

**Comparison of Results between Pylorus-preserving Pancreaticoduodenectomy and Subtotal Stomach-preserving Pancreaticoduodenectomy : Report at a Single Cancer Institute**

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## **ABSTRACT**

**Background/Aims:** Pylorus-preserving pancreaticoduodenectomy (PPPD) has the advantage of achieving good nutrition status postoperatively, but delayed gastric empty (DGE) is a frequent complication leading to a longer fasting period. Subtotal stomach-preserving pancreaticoduodenectomy (SSPPD) is an alternative option to preserve nutritional status and shorten the fasting period. We retrospectively compared clinical results between PPPD and SSPPD.

**Methodology:** Subjects comprised 28 patients who underwent PPPD and 27 patients who underwent SSPPD between 2000 and 2009.

**Results:** Pancreatic carcinoma was more frequent in the SSPPD group ( $p=0.041$ ). Operating time was longer in the SSPPD group (610 min) than in the PPPD group (540 min;  $p=0.031$ ). Blood loss was greater in the SSPPD group (1810 ml) than in the PPPD group (1306 ml;  $p=0.048$ ). Period of NG tube intubation and fasting period were shorter in the SSPPD group (6 days and 9 days, respectively) compared to the PPPD group (15 days and 19 days, respectively;  $p<0.01$  each). Severe DGE as defined by the International Study Group of Pancreatic Surgery (ISGPS) was 7% in the SSPPD group and 46% in the PPPD group ( $p<0.01$ ). Postoperative complications and nutritional status in the early period did not differ between groups, although incidence of fatty liver was higher in the SSPPD group (78%) than in the PPPD group (25%;  $p<0.01$ ).

**Conclusions:** SSPPD is a useful alternative for pancreaticoduodenectomy. Further prospective studies with longer follow-up are warranted to clarify the superiority and problems associated with this procedure.

**KEY WORDS:** Pancreaticoduodenectomy; Delayed gastric empty; Nutrition status

**ABBREVIATIONS:** pylorus-preserving pancreaticoduodenectomy (PPPD) , subtotal stomach-preserving pancreaticoduodenectomy (SSPPD), delayed gastric emptying (DGE)

## INTRODUCTION

Pancreaticoduodenectomy can now be safely performed thanks to improvements in surgical techniques, operative materials and perioperative management (1, 2). However, morbidities associated with surgical procedures remain problematic, such as delayed gastric emptying (DGE) (3-6). With the aim of maintaining gastrointestinal function and long-term nutritional status after PD, pylorus-preserving pancreaticoduodenectomy (PPPD) was reintroduced by Traverso and Longmire in 1978 to minimize impairment of nutrition and quality of life using the classic Whipple's pancreaticoduodenectomy (7, 8). PPPD has been widely applied to the treatment of benign and malignant peri-pancreatic diseases (9). However, many surgeons are concerned about the high incidence of DGE (14-61%) during the early postoperative period irrespective of the type of anastomosis (10-13), as this complication can delay patient recovery and increase the duration of hospitalization. Some groups have shown no differences in rates of postoperative complication between PPPD and standard pancreaticoduodenectomy (3, 4). However, PPPD might provide advantages of better nutritional conditions and postoperative weight loss was reportedly lower in patients following PPPD in comparison with standard pancreaticoduodenectomy in one prospective randomized controlled trial (4). An alternative procedure, subtotal stomach-preserving pancreaticoduodenectomy (SSPPD) has been used since the 1990s with the aim of maintaining gastric function and avoiding DGE by minimizing the range of resection in gastrectomy (6, 14, 15). Comparative studies of these two procedures have recently been reported (3-6), but the relative superiority of each procedure remains controversial. Clarifying the relative superiority and problems associated with PPPD and SSPPD based on early and long-term postoperative results is important. The present study examined 55 patients who

underwent PPPD or SSPPD and compared clinical data, surgical records, and patient outcomes in the early and late postoperative periods at a single cancer institute. Our goal was to clarify both the clinical superiority of SSPPD in terms of DGE and differences in nutritional status in the early and late postoperative periods at a single cancer institute.

