was graded according to the classification of the International Study Group on Pancreatic Fistula (ISGPF)[15].

Long term outcomes affected by remnant pancreatic atrophy

We used the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C-30 (EORTC QLQ-C30) (version 3) and the EORTC QLQ PAN26 module for the assessment of QOL. Questionnaires were self-reported by the patients after explanation of a trained nurse at preoperation

and 12 months after operation. Raw data of questionnaires were standardized to range from 0 to 100 as the EORTC scoring manual.

Nutritional status was assessed using RBW, BMI, serum protein, prealbumin, albumin level and serum transferrin level at preoperation and 12 months after operation.

Pancreatic exocrine function was assumed using stool elastase I activity measurement. Pancreatic exocrine deficiency was divided into 3 groups according to stool elastase level. Stool elastase over 200μg/g was no exocrine deficiency, stool elastase between 100μg/g and 200μg/g was mild to moderate exocrine deficiency and stool elastase under 100μg/g was severe exocrine deficiency.

We excluded the patients with preoperative diabetes in pancreas endocrine function analysis. Pancreatic endocrine function was evaluated using fasting blood sugar (FBS), post prandial 2 hour blood glucose (PP2), serum glycosylated hemoglobin (HbA1c), serum insulin and serum c-peptide level at preoperation and 12 months after operation.

Statistical analysis

Statistical analyses were performed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were compared using Pearson's chi-square or Fisher's exact test and continuous variables using Student's t-test or Mann-Whitney U test. P values ≤ 0.05 were considered statistically significant.

Results

Clinicopathological characteristics

The clinicopathological characteristics of the enrolled 122 patients are shown in Table 1. The patients included 69 (56.6%) men and 53 (43.4%) women, of mean age 61.9 years. Mean RBW was 111.3% and BMI was 23.7 kg/m^2. Approximately 20% of the patients (24/122) were diagnosed to have diabetes before operation. There were 38 patients with benign disease and 84 patients with malignant disease. In pancreatic texture, 93 patients had soft pancreas and 21 had firm or hard pancreas. Mean preoperative pancreatic duct size was 2.62mm. Conventional PD was performed in 18 patients and pylorus preserving PD was performed in 104 patients. Pancreatic duct drainage was done externally in 91 patients and internally in 31 patients. ISGPF grade B POPF was occurred in 25 patients (20.5%) and others showed no or ISGPF grade A POPF. Adjuvant chemoradiotherapy was carried out in 39.3 % (48/122) of the patients.

Pancreas volumetry

Median preoperative total pancreas volume was 72.3ml (Fig 2-a). Median remnant pancreas volume was 37.2 ml and 53.0% of preoperative total pancreas volume (Fig 2-b). At 12 months after operation, median pancreas volume was 20.0ml (Fig 2-c). During first 12 months after operation, the volume of remnant pancreas decreased 15.8 ml (median) and 45.1% of remnant pancreas volume

(Fig 2-d).

Risk factors for remnant pancreatic atrophy

The clinicopathologic factors that could affect to remnant pancreas atrophy were analyzed in Table 2. Age, sex, RBW, BMI, preoperative diabetes, pancreas texture, pancreatic duct size, operative method, pancreatic duct drainage method and POPF did not associated with the remnant pancreas atrophy in univariate analysis. The patients with malignant disease and patients underwent adjuvant chemoradiation therapy were more frequently found in more severe atrophy group (group II) in univariate analysis with statistical significance and diagnosis of malignant disease and performance of adjuvant chemoradiation therapy were independently associated with remnant pancreas atrophy over 50% in multivariate analysis.

Long term outcomes affected by remnant pancreatic atrophy

QOL scores at 12 months after operation were not different between group I and II (Table 3-a). In terms of changes of QOL score, global QOL score and hepatic symptom score were more improved in more severe atrophy group, group II (Table 3-b). Preoperative global QOL and hepatic symptom scores were significantly worse in group II (data was not shown).

