Surgical technique

Distal pancreatectomy with en block celiac resection for locally advanced pancreas carcinoma

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Running title: DP-CAR for pancreatic body cancer

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ABSTRACT

In locally advanced pancreatic body cancers, cancer infiltrates major vessels such as the celiac axis, common hepatic artery and superior mesenteric artery or vein, which is the borderline of resectability. Patients also suffer severe abdominal pain. Kondo and Hirano et al. developed a radical operation called "distal pancreatectomy with en block celiac resection (DP-CAR)" for such cases. We applied this procedure three times in two patients with pancreatic body carcinomas, in which combined vascular resection was necessary. Radical operation was eventually achieved.

KEYWORDS: DP-CAR, Vascular resection, Pancreatic body carcinoma

ABBREVIATIONS: Distal pancreatectomy with en block celiac resection (DP-CAR)

INTRODUCTION

In recent years, combined resection of the portal trunk vein (PV) or superior mesenteric vein (SMV) is often performed in patients with advanced pancreatic malignancies (1), and the resectability of these malignancies has been improved with the improvement of operative techniques for vascular resection (2). Pancreatic body carcinomas often invade the adjacent major vessels such as the splenic vein or artery, which can be resected in general (1, 2). Furthermore, other major vessels can be invaded, such as the celiac axis, common hepatic artery or superior mesenteric artery or vein and, in such cases, radical operation using Appleby's operation is usually avoided because of its lower curability and higher operative risk (3). Kondo and Hirano et al. developed an innovative operation: distal pancreatectomy with en block celiac resection (DP-CAR) for locally advanced pancreatic body carcinomas (4). By this procedure, pancreatic cancer can be completely resected with invading major vessels and pleural plexus. In addition, severe abdominal pain can be resolved. Patient survival in such advanced pancreatic carcinoma has been improved by this operation and, therefore, the usefulness of DP-CAR for prognosis was clarified (5-7). This technique has been gradually applied recently. We attempted this technique combined with vascular anastomosis superior mesenteric vein, and we experienced successful outcomes after DP-CAR in 2 cases with pancreatic body carcinoma. In the present report, we report our results using this operative technique.

METHODOLOGY

Operative procedures

The resected area proposed by Kondo and Hirano et al. is shown in Figure 1a, b (4, 5). In addition to resection of major surrounding vessels, celiac and superior mesenteric artery nerve plexus or ganglion and retroperitoneal tissues with left adrenal gland can be completely resected en block.

A few days prior to operation, intraarterial coil embolization in the common hepatic artery and left gastric artery was performed by an interventional radiologist in order to increase arterial flow via arcade from the superior mesenteric artery around the pancreatic head (Figure 2a, b) (4, 5). During operation, palpation of the proper hepatic artery or Doppler ultrasonography for intrahepatic blood flow were carefully examined.

According to the procedure by Kondo et al, Kocher's mobilization (8) is performed to distinguish the diverged trunk of the superior mesenteric artery and celiac axis from the abdominal aorta (Figure 3a). To fully expose these trunks, the surrounding nerve plexus or arcuate ligament must be cut. The exposed celiac trunk can be ligated at this point. In the next step, the distal pancreas was dissected from the peripheral superior mesenteric artery. By confirming the inferior mesenteric vein, the left renal vein or artery was exposed underneath the fusion fascia of Toldt. After ligation and cutting of the common hepatic artery, the pancreatic parenchyma was cut at the margin of the cancer-free region and the cut-end was often horizontally exposed due to tumor extension at the pancreas head (Figure 3b). In case of tumor involvement in the portal and superior mesenteric

venous trunk, combined resection of both pancreas and the adjacent vein was performed as below (Figure 3c). By removing the surrounding nerve plexus of the superior mesenteric artery, the cut line reached the ligated celiac axis and the celiac axis was cut at this point. By removing the left ganglion, left adrenal gland, Gerota's fascia or tissues en block, distal pancreatectomy was accomplished (Figure 3d).

In distal pancreatectomy, combined resection of the portal trunk or superior mesenteric vein is often required because of tumor invasion to this major venous trunk. Due to the severe congestion of the stomach or other organs, the portal vein and superior mesenteric vein must be reconstructed immediately. Passive bypass using a tube catheter between the superior mesenteric vein and the umbilical vein was not used during anastomosis in these cases. For venous anastomosis, direct end-to-end anastomosis using 5-0 Proline (Ethicon Inc., Cornelia, GA) was used to reconstruct both veins.