## **METHODOLOGY**

Subjects comprised 55 patients with peri-pancreatic pancreato-biliary diseases who underwent pancreaticoduodenectomy in the Division of Surgical Oncology at Nagasaki University Hospital (NUH) between 2000 and 2009. The patients consisted of 37 men and 19 women with a mean ( $\pm$ standard deviation (SD)) age of  $67.1 \pm 8.3$  years (range, 55-79 years). Underlying pancreato-biliary diseases among enrolled patients included pancreatic carcinoma (n=20), intraductal papillary mucin-producing neoplasm (n=10), chronic pancreatitis (n=2), ampullary carcinoma (n=8), bile duct carcinoma (n=14), and gall bladder carcinoma (n=1).

The present study compared clinical and operative findings and postoperative complications between PPPD and SSPPD groups. Postoperative follow-up with blood testing and measurement of body weight was performed every 3 months. Patients underwent contrast-enhanced computed tomography every 6 months. Gastroscopy was performed annually or if the patient reported upper abdominal symptoms. This study was a retrospective analysis, not a randomized control study. PPPD procedures were basically selected between 2000 and 2005 in cases where lymph node metastasis or direct invasion by the tumor was not observed around the pylorus lesions. SSPPD procedures were selected in cases with lymph node metastasis or direct invasion by the tumor around the pylorus or gastric lesions. This procedure was basically selected in all cases from 2006. All operations were performed by the same surgeons during this period. The study was approved by the Human Ethics Review Board of our institution. Data were collated from both anesthetic and patient charts plus the NUH database, covering the duration of the initial hospitalization following pancreatectomy.

PPPD was performed in 28 patients with the cut line at the duodenum 3 cm from the pylorus sphincter (**Figure 1A**)(a), and SSPPD was performed in 27 patients with the cut line at the gastric antrum 3 cm from the pylorus sphincter (**Figure 1A**)(b) (15). The intestinal anastomosis was completed as shown in **Figure 1B** and pancreatojejunostomy was performed in all patients, with the pancreas and seromuscular layer of the jejunum were anastomosed by interrupted suture using 4-0 polydioxanone (PDS) and the pancreatic duct was sutured to the jejunal wall by a running suture using 5-0 prolene with external tube drainage. The duodenum or gastric stump was anastomosed with an end-to-side procedure via the antecolic route (16). Anastomotic sites were routinely sprayed with 3.0 ml of fibrin glue (Beriplast P<sup>®</sup>; Aventis Behring, USA) to prevent pancreatic fistula (17).

Follow-up data were obtained from all patients retrospectively. Tube enteral nutrition was started on postoperative day 2. In general, the nasogastric (NG) tube was removed in cases where gastric retention was <300 ml/day after pancreaticoduodenectomy. Patients were allowed to resume liquid food intake after 5-7 days and gradually proceeded to a regular diet. All patients received stress ulcer prophylaxis in the form of H2 blockers or omeprazole during hospitalization. In cases with pancreatic fistula, octreotide was subcutaneously administered irrespective of suppressive influences on intestinal movement or exocrine function accompanying oral diet nutrition until the fistula was healed (1). According to the International Study Group of Pancreatic Surgery (ISGPS) classification (18), DGE was defined as the need for NG decompression for >7 days or as a delay in food intake because the patient could not proceed to a full regular diet within 14 days postoperatively (**Table 1**).

Data are expressed as mean  $\pm$ SD. Data from different groups were compared using one-way analysis of variance (ANOVA) and examined by Student's *t*-test or Dunnet's multiple comparison test. A two-tailed *P* value  $<0.05$  was considered significant. Statistical analyses were performed using STATISTICA<sup>TM</sup> software (StatSoft, Tulsa, OK).

