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Stomach-Preserving Distal Pancreatectomy with Combined Resection of the Celiac Artery: Radical Procedure for Locally Advanced Cancer of the Pancreatic Body

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Abstract To enhance the resectability of cancer of the pancreatic body, a new surgical technique should be developed. Of 25 patients with cancer of the pancreatic body who underwent distal pancreatectomy with curative intent, seven with cancer invasion around the celiac artery underwent stomach-preserving distal pancreatectomy with combined resection of the celiac artery. This procedure secured arterial blood supply to the whole stomach and liver via the inferior pancreaticoduodenal artery without arterial reconstruction. There was no postoperative mortality. One patient developed transient passage disturbance in the duodenum. Another one developed a minor pancreatic fistula. No patients had serious complications related to ischemia of the stomach or liver. The quality of life of the patients after surgery was well maintained, and planned adjuvant therapy was accomplished. Local recurrence was evident in only two patients. The median survival time of patients who underwent distal pancreatectomy with (n=7) or without (n=18) resection of the celiac artery was 19 and 25 months, respectively. The overall survival rate was not significantly different between the two groups (P=0.5300). The present study suggests that this surgical procedure is a rational approach to locally advanced pancreatic body cancer invading around the celiac artery. In view of the feasibility of this procedure, it can also be adopted for less advanced cancer of the pancreatic body to enhance local control and survival.

Keywords Cancer of the pancreas · Cancer of the pancreatic body · Distal pancreatectomy · Celiac artery resection · Preservation of the stomach

Introduction

Because the only long-term survivors with cancer of the pancreatic body have been those who have undergone resection, surgery still remains the only hope for prolonged survival. Results of surgical treatment, however, have not improved in recent years.[1,2] The resectability rate for cancer of the pancreatic body also remains poor despite the use of modern imaging techniques.[3] Most patients with cancer of the pancreatic body are unresectable at the time of diagnosis due to cancer invasion of large arteries. To increase resectability rates, surgical challenge against such an advanced pancreatic cancer is necessary.

Cancer of the pancreatic body often invades the origin of the common hepatic and/or splenic arteries arising from the celiac artery. More advanced cancer further invades the celiac artery itself with cancer infiltration of the surrounding nerve plexus. For such a case, we first performed stomach-preserving distal pancreatectomy with combined resection of the celiac artery (SP-DP-CA) in 1987. This operative procedure successfully secured arterial blood supply to the whole stomach and liver only via the inferior pancreaticoduodenal artery (IPDA) arising from the superior mesenteric artery (SMA). In 1991, we reported on two patients who underwent SP-DP-CA without any complications, showing the feasibility of SP-DP-CA for locally advanced cancer of the pancreatic body.[4] In that report, it was clarified that the whole stomach can be safely preserved without arterial reconstruction even if the celiac and common hepatic arteries are severed. We believe that preservation of the whole stomach significantly contributes

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to a better quality of life for patients who have undergone radical pancreatectomy. In the present study, we report our experience with SP-DP-CA for locally advanced cancer of the pancreatic body.

Material and Methods

Patient Number and Indication for SP-DP-CA

Between July 1987 and April 2003, 149 patients with cancer of the pancreatic body were admitted to the Tochigi Cancer Center Hospital. Among them, 25 patients underwent distal pancreatectomy with curative intent, and seven of these 25 patients underwent SP-DP-CA. SP-DP-CA was indicated for patients who had cancer invasion around the celiac artery and origins of the common hepatic artery and/or splenic artery, without tumor involvement of the SMA (Fig. 1). In all patients, preoperative angiography was carried out and variations of the IPDA were examined to safely perform SP-DP-CA.

Surgical Procedure

The abdominal cavity is explored through a wide upper midline incision. After confirming the absence of distant metastasis, the spleen and pancreatic tail and body are retracted medially from the retroperitoneum. To expose the origin of the celiac artery at the abdominal aorta, the left celiac ganglion, celiac nerve plexus, and a part of the left crus of the diaphragm are excised with en bloc dissection of the lymph nodes around the celiac artery and abdominal aorta. A polyester tape is then applied to the origins of the celiac artery and SMA that appears just below the celiac artery. In cases with tumors invading near the origin of the celiac artery, another polyester tape is also applied to the abdominal aorta just below the diaphragm, which enables the control of arterial bleeding by total clamping of the aorta. During these procedures, frozen section examination of surgical margins is repeatedly carried out to determine the curability of this operation.

