Appraisal of Arteriography for Assessment of Operability in Periampullary Cancer

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The preoperative arteriograms in 87 periampullary cancers were analyzed in relation to the extension of tumor as explored in surgery, the resectability and the survival time. Most of the patients in whom the pancreaticoduodenal arcades were intact (Group I-O) showed no extension of the lesion into the surroundings and survived more than two years after pancreatoduodenectomy. Those in which the invasion was confined to the anterior pancreaticoduodenal arcade (Group I-A) could also be resected with much anticipation of long survival. About a third of the patients, in whom either the posterior arcade (Group I-P) or both anterior and posterior arcades were invaded (Group I-AP), were resectable. Only a few patients with the involved gastroduodenal artery (Group 2-A) or with the involved superior mesenteric artery (Group 2-P) were treated by extended pancreatoduodenectomy, but they died of recurrence shortly after resection. Further extension of the lesion was explored in surgery when preoperative angiography showed invasion of both the gastroduodenal and superior mesenteric arteries (Group 2-AP) or of the extrapancreatic vessels such as the hepatic artery (Group 3-C), intestinal arteries (Group 3-M) and both (Group 3-CM). Survival in these cases was only a few months after by-pass operation.

ANGIOGRAPHERS have extensively pursued the arteriograms in cancer of the pancreas only from the viewpoint of differential diagnosis, but only a few have attempted to analyze these vascular roentgenograms in relation to the management of different stages of this disease. Although there are some discrepancies in the extant literature concerning the value of pancreatic angiography, we believe that no preoperative tools but arteriography could assess tumor growth, resectability and prognosis of this disease. In a previous study,[9] an attempt was made to stage the extent of lesions as judged by vascular morphology. However, for the purpose of its further appraisal in the field of surgery, the various stages of angiograms should be re-evaluated in relation to the state of lesions explored by laparotomy. In fact, there do not seem to be any systematic works throwing light on these problems. The purpose of this paper is to correlate these preoperative arteriograms with operative findings and survival times. Hopefully, it can also provide an actual basis for selection of the proper therapeutic procedure in periampullary cancer.

Materials and Method

During the past 10 years, preoperative arteriography was performed in our clinic on 87 patients with adenocarcinoma in the periampullary region. All underwent laparotomy within two weeks after angiography and had a proven diagnosis of periampullary cancer. They consisted of 30 patients whose lesions could be treated by pancreatoduodenectomy and 57 whose lesions could not be resected due to the advanced extension of tumors or to their poor general conditions. The resectable instances, in which the precise location of the lesions could be determined by the extirpated specimens, included 13 with cancer of the head of the pancreas, 8 with cancer of the ampulla of Vater, 7 with cancer of the terminal bile duct and 2 with cancer of the duodenum. Excluded from the present series were cystadenocarcinoma, islet cell carcinoma, carcinoid and other unusual types of tumors. Those with extensive involvement of the entire pancreas were also omitted, even if the primary lesions appeared to be in the periampullary region.

Selective arteriography was performed with the Seldinger technique.[7] Catheterization of the celiac trunk and the superior mesenteric artery was made under fluoro-

scopic control mainly using the Cook grey catheter with J-shaped tip. A 30 to 50 ml bolus of 66.8% sodium iothalamate was injected into each artery and the serial film was taken. In order to delineate the further detailed vascular morphology, the right oblique projection was added to the anteroposterior by use of superselective angiography, pharmacoangiography[10] or combined hypotonic duodenography.[11,12]

As described in a previous study,[9] the arteries relating to the pancreas were grossly divided into three types: 1) the arteries confined to the pancreas such as the pancreaticoduodenal arteries and their branches (group 1 artery); 2) the arteries adjacent to the pancreas such as the gastroduodenal artery and the proximal portion of superior mesenteric artery (group 2 artery); and 3) the arteries of the extrapancreatic organs such as the middle colic, jejunal, gastric, gastroepiploic and hepatic arteries (group 3 artery).