## RESULTS

Pancreas carcinoma was significantly more frequent in the SSPPD group than in the PPPD group, but no significant difference in patient demographics or laboratory data was apparent between groups (**Tables 2, 3**). Surgical records showed that blood loss and operating time were significantly higher in the SSPPD group than in the PPPD group (**Table 3**). **Table 4** shows postoperative laboratory data and complications in the early postoperative period. The duration of NG tube intubation was significantly longer in the PPPD group than in the SSPPD group. Time to oral intake was also significantly longer in the PPPD group than in the SSPPD group. Incidence of DGE and Grade C DGE were significantly higher in the PPPD group than in the SSPPD group. Serum amylase level was significantly lower in the SSPPD group. Weight loss, frequency of other complications and mortality rate were not significantly different between groups. Duration of hospitalization tended to be longer in the PPPD group than in the SSPPD group, but no significant was identified.

Fifteen patients in the SSPPD group (56%) and 21 in the PPPD group (75%) could maintain oral food intake without severe tumor relapse for 24 months after operation. Comparative analysis of nutritional status was examined between groups in the long-term period (24 months). **Figure 2** shows nutritional status in the long-term period after pancreaticoduodenectomy. Body weight was unchanged between groups. Serum albumin level was significantly lower at 1 month after pancreaticoduodenectomy in both groups and was significantly higher at 6 months in the PPPD group than in the SSPPD group. However, serum albumin level had recovered to the same as baseline at 12 and 24 months in the SSPPD group. Cholinesterase and total cholesterol levels did not differ significantly between groups. Frequency of fatty liver after the operation between 6 and

24 months after operation was significantly higher in the SSPPD group (73%) than in the PPPD group (24%;  $p < 0.01$ ) (**Figure 3**). While, frequency of postoperative peptic ulcer during this period did not differ significantly between the SSPPD group (20%) and the PPPD group (48%;  $p = 0.21$ ).

## DISCUSSION

Pancreaticoduodenectomy is a standard procedure performed to achieve complete removal of peri-pancreatic head malignancies with surrounding tissues. PPPD has been established to maintain gastric function (7-9), but DGE remains as a problematic complication that delays patient nutritional recovery (3-6, 10-13). At this stage, earlier oral food intake or tube enteral feeding after gastrointestinal surgery including pancreaticoduodenectomy is preferable to maintain nutrition and immune-function(19, 20). The complication of DGE is thus a significant obstacle to nutritional recovery after pancreaticoduodenectomy, and may lead to other complications or prolonged hospitalization. Although tube enteral feeding is possible in the early postoperative stage, this often causes related complications such as abdominal pain and diarrhea (21). Particularly in cases of pancreaticoduodenectomy with complicated intestinal anastomosis, our experience is that tube enteral feeding cannot always be achieved. Oral food intake in the early stages is thus quite important.

First, DGE may occur due to mechanical problems such as transient torsion or angulations of the anastomotic intestine (3, 22), which can be corrected by various types of intestinal reconstruction. Position of duodenojejunostomy as an antecolic or retrocolic route has also been suggested as a cause of DGE (3, 23), but antecolic duodenojejunostomy after PPPD has not been shown to improve the incidence of DGE (3). We have performed PPPD or the standard Whipple's pancreaticoduodenectomy via a retrocolic route and changed to an antecolic route from 2000, as we encountered severe compressive obstruction of the intestines in a couple of patients. In the present study, we selected an antecolic approach in all cases. Second, postoperative gastroparesis may cause transient interruption of gastric output, leading to DGE (3). In such a state, more

than 2-3 weeks is necessary to recover from gastroparesis in our experience with PPPD. In cases of PPPD, ligation of the right gastric artery (RGA) is controversial (5, 24). Preserving the RGA may fix location of the pylorus, which interrupts the operative procedure and intestinal movement, while ligation of the RGA may decrease arterial supply to the pylorus and gastric antrum, leading to dysfunction in this lesion. We have performed both preservation and ligation of RGA in PPPD series in the 1990s and we could not identify any advantage to RGA preservation (unpublished data). Therefore, in series since 2000, we have selected ligation of the RGA. Treatment of gastrointestinal hormones such as motilin has been noted (25), but we did not find no advantages in using a motilin agonist as erythromycin. Results of an RCT by Yeo et al. (26) seem to support our decision against using motilin agonists.