Serum prealbumin, albumin and protein level at 12 months after operation were slightly lower in group II than group I and there was no significant difference in RBW and BMI between both groups (Table 4-a). However, the change of

nutritional indexes was not significantly different between two groups during 12 months after operation (Table 4-b).

Steatorrhea symptom score was not different between group I and group II at preoperation and 12 months after operation. There was no significant difference in change of steatorrhea symptom score during 12 months (Table 5-a). Stool elastase level was not different at preoperation. Stool elastase level was found to be significantly decreased in group II at 3 months and 12 months after operation through consecutive follow-up. But, the change was not different (Table 5-b). At 12 months after operation, there were 14.6% of patients with no exocrine deficiency in group I, but there was no patient with normal exocrine function in group II. Also, patients with severe exocrine deficiency were more frequently found in group II (Table 5-c).

There was no difference in pancreatic endocrine function at preoperation according to the severity of atrophy (Table 6-a). However, new onset diabetes at 12 months after operation was more frequently found with statistical tendency and PP2 at 12 months was significantly higher in group II than group I (Table 6-b). HbA1c at 12 months after operation was found to be higher in group II than group I with statistical tendency through consecutive follow-up. There was no significant difference in change of pancreatic endocrine function indexes during 12 months (Table 6-d).

Discussion

This study evaluated the atrophy of remnant pancreas after PD, its risk factors and effects. The atrophic change of remnant pancreas after PD was generally known and previously reported in several studies. In early studies, the atrophic change was mainly described by morphologic changes and/or the pancreatic parenchymal thickness and pancreatic duct size [5-9]. As the radiologic technology advanced, more specific and accurate results of pancreas atrophy have been reported using CT volumetry.[10-12] In these report, postoperative remnant pancreas volume after PD was 44.2-71.4ml and decreased to 16.9-39.8ml after 3 to 12 months follow-up through the analysis of 32-57 enrolled patients. Our result of 122 enrolled patients was similar. We reported that remnant pancreas volume was 37.2ml and decreased to 20.0ml after 12 months follow-up in this study. During first 12 months after PD, remnant pancreas showed 45.1% of volume loss.

The degrees of volume change of remnant pancreas after PD were varied by individuals from 19.2% of increase to 78.8% of decrease. There must be risk factors that could affect development of remnant pancreas atrophy. In previous studies, preoperative diabetes, malignant diagnosis, dilated pancreatic duct, type of operation, type of pancreaticoenteric anastomosis, pancreatic drainage method, pancreas texture, presence of POPF and adjuvant chemoradiation therapy were mentioned to related factors.[10-14] We analyzed these factors in this study, consequently malignant diagnosis and performance of adjuvant

chemoradiation therapy were shown significant association with volume decrease over 50%.

Many reports showed that atrophic change of remnant pancreas after PD. However the explanation of atrophic change of remnant pancreas was not clearly demonstrated yet. There were only a few hypotheses. Pancreaticoenteric anastomosis stenosis and following chronic inflammation of remnant pancreas were mentioned one of major causes of remnant pancreas atrophy.[5, 6] In some studies, postoperative pancreatic duct dilatation and remnant pancreas atrophy were more severely observed in pancreatiogastrostomy (PG) cases than PJ cases due to more frequent pancreatic anastomosis stenosis and chronic inflammation in PG cases[7, 8]. However, because all patients enrolled this study were underwent PJ, we couldn't compare the differences between two pancreatic anastomosis methods. Postoperative pancreatic duct diameter was not associated with the severity of atrophic change in this study. The decreased secretion of the hormones that might have trophic effects on the pancreas was discussed one of the reasons in previous studies, and PD than pylorus-preserving PD was reported to be associated with more severe remnant pancreas atrophy due to the resection of duodenum and distal stomach which are the sources of these hormones [7, 9, 10]. However, type of operation was not related to remnant pancreas atrophy in this study. Malignancy and chemoradiation therapy were the independent risk factors of severe remnant pancreas atrophy. Patients with pancreatic cancer often have a hard pancreas with parenchymal fibrotic changes and impaired function [16]. This

preoperative change of remnant pancreas caused by malignant disease could be thought to be a reason of more severe atrophic change after PD. The suppression effect of cell proliferation of chemoradiation therapy could intensify the atrophic change of remnant pancreas. However, there was no definitive mechanism of remnant pancreas atrophy after PD as earlier mentioned. More studies about this issue will be needed.