Those in which tumor invasion was radiologically limited to the group 1 artery were further subdivided into Group 1-O, Group 1-A, Group 1-P and Group 1-AP cancers. In Group 1-O cancer the invasion was confined to the branches of pancreaticoduodenal arteries or with no evidence of vascular invasion found on the films. In Group 1-A the invasion was limited to the anterior pancreaticoduodenal arcade. In Group 1-P the invasion was limited to the posterior pancreaticoduodenal arcade; and in Group 1-AP the invasion extended to both anterior and posterior arcades.

Those in which tumor infiltration extended to the group 2 artery were subclassified into Group 2-A, Group 2-P and Group 2-AP cancers. In Group 2-A cancer the gastroduodenal artery was involved by tumor. In Group 2-P the proximal portion of superior mesenteric artery was invaded; and in Group 2-AP the vascular involvement was seen in both the gastroduodenal and superior mesenteric arteries.

Those in which the invasion extended farther into the group 3 artery were subclassified into Group 3-C, Group 3-M and Group 3-CM cancers: in Group 3-C the involvement was demonstrated in vessels belonging to the celiac territory such as the hepatic and gastric arteries; in Group 3-M the vascular invasion was shown in branches belonging to the superior mesenteric territory such as the jejunal and middle colic arteries; and Group 3-CM consisted of both the invaded Group 3-C and Group 3-M arteries.

Pancreatoduodenectomy was performed in either one or two stages in patients who showed no hematogenous metastasis, peritoneal dissemination or local extension into the surrounding structures such as portal vein, mesentery or hepatoduodenal ligament. The resecting procedure was not performed on those who were in extremely poor general condition, even when the lesions appeared removable. Those in whom pancreatoduodenectomy was not feasible underwent by-pass operations, including cholecystojejunostomy, cholecystostomy, choledochostomy, choledochoduodenostomy and gastrojejunostomy.

Correlations between each type of preoperative arteriogram and resectability, operative findings and survival time were reviewed.

Results

Results are summarized in Table 1.

Table 2 summarizes the incidence of each tumor growth into the surroundings, liver and peritoneum.

As shown in Table 2, of the 25 cases of Group 1-O, liver metastasis was demonstrated in two, one of which was accompanied by portal and mesenterial infiltration. Of the 8 cases of Group 1-P, portal involvement was revealed in 4; in one there was mesenterial invasion, and in one there was hepatoduodenal invasion and liver metastasis. Of the 11 cases of Group 1-AP, 4 showed portal involvement; one mesenterial involvement; one portal and mesenterial involvement; one portal and mesenterial involvement and peritoneal dissemination; and one portal and mesenterial involvement, peritoneal dissemination and liver metastasis.

Of the 11 cases of Group 2-A, three exhibited mesenterial invasion; two portal invasion; one mesenterial and portal invasion; one portal and hepatoduodenal invasion; one portal and mesenterial invasion and liver metastasis; one portal and hepatoduodenal invasion and liver metastasis; and one mesenterial and hepatoduodenal invasion, peritoneal dissemination and liver metastasis. The case with mesenterial invasion, as mentioned previously, was treated by transverse colectomy together with pancreatoduodenectomy. Portal involvement was disclosed in all of the 3 Group 2-P and 4 Group 2-AP patients. Tumor growth into the mesentery, hepatoduodenal ligament and liver was additionally determined in some of them, especially in the latter group. Only one resectable lesion in Group 2-P could not be removed without the combined resection of the pancreatic portion of the portal vein, as described above.

Surgery revealed that the lesions belonging angiographically to Group 3 were associated with their advanced local extension, which made almost all of them unresectable. In this group of 24 patients, liver metastasis and peritoneal dissemination were seen in 6 and 7, respectively. With regard to the mode of extension, hepatoduodenal infiltration was more evident in Group 3-C than in Group 3-M, while peritoneal dissemination was comparatively prominant in Group 3-M.