Results

Between 1994 and 2011, we experienced 33 patients with pancreatic carcinoma who underwent distal pancreatectomy, in which three patients underwent combined resection of portal or superior mesenteric vein and three underwent combined arterial resection. Of these patients, three patients underwent DP-CAR procedure. As shown in Table 1, two patients were male and one was female. The female patient had severe diabetes mellitus on admission and was scheduled to undergo control of blood sugar levels. The first case did not undergo preoperative coil embolization in the common hepatic artery. In one patient undergoing coil embolization, the coil migrated in the gastroduodenal artery, which was resolved using an interventional technique without severe complications. As shown in Table 1, the combined resection of the superior mesenteric vein and its reconstruction was performed in two patients. Mean operative time and blood loss were 7.8 hours and 923 mL, respectively. The first case did not show any postoperative complications. The second case showed delayed gastric emptying with watery diarrhea for a long period, and the third case showed Grade A (international study group (ISGPF) definition) (9) pancreatic fistula and duodenal penetration by ischemia. The latter two patients had no poor outcomes during their hospital stay. Severe abdominal pain disappeared and symptoms of ischemic gastropathy were not observed in any patients. All patients had recurrences of liver or bone metastasis in the early period after operation and died within 13 postoperative months.

Case presentation

Case 2 was a patient with pancreatic body carcinomas involving the celiac axis and surrounding nerve plexus (Figure 4). CEA was 1.4ng/ml and CA19-9 was 70.6U/ml. This patient had severe back and upper abdominal pain, which were remarkably improved after operation. Histological findings showed the following: invasive ductal adenosquamous carcinoma, 6.5×4cm, moderate lymphatic and venous infiltration and perineural infiltration, invasion to the splenic artery and vein, and locoregional node metastasis. AJCC Stage IIb, R0 operation was achieved.

Case 3 was a patient with pancreatic body carcinomas involving the common hepatic artery and superior mesenteric vein (Figure 5), who had diabetes and chronic hepatitis C. CEA was 778 ng/ml and CA19-9 was 255 U/ml. This patient also had severe upper abdominal pain, which was remarkably improved after operation. Histological findings showed invasive ductal adenocarcinoma, measuring 5.5×3.5cm. We observed moderate lymphatic and venous infiltration and perineural infiltration, invasion to superior mesenteric vein, and node metastasis. AJCC Stage IIb, R0 operation was achieved as well.

DISCUSSION

Aggressive surgical exploration for pancreatic malignancies combined with vascular resection has been recently reported (1-7) and the techniques and perioperative management have remarkably improved. We also actively performed vascular resection for complete tumor resections (R0) so far. DP-CAR is a newly developed radical operation for borderline resectable pancreatic carcinoma (4-7). Safety and usefulness of DP-CAR has been reported even though the celiac or portal trunk was resected. Based on the recent NCCN guideline, pancreas carcinoma involvement of the major vascular trunk was considered "borderline resectable" (10), in which resectability is dependent on the surgeon's policy. Recently, many expert surgeons at high volume institutes have attempted radical pancreatectomy with combined vascular resection (2-7).

Before performing DP-CAR, preoperative management by interventional radiology is necessary because hepatic arterial flow and postoperative ischemic gastropathy are concerns (5,11, 12). By using arterial coil embolization in the common hepatic artery, arterial redistribution via the pancreatic head arcade from the superior mesenteric artery can be performed at the time of radical operation. By that in the left gastric artery, arterial redistribution via right gastroepiploic artery from the superior mesenteric artery is increased. To prevent lower hepatic flow and ischemic gastropathy, this preoperative management is useful. In our series, two patients underwent coil embolization and had no severe complications. Arterial redistribution by embolization could be completed. In case 3, the placed coil migrated into the gastroduodenal artery and, fortunately, the migrated coil could be removed using an interventional technique at the same time. During operation, mild hematoma was observed around the pancreas head. This complication often happens, and careful management of embolization is necessary.

According to the original DP-CAR by Kondo and Hirano et al., en block radical pancreatectomy can be easily performed (4, 5). When the portal or superior mesenteric vein is resected, congestion of the stomach, small intestine and pancreas were remarkably observed. Anastomosis itself is relatively difficult because veins were fixed with pancreatic parenchyma. We carefully performed vascular anastomosis in this vein without stenosis or kink. After reconstruction was completed, congestion was rapidly improved. When severe congestion occurred, portal flow bypass or transient clamp of arterial inflow is necessary. As the present report showed, parachute anastomosis is feasible for portal or superior mesenteric vein anastomosis. This technique is basically applied for arterial anastomosis in cardiovascular surgery (13). Concerning ligation and cutting of the common hepatic artery, we could easily perform these techniques; however, removal of the intra-arterial coil was necessary in one case. By previous reports (11, 12), removal of the placed coil might be possible without severe complication. We eventually performed R0 resection by en block operation of DP-CAR in the present series.

