ORIGINAL ARTICLE

A Dog Model of Pancreaticojejunostomy Without Duct-to-Mucosa Anastomosis

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ABSTRACT

Context Various anastomosis techniques have been introduced for the safe pancreaticoenterostomy. **Objective** In the present study, we developed an experimental animal model for simple pancreaticojejunostomy and evaluated the feasibility, safety, and efficacy of this technique. **Animals** Ten dogs were studied. **Intervention** The dogs underwent the simple approximation ("docking") method for pancreaticojejunostomy and were re-explored on the 30th post-operative day. **Main outcome measure** After excision of the remnant pancreas with the jejunal segment of the pancreaticojejunostomy, the degrees of fibrosis in the remnant pancreas were analyzed according to the patency of the pancreaticojejunostomy. **Results** There were no mortalities and clinically significant complications. The patency of pancreaticojejunostomy remained in six cases and was obliterated in four cases. It was noted that obliterated pancreaticojejunostomy accompanied cases with more dilated pancreatic ducts (3.1±0.4 mm *vs*. 5.5±0.6 mm, P=0.008). The grade of pancreatic fibrosis was significantly correlated with the obliterated pancreaticojejunostomy (P=0.038) and the size change of the remnant pancreatic duct (P=0.040). **Conclusions** The suggested simple pancreaticojejunostomy method is easy and shows no evidence of significant pancreatic fistula. However, the potential risk of dysfunction in the remnant pancreas limits its possible clinical applications. The meticulous duct-to-mucosa pancreaticojejunostomy is highly preferred to manage the remnant pancreas following pancreaticoduodenectomy.

INTRODUCTION

The pancreaticointestinal anastomosis is thought to be one of the most important procedures in pancreatic surgery. With the development of surgical experience and techniques, the operative mortality and morbidity of pancreatic surgery have been reduced to within an acceptable range [1, 2, 3, 4]; however, the complications related to pancreatic leakage still threaten both patients and pancreatic surgeons. Pancreatic leakage is one of the main obstacles for inexperienced surgeons in the performance of advanced pancreatic surgery. In addition, the number of soft pancreas cases (soft texture with a small pancreatic duct) after pancreatic resection seems to be increasing, indicating that the potential risk of post-operative pancreatic leakage might be also increasing [5, 6]. Even though duct-to-mucosa pancreaticojejunostomy generally has been performed in clinical practice for pancreaticointestinal anastomosis following pancreatectomy, delicate surgical techniques and experience are needed. Therefore, it might be necessary to develop an easy and safe technique for pancreatico-intestinal anastomosis, especially for beginning young pancreatic surgeons. Using an animal model, we developed a simple approximation method, the so-called, "docking" method, for pancreaticojejunal anastomosis and evaluated the feasibility, safety, and efficacy of this technique, as well as its potential application to the clinical setting.

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Key words Models, Animal; Pancreatic Fistula; Pancreatico-jejunostomy

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MATERIALS AND METHODS

Animals

Ten dogs with a median body weight of 21 kg (range: 20-23 kg) were used to evaluate the feasibility and efficacy of this method.

Surgical Technique

Under general endotracheal anesthesia, the dog was placed in the supine position. A sterile drape was used and preparations for the operative field were made. The