To evaluate the effects of remnant pancreas atrophy was the final purpose of this study. The relationship between pancreas atrophy and decreased pancreatic exocrine/endocrine functions has been published previously in patients with chronic pancreatitis and diabetes mellitus [17-21]. The studies about these relationship in the patients underwent PD also has been reported but the results were controversial. [6, 7, 10-14, 22] We evaluated the differences in QOL scores after PD according to the severity of remnant pancreas atrophy using prospectively collected QOL questionnaires. As far as we know, this was the first report about this issue. In terms of QOL, there was no significant difference in QOL scores according to the atrophy. Relatively decreased QOL scores of group II at preoperation, recovered and showed no difference compared with group I after 12 months follow-up. In nutritional status, group II showed slightly lower laboratory results but anthropometric indexes were not different according to atrophy. Pancreatic exocrine function was more decreased in group II. Stool elastase level at 12 months after operation was significantly lower in group II and there were more patients categorized to severe exocrine deficiency in group II. However, its clinical effect was not clearly shown. The symptom

score about steatorrhea in QOL questionnaire was not different between 2 groups and the nutritional indexes that could be affected by exocrine function, also not clearly different. This could be thought that the effects of proper administration of pancreatic enzyme supplementations. After operation, all patients have been recommended to take 2 capsules of pancreatic enzyme supplementations which included lipase 25,000 FIP, amylase 22,500 FIP and protease 1,250 FIP during every meal. The differences of endocrine deficiency according to the severity of remnant pancreas atrophy were more apparently detected in our study than previous studies. At 12 months after PD, patients in group II showed more frequent new onset diabetes and higher serum HbA1c level. PP2 was also significantly higher in group II than group I at 12 months after operation. More careful monitoring and management of blood glucose level were needed for the patients who were more susceptible for remnant pancreas atrophy development.

This study was designed to retrospective. This is major limitation of this study. However, relatively large sample size than previous studies about similar issue and prospectively collected data including QOL questionnaires, nutritional indexes and laboratory tests could be the strength of this study.

In summary, remnant pancreas after PD showed atrophic change in most of cases and diagnosis of malignancy and performance of adjuvant chemoradiation therapy independently associated with severe atrophy. Atrophic changes did not significantly influence on QOL and nutritional status, however, pancreatic exocrine/endocrine deficiency after PD was related with the severity

of atrophic change. In conclusion, there will be a need of more careful monitoring and proper management of pancreatic exocrine and endocrine deficiency in the patients who underwent PD due to malignancy and who carried out adjuvant chemoradiation therapy in follow-up after PD.

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Table 1. Clinicopathological characteristics

Characteristics		N=122
Age (years)		61.9 ± 10.7
Sex	Male : Female	69 : 53 (56.6% : 43.4%)
Relative body weight (%)		111.3 ± 16.4
Body mass index (kg/m^2)		23.7 ± 3.1
Preoperative diabetes		24 (19.7%)
Disease	Benign	38 (31.1%)
	Malignancy	84 (68.9%)
Pancreas texture	Soft : Firm/Hard	93 (81.6%) : 21 (18.4%)
Pancreatic duct Size (mm)	Preoperation	2.62 ± 1.86
	12 months	2.68 ± 1.83
Operation	Whipple : PPPD	18 (14.8%) : 104 (85.2%)
PJ stent	External : Internal	91 (74.6%) : 31 (25.4%)
POPF	No & Grade A : Grade B	97 (79.5%) : 25 (20.5%)
Adjuvant Chemoradiotherapy		48 (39.3%)

