

Fat Tissue Infiltration into the Pancreas Parenchyma and Its Effect on the Result of Surgery

Purpose: In Korea, there are few reports regarding the infiltration of fat tissue in pancreatic parenchyma in surgically resected organs. It is necessary to ascertain the correlation between the presence of fat tissue in the resection margin of the pancreas and the surgery outcome.

Methods: Fifty four patients who underwent pancreatic resection from Jan. 2007 to Nov. 2008 were enrolled in this study. Pathologic examination was performed to determine the presence of fat tissue in resected pancreatic parenchyma. Statistical correlation between the presence of fat tissue with clinical parameters and postoperative complication rates was analyzed.

Results: Among the specimens of all fifty four patients, fat tissue was found in 32 specimens of patients (59.3%). Female gender and patients whose body mass index exceeded 24 kg/m² were statistically correlated with the presence of the fat tissue in pancreatic parenchyma. There was no statistical relationship between infiltration of fat tissue with postoperative complications.

Conclusion: This study may serve as the base data for study in radiological imaging in detecting pancreatic tissue. A further larger scaled study is needed to validate the result of this study.

Key Words : Pancreas, Fat, Pancreaticoduodenectomy

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Introduction

Pancreaticoduodenectomy is a technically difficult procedure, and the incidence of postsurgical complications is high. Particularly, pancreaticojejunostomy leakage is a very serious complication, and it has been shown that the most prevalent cause of death after pancreaticoduodenectomy is pancreatic juice leakage due to the failure of pancreatico-enterostomy that may develop during reconstruction of the pancreatic duct. If a pancreatic fistula develops, this

leads to pancreatic juice leakage into the abdominal cavity, and adjacent vascular walls or intestinal walls may be damaged because of the potent self digestion capacity of the pancreatic juice. Consequently intraabdominal hemorrhage, abscess formation, sepsis and other fatal conditions develop, possibly leading to death.¹ Although the incidence of pancreatic anastomosis leakage has been reported to vary according to different investigators, it has been reported that after pancreaticoduodenectomy pancreatic anastomosis leakage occurs in approximately 5~40% cases.²⁻⁴ Numerous risk factors for leakage of the pancrea-

tico-enterostomy area have been reported, such as the size of the pancreatic duct, the presence or absence of pancreatitis, insufficient blood supply to the anastomosis site, hemorrhage in the anastomosis site, the level of tension in the anastomosis site, the weak tissue of the pancreas, and the experience of surgeons have been reported.^{1,5-8} For safe pancreatic anastomosis, diverse surgical techniques have been and studied that compared the outcomes of combination surgical methods such as pancreaticojejunostomy, pancreaticogastrostomy, duct-to-mucosa surgical methods, dunking surgical methods, or with or without stent installation. However, no significant differences in the development of pancreatic juice leak were observed, and until recently, a means that reduces the development of complications is as yet unavailable.⁹

Mathur et al. have reported recently that the incidence of pancreaticojejunostomy leakage is increased in patients with infiltration of fat tissue into the pancreatic parenchyma in the vicinity of the anastomosis site.¹⁰ In 1933, Ogilvie confirmed the infiltration of fat tissue in the pancreatic parenchyma by autopsy, and reported that it was detected in 9% of normal weight cases and 17% of obese cases.¹¹ Later, Olsen has observed that as age and weight increased, the extent of fat tissue infiltration into the pancreatic parenchyma was more severe.¹² Also, several investigators have reported the correlation of fat infiltration within the pancreas to obesity.¹³ In addition, some investigators have reported studies suggesting the possibility of the increase in the incidence of pancreatic anastomotic leakage after pancreaticoduodenectomy in patients with infiltration of fat tissue within the pancreas.^{10,14}

Therefore, in our study, by examining the infiltration of fat tissue in the pancreatic parenchyma of patients who received pancreatectomy, the association with clinical markers such as the patient obesity, the presence or absence of diabetes, etc. was investigated. In addition, it was examined whether infiltration of fat tissue correlates with development of pancreaticojejunostomy leakage after pancreaticoduodenectomy.

Methods

From January 2007 to November 2008, 54 patients received pancreatectomy at our institution. Among them 35 patients were male (64.8%), 19 were female (35.2%), and the mean age was 58.5 ± 11.1 years (range; 22~73 years).

With regard to surgical method, pancreaticoduodenectomy was performed in 37 patients, distal pancreatectomy in 17 patients, and the mean body mass index (BMI) was 22.8 ± 2.9 kg/m². The range of the BMI was from a minimum 16.3 kg/m² to a maximum 30.9 kg/m². There were 35 normal group patients whose BMI was lower than 24 kg/m² was, and 16 were obese patients with higher than 24 kg/m² BMI. Five patients were associated with diabetes.

