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Authors' Contribution: Study Design A Data Collection B Statistical Analysis C Data Interpretation D Manuscript Preparation E Literature Search F Funds Collection G Imanaga's First Method for Reconstruction with Preservation of Mesojejunal Autonomic Nerves During Pylorus-Preserving Pancreatoduodenectomy

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Pancreatic diseases

Imanaga's first method

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Case series Patient: Final Diagnosis: Symptoms: Medication: Clinical Procedure: Specialty:

> Objective: Background:

Unusual or unexpected effect of treatment

Postoperative physiologic function

Pancreatic surgeries have undergone substantial development. Pancreaticoduodenectomy and pylorus-preserving pancreatoduodenectomy inherently require reconstruction. In 1960, Professor Imanaga introduced a reconstructive technique performed in the order of the gastric remnant, pancreatic duct, and biliary tree from the viewpoint of physiologic function after pancreaticoduodenectomy. We herein report our experience with Imanaga's first method during pylorus-preserving pancreatoduodenectomy and retrospectively evaluate the short- and long-term outcomes. Technicalities and pitfalls are also discussed.

Case Report:

Report: Eight patients were evaluated (mean follow-up period, 16.7±1.0 years). Mesojejunal autonomic nerves were preserved without tension to the greatest extent possible for reconstruction. Intentional dissection of regional lymph nodes and nerves was performed in five and two patients, respectively. During the short-term post-operative period, one patient developed pancreatic leakage resulting in an intraperitoneal abscess, and endo-scopic transgastric drainage was required. Two patients developed delayed gastric emptying. In three patients, passage from the duodenojejunostomy to pancreaticojejunostomy was mechanically disturbed, and endoscop-ic dilations with a balloon bougie were repeated. Repeated cholangitis was observed in three patients. During the long-term postoperative period, neither cachexia nor sarcopenia was observed, although two patients had diabetes. Two patients were free from all medications. Three patients who did not undergo intentional dissection of lymph nodes and nerves showed acceptable short- and long-term period.

Conclusions

Imanaga's first reconstruction may have potential benefits, especially for diseases that do not require intentional dissection. Adequate mobilization of the pancreatic remnant is important for successful reconstruction.

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MeSH Keywords:

Imanaga • Pancreaticoduodenectomy • Pylorus • Reconstructive Surgical Procedures

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Background

Pancreaticoduodenectomy (PD) was first attempted by Codivilla in 1898 [1] and was thereafter successfully performed by Kaush in 1912 [2]. In 1935, Whipple demonstrated that PD was technically feasible and compatible with reasonable function after recovery [3]. Pylorus-preserving PD (PpPD) was first introduced by Watson in 1944 [4], and Traverso and Longmire subsequently documented the usefulness of this surgery [5]. The artery-first approach was reported by Weitz in 2010 [6]. Pancreatic surgeries for pancreatic diseases are now performed worldwide.

PD, subtotal stomach-preserving PD (SSpPD), and PpPD inherently require three reconstructions: digestive tract, biliary tree, and pancreatic duct. Reconstructive surgeries such as the Whipple and Child procedure have been introduced [3,7–9] and have already undergone some modifications [10,11]. In the Japanese guidelines [12], reconstructive techniques are categorized based on the order of the gastric remnant, biliary tree, and pancreatic duct as follows: type 1 is defined as the biliary tree, pancreas, and stomach in that order (e.g., the Whipple procedure) [3]; type 2 is defined as the pancreas, biliary tree, and stomach in that order (e.g., the Child procedure) [8]; and type 3 is defined as the stomach, pancreas, and biliary tree in that order (e.g., the Cattell method) [13].

Hajime Imanaga (1902–1997) was a professor at the Department of Surgery, Nagoya University (Nagoya, Japan) [14] who focused on surgical treatments for pancreatic disease and portal hypertension [14,15]. He introduced a reconstructive technique involving the gastric remnant, pancreatic duct, and biliary tree in that order from the viewpoint of physiologic functions after PD [14]. This technique, established in 1960, is called "Imanaga's first method" and is categorized as type 3 according to the Japanese guidelines [12]. Pancreatic surgeons have since modified his method, further developing this reconstructive technique. We herein report our experience with Imanaga's first method during PpPD and retrospectively evaluated the short- and long-term outcomes. The technical specifications and surgical pitfalls of the procedure are also discussed.