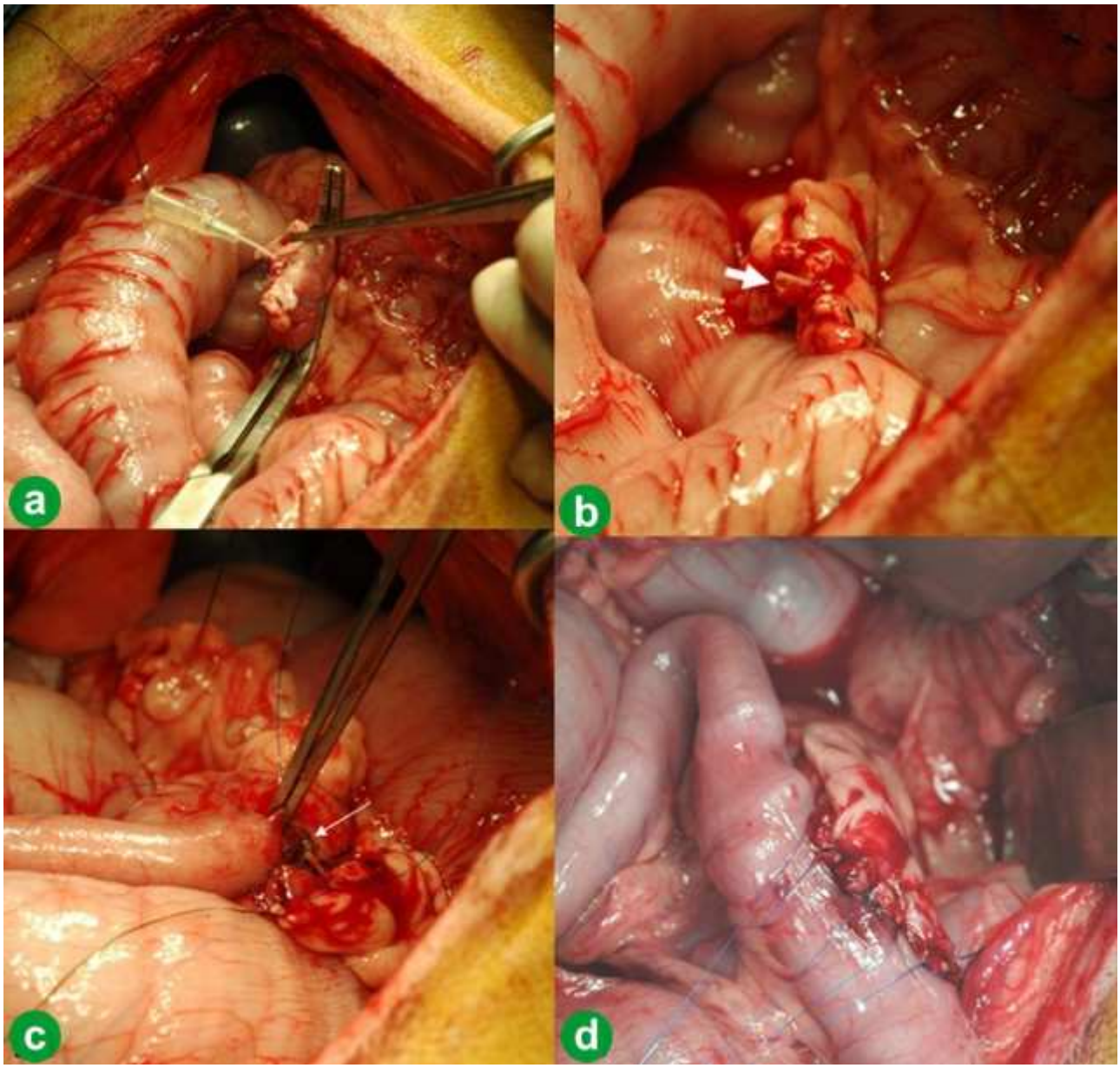

Figure 1. Establishment of an animal model for the docking method. After dividing the pancreatic neck portion, a 22 G angiocatheter was inserted into the pancreatic duct (**a.**). Note the clear pancreatic juice from the inserted pancreatic duct stent (**b.**). The pancreatic stent is inserted into the small jejunostomy site (white arrow)-docking (**c.**). Simple interrupted sutures to approximate the pancreas and jejunal wall (**d.**)