With the aim of minimizing DGE as described above (3-6), we have routinely applied SSPPD since 2006 although SSPPD was selected only in cases with suspected node metastasis or direct invasion in the peri-pyloric region until 2005. The present study was thus a historical comparative analysis, not a controlled trial. Based on a series between 2000 and 2005, pancreatic cancer was significantly more frequent in the SSPPD group and operating time and blood loss were therefore significantly higher, as in other retrospective reports (4, 6, 14). No other significant differences between groups were identified in patient background or preoperative organ functions.

As reported in other studies (6, 14, 15), DGE was significantly more frequent and DGE grade was more severe in the PPPD group compared with the SSPPD group in the present study. Most patients with PPPD showed DGE, including mild grade A DGE (18). Oral food intake was delayed until 4-5 weeks after pancreaticoduodenectomy in most of these patients, with 2 patients needing endoscopic pyloric dilatation at 8 weeks.

Conversely, even in SSPPD with vertical anastomosis and wide orifice, grade B and C DGE occurred in only 6 patients (22%). In those patients, gastroparesis was observed for a few weeks, but no stenosis of gastrojejunostomy was seen (24). Four patients who underwent SSPPD showed symptoms due to bile reflux into the stomach. These patients did not have an enteric loop anastomosis between the efferent and afferent jejunum, known as Braun's enteroanastomosis (27). We therefore started to routinely perform Braun's enteroanastomosis in pancreaticoduodenectomy, as bile or output reflux often causes gastritis leading to poor feeding and malnutrition (28). With respect to other PD-related complications, no differences in frequency were apparent between groups in the present study, although Mark et al. reported that intraabdominal complications were a major risk factor for DGE (5). Duration of hospitalization tended to be longer in the PPPD group, which might be mainly due to the longer period of DGE. van Berge Henegouwen et al. reported shortened hospitalization in the PPPD group even though frequency of DGE was lower in the SSPPD group (5).

Tran et al. (4) performed long-term follow-up of nutritional status after the standard Whipple's pancreaticoduodenectomy. That report found no differences in body weight between groups with pancreaticoduodenectomy or PPPD up to 6 months postoperatively. Hayashibe et al. reported a comparison of serum albumin levels for 24 months between SSPPD and PPPD groups (6), showing no differences in albumin level at any postoperative period. In the present study, however, body weight and serum albumin level were lower in the SSPPD group up to 6 months after pancreaticoduodenectomy, showing similar recovery to the PPPD group. In the present study, some patients dropped out after 6 months due to tumor recurrence and progression. We therefore only examined patients who could visit our clinic. To the best of our knowledge, detailed analyses of nutritional

status for a long period after SSPPD are rare. In the long term after pancreaticoduodenectomy, nutritional status does not appear to differ markedly between groups. Recently, non-alcoholic steatohepatitis has been noticed as a malnutritional status among patients undergoing pancreaticoduodenectomy (29). In the present study, incidence of fatty liver tended to be higher in the SSPPD group than in the PPPD group. Kato et al. described pancreatic adenocarcinoma and postoperative diarrhea as factors associated with postoperative hepatic steatosis (29). Fatty liver was caused by reduced localized blood supply and malabsorption of lipoproteins after pancreaticoduodenectomy (30). In the SSPPD group in our study, pancreas carcinoma was more frequent compared with the PPPD group and postoperative diarrhea was also more frequent due to aggressive resection of the nerve plexus (31). Although this status was not reflected in blood tests, fat absorption might have been affected in patients with pancreas carcinoma. Peptic ulcer represents another postoperative complication after pancreaticoduodenectomy (32). In the present study, peptic ulcer was observed in both PPPD and SSPPD groups. Vagotomy was not always performed, but prophylactic H2 blockers were routinely administered.