The type of disease consisted of pancreatic cancer in 12 patients, benign pancreatic tumor in 15 patients, biliary tract cancer in 13 patients, ampulla of Vater cancer in 5 patients, gastric cancer in 3 patients, duodenal cancer in 2 patients, and other diseases in 4 patients (Table 1).

In particular, the incidence of complications after pancreaticoduodenectomy or pylorus-preserving pancreaticoduodenectomy (PPPD) was compared with end-to-side duct-to-mucosa pancreaticojejunostomy as the standard procedure. Suture methods were interrupted sutures, and pancreatic stent insertion was performed. For the assessment of pancreatic juice leakage and drainage, draining tubes were installed in the area adjacent to the pancreaticojejunostomy area. Patient progress was assessed by performing serum tests on the days 1, 3 and 7 after surgery, and the presence or absence of pancreatic juice leakage was determined by measuring the amylase and lipase levels in the body fluid drained by the draining tube. By assessing the presence or absence of the development of pancreaticojejunostomy leakage after pancreaticoduodenectomy and pylorus-preserving pancreaticoduodenectomy, as well as on the day of the removal of the draining tube, the correlation with the infiltration of fat tissue in the pancreatic parenchyma was analyzed.

Table 1. Demographics and operative data

Variables	n
Sex	M/F 35/19
Age	Mean±SD (range, 58.5±11.1 (22~73) year)
DM	No/Yes 49/5
BMI (kg/m ²)	≤24/24< 36/18
Preop cholesterol (mg/dl)	≤200/200< 44/10
Disease	
Pancreatic benign tumor	12
Pancreatic malignant tumor	15
Bile duct cancer	13
Ampulla of Vater cancer	5
Stomach cancer	3
Duodenal cancer	2
Others	4
Operation	DP*/PD [†] 17/37
Fatty tissue in pancreas	No/Yes 22/32 (59.3%)

*DP=distal pancreatectomy; †PD=pancreaticoduodenectomy

By histological examination of pancreatic tissues extracted from 54 patients who received surgery the presence of fatty tissue in the pancreatic parenchyma was assessed, and the patients were assigned to the Non-fat group and the Fat group. The correlation of the presence or absence of fatty tissues in the pancreatic parenchyma to clinical markers was analyzed. In addition, in patients who received pancreaticoduodenectomy, the incidence of complications according to the presence or absence of fatty tissue was compared.

As the objective standard, pancreatic leakage was defined as a concentration of amylase obtained from the drainage that was more than three times higher than normal serum values, and more than 50 ml/day drainage after the 11th post-operative day¹⁵. In addition, to compare the level of leakage, the standard of Bassi et al. was applied (Table 2).¹⁶

Table 2. Grade of postoperative pancreatic fistula (Bassi et al.¹⁵)

Grade	A	B	C
Clinical conditions	Well	Often well	III appearing/bad
Specific treatment	No	Yes/No	Yes
US/CT (if obtained)	Negative	Negative/positive	Positive
Persistent drainage (after 3 weeks)	No	Usually yes	Yes
Reoperation	No	No	Yes
Death related fistula	No	No	Possibly yes
Signs of infections	No	Yes	Yes
Sepsis	No	No	Yes
Readmission	No	Yes/No	Yes/No

Results

1. The association of the presence or absence of fatty tissue in the pancreas with clinical features in the entire patients

In 32 among the total of 54 patients, fat tissue was detected in the pancreatic tissue of patients (59.3%). With regard to distribution of fat tissue, it was present in the pancreatic lobules or the interlobal space. The gender and mean age of the Non-fat group were similar to the Fat group (Non-fat group, 56.9±13.3 years vs. Fat group 59.6±9.4 years, *p*=0.133). Similarly, there was no statistically significant difference in terms of the presence or absence of adipose tissues in the pancreas, as well as with or without the association with (Non-fat group, 3/22 vs. Fat group 2/32, *p*=0.304). In the obese patients whose pre-operative BMI was greater than 24, the presence of fat tissue in the pancreatic parenchyma was statistically higher (Non-fat group, 3/22 vs. Fat group 13/32, *p*=0.027). A trend of a higher pre-operative serum cholesterol level was observed in the Fat group (Non-fat group, 148.3±42.9 vs. Fat group, 172.4±49.4, *p*=0.069), but no statistical difference (Table 3).