Hirano et al. summarized the postoperative complications of DP-CAR (4, 5) as follows: frequent pancreatic fistula due to horizontal wide cut-end of the pancreas stump (17.4%), ischemic gastropathy (13%), and watery diarrhea (34.8%). In case 3, grade A pancreatic fistula was observed; however, this did not develop into severe status. Gastropathy or gastritis was not observed with postoperative gastroscopy in any patients in our series.

Subjects who undergo DP-CAR have locally advanced pancreatic carcinoma, usually with advanced cancer stages (6, 7). Hirano et al. reported that 1 and 5 year survival was 71 and 42%, respectively (5). By examining cases in each Japanese stage, 5 year survival in stage IVa was 36% and patients with stage IVb had no survival over 16 months. Liver metastasis was dominantly observed, while local recurrence was rarely observed. Local recurrence might be controlled by DP-CAR (5). By comparing other reports on advanced pancreatic carcinomas, results of DP-CAR might show a better prognosis (6). In our series, all patients died within 13 months and distant metastasis was observed in the early period but with no local recurrence. To improve patient outcomes, neoadjuvant chemoradiation therapy would be necessary to perform such a radical operation for locally advanced pancreatic carcinoma (14).

In conclusion, we applied DP-CAR for locally advanced pancreas body carcinoma involving the celiac axis or portal trunk in three patients. To prevent ischemic gastropathy or lower arterial hepatic flow, preoperative coil embolization by interventional radiology was performed. When the carcinoma invaded the portal or superior mesenteric vein, reconstruction of the veins was safely performed. Future study and appropriate analysis regarding this surgical technique in a larger number of patients is necessary to evaluate feasibility. DP-CAR might reduce organ damage and en-block resection provided R0 resection and operative safety. Acknowledgement

We greatly appreciate the work of the late Professor Satoshi Kondo in the development and instruction of his original DP-CAR operation.

Figure legends

Figure 1. Scheme of DP-CAR reported by Kondo and Hirano et al. (2007)

CHA; common hepatic artery, SA; splenic artery, CA; celiac axis; SV; splenic vein, PV; portal vein, Ao; Aorta, Panc; pancreas, Du; duodenum, IVC; inferior vena cava, g; ganglion, adr; adrenal gland, LGA; left gastric artery, PHA; proper hepatic artery, SMA; superior mesenteric artery, GDA; gastroduodenal artery, GEA; gastroduodenal artery

Figure 2. Preoperative interventional coil embolization. (a) Proximal common hepatic artery was involved by tumor (arrow) (b) Common hepatic artery (arrow) and left gastric artery (dotted arrow) were embolized by coil.

Figure 3. Operative findings. (a) Bifurcation of celiac axis and SMA was exposed. (b)Horizontally cut-end of pancreatic transection. (c) Combined resection of portal andsuperior mesenteric vein. (d) Resected area of DP-CAR.

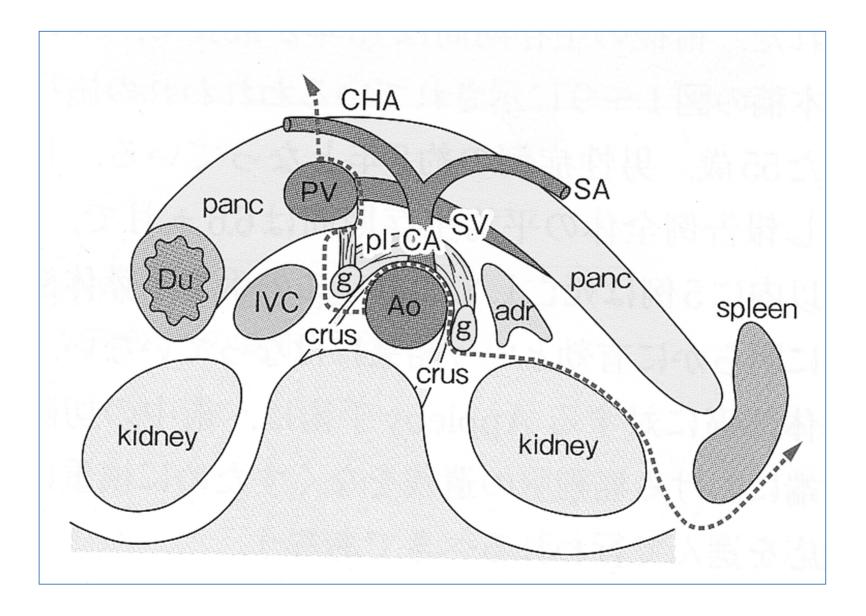
- Figure 4. Case 2. CAT scan finding. Arrow showed the cancer infiltration to the celiac axis and surrounding nerve plexus.
- Figure 5. Case 3. Arrow shows the tumor involvement to hepatic artery and arrow head shows involvement to confluent between splenic vein and portal vein.