As stated above, liver metastasis and peritoneal dissemination were surgically explored in the various groups. The angiographic confirmation of these discontinuously spreading lesions was assessed. As indicated in

TABLE 1. *Correlation Between Preoperative Arteriograms and Resectability in 87 Periampullary Cancers*

Anteriogram	Number of Patients	Resectable cases and location					Unresectable cases	Resectable rate (%)
		Head of the Pancreas	Ampulla of Vater	Terminal Bile Duct	Duodenum	Total		
Group 1-O	25	3*	8	7**	1	19	6§	76
Group 1-A	1	1	0	0	0	1	0	100
Group 1-P	8	3	0	0	0	3	5‖	37
Group 1-AP	11	3	0	0	0	3	8	27
Subtotal	45	10	8	7	1	26	19	
Group 2-A	11	2***	0	0	0	2	9	18
Group 2-P	3	1†	0	0	0	1	2	33
Group 2-AP	4	0	0	0	0	0	4	0
Subtotal	18	3	0	0	0	3	15	
Group 3-C	3	0	0	0	0	0	3	0
Group 3-M	18	0	0	0	1‡	1	17	5
Group 3-CM	3	0	0	0	0	0	3	0
Subtotal	24	0	0	0	1	1	23	
Total	87	13	8	7	2	30	57	34 (average)

*One total pancreatectomy
**Two total pancreatectomies
***One resection of transverse colon; one total pancreatectomy
†Total pancreatectomy and resection of portal vein
‡Resection of transverse colon
§Four unresected due to poor risk state, although lesions were removable
‖One unresected due to poor risk state, although lesion was removable

Table 3, the presence of liver metastasis could be accurately evaluated on the films in 11 of 17 patients (2 of Group 1, 4 of Group 2 and 5 of Group 3), and that of peritoneal dissemination could be predicted in three of 11. These angiographically confirmed three patients belonged to Group 3.

Excluding those who died immediately after operation or are still alive, survival time after operation was reviewed. The average survival of the patients with whole resectable and unresectable cancers was 17.3 and 4.5 months, respectively. The average survival times of the patients with resectable cancer were as follows: 24.3 months for 8 Group 1-O cases; 10.6 months for one Group 1-P; 9.6 months for three Group 1-AP; 8.9 months for two Group 2-A; and 7.6 months for one Group 2-P. Of these patients, including those still living, 8 Group 1-O and one Group 1-A showed a survival time of more than 3 years after pancreatoduodenectomy.

Fig. 1 illustrates the survival time of each pancreatoduodenectomized patient.

The survival time of the unresectable cancer cases in Group 1 was 6 or 7 months, and that of unresectable cases in Group 2 and 3 was 2 to 4 months after by-pass operations. Of these 57 unresectable patients, only 13 survived more than 6 months. They consisted of three each of Group 1-O, Group 1-P and Group 1-AP; two Group 2-A; and one each of Group 3-M and Group 3-CM cancer. Excluding those with liver metastasis, the survi-

TABLE 2. *Correlation Between Preoperative Arteriograms and Operative Findings in 87 Periampullary Cancers*

Arteriogram	Total Patients	Local Invasion of Tumors			Liver Metastasis	Peritoneal Dissemination
		Portal Vein System	Mesentery	Hepatoduodenal Ligament		
Group 1-O	25	1	1	0	2	0
Group 1-A	1	0	0	0	0	0
Group 1-P	8	4	1	1	1	0
Group 1-AP	11	7	4	0	1	2
Group 2-A	11	6	6	3	3	1
Group 2-P	3	3	1	1	1	0
Group 2-AP	4	4	3	2	3	1
Group 3-C	3	3	2	3	1	0
Group 3-M	18	16	17	7	4	5
Group 3-CM	3	3	3	2	1	2
Total	87	47	38	19	17	11

TABLE 3. *Angiographic Confirmation of Liver Metastasis and Peritoneal Dissemination*

Anteriogram	Liver metastasis		Peritoneal Dissemination	
	Surgically confirmed	Angiographi-cally confirmed	Surgically confirmed	Angiographi-cally confirmed
Group 1-O	2	1	0	–
Group 1-A	0	–	0	–
Group 1-P	1	0	0	–
Group 1-AP	1	1	2	0
Group 2-A	3	2	1	0
Group 2-P	1	0	0	–
Group 2-AP	3	2	1	0
Group 3-C	1	1	0	–
Group 3-M	4	4	5	1
Group 3-CM	1	0	2	2
Total	17	11 11/17=64%	11	3 (3/11=27%)

val time of the unresectable Group 1-O and Group 1-P accounted for over 8 months.