Table 2. Clincopathological factors according to atrophy

		Group I (n=72)	Group II (n=50)	p value	Relative risk (95% CI)	p value
Age (years)		61.1 ± 10.6	63.1 ± 10.9	0.315		
Sex	Male	40 (58.0%)	29 (42.0%)	0.854		
	Female	32 (60.4%)	21 (39.6%)			
Relative body weight (%)		112.1 ± 17.0	110.2 ± 15.6	0.516		
Body mass index (kg/m^2)		23.8 ± 3.2	23.5 ± 3.1	0.532		
Preoperative diabetes	Yes	15 (62.5%)	9 (37.5%)	0.818		
	No	57 (58.2%)	41 (41.8%)			
Diagnosis	**Malignancy**	**39 (46.4%)**	**45 (53.6%)**	**<0.001**	**4.334 (1.398-13.433)**	**0.011**
	Benign	**33 (86.8%)**	**5 (13.2%)**			
Pancreas texture	Soft	55 (59.1%)	38 (40.9%)	0.629		
	Firm/Hard	11 (52.4%)	10 (47.6%)			
Pancreas duct size (mm)	Preoperation	2.7 ± 1.7	2.5 ± 2.1	0.502		
	12 months	2.8 ± 1.8	2.4 ± 1.9	0.259		
Operation	Whipple	9 (50.0%)	9 (50.0%)	0.443		
	PPPD	63 (60.6%)	41 (39.4%)			
PJ stent	External	53 (58.2%)	38 (41.8%)	0.834		
	Internal	19 (61.3%)	12 (38.7%)			
POPF	No & A	58 (59.8%)	39 (40.2%)	0.821		
	B	14 (56.0%)	11 (44.0%)			
Adjuvant chemoradiotherapy	**Yes**	**17 (35.4%)**	**31 (64.6%)**	**<0.001**	**2.988 (1.245-7.172)**	**0.014**
	No	**55 (74.3%)**	**19 (25.7%)**			

Table 3. Quality of life scores according to the atrophy

a) at 12 months after operation

	Group I (n=72)	Group II (n=50)	p value
Physical*	85.0 ± 15.1	83.5 ± 13.7	0.579
Role*	86.1 ± 20.2	80.7 ± 19.4	0.139
Emotional*	88.3 ± 14.4	87.2 ± 18.8	0.705
Cognitive*	88.4 ± 14.2	89.0 ± 16.0	0.834
Social*	89.4 ± 18.2	84.7 ± 22.5	0.208
Global QOL*	72.3 ± 19.9	72.5 ± 18.6	0.948
Pancreatic pain†	12.2 ± 13.6	15.0 ± 14.2	0.280
Digestive†	12.7 ± 20.4	15.3 ± 18.7	0.468
Hepatic†	7.6 ± 14.0	6.3 ± 11.1	0.584
Bowel habit†	10.7 ± 15.1	11.7 ± 14.8	0.712
Body image†	19.2 ± 19.9	20.0 ± 25.0	0.847
Satisfaction†	42.6 ± 28.9	45.5 ± 23.3	0.563
Sexuality†	73.3 ± 25.0	64.1 ± 36.6	0.165

