Strategies for the treatment of invasive ductal carcinoma of the pancreas and how to achieve zero mortality for pancreaticoduodenectomy

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Abstract
Although various therapeutic modalities are available for carcinoma of the pancreas, "curative resection" is the most important. Thus, the aim of surgery for carcinoma of the pancreas is local complete resection of the carcinoma. Carcinoma of the head of the pancreas invades through the pancreatic parenchyma, following the arteries, veins, and especially nerves between the parenchyma and fusion fascia, and then spreads horizontally toward the superior mesenteric artery or celiac axis. We suggest techniques for resection of the extrapancreatic nerve plexus in the head of the pancreas during a Whipple procedure for carcinoma of the pancreas, from the perspective of surgical anatomy and pathology, to achieve "curative resection". We suggest that: (1) en-bloc resection of the right side of the superior nerve plexus and the first and second nerve of the pancreatic head should be performed. With this technique, it is possible to avoid cutting these nerves. It is easy to perform this procedure, as follows. First, the superior mesenteric artery and vein are encircled with tape. Next, the superior mesenteric artery should be moved to the right side of the superior mesenteric vein under this vein. In addition, (2) the entire cut end of the nerve plexus should be investigated during the operation, using frozen specimens, and confirmed to be negative for cancer. If the cut end is positive for cancer, additional resection of the nerve plexus should be performed to achieve curative resection. It is impossible to completely determine whether the cut end of the nerve plexus is positive or negative for carcinoma after surgery, because the cut end is long and some specimens are deformed by formalin fixation; thus, it is difficult to identify the true surgical cut end. With regard to reconstruction, we perform a modified Child method with pancreaticojejunostomy (end-to-side), choledochoduodenostomy (also end-to-side), and gastrojejunostomy with Braun's anastomosis. The greater omentum is set around the pancreaticojejunostomy to prevent pancreatic juice from spreading in the abdomen. Careful management of the intraabdominal drainage tubes after the operation is crucial. With the operative procedure and postoperative controls described above, operative mortality was zero in 114 consecutive patients in our series who underwent pancreaticoduodenectomy.

Key words Curative resection · Horizontal spread · En-bloc resection · Nerve plexus · Modified Child method · Greater omentum around PJ · Operative mortality

Introduction

Although various therapeutic modalities are available for carcinoma of the pancreas, "curative resection" is the most important. Thus, the aim of surgery for carcinoma of the pancreas is local complete resection of the carcinoma.

For this purpose, surgeons have to know how and where, or in which direction, carcinoma of the pancreas invades and spreads.

Fusion fascia

Figure 1 shows the fusion fascia of the head of the pancreas in an autopsy case.[1] The fascia is composed of loose connective tissue. With Kocher's maneuver, the fascia adheres to the pancreatic parenchymal side, but not to the vena caval side. All of the important pancreaticoduodenal arcades of arteries, veins, and nerves are situated on this fusion fascia.[1,2]

Figure 2 shows a posterior view of the head of the pancreas. The posterior surface of the pancreas is covered with the fusion fascia of Treitz. The cut end of the portal vein and the superior mesenteric artery (SMA; shown at the top of Fig. 2) are also covered with fusion fascia and exist on the ventral side. Thus, the pancreatic parenchyma, extrapancreatic nerve plexuses, SMA, and portal vein are wrapped within the fusion
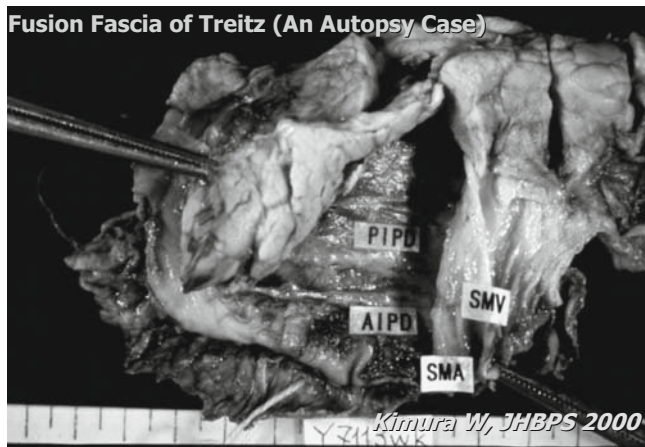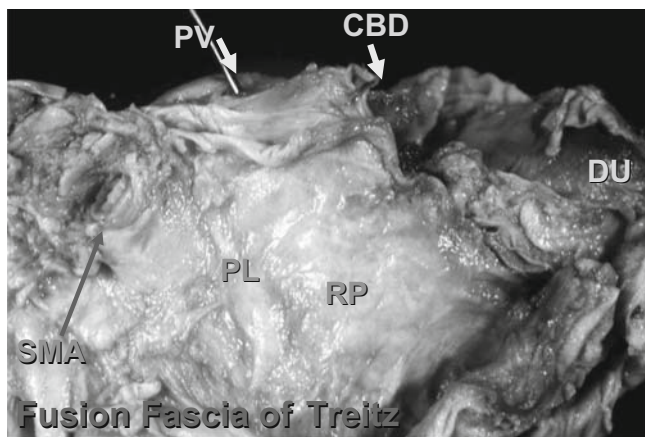
Fig. 1. The fusion fascia of the head of the pancreas in an autopsy case.[1] All of the important pancreaticoduodenal arcades of arteries, veins, and nerves are situated on this fusion fascia. *PIPD*, posterior inferior pancreaticoduodenal artery; *AIPD*, anterior inferior pancreaticoduodenal artery; *SMV*, superior mesenteric vein; *SMA*, superior mesenteric artery