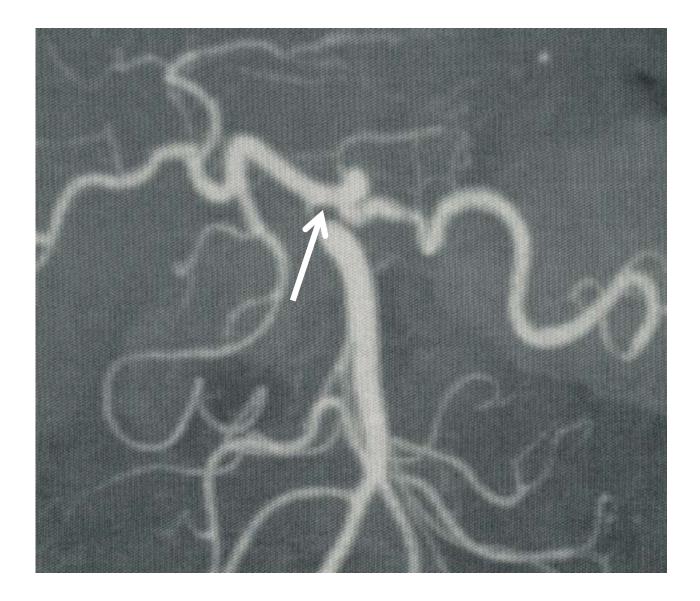
REFERENCES

- Nimura Y: Extended surgery in bilio-pancreatic cancer: the Japanese experience. Semin Oncol 2002;29:17-22
- Li B, Chen FZ, Ge XH, Cai MZ, Jiang JS, Li JP, Lu SH: Pancreatoduodenectomy with vascular reconstruction in treating carcinoma of the pancreatic head. Hepatobiliary Pancreat Dis Int. 2004;3:612-615.
- Kimura W, Han I, Furukawa Y, Sunami E, Futakawa N, Inoue T, Shinkai H, Zhao B, Muto T, Makuuchi M, Komatsu H. Appleby operation for carcinoma of the body and tail of the pancreas. Hepatogastroenterology. 1997;44:387-393.
- Hirano S, Kondo S, Hara T, Ambo Y, Tanaka E, Shichinohe T, Suzuki O, Hazama K: Distal pancreatectomy with en bloc celiac axis resection for locally advanced pancreatic body cancer: long-term results. Ann Surg.;246:46-51.
- Hirano S, Kondo S, Tanaka E, Shichinohe T, Tsuchikawa T, Kato K, Matsumoto J. Postoperative bowel function and nutritional status following distal pancreatectomy with en-bloc celiac axis resection. Dig Surg. 2010;27:212-216.
- Yamamoto Y, Sakamoto Y, Ban D, Shimada K, Esaki M, Nara S, Kosuge T. Is celiac axis resection justified for T4 pancreatic body cancer? Surgery. 2012;151:61-69.
- Sperti C, Berselli M, Pedrazzoli S. Distal pancreatectomy for body-tail pancreatic cancer: is there a role for celiac axis resection? Pancreatology. 2010;10:491-498.
- Dudley HA, Thomas CV. Kocher's maneuver. Surg Gynecol Obstet. 1966;122:604-606.
- Pratt WB, Maithel SK, Vanounou T, Huang ZS, Callery MP, Vollmer CM Jr. Clinical and economic validation of the International Study Group of Pancreatic Fistula (ISGPF)classification scheme. Ann Surg. 2007;245:443-451.
- Evans DB, Erickson BA, Ritch P. Borderline resectable pancreatic cancer: definitions and the importance of multimodality therapy. Ann Surg Oncol. 2010;17:2803-2805.
- 11. **Tanaka E, Hirano S, Tsuchikawa T, Kato K, Matsumoto J, Shichinohe T.** Important technical remarks on distal pancreatectomy with en-bloc celiac axis

resection for locally advanced pancreatic body cancer (with video). J Hepatobiliary Pancreat Sci. 2012;19:141-147.