Figure 1 Computed tomography scan demonstrating a tumor mass invading around the bifurcation of the splenic and common hepatic arteries (patient 5).

Following division of the short gastric vessels, the peripheries of the left gastric artery and vein are divided near the gastric wall, preserving the ascending branches of the left gastric vessels. By lifting the stomach upward, an anterior approach to the tumor is facilitated. Dissecting the lymph nodes and neural plexus around the common hepatic artery, the confluence of the gastroduodenal artery and common hepatic artery is exposed. The right gastric and gastroepiploic arteries should be preserved with certainty. The common hepatic artery is then severed with a transfixing suture just proximal to the origin of the gastroduodenal artery after confirming a well-palpable pulsation of the proper hepatic artery during a 3-min-long occlusion of the common hepatic and celiac arteries with vascular clamps.

The portal vein (PV) is dissected above and below the pancreas and finally freed from the dorsal side of the pancreas. The pancreas is divided over the right side of the PV. The pancreatic margin is routinely investigated by frozen section. The splenic vein is divided immediately before the junction with the superior mesenteric vein (SMV). When tumor invasion of the SMV–PV confluence is encountered or suspected, portal reconstruction is required.

Lifting up the cut end of the caudal pancreas with the tumor, the SMA is dissected from the surrounding lymph nodes and nerve plexus toward its origin. Great care should be taken to preserve the IPDA arising from the SMA or first jejunal artery. Therefore, dissection at the right side of the SMA is relatively compromised. The origin of the celiac artery is then totally dissected with excision of the right celiac ganglion and celiac nerve plexus. Pulling the polyester tape, already applied to the origin of the celiac artery, makes this dissection safe without difficulty. Finally, the celiac artery is divided at its origin via transfixing suture. When the tumor threatens the origin of the celiac artery, a side vascular clamp is applied to the aorta and then the celiac artery is severed at its origin. In such a case, the cut end of the celiac artery at the aorta is closed with sutures. The status after completion of SP-DP-CA is shown in Figs. 2 and 3.

Survival Time and Statistical Analysis

To evaluate the survival time of SP-DP-CA patients, the 18 patients with cancer of the pancreatic body who underwent distal pancreatectomy without combined resection of the celiac artery were used as a control.

Survival time was measured from the time of surgery and recorded in months. Cumulative survival rates were estimated based on the Kaplan–Meier method. The log-rank test

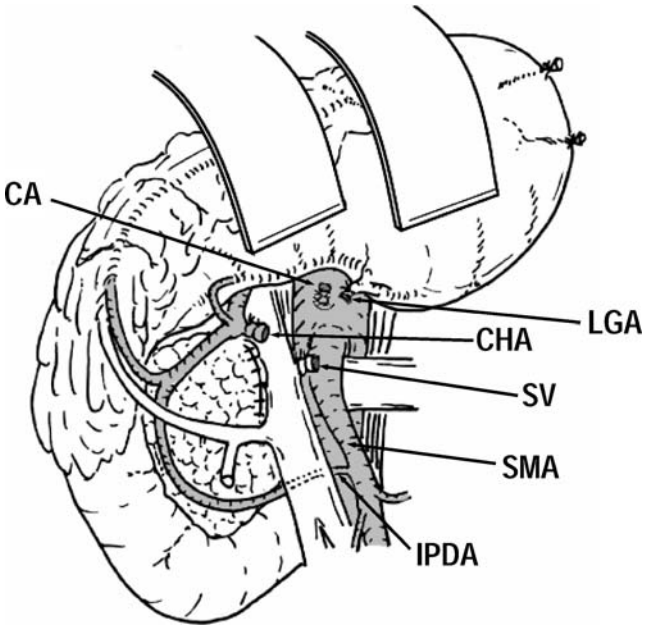

Figure 2 Completion of SP-DP-CA. The stomach is lifted upward. The blood supply to both the stomach and liver is maintained via the IPDA arising from the SMA. *CA* stump of the celiac artery, *LGA* distal stump of the left gastric artery, *CHA* stump of the common hepatic artery, *SV* stump of the splenic vein.

was used to compare the outcome between the two patient groups, and significance was accepted at the 5% level.