These results are summarized in Table 4.

Discussion

The present documentations provide further knowledge from that gained in our previous series[9,13–16] on the correlation between arteriograms and clinical aspects in cancer of the pancreas. We have since made use of these vascular roentgenograms for the management of this malignoma, but the increasing number of observations have necessitated the further analysis of the vascular

morphology of the pancreas. The curability as well as resectability of periampullary cancer depends on whether the tumor extends farther into the surrounding structures such as the portal vein, vena cava, mesentery or hepatoduodenal ligament, and whether the tumor is accompanied by liver metastasis or peritoneal implants. In addition, the clinical course is not only affected by the extent of the tumor but, as we stressed previously,[14,15] deeply influenced by the location of the lesion within the gland. These factors are certainly of the greatest importance for the management of these patients. However, there have been no preoperative criteria to assess them accurately, nor have any particular efforts to establish them been provided. In an attempt to resolve such problems the intrapancreatic and peripancreatic arteries each were further reclassified into those located in the anterior side of the gland and those in the posterior side; the associated vascular involvement was correlated with the extension of tumor as explored in surgery, the resectability and the followup results.

With Group 1-O, in which no evidence of invasion was found along the pancreaticoduodenal arteries, almost none of the patients showed any extension of the lesion into the surrounding areas and such patients could be treated by pancreatoduodenectomy. These patients showed an average survival time of more than two years. One Group 1-A cancer patient, in whom the vascular involvement was confined to the anterior superior pancreaticoduodenal artery, could also be resected and is now living well 6 years after surgery.

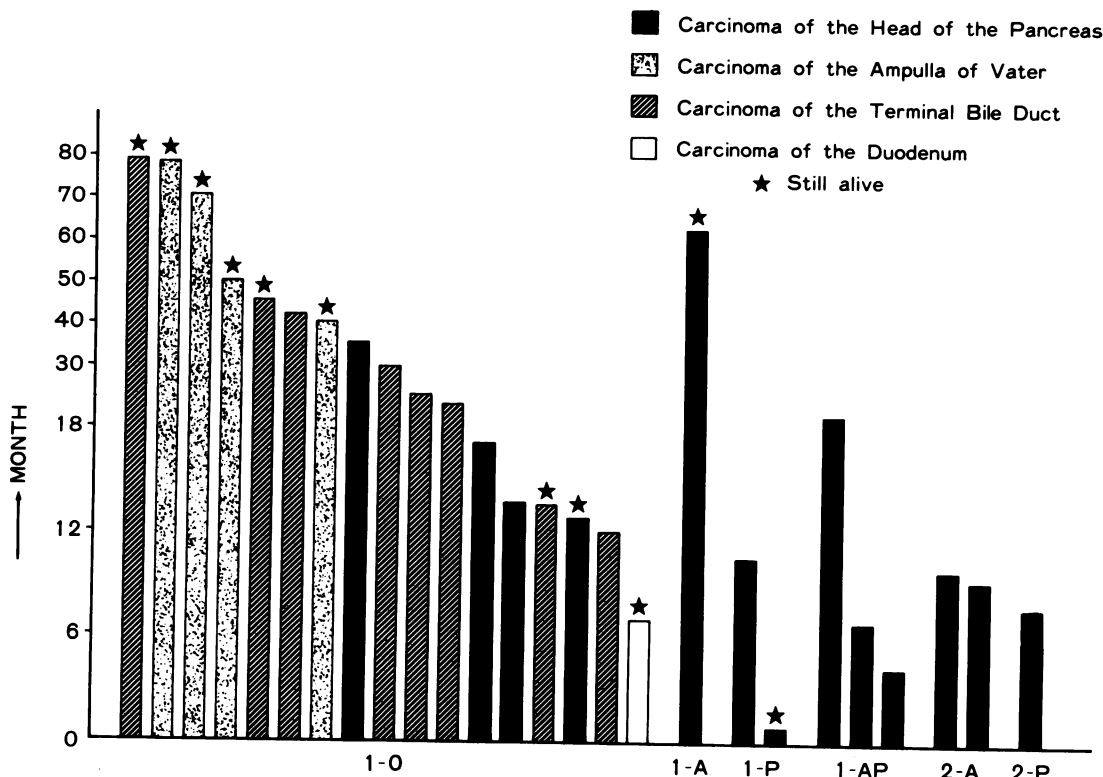In contrast, resectability as well as survival after pan-