Case Report

From June 2000 to March 2003, we performed Imanaga's first method for reconstruction during PpPD (Figure 1). Approximately 20 cm of the distal jejunum was sacrificed as close to the jejunal wall as possible, according to one segment of jejunal vessels. The jejunum was then lifted in a retrocolic manner. Even subtle tension of the mesojejunum was avoided, and the autonomic nerves in the mesojejunum of the lifted jejunal limb were preserved to the greatest extent possible (Figure 2). Isoperistaltic duodenojejunostomy was performed



Figure 1. Reconstruction by Imanaga's first method during PpPD. Extracorporeal tubes were placed in the biliary tree (dotted blue arrow) and main pancreatic duct (dotted red arrow).

in an end-to-end fashion, and pancreatojejunostomy and choledochojejunostomy were performed in an end-to-side fashion. The parenchyma of the pancreatic remnant and seromuscular layers of the jejunum were sutured in an interrupted pattern. The main pancreatic duct was anastomosed to the jejunal mucosa by interrupted sutures. Extracorporeal tubes were placed in the biliary tree and main pancreatic duct. The biliary tube was removed on postoperative day (POD) 14, and the pancreatic tube was removed on POD 21 (Figure 1).

The postoperative course was followed in eight patients who underwent PpPD. Data are presented as mean and standard deviation. The follow-up duration was 16.7 ± 1.0 years. The average patient age was 47.4 ± 10.6 years, and the patients were four men and four women. The operative time was 441.3 ± 57.9 minutes, and the blood loss volume was 506.5 ± 197.8 ml. Clinical diagnoses based on histological examination of resected specimens included neuroendocrine tumors in three patients, ampullary carcinoma in three patients, and intraductal papillary mucinous carcinoma in two patients. Intentional dissection of regional lymph nodes and nerves was performed in five and two patients, respectively.

According to the International Study Group of Postoperative Pancreatic Fistula in 2005 [16], pancreatic leakage was categorized as grade A in four patients, grade B in three patients, and grade C in one patient. In one patient who developed a stenosis of the pancreatojejunostomy site, pancreatic leakage resulted in an intraperitoneal abscess, and endosonography-guided transgastric drainage was required. Delayed gastric emptying (DGE) was observed in two patients. In three patients, passage from the duodenojejunostomy to the pancreaticojejunostomy



Figure 2. Approximately 20 cm of distal jejunum (solid red lines) was sacrificed as close to the jejunal wall as possible, according to one segment of jejunal vessels (dotted blue line). The jejunum was then resected and lifted up (dotted red line). Even subtle tension of the mesojejunum was avoided, and the autonomic nerves in the mesojejunum of the lifted jejunal limb were preserved to the greatest extent possible (green arrows).

was mechanically disturbed, and endoscopic dilation with a balloon bougie was repeated. The total amount of dietary intake was sufficient on POD 22.5±13.5. Repeated cholangitis was observed in three patients on POD 82.5±49.2 (range, POD 22–166). Surgical site infection was observed in two patients, and adhesive ileus occurred in one patient. According to the Clavien–Dindo classification [17], postoperative complications were categorized as grade Illa in four patients, grade I in two patients, and grade II in two patients. The postoperative hospital stay was 44.9±19.4 days.

During the long-term postoperative period, neither cachexia nor sarcopenia was observed, and the amount of body weight loss from the preoperative period was 6.4±4.1 kg. Although malnutrition was not observed, two patients had diabetes. Although six patients received some medications (e.g., digestive enzymes, proton pump inhibitors, or diabetes medication), two patients remained free from all medications. Because some patients had two or more complications, we summarize characteristics and properties of all patients in Table 1.

Discussion

According to the Clavien-Dindo classification [17], grade IIIa postoperative complications were observed in four patients (50%) in this study; no fatal complications (e.g., grade IV and V) were observed. The risk of PD has fallen to 5% to 10% [11]. The rate of postoperative complications and the need for blood transfusions have also been reduced [11]. Furthermore, a normal, productive life without the need for medication and without digestive disorders can be expected [11]. Approximately 70% of patients can return to their preoperative occupation [11].

Pancreatojejunostomy is crucial for an uneventful postoperative course [11], and pancreatic leakage is the major cause of procedure-related death [18]. PD, PpPD, and SSpPD result in a pancreatic leakage at a rate of 10% to 15% [19]. In the present study, pancreatic leakage resulted in an intraperitoneal abscess in one patient (12.5%), and endoscopic transgastric drainage was required (grade C based on the International Study Group of Postoperative Pancreatic Fistula in 2005 [16]). To overcome fatal complications associated with pancreatic leakage, randomized controlled trials of pancreatojejunostomy versus pancreatogastrostomy have been performed [20, 21] and various pancreatic tube designs made [22,23]. Additionally, a new standardized technique for pancreaticojejunostomy was introduced in 2003 to minimize postoperative pancreatic leakage [24]. This transpancreatic U-suture technique, also called "Blumgart's pancreaticojejunal anastomosis," was originally devised by Blumgart at the Memorial Sloan-Kettering Cancer Center in New York; however, its clinical results have not yet been published [24,25]. Blumgart's anastomosis has been updated [18], and this anastomosis with or without modifications has become globally widespread [24,26].