Results

Details of Patients and Surgical Procedures

Involved major vessels confirmed by preoperative imaging studies and/or by surgery are listed in Table 1. Patient 2 underwent combined resection of the involved SMV–PV confluence with end-to-end anastomosis. Patient 1, who also had cancer of the transverse colon, underwent additional transverse colectomy. In four patients (patients 2, 4, 5, and 7), adjacent structures were resected en bloc because of tumor invasion (Table 1). Patients 4 and 7 with invasion of the stomach underwent partial resection of the gastric wall. In three patients (patients 2, 5, and 7), en bloc resection of the transverse mesocolon, preserving the transverse colon with marginal vessels, was performed because of tumor invasion of the mesocolon near the ligament of Treitz. Prophylactic cholecystectomy was carried out in four patients (patients 1, 2, 4, and 6). In two patients (patients 2 and 6), repeat frozen section examination of the pancreatic cut margins disclosed cancer deposits in the small pancreatic ducts. We finally abandoned the idea of an additional resection of the pancreas because of the risk of sacrificing the pancreaticoduodenal arterial arcade, and we consequently administered intraoperative electron beam radiotherapy.

Pathological Findings of the Resected Specimens

The sixth edition of the International Union Against Cancer pTNM classification[5] was used to determine the stage grouping (Table 1). In patient 1, the dissected margin adjacent to the SMA wall was found to be positive for cancer, and the stage, therefore, was judged to be stage III (pT4, pN0, M0). In two patients (patients 2 and 6), positive pancreatic margins were reconfirmed. As a result, three of seven patients were found to have positive surgical margins. Four patients were found to have regional lymph node metastasis. Minute peritoneal nodules near the primary lesion proved to be cancer dissemination in patient 7, who was judged to have stage IV disease. In all patients, pathological examination of the resected specimens disclosed cancer infiltration of the nerve plexi encompassing the celiac, common hepatic, and/or splenic arteries. No patients, however, had direct cancer invasion of the celiac arterial wall.

Adjuvant Therapy Performed

One patient (patient 4) had not been scheduled for adjuvant therapy because of her poor general condition before surgery (Table 1). Adjuvant therapy could be delivered as scheduled in the remaining six patients. Intraoperative electron beam radiotherapy (16 to 30 Gy) was delivered in six patients, excluding patient 4 (Table 1). In addition, patients 1 and 2 received planned 45 and 40.5 Gy of postoperative external

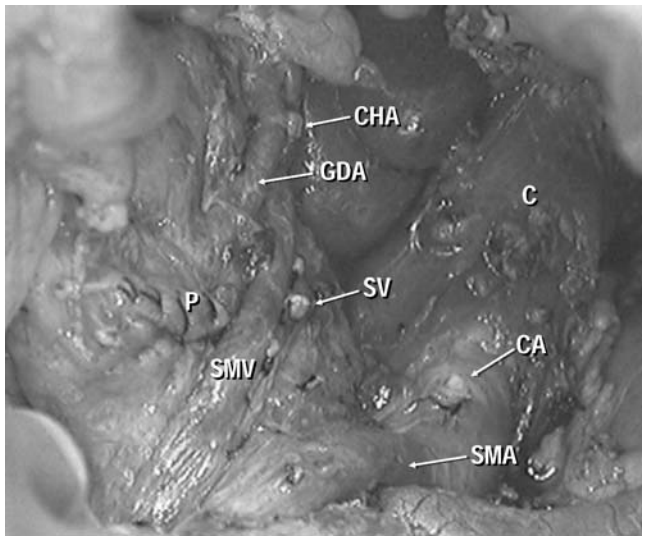

Figure 3 Operative field following SP-DP-CA. *CHA* stump of the common hepatic artery, *C* crus, *GDA* gastroduodenal artery, *SV* stump of the splenic vein, *CA* stump of the celiac artery, *SMA* superior mesenteric artery, *SMV* superior mesenteric vein, *P* stump of the pancreas.

Table 1 Patient Characteristics

Patient no.	Age and Gender	Preoperative Epigastric and/or Back Pain	Involved Major Vessels	Other Resected Structures	Surgical Margin	UICC Stage					Adjuvant Therapy
						pT	pN	Positive Nodes	pM	pTNM	
1	62 M	+	CHA, SA, CA	Transverse colon, gallbladder	Positive	4	0	(0/33)	0	III	IORT (20 Gy), EBRT (45 Gy)
2	60 F	+	SA, CA, SMV/PV	Transverse mesocolon, gallbladder	Positive	3	1	(3/41)	0	IIB	IORT (16 Gy), EBRT (40.5 Gy)
3	79 M	+	CA	None	Negative	3	1	(1/33)	0	IIB	IORT (30 Gy), PHI (20 Gy)
4	74 F	+	SA	Stomach (partial), left adrenal, left kidney (partial), jejunum, gallbladder	Negative	3	0	(0/7)	0	IIA	None
5	54 F	+	CHA, SA	Transverse mesocolon, left adrenal, left kidney	Negative	3	1	(2/51)	0	IIB	IORT (30 Gy), PHI (22 Gy)
6	73 M	+	CHA, SA, CA	Gallbladder	Positive	3	0	(0/29)	0	IIA	IORT (30 Gy)
7	45 M	+	CHA, SA	Transverse mesocolon, stomach (partial), left adrenal	Negative	3	1	(3/21)	1	IV	IORT (30 Gy), chemotherapy with GEM