FIG. 1. Survival after pancreatoduodenectomy in each group of patients, excluding those dying surgically.

TABLE 4. *Correlation Between Preoperative Arteriograms and Survival Time in 87 Periampullary Cancers*

| | Resectable Cases | | | | Unresectable cases | | | | |
| | | | | | | | Average Survival After Surgery* (mon) | | |
Arteriogram	Total Patients	Patients dying surgically or still alive	Average survival after surgery* (mon)	Survival >3 yrs	Total Patients	Patients dying surgically or still alive	Including liver metastasis	Excluding liver metastasis	Survival > 6 mon
Group 1-O	19	11	24.3	8	6	2	7.3	8.7	3
Group 1-A	1	1	—	1	0	—	—	—	—
Group 1-P	3	2	10.6	0	5	0	7.0	8.3	3
Group 1-AP	3	0	9.6	0	8	3	6.1	6.1	3
Group 2-A	2	0	8.9	0	9	2	4.6	5.2	2
Group 2-P	1	0	7.6	0	2	0	2.5	3.1	0
Group 2-AP	0	0	—	—	4	1	2.5	2.0	0
Group 3-C	0	0	—	—	3	1	3.2	3.2	0
Group 3-M	1	1	—	0	17	3	3.8	4.4	1
Group 3-CM	0	0	—	—	3	0	3.4	2.7	1
Total	30	15	17.3 (average)	9	57	12	4.5 (average)	5.6 (average)	13

*Excluding those dying surgically or still living

creatoduodenectomy became abruptly unfavorable when the lesions involved the posterior pancreaticoduodenal arcade; that is, about half of the Group 1-P and Group 1-AP cancers exhibited portal vein invasion, and a few in the latter group additionally disclosed mesenteric involvement and peritoneal dissemination. Thus, localization of lesions within the periampullary region exerts an influence on the clinical course. Such localization could be determined by the vascular morphology as classified in this study. Of the Group 2 cancers, in which tumors extended to the peripancreatic arteries, only a few lesions growing anteriorly (Group 2-A) were resectable with the transverse colon, but recurrence shortly after resection could not be avoided. One Group 2-P patient, in whom the tumor grew posteriorly, underwent resection of the pancreatic segment of portal vein and the entire pancreas, but he survived only 7 months. Furthermore, the majority of Group 2 cancers already revealed mesenterial core formation, liver metastasis or hepatoduodenal invasion. This suggested that when the extrapancreatic vessels were radiologically involved, there was little hope for cure, even if extended pancreatoduodenectomy was performed. In fact, when comparing the survival rate of Group 1 treated by by-pass operations alone with that of Group 2 treated by radical procedures, no difference between their postoperative clinical course could be found.

Hermneck and colleagues[5] also have classified cancer of the pancreas into four stages on the basis of the extent of lesion as judged by operative and histologic findings at the time of operation. According to his results, survival times after resection for stage 1 (local disease only) and stage II (invasion of surrounding tissues) were 1.4 and 1.2 years, respectively. However, resection for stage III (re-

gional node metastases) and stage IV (generalized carcinoma) resulted in survival times almost identical to that observed with palliative procedures only. According to Smith and colleagues' review[8] of cancer of the pancreas, the long-term survivors were included among the patients who had by-pass operations. His conclusion was that pancreatoduodenectomy should be reserved for those with early tumors in whom evidence of local invasion or spread to regional lymph nodes was not demonstrable; and that by-pass operation should be selected if the presence of local or nodal invasion was probable. According to Crile's observation[2] on some early stages of adenocarcinoma of the head of the pancreas, the average period of survival of those who were treated with by-pass procedure was longer than that of those treated by radical operations. Based on these facts, he insisted that when nothing but adenocarcinoma of the head of the pancreas and only those large enough to be readily palpable were considered, radical operation appeared to disseminate the disease and shorten life.