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Fig. 2. Posterior view of the head of the pancreas. The posterior surface of the pancreas is covered with fusion fascia of Treitz. The cut end of the portal vein (*PV*) and the SMA, shown *at the top of the figure*, are also covered with fusion fascia and exist on the ventral side. Thus, the pancreatic parenchyma, extrapancreatic nerve plexuses, SMA, and portal vein are wrapped within the fusion fascia and exist in the same space. *PL*, Nerve plexus; *RP*, retroperitoneal tissue; *DU*, duodenum; *CBD*, common bile duct

fascia and exist in the same space. Cancer of the head of the pancreas spreads within the fusion fascia and rarely spreads directly to the inferior vena cava.

Nature of the spread of carcinoma

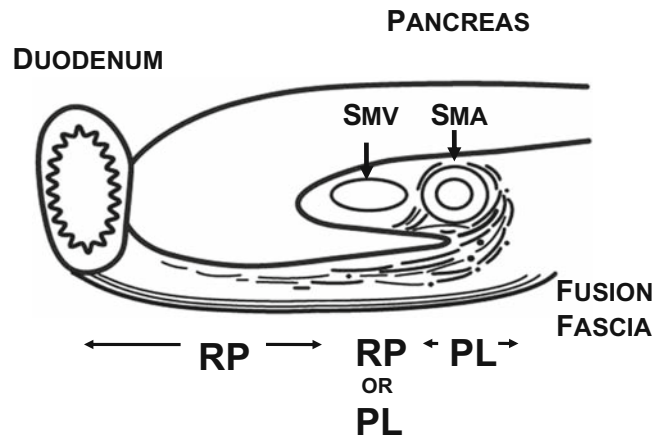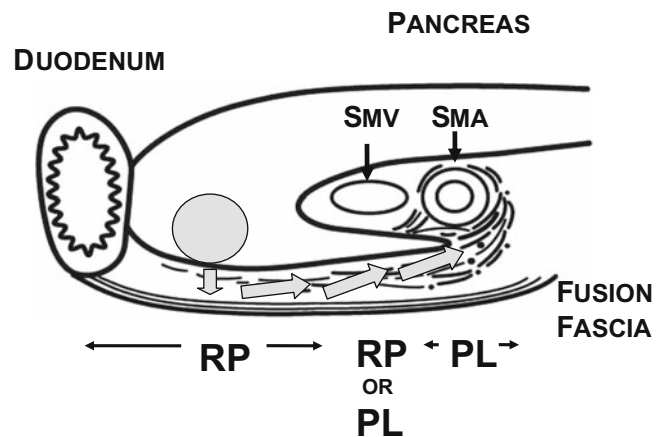We have concluded that carcinoma of the head of the pancreas may spread as follows (Fig. 3). Carcinoma of

Fig. 3. Nature of the spread of carcinoma of the head of the pancreas

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Fig. 4. Carcinoma of the head of the pancreas invades through the pancreatic parenchyma, following the nerves between the parenchyma and fusion fascia, and then spreads horizontally toward the SMA or celiac axis

the head of the pancreas invades through the pancreatic parenchyma, following the arteries, veins, and especially nerves, between the parenchyma and fusion fascia, and then spreads horizontally toward the SMA or celiac axis (Fig. 4).[3–5]

Histologically, a large number of arteries, arterioles, veins, and nerves exist between the fusion fascia of Treitz and the pancreatic parenchyma and around the SMA (Fig. 5).