CHA = common hepatic artery, SA = splenic artery, CA = celiac artery, SMV = superior mesenteric vein, PV = portal vein, IORT = intraoperative radiotherapy, EBRT = postoperative external beam radiotherapy to the tumor bed, PHI = prophylactic hepatic irradiation, GEM = gemcitabine

beam radiotherapy to the tumor bed, respectively. Patients 3 and 5 were able to receive planned 20 and 22 Gy of postoperative prophylactic hepatic irradiation, respectively.[6] Patient 7 received postoperative chemotherapy with three courses of full-dose gemcitabine.

Of the 18 patients in the control group, four received no adjuvant therapy. The remaining 14 received adjuvant therapy as follows, similarly to the SP-DP-CA patients: 14, intraoperative electron beam radiotherapy (16 to 30 Gy); seven, postoperative prophylactic hepatic irradiation (19.8 to 20 Gy); two, postoperative external beam radiotherapy to the tumor bed (39.6 and 25.2 Gy, respectively); two, postoperative chemotherapy with gemcitabine and 5-fluorouracil, respectively.

Postoperative Complications

There was no postoperative mortality. Postoperative complications occurred in two patients (patients 3 and 6) (Table 2). Patient 3 developed transient passage disturbance in the second portion of the duodenum, resulting in the delayed start of oral intake (Table 2). An upper gastrointestinal series showed decreased motility of the duodenum without stenosis. The passage disturbance was conservatively improved. Patient 6 developed a minor pancreatic fistula, but it spontaneously closed without surgical intervention. Although two patients (patients 6 and 7) showed a transient elevation of serum transaminase levels that peaked on postoperative day 2 and promptly declined thereafter, no patients showed significant evidence related to ischemia of the stomach or liver (Table 2).

Long-term Outcome and Survival

Diarrhea, which sometimes needed loperamide and/or opium tincture to be controlled, was observed in five patients (Table 2). No patients developed insulin-dependent diabetes mellitus. Until death, all but one patient (patient 6) showed a complete resolution of epigastric and/or back pain that they had preoperatively had (Table 1). Patient 6 developed epigastric and back pain along with local recurrence that was confirmed by computed tomography (CT) scan 13 months after surgery. Patient 2 committed suicide without follow-up examinations. The reason for suicide was mental and not related to severe postoperative morbidity. The other six patients had been able to maintain a good quality of life until they required readmission due to the progression of recurrent lesions.

Table 2 Postoperative Course

Patient no.	Start of Oral Intake (POD)	Early Postoperative Complication	Diarrhea	Insulin-dependent Diabetes Mellitus	Epiagstric/ Back Pain	Pattern of Recurrence				Autopsy	Survival Time (months)	Cause of Death
						Local	Liver	Lung	Peritoneum			
1	9	None	Controllable	None	Disappeared	None	None	None	+	+	42	DOC
2	8	None	Controllable	None	Disappeared	Unknown	Unknown	Unknown	Unknown	None	4	Suicide
3	29	Transient passage disturbance in the duodenum	Controllable	None	Disappeared	None	None	None	+	+	17	DOC
4	18	None	None	None	Disappeared	None	+	None	None	None	21	DOC
5	11	None	Controllable	None	Disappeared	+	None	+	None	+	78	DOC
6	10	Pancreatic fistula, transaminase elevation POD2 (AST=641, ALT=443)	None	None	+	+	+	+	+	+	19	DOC
7	8	Transaminase elevation POD2 (AST=1546, ALT=1680)	Controllable	None	Disappeared	None	None	None	+	None	13	DOC

POD = postoperative day, ALT = alanine aminotransferase, AST = aspartate aminotransferase, DOC = died of cancer