These reports might be partly true if we compared our results between those with unresectable Group 1 and those with resectable Group 2. However, the ablative procedure should be executed for Group 1 cancer, in which most of the tumors had not yet extended far beyond the capsule of the gland. In addition, even when the lesions with Group 1 are not removed, local infusion chemotherapy by means of our method[17] probably has much to offer.

According to our previous study[14,15] on the correlation of survival time with the location and size of tumor, the cancers situated in the posterior side of the head of the pancreas or in the uncinate process were prone to be unresectable. This was true even when they were detected at

a comparatively early stage. When such cancers were resected with the routine method, the patients died of recurrence within as little as one year after surgery. This poor survival time might be due to the cancerous tissue remnants around the portal vein system where aggressive manipulation could not be performed. These data suggest that some patients in Group 1, especially in Group 1-P and Group 1-AP, could benefit from further extended surgery such as total pancreatectomy combined with portal resection. Fortner[3] has advocated a new en-bloc resection of the lesion in which the entire pancreas, portal vein, celiac axis, proximal portion of the superior mesenteric artery, lymph nodes and lymphatic vessels adjacent to the pancreas were all removed. He recommended this bold procedure for adenocarcinoma that was clinically confined to the pancreas. If the operative mortality can be held to acceptable levels, such new efforts appear promising. For selection of these various degrees of procedures, the vascular patterns proposed in the present study could be of great help.

In the Group 3 cancers, the most frequently involved vessel of the celiac territory was the hepatic artery, and in the superior mesenteric territory it was the middle colic artery or jejunal arteries. The former (Group 3-C) was correlated with a high incidence of invasion of the hepatoduodenal ligament, while the latter (Group 3-M) was correlated with peritoneal dissemination in addition to mesenterial core formation. Of course, almost all cases were beyond resection and the patients survived only 3 to 4 months on the average.

As to resectability in periampullary cancer, Sato and associates[6] have observed that lesions with abnormalities limited to the superior pancreaticoduodenal artery could be resected, but that lesions with abnormalities in other arteries were unresectable. According to a recent report by Goldstein and colleagues,[4] the signs of nonresectability were invasion or occlusion of the portal or superior mesenteric vein, or encasement of the celiac, superior mesenteric, hepatic, gastric or intestinal arteries; lack of resectability was predictable in 25 of 29 cancers. Following Buranasiri and Baum,[1] many radiologists have stressed the importance of the venous phase in diagnosis of this disease. In the present research the state of the portal system was also evaluated, but a clearer venous visualization was not always accomplished in all of the instances presumably due to the lack of a large dose of contrast medium. Thus, the venous factor, regrettably, could not be statistically assessed in the present series.

Most cases of peritoneal dissemination belonged to Group 3, but there was no marked difference in the incidence of liver metastasis among the groups. Surprisingly, two of Group 1-O already had liver metastasis, which prevented execution of the resecting procedure. These metastatic lesions were usually so hypovascular that the angiographic manifestation, especially of

peritoneal implants, was discouraging.[18] Diagnosis of some cases of Group 1-O cancer by angiography alone was also obscure because the finer branches of the arcades were not always sharply visualized. In order to compensate for this disadvantage, the routine use of the simultaneous projection of hypotonic duodenograms with angiograms was adopted, this procedure being reported elsewhere.[11,12] Irrespective of these diagnostic problems, we wish to emphasize that the majority of Group 1-O cancer as well as Group 1-A could be treated by routine pancreatoduodenectomy, which is usually followed by a longer survival period. It is also possible that the curability of group 1-P and Group 1-AP cancers could be improved by means of further extended resections of the lesions.

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