In conclusion, at this stage, prospective and randomized controlled trials comparing PPPD and SSPPD have yet to be undertaken. In the next step, such trials should be used to clarify differences between these procedures. DGE was significantly decreased in the SSPPD group and nutritional condition was maintained in the early and late periods after operation in comparison with PPPD. Postoperative fatty liver was more frequent in the SSPPD group and careful management of lipid absorption appears necessary to improve nutritional status. SSPPD is a useful alternative to pancreaticoduodenectomy and further prospective studies with longer follow-up are warranted to clarify the benefits and problems associated with this procedure.

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## FIGURE LEGENDS

**FIGURE 1** Operative techniques(A). Cut lines were: (a) PPPD; and (b) SSPPD. The modified Child's reconstruction was performed with end-to-side gastro- or duodeno-intestinal anastomosis via an antecolic route (B).

**FIGURE 2** Nutritional status in the late period (>6 months) after PD. Solid line, PPPD group; dotted line, SSPPD group. #  $p < 0.05$  vs. preoperative value; \*  $p < 0.05$  vs. PPPD.

**FIGURE 3** Prevalence of fatty liver and peptic ulcer after PD. Open bar, PPPD group; closed bar, SSPPD group.

TABLE 1 ISGPS Classification for DGE (18)

Grade	NG tube	Oral intake
A	Intubation for 4-7 days Reinsertion after 4 days	Until 7 days
B	Intubation for 8-14 days Reinsertion after 8 days	Until 14 days
C	Intubation >14 days Reinsertion after 14 days	Until 21 days

TABLE 2 Comparison of patient demographics (continuous data) and operative findings between PPPD and SSPPD.

	PPPD (n=28)	SSPPD (n=27)	P value
Age (years)	68±8	66±12	0.56
Preoperative laboratory values			
Total protein (g/dl)	6.8±0.6	6.7±0.5	0.88
Albumin (g/dl)	3.9±0.3	3.9±0.4	0.94
Bilirubin (mg/dl)	3.0±3.6	2.1±1.9	0.68
Amylase (IU/L)	82±52	134±188	0.13
Cholinesterase (IU/L)	150±77	188±83	0.06
Total cholesterol (mg/dl)	195±92	171±37	0.56
Blood sugar (mg/dl)	130±47	115±34	0.41
Hemoglobin A1C (%)	6.0±1.4	5.7±0.9	0.77
Exocrine pancreatic function test (%)	58±19	64±11	0.45
Length from bile duct to gastro- or duodeno-intestinal anastomosis (cm)	41±7	46±7	0.447
Intraoperative bleeding (ml)	1306±776	1810±1054	0.023
Red cell transfusion (ml)	482±691	709±889	0.18
Operating time (min)	540±148	610±209	0.031

Continuous data are expressed as mean ± SD.

TABLE 3 Comparison of patient demographics (categorical data) and operative findings between PPPD and SSPPD.

	PPPD (n=28)	SSPPD (n=27)	P value
Gender			
Male/Female	21/7	15/12	0.22
Diseases			
Pancreas cancer	6	14	
IPMN*	6	4	
Chronic pancreatitis	1	1	
Biliary tract cancer	9	5	0.041
Ampullar cancer	6	2	
Gall bladder cancer	0	1	
Background of pancreas			
Normal pancreas/chronic pancreatitis	6/22	5/22	1.0
Diabetes (no/yes)	10/18	8/19	1.0
Smoking (no/yes)	13/15	6/21	0.40
Alcoholism (no/yes)	15/13	8/19	0.53
Hardness of pancreas (soft/hard)	21/7	11/16	0.25
Dilated pancreatic duct >5 mm (no/yes)	8/20	9/18	0.46
Tube drainage (external drainage/lost tube)	22/6	20/7	0.89
Additional jejunostomy	3/25	7/20	0.17
Lymph node dissection (D0/1/2)	1/3/24	0/2/25	0.37
Combined resection of portal vein (no/yes)	4/24	7/20	0.33
Re-operation (no/yes)	27/1	27/0	1.0
Intravenous albumin administered (no/yes)	3/25	3/24	1.0