Techniques for complete resection

We now suggest techniques for resection of the extra-pancreatic nerve plexus in the head of the pancreas during a Whipple procedure for carcinoma of the pan-
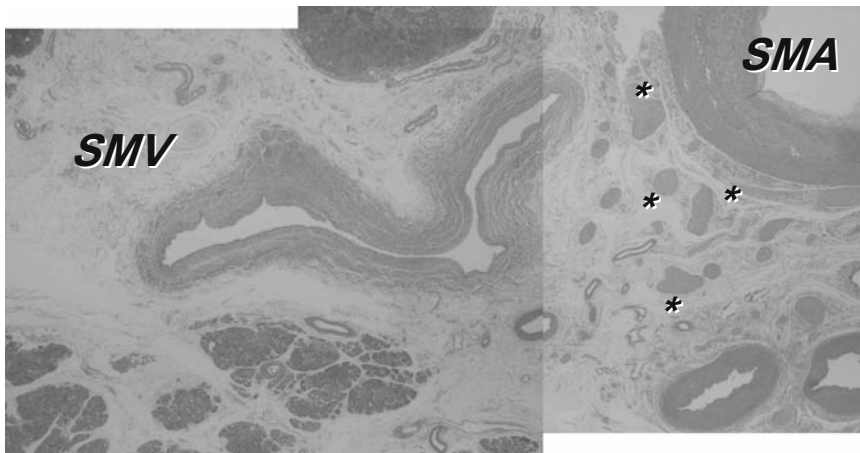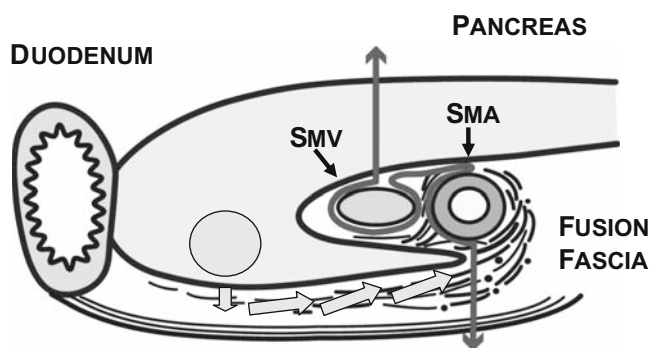
Fig. 5. Histologically, a large number of nerves (*asterisks*) exist around the SMA (H&E)

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Fig. 6. En-bloc resection of the right side of the superior nerve plexus and the first and second nerve plexuses of the pancreatic head. The surgical resection line is shown in *red*

creas, from the perspective of surgical anatomy and pathology, to achieve "curative resection".

We offer two suggestions (Fig. 6):[4,5]

1. En-bloc resection of the right side of the superior nerve plexus and the first and second nerve plexus of the pancreatic head should be performed. With this technique, it is possible to avoid cutting these nerves. The surgical resection line is shown in red in Fig. 6. It is easy to perform this procedure, as follows (Fig. 7). First, the SMA and superior mesenteric vein (SMV) are encircled with tape. Next, the SMA should be moved to the right side of the SMV under this vein.

2. The entire cut end of the nerve plexus should be investigated during the operation, using frozen specimens, and confirmed to be negative for cancer. If the cut end is positive for cancer, additional resection of the nerve plexus should be performed to achieve curative resection. It is impossible to completely determine whether the cut end of the nerve plexus is positive or negative for carcinoma after surgery,

because the cut end is long and some specimens are deformed by formalin fixation; thus, it is difficult to identify the true surgical cut end.

Figure 8 shows a computed tomography (CT) scan in a 59-year-old woman with carcinoma of the head of the pancreas. Carcinoma did not seem to exist around the superior mesenteric artery (SMA). However, when 27 parts of the cut end of the nerve plexus of the SMA and the first and second nerve plexuses of the pancreatic head were histologically investigated by frozen section during the operation, five parts were diagnosed to be positive for carcinoma. Additional resections were performed to ensure that the cut ends of these parts were negative for carcinoma. Stitches (arrows in Fig. 9) indicate additional resections of the nerve plexuses in this patient.

Key parts of our Whipple procedures

The key parts of our Whipple procedures are as follows:[6]

1. After tunneling, the pancreas is cut above the portal vein.
2. When the SMV is not involved in carcinoma, it is detached from the head and uncus of the pancreas.
3. The SMA is moved to the right side of the SMV under this vein.
4. The right side of the nerve plexus of the SMA is dissected with a cancer-free margin for R0 resection.
5. The right side of the nerve plexus of the SMA is completely resected.
6. Paraaortic lymph node dissection is also performed in our procedures.