dog underwent laparotomy through a midline incision. After upward retraction of the stomach, the pancreas was identified. After careful dissection of the pancreatic neck above the superior mesenteric vein-splenic vein-portal vein confluence, the pancreatic neck was divided using a surgical knife. The proximal pancreatic stump was controlled by continuous interlocking sutures (4-0 prolene). The pancreatic duct of the distal pancreas was identified using a 22 G angiocatheter (Figure 1a) and the catheter was inserted into the pancreatic duct and fixed to the pancreas. After confirming the flow of pancreatic juice through the pancreatic duct stent (Figure 1b), the proximal jejunum was transected at 30 cm from the origin of the small bowel. The simple approximation method for pancreaticojejunostomy was performed in Roux-en-Y fashion. An approximately 2-3-mm sized jejunostomy was made at the potential site of the jejunum for pancreaticojejunostomy. After the pancreatic duct stent (angiocatheter) was inserted into the small jejunostomy site ("docking") (Figure 1c), five or six simple interrupted sutures were applied to approximate the pancreas and the jejunum without duct-to-mucosa anastomosis (Figure 1d). No biologic fibrin glue was applied and no drain was inserted. The abdominal wall was closed in two layers and a skin stapler was applied. Post-operatively, the dogs were extubated and fluid intake was administered upon recovery from anesthesia. Intramuscular gentamicin was given for three days after surgery. All dogs (n=10) were re-explored and scarified on the 30th post-operative day. The abdominal cavity, anastomosis site, and the pancreas were carefully observed for adhesions, signs of peritonitis, abscess, and anastomosis leakage. The

pancreaticojejunostomy sites were excised for gross and histologic examination. After fixation in 10% formalin solution, specimens were paraffin-embedded for histologic examination with hematoxylin-eosin and Masson-trichrome staining. Fibrosis that follows as a physical healing process after transection of the pancreatic parenchyma affects the pancreatic duct especially if has a small diameter at the initial operation leading to its constriction, and thus increasing the chance of development of a persistent pancreatic fistula [7, 8, 9]. Based on Newman's previous study [10], the severity of pancreatic fibrosis was subsequently graded as follows: grade 1, less than 10% of the section affected; grade 2, 10-40% of the section affected; and grade 3, more than 40% of the section affected.

STATISTICS

The continuous variables were expressed as mean±standard deviation (SD), and categorical variables were described as frequencies. Non-parametric analyses (Wilcoxon signed rank test, Mann-Whitney U test and Spearman rank correlation were applied to comparative data. The linear-by-linear association chi-square test was used in the analysis of categorical variables. A P value less than 0.05 was accepted as statistical significance. The SPSS (Version 15.0 for Windows, SPSS Inc., Chicago, IL, USA) was used for the statistical analysis.

ETHICS

The present study was performed under protocols approved by the Animal Care and Use Committee of the College of Medicine of Yonsei University. All animals received humane care according to the criteria outlined in the "Guide for the Care and Use of Laboratory Animals (1996)" prepared by the National Academy of Sciences.

RESULTS

Post-operative Course, Morbidity, and Mortality

All animals resumed oral intake within one day after surgery. During 30 days after surgery, no mortality was noted. There were no clinically significant complications, such as peritonitis, abscess, or bleeding, and only superficial wound infection was noted in two dogs. At re-exploration on the 30th day after the initial