b) change between preoperation and 12 months after operation

	Group I (n=72)	Group II (n=50)	p value
Physical*	0.5 ± 17.7	2.2 ± 20.1	0.625
Role*	-0.1 ± 0.9	-0.1 ± 1.1	0.954
Emotional*	15.3 ± 23.7	18.2 ± 27.3	0.535
Cognitive*	1.9 ± 21.2	5.7 ± 25.8	0.378
Social*	8.9 ± 29.0	12.6 ± 36.1	0.540
Global QOL*	**11.2 ± 32.7**	**26.7 ± 31.3**	**0.011**
Pancreatic pain†	-1.6 ± 18.5	-8.6 ± 26.6	0.113
Digestive†	-7.5 ± 26.1	-1.7 ± 28.4	0.250
Hepatic†	**-8.7 ± 26.3**	**-22.7 ± 30.3**	**0.008**
Bowel habit†	-4.5 ± 21.2	-3.3 ± 26.3	0.785
Body image†	-4.5 ± 33.6	-11.2 ± 35.9	0.294
Satisfaction†	0.9 ± 35.7	7.4 ± 27.5	0.291
Sexuality†	8.8 ± 45.0	1.0 ± 43.1	0.432

* European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C-30 (EORTC QLQ-C30) (version 3) domains; Higher score means better quality of life.

† EORTC QLQ PAN26 domains; Higher score means worse symptom.

Table 4. Nutritional status according to atrophy

a) at 12 months after operation

	Group I (n=72)	Group II (n=50)	p value
RBW (%)	106.5 ± 21.2	103.8 ± 14.6	0.454
BMI (kg/m^2)	22.5 ± 2.8	22.2 ± 2.4	0.543
Transferrin	274.5 ± 39.5	266.3 ± 53.1	0.376
Prealbumin	**25.3 ± 5.6**	**22.5 ± 5.1**	**0.015**
Albumin	**4.3 ± 0.3**	**4.2 ± 0.4**	**0.005**
Protein	**7.2 ± 0.4**	**7.1 ± 0.4**	**0.017**

b) change between preoperation and 12 months after operation

	Group I (n=72)	Group II (n=50)	p value
RBW (%)	5.7 ± 14.3	6.6 ± 9.6	0.684
BMI (kg/m^2)	1.3 ± 2.3	1.4 ± 2.0	0.857
Transferrin	50.6 ± 54.7	33.6 ± 47.3	0.106
Prealbumin	-1.2 ± 9.8	-2.5 ± 8.6	0.533
Albumin	0.3 ± 0.4	0.4 ± 0.5	0.797
Protein	0.4 ± 1.1	0.3 ± 0.7	0.899

Table 5. Pancreatic exocrine function according to atrophy

a) Steatorrhea symptom score

Steatorrhea	**Group I (n=72)**	**Group II (n=50)**	**p value**
Preoperation	16.2 ± 24.4	22.7 ± 31.9	0.207
12 months	11.6 ± 18.7	11.3 ± 19.8	0.947
Change (during 12 months)	-4.7 ± 30.0	-12.2 ± 32.4	0.192

b) Stool elastase level

Stool elastase	**Group I**	**Group II**	**p value**
Preoperation	312.6 ± 157.8 (n=36)	287.9 ± 176.5 (n=21)	0.586
3 months	**78.4 ± 73.2 (n=43)**	**31.6 ± 31.6 (n=24)**	**0.001**
6 months	92.3 ± 157.8 (n=47)	55.4 ± 89.7 (n=25)	0.149
12 months	**104.1 ± 134.5** (n=41)	**33.6 ± 43.8** (n=25)	**0.003**
Change (during 12 months)	-207.7 ± 163.9 (n=31)	-249.8 ± 126.5 (n=16)	0.374

b) Exocrine deficiency grade at 12 months

Exocrine deficiency grade	**Group I (n=41)**	**Group II (n=25)**	**p value**
No exocrine deficiency (stool elastase ≥ 200)	14.6% (6/41)	0% (0/25)	0.133
Mild to moderate exocrine deficiency (100 ≤ stool elastase < 200)	7.3% (3/41)	8.0% (2/25)	
Severe exocrine deficiency (stool elastase < 100)	78.0% (32/41)	92.0% (23/25)	