In some cases, we also perform portal vein resection, as shown in Fig. 10, and sometimes we apply intraoperative radiation therapy (Fig. 10).
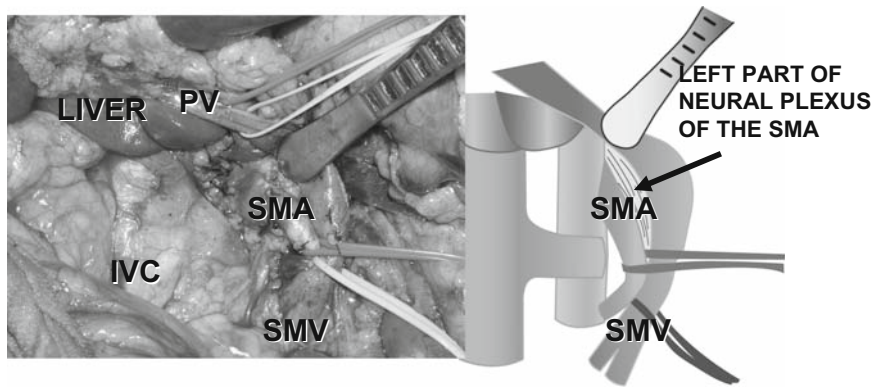
LIVER PV

IVC

SMA

SMV

LEFT PART OF
NEURAL PLEXUS
OF THE SMA

SMA

SMV

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Fig. 7. For the procedure, the superior mesenteric artery (*SMA*) and superior mesenteric vein (*SMV*) are encircled with tape. Next, the SMA should be moved to the right side of the SMV under this vein. *PV*, Portal vein; *IVC*, inferior vena cava

Tumor   SMA

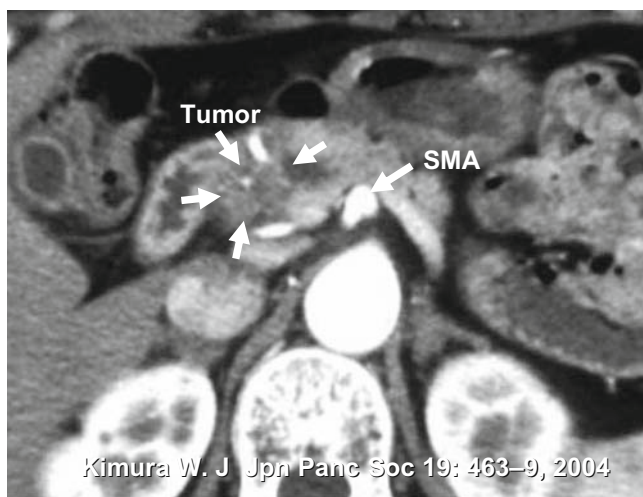Kimura W. J Jpn Panc Soc 19: 463–9, 2004

Fig. 8. Computed tomography (CT) scan in a 59-year-old woman with carcinoma of the head of the pancreas. Carcinoma did not seem to exist around the superior mesenteric artery (SMA)
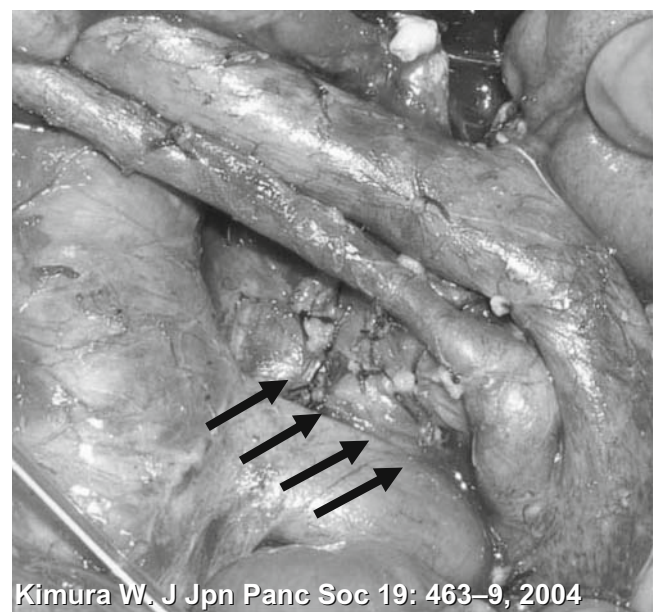

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Fig. 9. In the patient whose scan is shown in Fig. 8, when 27 parts of the cut end of the nerve plexus of the SMA and the first and second nerve plexuses of the pancreatic head were histologically investigated by frozen section during the operation, five parts were diagnosed to be positive for carcinoma. Stitches (*arrows*) indicate additional resections made to ensure that the cut ends of these parts were carcinoma-negative

Reconstruction

Our method of reconstruction in a pancreaticoduodenectomy is the Whipple procedure (Fig. 11). We perform a modified Child method with pancreaticojejunostomy (end-to-side), choledochoduodenostomy (also end-to-side), and gastrojejunostomy with Braun's anastomosis.