DGE is a critical problem in pancreatic surgeries [27]. The route of reconstruction (retrocolic or antecolic) [28] and whether pylorus resection is performed [29] do not affect DGE after PD/ PpPD/SSpPD. In the present study, DGE was observed in two patients (25.0%). However, we found that digestive symptoms caused by mechanical obstruction are intractable, even when only a subtle disturbance of passage from the duodenojejunostomy to the pancreaticojejunostomy has occurred. Although the effectiveness of repeated use of balloon bougies is unclear, interventional radiology via an endoscopic approach (grade IIIa according to the Clavien-Dindo classification [17]) was performed in three patients (37.5%). Based on our experience, we suggest that the pancreatic remnant should be well mobilized before pancreaticojejunostomy for successful performance of Imanaga's first method (Figure 3). Because

Primary disease	Lymphnode* (Y/N)	Nerve** (Y/N)	Repeated cholangitis (The last onset day [POD])	Passage disturbance***	Pancreatic leakage (grade)****	DGE	Sufficient dietary intake (POD)	Other complications
IPMC	Yes	Yes	166	-	C	+	22	Pancreatojejuno- stomy stenosis Intraperitoneal abscess Wound infection
IPMC	Yes	Yes		+	В	_	23	
NET	No	No		-	A	-	6	
NET	No	No	134	-	A	_	10	
NET	No	No		-	A	-	8	Adhesional ileus Wound infection
AC	Yes	No		+	В	_	35	
AC	Yes	No		+	В	-	38	
AC	Yes	No	106	-	A	+	38	

 Table 1. Characteristics of the eight patients who underwent the pylorus-preserving pancreatoduodenectomy method of Imanaga (PPPD-Imanaga), or 'Imanaga's first method' with preservation of the autonomic nerves in the lifted jejunal limb.

Drimory	Complication	Treatments	Hospital	Long-term after surgery			
Primary disease	(grade) *****	for complications	discharge	Body weight loss (kg)	Medications	Diabetes	
IPMC	Illa	Transgastric drainage	38	4	+	-	
IPMC	Illa	Balloon bougie	52	8	+	-	
NET	I		25	2	-	-	
NET	II		26	0	-	-	
NET	I		24	7	+	-	
AC	Illa	Balloon bougie	57	10	+	+	
AC	Illa	Balloon bougie	75	12	+	-	
AC	II		62	8	+	+	

AC – ampullary carcinoma; DGE – delayed gastric emptying; IPMC – intraductal papillary mucinous carcinoma; NET – neuroendocrine tumor; POD – postoperative day; PpPD – pylorus-preserving pancreaticoduodenectomy. * Intentional dissection of regional lymph nodes; ** intentional dissection of nerves; *** mechanical disturbance of passage from the duodenojejunostomy to the pancreaticojejunostomy; **** International Study Group of Postoperative Pancreatic Fistula; ***** Clavien-Dindo classification.

the pancreaticojejunostomy is located very close to the duodenojejunostomy site, insufficient mobilization easily causes a winding route and impaired passage (Figure 4).

Refractory cholangitis was observed in three patients (37.5%) in the early postoperative period. Imanaga's first method involves isoperistaltic reconstruction in the order of the gastric remnant, pancreatic duct, and biliary tree. Therefore, one possible explanation for repeated cholangitis may be that the biliary tract is not separated from the dietary contents containing digestive juice. However, the frequency of cholangitis decreased with the passage of time, and the latest day on which acute cholangitis developed was POD 166. Acute cholangitis may recur in the short-term period after Imanaga's first

method. Although the cause is unknown, postoperative cholangitis seems to resolve as time passes. We speculate that postoperative recovery of digestive peristalsis will resolve stagnation at the time of choledochojejunostomy.

During the long-term period after Imanaga's first reconstruction in the present study, two patients did not develop digestive disorders and required no medications. These two patients had not undergone intentional dissection of lymph nodes and nerves, although such dissection is usually required for treatment of pancreatic malignancy. Imanaga's first reconstruction may have benefits with respect to long-term outcomes, especially for patients with benign diseases that do not require intentional dissection of lymph nodes and nerves. Of





course, this was a retrospective study in a single institution, and the results may have been affected by several types of bias, mostly selection bias. Therefore, the conclusions must be interpreted with extreme caution. Many pancreatic surgeons focus on technical aspects of reconstructive or advanced surgery [30,31]. In summary, we used Imanaga's first method and suggest that this isoperistaltic reconstruction technique may have potential benefits.

Conclusions

Two decades have passed since Professor Imanaga died. Should Imanaga's first method be reevaluated? Future studies are still needed to elucidate the potential benefit of his signature reconstruction technique from a physiological viewpoint. This represents an important frontier in the field of pancreatic surgery.

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Figure 4. Technicalities and surgical pitfalls of the procedure are summarized. Adequate mobilization of the pancreatic remnant before pancreaticojejunostomy (solid red arrow) is important for excellent digestive passage (dotted red arrow). Because the pancreaticojejunostomy is located very close to the duodenojejunostomy, insufficient mobilization (solid blue arrow) easily causes a winding route and impaired passage (dotted blue arrow).

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Conflict of interest

None.

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