Patterns of recurrence confirmed by CT and/or autopsy are listed in Table 2. Local recurrence was clarified in two (patients 5 and 6) of four patients who underwent autopsy, one (patient 6) of whom had had a positive surgical margin. Patient 5, with negative surgical margins, was first found at autopsy to have had local recurrence around the stump of the celiac artery, which had not been detected by CT scan before death. This patient developed pulmonary metastasis and was administered more than 10 courses of full-dose gemcitabine. As a result, patient 5 could survive for more than 6 years. The local control achieved in patient 1 may have been attributed to adjuvant radiotherapy composed of intraoperative electron beam radiotherapy (20 Gy, 9 MeV) and postoperative external beam radiotherapy (45 Gy). The median survival times of patients who underwent distal pancreatectomy with (n=7) or without combined resection of the celiac artery (n=18) were 19 and 25 months, respectively. The overall survival rate was not significantly different in the two groups (P=0.5300, Fig. 4).

Discussion

Some instances of locally advanced cancer of the pancreatic body show invasion around the bifurcation of the common hepatic, splenic, and celiac arteries without cancer involvement of the SMA. For such a case, the Appleby operation.[7] might be a radical procedure. The Appleby operation, devised for advanced gastric cancer, allows en bloc resection of the stomach, caudal pancreas, and common hepatic and celiac arteries with surrounding lymph nodes. Using the Appleby operation, cancer of the pancreatic body invading around the celiac artery can theoretically be resected without any arterial reconstructions because

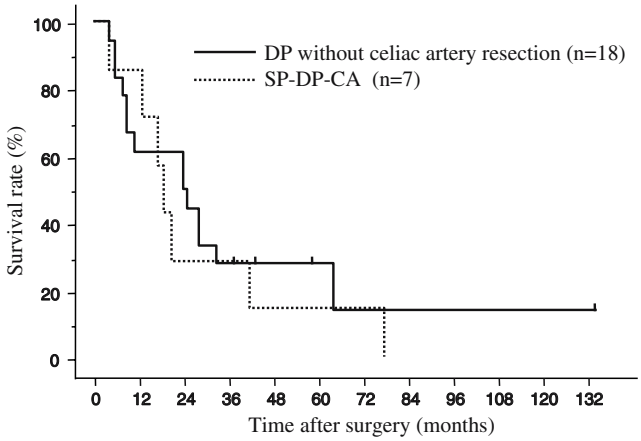

Figure 4 Survival curves of patients who underwent distal pancreatectomy with or without celiac artery resection for cancer of the pancreatic body. There was no significant difference in the survival rate between the two groups (P=0.5300).

arterial blood supply to the liver is maintained via the IPDA arising from the SMA. There have been several reports on the Appleby operation adopted for patients with advanced cancer of the pancreatic body.[8–12] The greatest disadvantage of the Appleby operation, when adopted for cancer of the pancreatic body, is that an intact stomach is totally resected. Total gastrectomy that might be unrelated to the surgical radicality for pancreatic cancer inevitably has negative effects upon the quality of life of patients undergoing pancreatectomy. As a result, such patients may lose the chance to receive adjuvant therapy that is likely to enhance postoperative survival. The Appleby operation provided us with some useful hints for developing SP-DP-CA. SP-DP-CA, however, fundamentally differs from the Appleby operation in terms of preserving the whole stomach. We believe that the preservation of the whole stomach maintains a more normal gastrointestinal hormonal milieu, which in turn results in a better nutritional status. It is our policy that a good nutritional status is necessary for resected patients to complete planned postoperative adjuvant therapy. On the basis of these concepts, we first performed SP-DP-CA for locally advanced cancer of the pancreatic body in 1987. Our primary concern was arterial blood supply to the liver and stomach only via the IPDA. Fortunately, a postoperative arteriogram of the SMA showed sufficient blood flow to the liver and stomach via the IPDA, and the clinical course of the patient following the first SP-DP-CA was uneventful.[4] Patients fulfilling the indication criteria for SP-DP-CA have been very limited. A majority of patients with locally advanced cancer of the pancreatic body had tumor invasion not only around the celiac artery, but also around the SMA. Furthermore, CT with arterial portography often disclosed small liver metastases in patients who were supposed to be candidates for SP-DP-CA. Our series, therefore, includes only seven patients who underwent SP-DP-CA. On the other hand, owing to precise preoperative evaluation by imaging studies, we never experienced a patient in whom planned SP-DP-CA was discontinued before completing the resection because of local disease or positive intraoperative biopsies.