Pancreaticojejunostomy

In our procedure, a pancreatic tube with a knot is used in almost all cases. The tube is inserted into the main pancreatic duct, and a mark is made with PDS-II near the knot. Stitches are applied to fairly thick pancreatic

parenchyma and seromuscle layers of the jejunal wall of the posterior part of the anastomosis (Fig. 12). The end of this tube is taken outside through the end loop of the jejunum.

The wall of the main pancreatic duct, as well as a small amount of the pancreatic parenchyma and all layers of the jejunal wall, are then sutured (Fig. 13). At least five stitches should and can be set in the posterior wall of a normal-size main pancreatic duct.
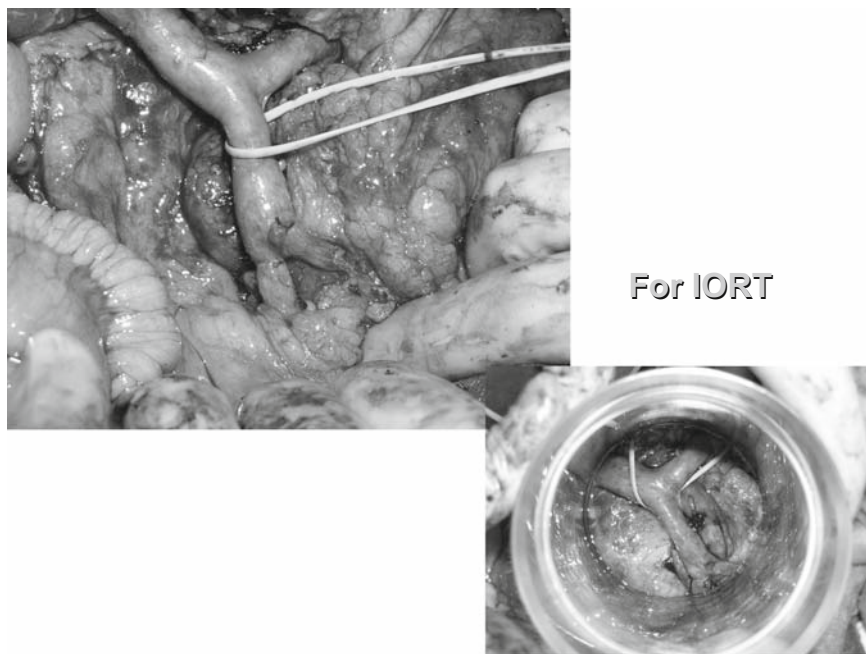
For IORT

Fig. 10. Portal vein resection and intra-operative radiation therapy (*IORT*)

1. Pancreaticojejunostomy

2. Choledochojejunostomy
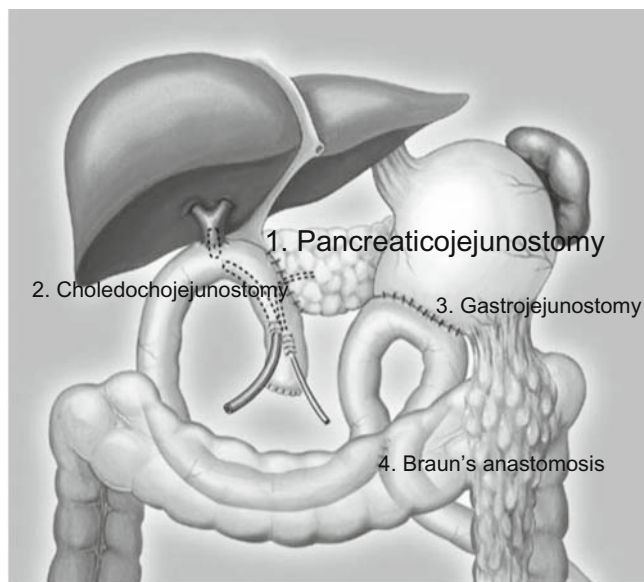
3. Gastrojejunostomy

4. Braun's anastomosis

Fig. 11. Our method of reconstruction for pancreaticoduodenectomy: Whipple procedure. We perform a modified Child method with pancreaticojejunostomy, end-to-side, choledochoduodenostomy, also end-to-side, and gastrojejunostomy with Braun's anastomosis