Table 3. Comparison of clinical data according to the presence of intrapancreatic parenchymal fat

		Pancreatic fatty tissue		<i>p</i> -value
		-	+	
Sex	M	18	17	0.030
	F	4	15	
Age (years)	≤60	10	18	0.435
	60<	12	14	
DM	No	19	30	0.328
	Yes	3	2	
BMI (kg/m ²)	≤24	18	18	0.050
	24<	4	14	
Preoperative cholesterol level (mg/dl)	≤200	19	25	0.444
	200<	3	7	

Table 4. Postoperative data of pancreaticoduodenectomy patients (n=37)

Variables		n
Sex	M : F	28 : 9
Age	Mean ±SD (range, year)	61.1 ± 9.1 (34 ~ 73)
Pancreatic fat	No/yes	17/20
	At resection margin	15
Complication	No/yes	22/15
Pancreatic leak	No/yes	28/9
	Grade A	3
	Grade B	1
	Grade C	5
Mortality		3

2. Difference of clinical features of pancreaticoduodenectomy patients

Among the total of 54 patients, pancreaticoduodenectomy was performed in 37 patients. Postsurgical pancreaticojejunostomy leakage developed in 9 patients (21.05%). In patients with leakage, severity ISGPF grade¹⁶ A occurred in 3 patients, grade B in 1 patient, and grade C in 5 patients. Clinically, grade B and C patients were classified as major leakages. In patients who received pancreaticoduodenectomy, 15 patients demonstrated fat tissue

Table 5. Comparison of clinical data according to the presence of intrapancreatic parenchymal fat in pancreaticoduodenectomy patients

	Pancreatic resection margin fat		<i>p</i> -value
	-	+	
PJ leak	No	15	0.198
	Yes	7	
No leak + grade A leak	18	13	0.694
Grade B+C leak	4	2	

presence in the resection margin of the pancreas. The incidence of the complications of the pancreaticojejunostomy site according to the presence or absence of fat tissue in the resection margin was compared, and showed that 31.8% (7/22) had fat tissue, while 13.3% (2/15) did not, showing no statistical difference ($p=0.186$). The rate of major leakage in the Non-fat group was 18.2% (4/22), and 13.3% (2/15) in the Fat group, again demonstrating no statistical difference ($p=0.532$) (Tables 4, 5).

Discussion

Presently in Korea, reports on the infiltration of fat tissue into the pancreatic parenchyma of surgical tissues and its clinical significance are few.

Gaujoux et al.¹⁴ have reported in a study which was conducted on 100 patients who received pancreaticoduodenostomy that in patients with infiltration of fat tissue into the pancreas, patients without fibrosis findings in the pancreas, and patients with a body mass index higher than 25 kg/m², the incidence of complications was increased. The result of our study showed that in obese patients whose pre-operative BMI was higher than 24, the probability of the presence of fat tissue in the pancreatic parenchyma was statistically high. The incidence of pancreaticojejunostomy leakage according to the presence or absence of fat tissue was not statistically different.

In our study, tissues were collected from the dissection surface of the resected pancreas, as well as from random

sites, prepared as slides, and examined under light microscopy, and thus the possibility of the presence of fat tissue in unexamined areas cannot be ruled out. Therefore, to assess the presence or absence of fat tissue, it may be necessary to establish a regular standard method for tissue collection. However, since it is considered that fat tissue on the resection surface are involved in the association with surgical complications, the authors of this study regard the method of our study to be valid.

In the present study, the development of pancreatic duct leakage that manifested after pancreaticoduodenectomy was not statistically associated with the presence of fat tissue on the resection surface of pancreas. Lee et al.¹⁷ have pointed out that the increase of fat found during magnetic resonance imaging, which was performed for predicting the development of pancreatic fistulas in the pancreas, was a risk factor for post-operative pancreatic fistula formation. This report was based on radiological examination and did not confirm the resected samples of actual tissues, and thus it was different from our study.

Conclusion

In our patient groups, fat tissue was detected in the pancreatic parenchyma in 59.3% of the total patients. A higher detection trend was observed among the female patients, and in patients with a body mass index greater than 24 kg/m² was shown. This infers that in obese patients, the possibility of the presence of fat tissue in the pancreatic parenchyma is high. However, in our subject patients, highly obese patients whose BMI was greater than 35 were not included, and thus additional studies on such a cohort may be required. In addition, the development of complications after pancreaticoduodenectomy as well as the association with accompanying diabetes was not be observed, which may be due to the small number of subject patients. Therefore, it is thought that studies on a larger number of patients are recommended.

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