Table 6. Pancreatic endocrine function according to atrophy

a) at preoperation

	Group I (n=52)	Group II (n=37)	p value
FBS	93.4 ± 10.3	95.3 ± 9.4	0.394
PP2	147.9 ± 32.3	141.3 ± 26.9	0.429
HbA1c	5.7 ± 0.3	5.7 ± 0.4	0.454
C-peptide	3.9 ± 4.2	3.4 ± 2.2	0.522
Insulin	13.7 ± 16.8	14.4 ± 15.5	0.854

b) at 12 months after operation

	Group I (n=56)	Group I (n=41)	p value
FBS	97.7 ± 10.8	98.3 ± 16.3	0.819
PP2	**133.6 ± 43.8**	**163.7 ± 74.7**	**0.035**
HbA1c	**5.7 ± 0.5**	**6.0 ± 1.0**	**0.088**
C-peptide	1.9 ± 1.1	1.7 ± 1.4	0.507
Insulin	6.6 ± 4.5	6.6 ± 4.8	0.972
New onset diabetes	**6/57 (10.5%)**	**11/41 (26.8%)**	**0.057**

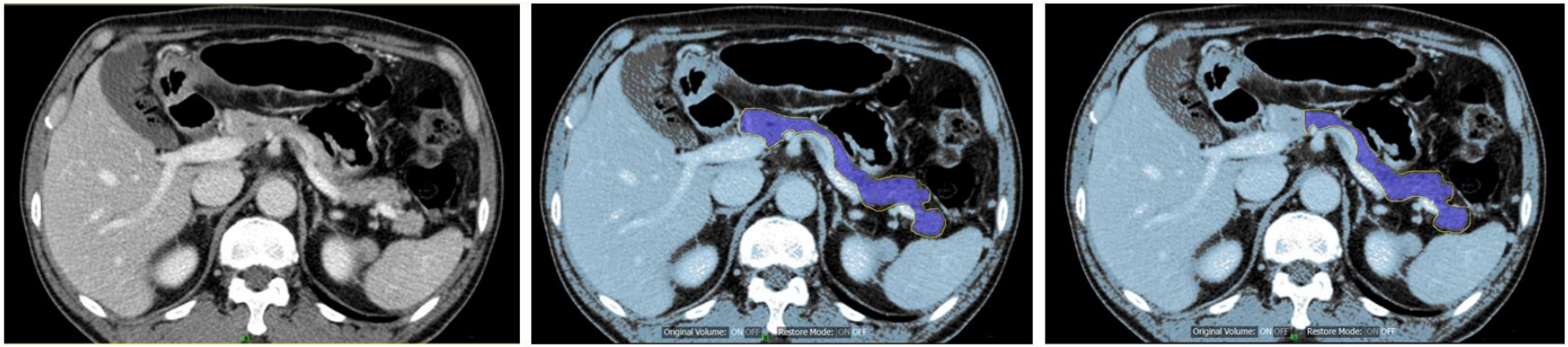
c) Consecutive change of HbA1c

HbA1c	**Group I**	**Group II**	**p value**
Preoperation	5.7 ± 0.3 (n=47)	5.7 ± 0.4 (n=35)	0.454
3 months	5.8 ± 0.4 (n=46)	5.9 ± 1.0 (n=31)	0.607
6 months	5.6 ± 0.4 (n=47)	5.8 ± 0.7 (n=32)	0.391
12 months	**5.7 ± 0.5 (n=47)**	**6.0 ± 1.0 (n=30)**	**0.088**