Fig. 12. In pancreaticojejunostomy, stitches are applied to a fairly thick pancreatic parenchyma and seromuscle layers of the jejunal wall of the posterior part of the anastomosis

Pancreatic tube

Pancreaticoduodenostomy without a pancreatic tube was performed in only 3 of the 114 patients in this series. With a tube, we can easily observe the pancreatic duct and the entire jejunal wall at the anastomosis during the operation. Without a tube, it is sometimes difficult to observe the pancreatic wall, and the stitches for the anterior wall may mistakenly be applied to the posterior wall of the anastomosis, although Tani et al.[7] have recommended that no stent be used for pancreaticojejunostomy.

The pancreatic tube is inserted into the main pancreatic duct and fixed to the anastomosis with PDS-II. The tube is fixed with a Witzel procedure.

The stitching of the anterior wall anastomosis is the same as that used for the posterior wall. We then complete the pancreaticojejunostomy.
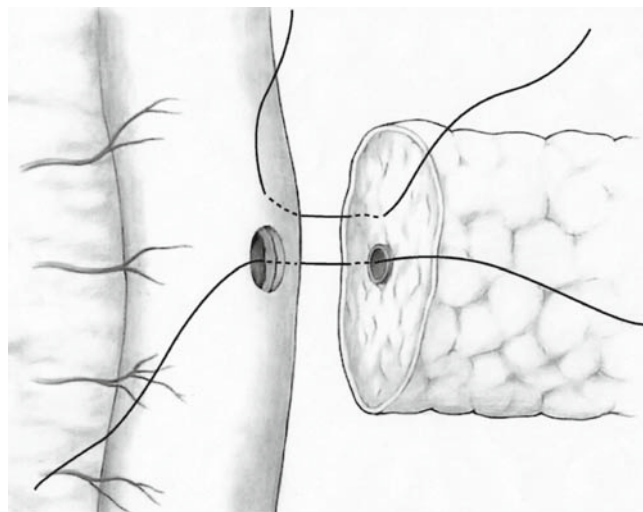
Choledochojejunostomy

With regard to choledochojejunostomy, a stent, about 2 cm long, with many holes (Fig. 14) is set in the anastomosis of the choledochojejunostomy.[8] The middle of the stent is marked with PDS-II. The choledochojejunostomy is performed with the hepatic duct and all layers of the jejunal wall, with one layer of interrupted sutures. Monofilament absorbable 4-0 PDS-II is used.
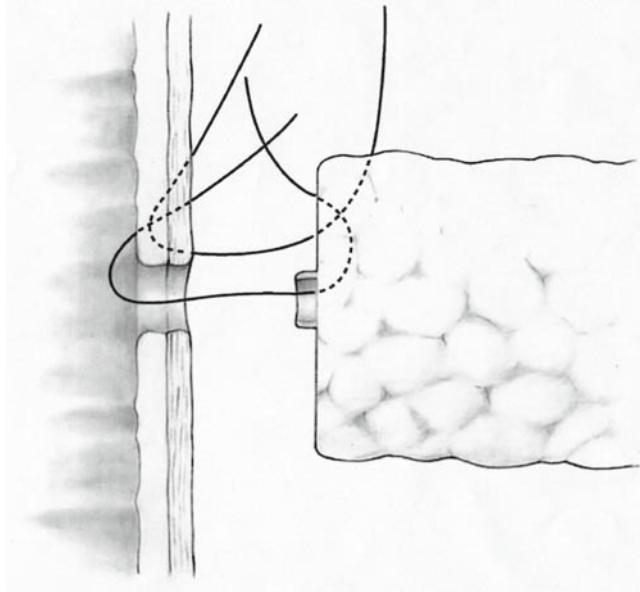

Fig. 13. The wall of the main pancreatic duct, as well as a small amount of the pancreatic parenchyma, and all layers of the jejunal wall are sutured

Greater omentum around the pancreaticojejunostomy

The greater omentum is set around the pancreaticojejunostomy to prevent pancreatic juice from spreading in the abdomen (Fig. 15a–c).[6] Four sets of single-lumen ficon drains are set in the abdomen around the pancreaticojejunostomy and choledochojejunostomy (Fig. 15a,b).