- 12. Abo D, Hasegawa Y, Sakuhara Y, Terae S, Shimizu T, Tha KK, Tanaka E, Hirano S, Kondo S, Shirato H. Feasibility of a dual microcatheter-dual interlocking detachable coil technique in preoperative embolization in preparation for distal pancreatectomy with en bloc celiac axis resection for locally advanced pancreatic body cancer. J Hepatobiliary Pancreat Sci. 2011 Sep 21. Epub
- Isomura T, Hisatomi K, Hirano A, Nishimi M, Satoh T, Kumate M, Ohishi K. Improvement of postoperative graft patency rate for coronary revascularization. Minerva Cardioangiol. 1995;43:475-479.
- 14. **van Tienhoven G, Gouma DJ, Richel DJ.** Neoadjuvant chemoradiotherapy has a potential role in pancreatic carcinoma. Ther Adv Med Oncol. 2011;3:27-33.







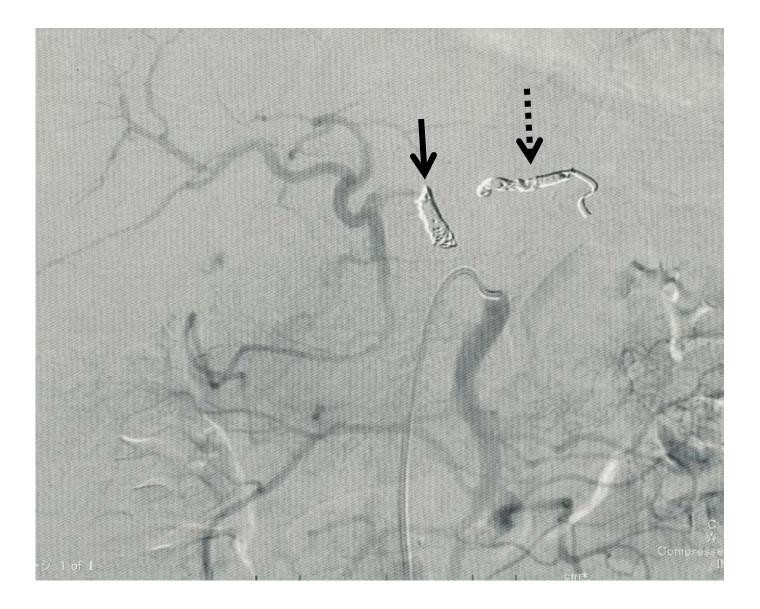


Fig. 3a

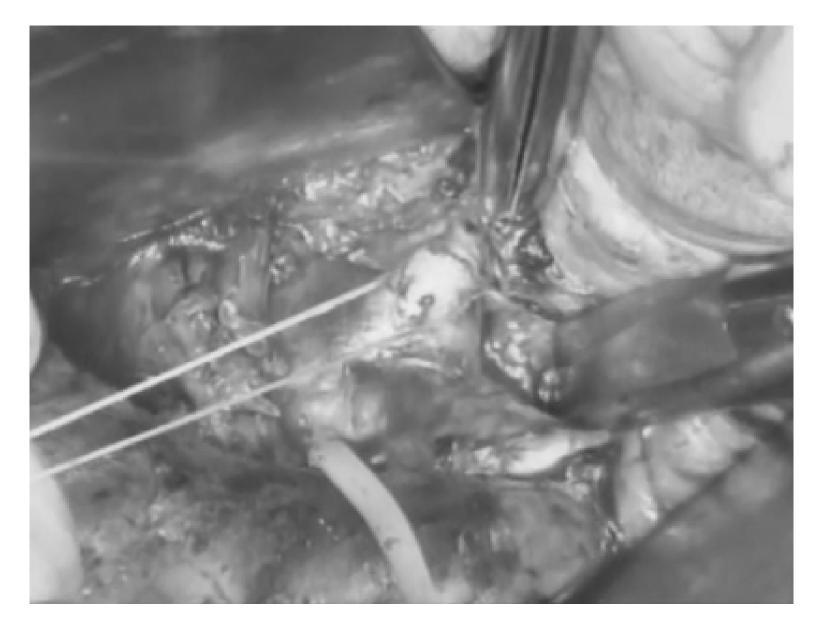


Fig. 3b