d) change between preoperation and 12 months after operation

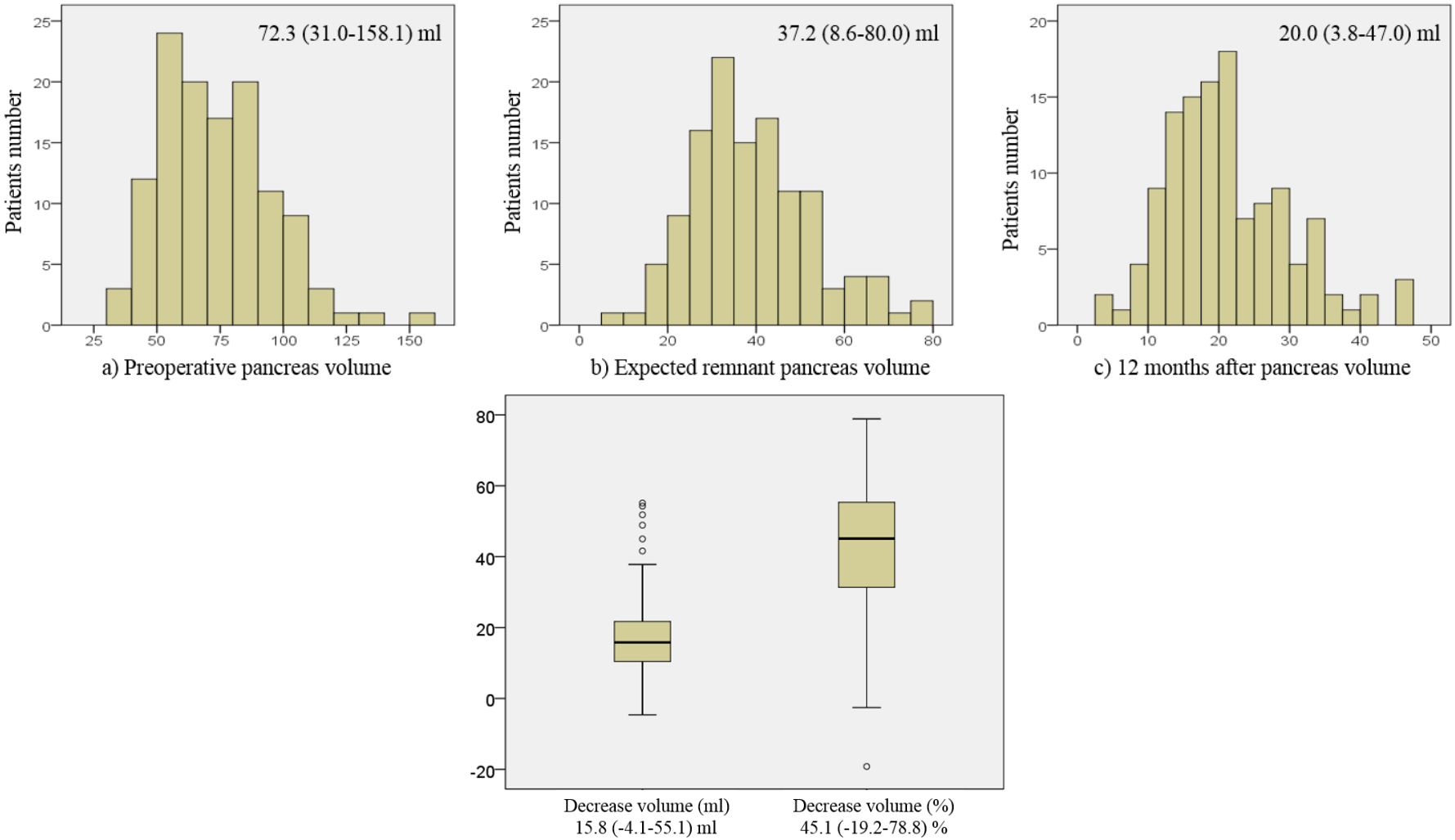
	Group I	Group II	p value
FBS	4.1 ± 12.3 (n=51)	0.8 ± 16.6 (n=37)	0.289
PP2	-15.9 ± 49.6 (n=34)	7.2 ± 71.6 (n=19)	0.172
HbA1c	-0.1 ± 0.3 (n=38)	0.3 ± 1.1 (n=25)	0.101
C-peptide	-2.3 ± 4.5 (n=40)	-1.8 ± 2.7 (n=27)	0.610
Insulin	-8.7 ± 16.9 (n=41)	-8.1 ± 16.0 (n=32)	0.905