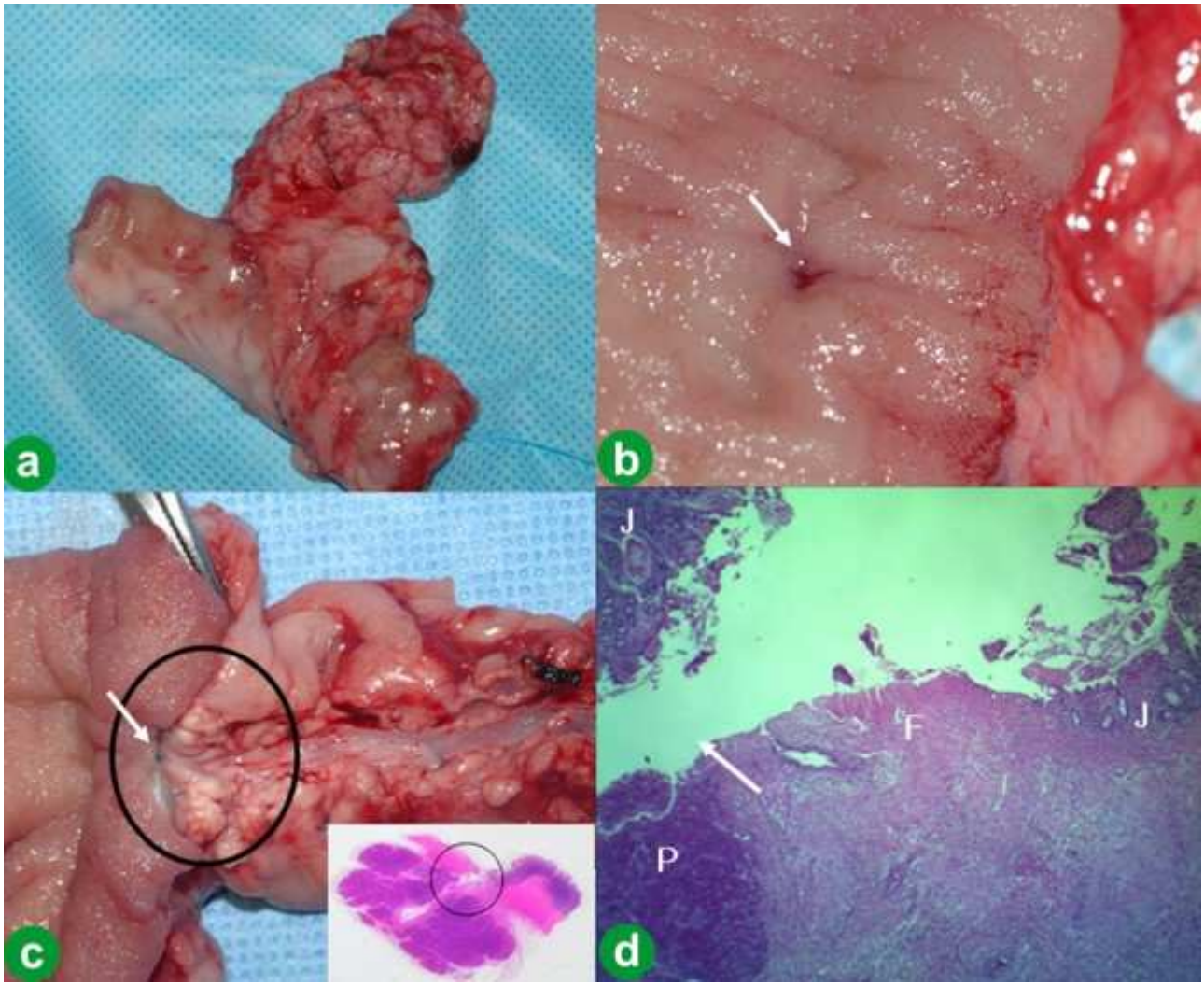

Figure 2. Relaparotomy and specimen examination on the 30th day after the initial operation. Excised specimen of a previous pancreaticojejunostomy (**a.**), Note the pancreatic duct opening (white arrow and black circle) in the jejunum and the longitudinal opening along the pancreatic duct (**b.**, **c.**). Pancreatic duct (P) was connected to the jejunum (J) by thick fibrosis (F) (**d.**) (H&E x40).

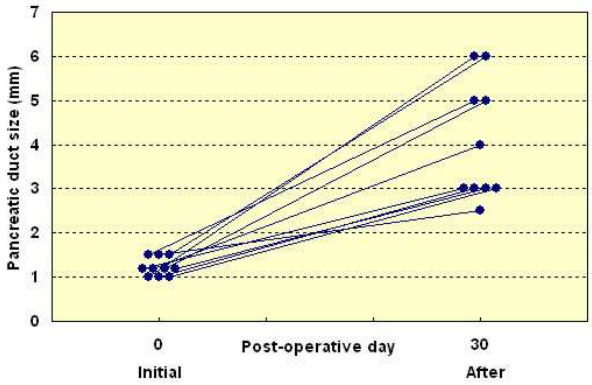

Figure 3. Change in pancreatic duct size after using the simple approximation method. (Wilcoxon signed rank test, P<0.001).

operation, only mild to moderate adhesion was noted around the pancreaticojejunostomy site, and there were no signs of anastomosis leakage, abscess, peritonitis, or bleeding.