\* Intraductal papillary mucin-producing neoplasm

TABLE 4 Comparison of postoperative outcomes between PPPD and SSPPD

	PPPD (n=28)	SSPPD (n=27)	P value
NG tube intubation	15±7	6±5	<0.01
Reinsertion of NG tube	4/24	2/25	0.67
Day to solid diet intake (days)	19±16	9±13	<0.01
Delayed gastric empty (no/yes)	1/27	11/16	<0.01
Grade A / B / C	1/13/13	10/4/2	<0.01
Changes of body weight at 1 month (kg)	-2.3±2.7	-3.0±3.3	0.58
Postoperative laboratory values			
Total protein (g/dl)	5.2±0.6	5.2±0.8	0.79
Albumin (g/dl)	2.9±0.4	2.8±0.4	0.57
Bilirubin (mg/dl)	2.8±2.2	2.5±2.8	0.09
Amylase (IU/L)	166±100	132±150	0.032
Cholinesterase (IU/L)	81±38	96±52	0.35
Total cholesterol (mg/dl)	93±22	95±20	0.57
Pancreatic fistula (no/yes)	24/4	23/4	1.0
Intra-abdominal infection (no/yes)	23/5	24/3	0.71
Postoperative bleeding (no/yes)	27/1	26/1	1.0
Massive ascites (no/yes)	25/3	25/2	1.0
Postoperative diabetes* (no/yes)	19/9	21/6	1.0
Mortality	28/0	26/1	1.0
Hospital stay (days)	42±18	31±26	0.06

\* Insulin infusion was for >7 days postoperatively.