Figure 1. Pancreas volumetry procedure using Xelis 3D program



a) Portal phase CT image b) Preoperative pancreas volume measurement c) Expected remnant pancreas volume measurement

Figure 2. Pancreas volumetry results



국문초록

췌십이지장절제술 후 잔존 췌장의 위축; 위험 인자와 삶의 질, 영양 상태 및 췌장 기능에 미치는 영향

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서론: 췌십이지장절제술 후 잔존 췌장의 위축은 이전 연구들에서 보고되어왔다. 하지만 이러한 위축성 변화를 심화시키는 인자들과 위축에 따른 영향에 대해서는 잘 연구되지 않았다. 이 연구에서는 잔존 췌장의 위축에 영향을 미치는 임상 인자들을 확인하고, 잔존 췌장의 위축이 삶의 질, 영양 상태 및 췌장의 외분비/내분비 기능에 미치는 영향을 확인하고자 하였다.

방법: 췌십이지장절제술 후 CT 및 삶의 질에 관한 설문지를 포함하여 12 개월의 경과 관찰을 완료한 122 명의 전향적으로 수집한 자료를 분석하였다. 수술 전, 수술 후 잔존 및 12 개월 후 췌장 용적을 CT 용적측정술 프로그램을 이용하여 측정하였다. 환자들을 12 개월 동안 감소한 췌장용적을 기준으로 두 군으로 나누어 분석하였다. 12 개월간 췌장 용적이 50% 미만으로 감소한 환자들을 I 군으로, 50% 이상 감소한 환자들을 II 군으로 분류하였다. 수술 전 당뇨가 있었던 환자들은 내분비 기능 분석에서는 제외하였다.

결과: 수술 후 12 개월동안 잔존 췌장의 용적은 45% 감소하였다. 악성질환과 수술 후 항암방사선치료는 다변량 분석에서 50% 이상의 용적 감소와 유의한 관련성을 보였다. 대부분의 삶의 질 점수와 영양상태 지표들은 수술 후 12 개월에 잔존 췌장의 위축 정도와 연관성을 보이지 않았다. 하지만, 대변 elastase 는 II 군에서 유의하게 더 많이 감소하였다 (33.6 μg/g vs. 104.1 μg/g, p=0.003). I 군에서 14.6%의

환자들이 췌장 외분비 기능 장애를 보이지 않았고 (대변 elastase ≥ 200 μg/g) 78.0%의 환자들이 심한 췌장 외분비 기능 장애 (대변 elastase < 100 μg/g) 를 보인 반면, II 군에서는 92.0%의 환자들이 심한 외분비 기능 장애를 보였고, 정상 외분비 기능을 유지한 환자는 없었다. 수술 후 12 개월에 당뇨는 II 군에서 더 많이 새롭게 확인되었다 (26.8% vs. 10.5%, p=0.057). 공복 혈당은 두 군간에 차이를 보이지 않았으나, 식후 2 시간 혈당은 II 군에서 유의하게 높게 확인되었고 (163.7 mg/dl vs. 133.6 mg/dl, p=0.035) 당화혈색소 또한 II 군에서 높은 경향성을 보였다 (6.0% vs. 5.7%, p=0.088).

결론: 췌십이지장절제술 후 잔존 췌장의 위축은 악성질환으로 수술 받았거나, 수술 후 항암방사선치료를 받은 환자에서 더 심하게 진행하는 것으로 확인되었다. 삶의 질과 영양 상태는 잔존 췌장의 위축 정도에 따라 유의한 영향을 받지 않았으나, 췌장의 외분비/내분비 기능은 위축의 심한 정도와 관련성을 보였다. 악성질환으로 수술을 받았거나 수술 후 항암방사선치료를 받은 환자들에게는 췌장의 외분비 및 내분비 기능 장애에 대한 더욱 주의 경과 관찰 및 적극적인 치료가 필요할 것이다.

주요어 : 췌십이장절제술, 위축, 삶의 질, 췌장 기능

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