Several investigators have reported on SP-DP-CA with or without modification.[13–19] The major items of concern involve blood flow of the proper hepatic artery following resection of the common hepatic artery because abrupt reduction of blood flow of the proper hepatic artery may result in both hepatic and gastric ischemia. Of four patients in the series of Konishi et al.[15], two patients underwent reconstruction of the hepatic artery using a graft of the splenic artery taken from the resected specimen between the cut end of the common hepatic and celiac arteries because of weak pulsation of the proper hepatic artery. Lin et al.[17] modified SP-DP-CA by reanastomosis between the stump of the celiac and common hepatic arteries without a vascular graft. Kondo et al.[18] reported that preoperative embolization of the common hepatic artery was successfully performed to enhance the collateral arterial flow via the IPDA. Kondo et al.[18] also showed that postoperative gastric ulcer was rare in patients who underwent preoperative embolization of the common hepatic artery. None of the seven patients in our series underwent reconstruction of the hepatic artery or any attempts to enhance arterial blood flow via the IPDA. Well-palpable pulsation of the proper hepatic artery after occlusion of the common hepatic and celiac arteries can be considered valid evidence for a sufficient arterial flow to the liver and stomach. Intraoperative Doppler ultrasonography may be useful to evaluate hepatic arterial flow after occlusion, especially in cases with poor pulsation of the proper hepatic artery.[11] To ensure hepatic and gastric arterial flow following SP-DP-CA, accidental intraoperative injury to the IPDA must be avoided. Clearance of the lymph nodes and nerve plexus around the SMA is, therefore, inevitably compromised to secure the IPDA arising from the SMA. Preoperative evaluation for individual variation of the IPDA by angiography is also recommended to safely perform SP-DP-CA. We have never had a patient in whom SP-DP-CA was aborted because of poor pulsation of the proper hepatic artery after occlusion of the common hepatic and celiac arteries.

It is well known that extended pancreatectomy with the combined resection of major arteries, so-called regional pancreatectomy, is associated with high morbidity and mortality rates.[20] In contrast to regional pancreatectomy, SP-DP-CA does not require any arterial or gastrointestinal reconstruction. Kondo et al.[18] showed that the morbidity rate following SP-DP-CA was as high as 62%, but there was no mortality in their series. In addition, postoperative mortality following SP-DP-CA has not been documented in any other report on SP-DP-CA.[14–17,19] Zero mortality following SP-DP-CA may be attributed to the absence of arterial, pancreatico-biliary, and gastrointestinal reconstruction in this procedure. Furthermore, our SP-DP-CA patients were able to survive for as long as those who underwent distal pancreatectomy without resection of the celiac artery. These results show that SP-DP-CA is justified as a radical procedure for locally advanced cancer of the pancreatic body. Gagandeep et al.[19] also conclude that SP-DP-CA can result in prolonged survival and should be considered in central and distal pancreatic cancers invading the celiac artery. Adjuvant therapy performed following SP-DP-CA may also contribute to the survival of SP-DP-CA patients. SP-DP-CA patients in this series were able to complete planned adjuvant therapy or receive full-dose chemotherapy after cancer recurrence, owing to their well-maintained performance status following surgery. As a result, 3- and 5-year survivors could be obtained.

Recently, we reported that autopsy of patients with resectable pancreatic cancer revealed a high rate of local recurrence even after curative resection.[21] The control of local recurrence is one of the major goals of surgery for pancreatic cancer. It is noteworthy that local recurrence was evident in only two patients (patients 5 and 6), although all patients in this series had locally advanced pancreatic cancer involving major arteries. Furthermore, SP-DP-CA that is associated with a low mortality rate and good local control has the possibility of becoming a standard procedure for cancer of the pancreatic body without cancer invasion of the major arteries.

Conclusion

This study showed that SP-DP-CA is a rational approach to locally advanced pancreatic body cancer that invades around the celiac artery. Using SP-DP-CA, the resectability of advanced cancer of the pancreatic body will be improved without increased mortality rates. If limited to one institute, the accumulation of candidates for SP-DP-CA with the present indication criteria, however, will take a long time because the majority of locally advanced cancer of the pancreatic body is associated with not only the celiac artery but also SMA involvement. To determine the implications of SP-DP-CA for locally advanced cancer, multicentric clinical studies will be necessary. In view of the feasibility of SP-DP-CA, it may also be worthwhile to adopt SP-DP-CA for less advanced cancer of the pancreatic body to enhance local control and survival.

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