Figure 1A

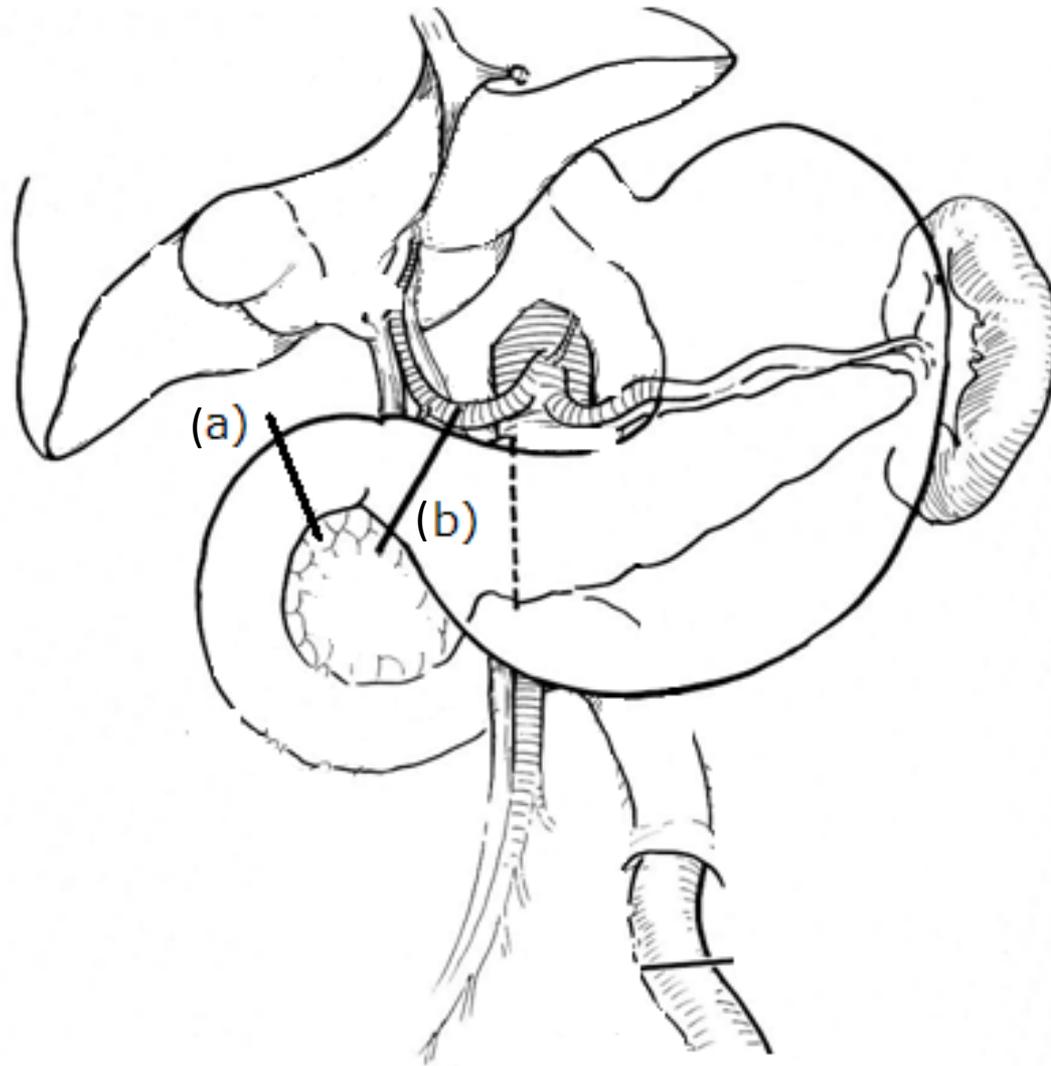


Figure 1B

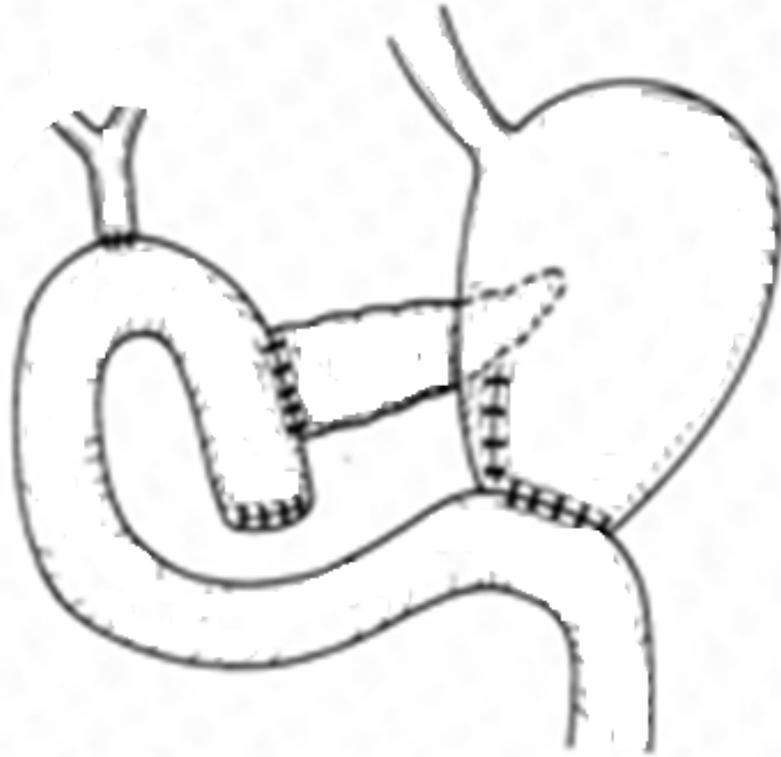
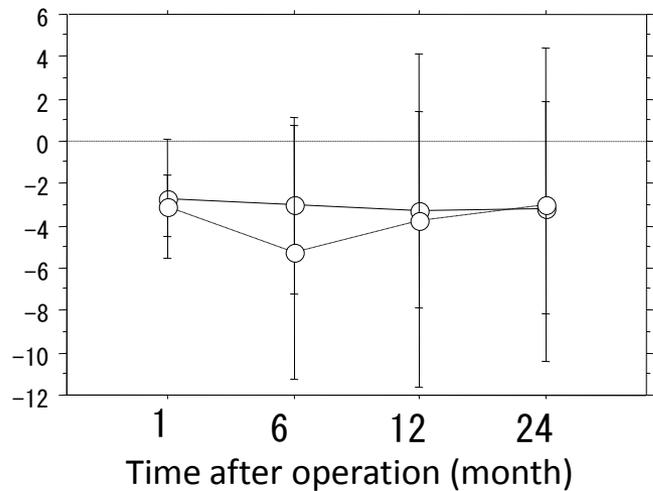
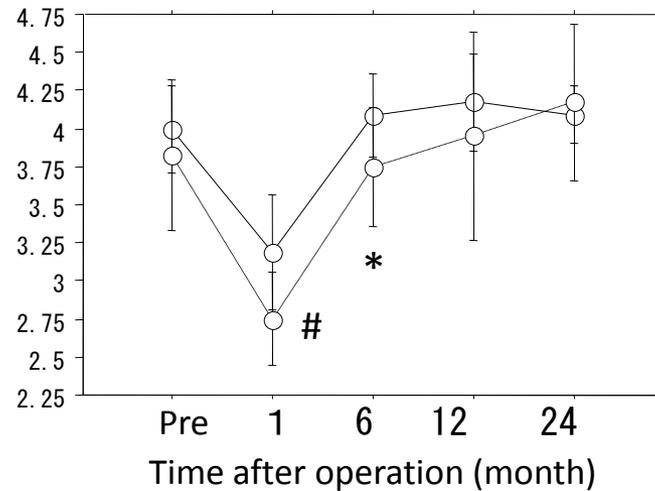