The Morphologic Changes of the Remnant Pancreas Using the Docking Method

When examining the excised specimens, the patency of pancreaticojejunostomy was sustained in six animals (Figure 2abc); however, the patency of the pancreatic duct was obliterated in the other animal models. The initial size of the pancreatic duct of the experimental animals was less than 2 mm (1.2±0.2 mm); however, the lumen was noted to be dilated (4.1±1.3 mm) 30 days after the initial operation (Figure 3, Wilcoxon signed rank test, P<0.001). The size of the pancreatic duct examined at the second operation was significantly different according to pancreatic duct patency (3.1±0.4 mm *vs*. 5.5±0.6 mm, duct patent group *vs*. duct obliterated group, respectively; Mann-Whitney U test, P=0.008). Upon routine histologic examination (H&E) of the remnant pancreas with a patent pancreatic duct, the pancreatic duct was connected to the small bowel mucosa through the bridge of the fibrotic band (Figure 2d).

Pancreatic Fibrosis and Correlation with Morphologic Changes in the Remnant Pancreas

Pancreatic fibrosis grade 1 (less than 10%) was observed in three animals, grade 2 (10-40%) in four animals, and grade 3 (more than 40%) was noted in three animals (Figure 4). When the pancreatic fibrosis grade system was correlated with the patency of the pancreaticojejunostomy, it was noted that pancreatic fibrosis was more prominent in the animals with obliterated pancreatic ducts (P=0.038, linear-by-linear