Management of intraabdominal drainage

Careful management of the intraabdominal drainage tubes after the operation is crucial (Fig. 16). The drainage tubes should not be closed by coagulation of the blood or by other substances. Therefore the drainage tubes should be cleaned every day. The tubes should be filled with saline to provide the drain with negative pressure.

If the amylase value of the drainage fluid is high and if there is a large amount of fluid, irrigation is performed daily with about 500 to 3000 ml saline. This procedure is very important for preventing postoperative intra-abdominal bleeding due to pancreatic fistula and infection.

Outcome of our Whipple procedures

With the operative procedures and postoperative controls described above, none of the 114 consecutive patients (see Table 1 for the patients' demographics) in
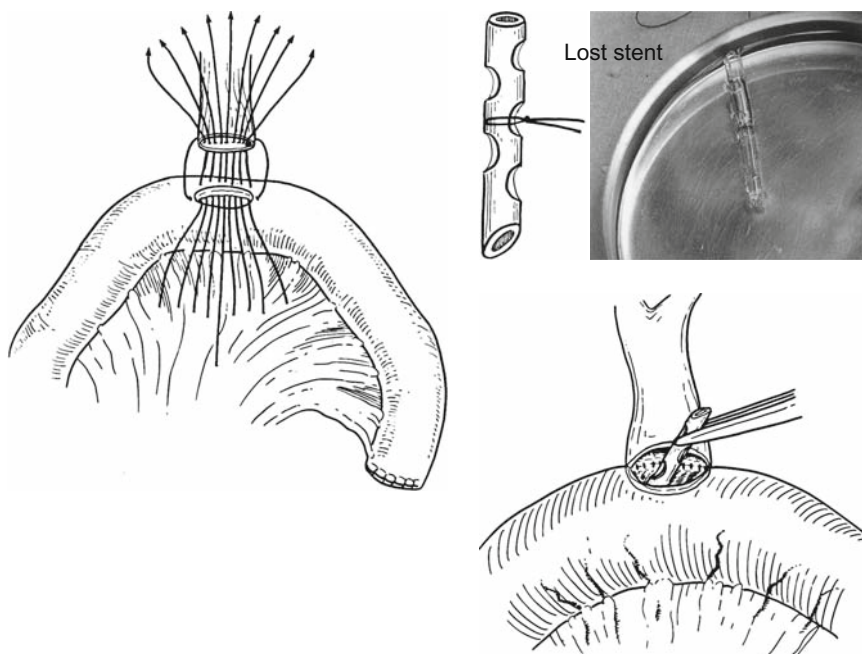