Figure 2

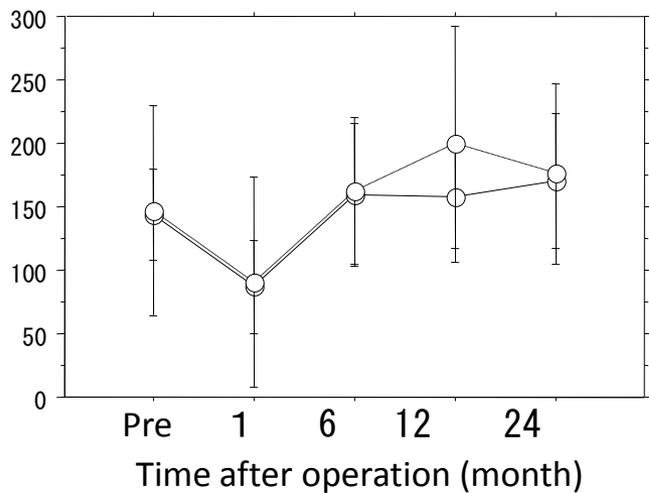
Changes of body weight before operation (kg)



Serum albumin (g/dl)



Chorine esterase (IU/L)



Total cholesterol (mg/dl)

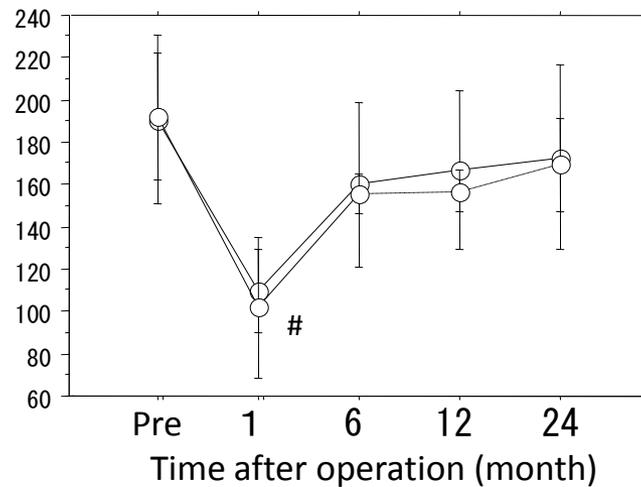


Figure 3