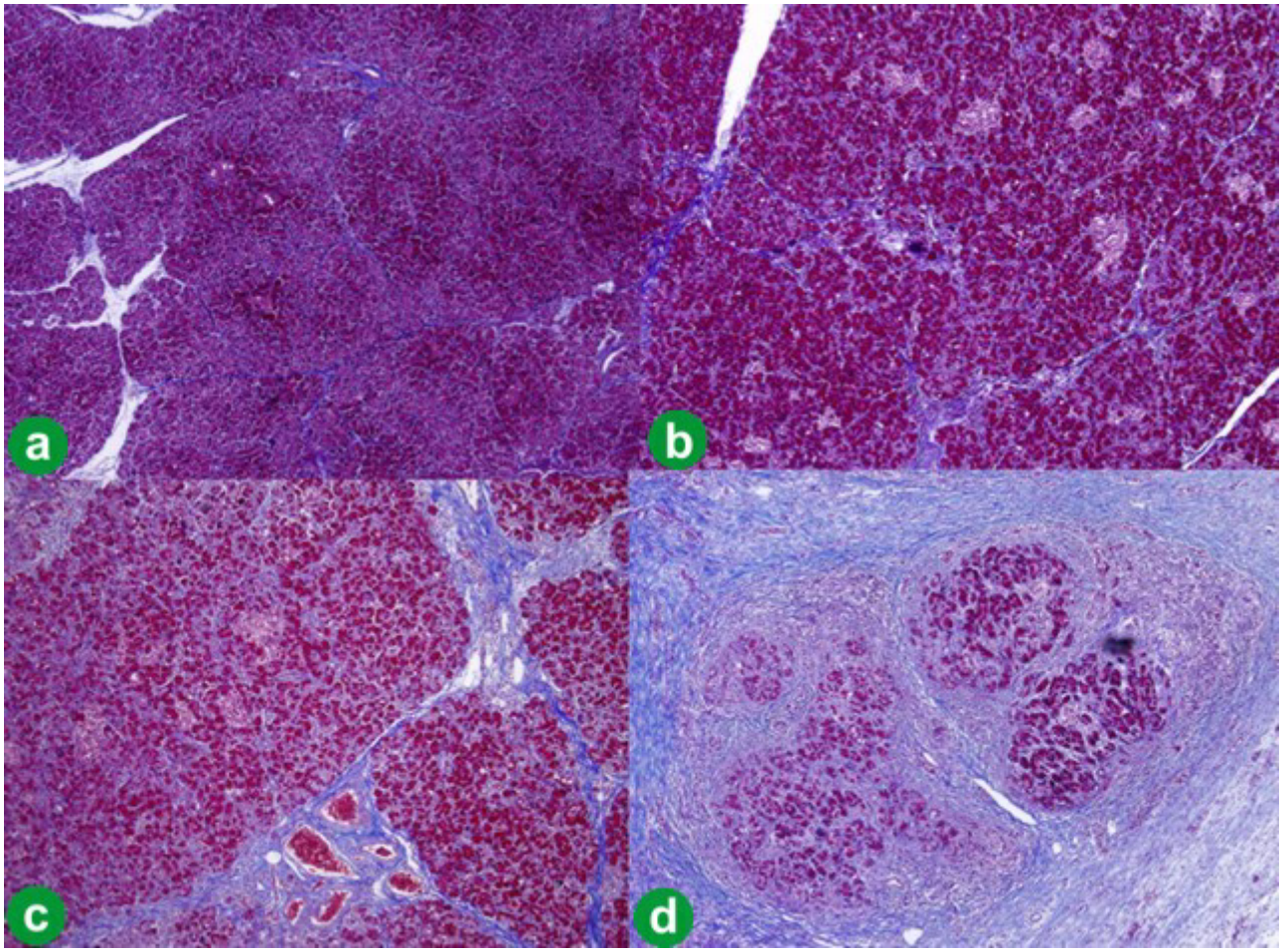

Figure 4. Fibrosis grading and morphological correlation. Normal (**a.**). Severity of pancreatic fibrosis was graded: grade 1 (**b.**, less than 10% of the section affected); grade 2 (**c.**,10-40% of the section affected); and grade 3 (**d.**, more than 40% of the section affected).

Table 1. Correlation between pancreatic duct (anastomosis) patency and pancreatic fibrosis.

	Grade 1: less than 10% (n=3)	Grade 2: 10-40% (n=4)	Grade 3: more than 40% (n=3)	P value [a]
Obliterated (n=4)	0	1 (25%)	3 (75%)	0.038
Patent (n=6)	3 (50%)	3 (50%)	0	

[a] Linear-by-linear association chi-square test

association, Table 1). In addition, the size change of the remnant pancreatic duct at the second operation was significantly correlated with the pancreatic fibrosis grade (P=0.040, Spearman rank correlation, Table 2).

DISCUSSION

A clinically evident post-operative pancreatic fistula is still a threatening post-operative complication and may be related to vascular complications, bleeding, abscess, sepsis, wound infection, or delayed gastric emptying, resulting in increased medical costs and prolonged hospital stay [6, 7, 8]. Therefore, many pancreatic surgeons have attempted to develop a more effective and safe surgical technique to reduce post-operative pancreatic fistula. Many clinicopathological factors are proposed as risk factors for pancreatic fistula. Among them, a soft remnant pancreas with a small pancreatic duct is known to be closely related to post-operative pancreatic fistula [7, 8, 9]. With the development of socioeconomic status, the diagnosis of pancreatic neoplasm without any clinical symptoms seems to be increasing, and the chance of encountering a soft remnant pancreas is also increasing, which provides a challenging pancreaticojejunal anastomosis to inexperienced pancreatic surgeons.