Lost stent

Fig. 14. A stent, about 2 cm long, with many holes, is set in the anastomosis of a choledochojejunostomy. Choledochojejunostomy is performed with the hepatic duct and all layers of the jejunal wall, with one layer of interrupted sutures
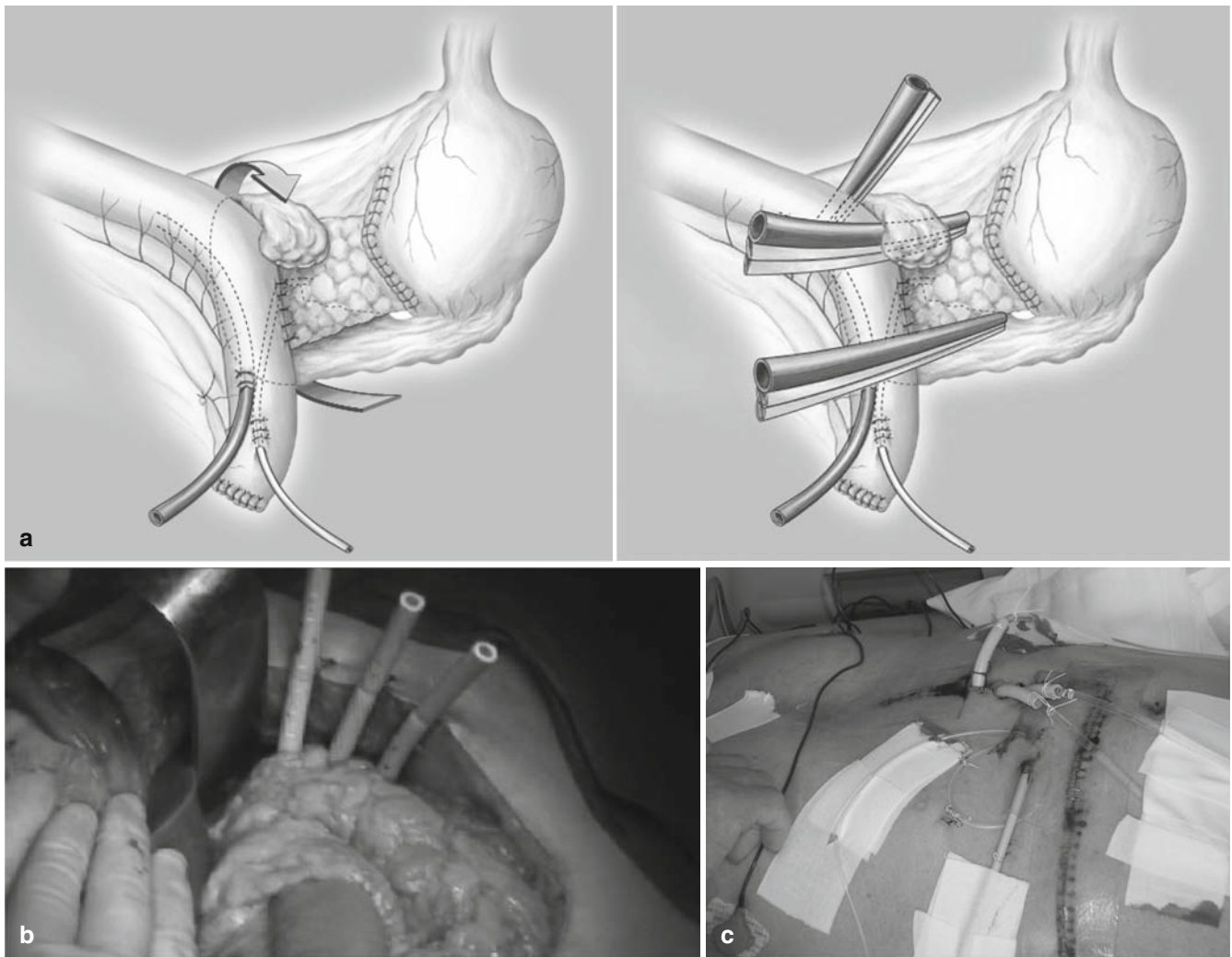
Fig. 15a–c. The greater omentum is set around the pancreaticojejunostomy to prevent pancreatic juice from spreading in the abdomen. Four sets of single-lumen ficon drains are set in the abdomen around the pancreaticojejunostomy and choledochojejunostomy

our series of pancreaticoduodenectomies died in the postoperative period (Table 2). Thus, operative mortality was zero. Intraabdominal bleeding was observed in 3 patients. Bleeding caused by pancreatic juice with infection was found in 2 patients; after trying interventional radiological methods without success, we managed to stop the bleeding by operation in both patients, and irrigated daily with 3000 ml saline for several days after the operation.

With regard to the definition of pancreatic fistula, we used the definition of Buechler et al.:[9] secretion of 30 ml or more of amylase-rich drainage fluid (more than 5000 units) per day for more than 10 days. According to this definition, 5 (4.3%) of the 114 patients in our series had pancreatic fistula.

In conclusion, pancreaticoduodenectomy was performed safely in all of our 114 patients, although death

Fig. 16. Postoperative management of the intraabdominal drainage tubes. The tubes should be filled with saline to give the drain a negative pressure

Table 1. Diseases in the patients who underwent pancreaticoduodenectomy in our series (1998–2007)

	Diagnosis	Number of patients
Pancreaticoduodenectomy	Pancreatic cancer	32
Number of patients, 114	IPMN	35
Male:Female, 74:40	IPMC	12
Age, 38–80 years	IPMA	23
(mean age, 65.8 years)	Carcinoma of the papilla of Vater	17
	Bile duct cancer	23
	Chronic pancreatitis	2
	Groove pancreatitis	1
	Neuroendocrine cell carcinoma	1
	Serous cystadenoma	1
	GIST of duodenum	1
	Gallbladder cancer	1

Table 2. Various reports on the outcome of pancreaticoduodenectomy in the postoperative period

Authors	Year	No. of cases	Pancreatic fistula (%)	Intraabdominal bleeding (%)	Intraabdominal abscess (%)	Operative death (%)
Trede and Schwall[10]	1988	285	8.8	1.4	0.7	3.1
Yeo[11]	1997	650	14	—	5.0	1.4
Petrazzoli[12]	1998	81	9.9	7.4	2.5	4.9
Buechler[13]	2003	617	3.2	3.2	2.0	1.6
Behman[14]	2004	125	8	6.4	14.4	4.8
Kimura (present study)	2007	114	4.3	2.6	—	0

has been reported after a Whipple operation even at high-volume centers (Table 2).[10–14]

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