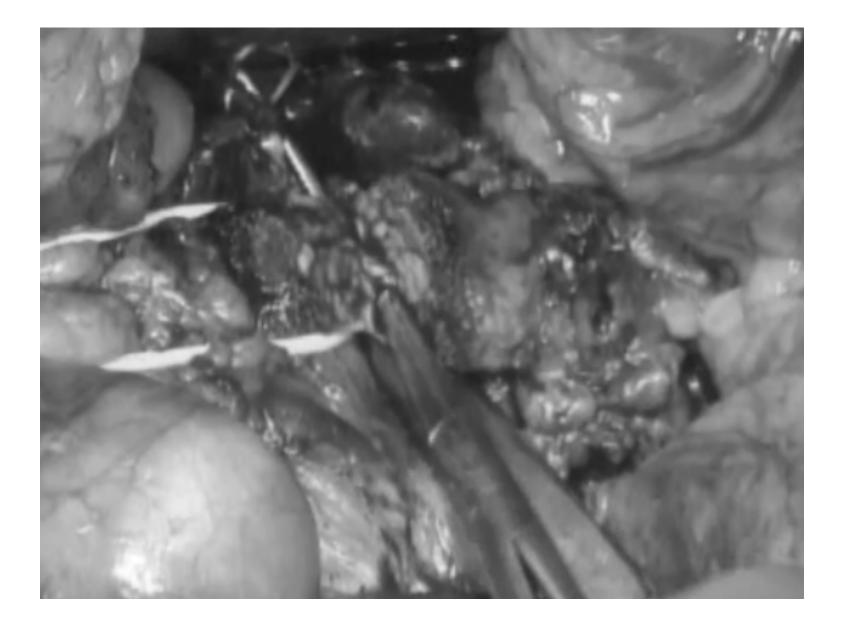




Fig. 3d

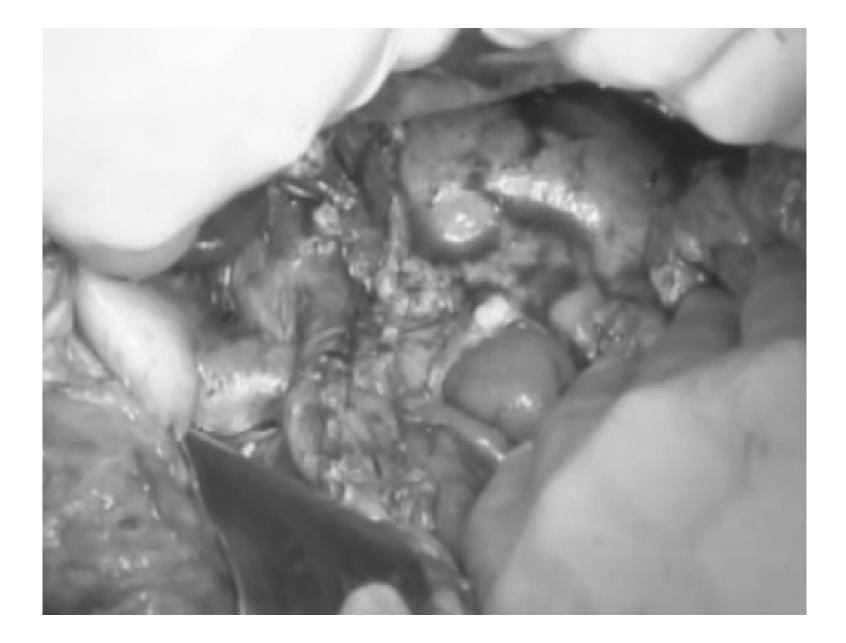






TABLE 1	Demographics of three patients w	with pancreatic carcinoma	who underwent DP-CAR
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	Age(y.o.),	Location of	Co-morbidity	Preoperative	Combined	Operating	Blood	Complications	Prognosis
	Gender	carcinoma		arterial	vascular	time	loss		(M; month)
				embolization	resection	(minutes)	(mls)		
1	63, Male	Body	None	No	Yes	345	540	None	Liver met. (4M)
									Cancer death (14M)
2	65, Male	Body and tail	None	Yes	No	496	850	DGE	Liver met. (4M)
									Survival (12M)
3	72, Female	Body and tail	DM	Yes	Yes	556	980	PF and	Bone met. (1M)
								duodenal ischemia	Dead of cerebral infarction
									(5M)

DM; diabetes mellitus, DGE; delayed gastric empty, PF; pancreatic fistula, met; metastasis