In this pancreaticojejunal anastomosis model (the so-called “docking method”), we attempted to develop an easy method for managing a soft remnant pancreas. Kuroda *et al*. [11] introduced a new technique for pancreaticointestinal anastomosis with canine model in which suturing of the pancreatic parenchyma is not required. They showed that the clinical outcome was based on the clinical treatment of the soft remnant pancreas. However, it is thought that the preparation for pancreatic duct anastomosis in their model is difficult. In contrast, our simple approximation method is thought to be easy and safe. As described in the materials and methods, this surgical procedure is very simple, and we observed neither post-operative mortality nor significant pancreatic fistula related to abscess, bleeding, or sepsis. Only in two out of ten dogs superficial wound infections were observed. However, the sizes of the remnant pancreatic ducts were significantly increased (1.2±0.2 mm *vs*. 4.1±1.3 mm; P<0.001), and the losses of pancreatic duct patency were noted in four animals. Histologic examination suggested that the anastomosis was completed by fibrotic change between the jejunum and pancreas. This fibrotic change facilitated the stenosis around pancreatic duct, which could result in chronic inflammation (fibrosis) of the remnant pancreas. As shown in our experimental model, pancreatic duct patency is related to significant luminal dilatation of the remnant pancreatic duct, which is associated with the degree of remnant pancreatic fibrosis (Tables 1 and 2). Even though no significant post-operative morbidity was found in this animal study, these observations might suggest a potential risk of functional deterioration of the remnant pancreas when using this method. Greene *et al*. [12] have reported that duct-to-mucosa anastomosis is superior to the simple invagination method for anastomotic patency in their animal model. In addition, recent morphologic and functional studies of remnant pancreas management showed similar findings [13, 14]; this conclusion is also supported by our results of the current study.

Some authors have suggested pancreatic duct closure without anastomosis for the management of a remnant pancreas following pancreaticoduodenostomy [15, 16]; however, this method is known to be greatly associated with perioperative morbidities, such as acute pancreatitis, pancreatic fistula, and diabetes. Our described pancreaticojejunal anastomosis model is easy and shows no evidences of significant pancreatic fistula. However, the potential risk of dysfunction in the remnant pancreas was highly expected by the loss of pancreatic duct patency, a dilated pancreatic duct in the remnant pancreas, and subsequent moderate to

Table 2. Correlation between the size change of the remnant pancreatic duct and pancreatic fibrosis

Change in the duct size (mm) [a]	Grade 1: less than 10% (n=3)	Grade 2: 10-40% (n=4)	Grade 3: more than 40% (n=3)	P value [b]
1	0	1 (25%)	0	**0.040**
1.8	2 (67%)	0	0	
2	1 (33%)	1 (25%)	0	
2.8	0	1 (25%)	0	
3.5	0	0	1 (33%)	
3.8	0	0	1 (33%)	
4.5	0	0	1 (33%)	
5.0	0	1 (25%)	0	
Mean±SD	**1.9±0.1**	**2.7±1.7**	**3.9±0.5**	

[a] Change in the duct size after using the simple approximation method: post-operative day 30 *versus* initial value (post-operative day 0).
[a] Spearman rank correlation

severe pancreatic fibrosis. Therefore, this anastomosis model seems to be applicable in only certain difficult clinical situations that are recommended ligation of the pancreatic duct.

In terms of remnant pancreatic function, previous studies have demonstrated that the degree of pancreatic duct patency is closely related with exocrine and endocrine function of the remnant pancreas [17, 18, 19, 20]. Therefore, it is essential to preserve anastomotic patency, which is the important factor for maintaining remnant pancreatic function. As our results showed, the physical healing process following surgical transection of pancreatic parenchyma could lead to stenosis of the pancreatic duct, which had greater chance to become clinically evident when the size of the duct at the initial operation is smaller. Therefore, duct-to-mucosa anastomosis seems superior as mechanically opposes the forces of fibrotic constriction. The duct-to-mucosa anastomosis may be the first choice for a safe pancreaticojejunostomy. More clinical experience and a meticulous surgical technique may be a key to the safe reconstruction of pancreaticointestinal anastomosis.

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Conflict of interest The authors have no potential conflict of interest

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