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Do 2-cm pancreatic tumors localize in the pancreas? Analysis of the greatest and smallest diameters of the autopsied pancreas

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ABSTRACT

Background: Local tumor growth and tumor size are key factors that determine the prognosis of patients with pancreatic cancers. In the present study, we measured the the greatest and smallest diameters of the pancreas to clarify the largest pancreatic ductal adenocarcinomas that can be confined to the pancreas.

Materials and Methods: Pancreatic tissues obtained from 10 autopsied patients were cut into 5-mm sections vertical to the main pancreatic duct. Each slice was processed for microscopic examination and was captured using a virtual slide scanner. We measured the greatest diameter of the pancreas in each slide.

Results: The average greatest diameters of the pancreatic body and tail were less than 2 cm in 2 cases for the pancreatic body and 5 cases for the pancreatic tail. All cases contained slides for which the greatest pancreatic diameter measured less than 2 cm, with 5 cases for the pancreatic head and body and 9 cases for the pancreatic tail. The average smallest diameters of the pancreatic head, body, and tail were less than 2 cm for all cases, and there were 3 cases in which they were less than 1 cm.

Conclusion: Our study, which evaluated the entire pancreatic parenchyma from autopsy tissues, revealed that the pancreas has many areas where diameters are less than 2 cm, suggesting that most 2-cm tumors cannot be limited to the pancreas.

Key words: pancreas; autopsy; greatest dimension; early cancer

Introduction

Pancreatic cancer mortality has been increasing worldwide[1] and in Japan[2]. Despite advances in diagnostics and therapeutics, pancreatic cancer prognosis remains poor, with an overall 5-year survival rate of 6%, due in part to difficulties in diagnosing carcinoma at an early stage[1]. Previously, we retrospectively evaluated 8,339 autopsies performed at our hospital and found that distant metastases were present in 27% of cases of occult pancreatic ductal adenocarcinoma (PDAC)[3], suggesting that PDAC exhibits aggressive behavior even at early stages.

Local tumor growth and tumor size are the key factors that determine the prognosis of patients with PDAC[4, 5]. Therefore, we evaluated tumors according

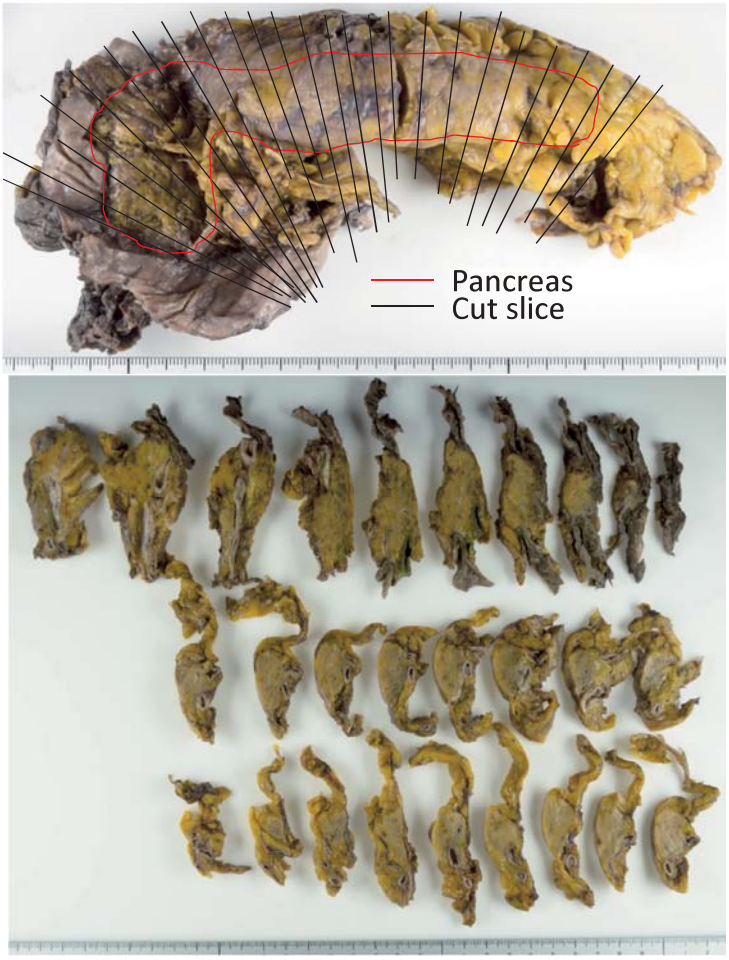

Figure 1. Gross examination of the pancreas from an autopsy case. The pancreas was cut into 5-mm sections vertically (black line) to the main pancreatic duct (cross section), and each slice was carefully examined before processing for microscopic examination. The red line indicates the pancreas.

to the Japanese classification of pancreatic carcinoma. T1 tumors are limited to the pancreas and measure less than 2 cm at the greatest dimension. T2 tumors are limited to the pancreas and measure larger than 2 cm at the greatest dimension. T3 tumors extend beyond the pancreas but do not involve the large vessels, while T4 tumors involve the portal vein, celiac axis, or the superior mesenteric artery. T1 and T2 PDACs are expected to have good prognoses owing to limited pancreatic localization[6]. However, we often see that small PDACs expand beyond the pancreas and involve the peripancreatic adipose tissue or duodenum because the pancreas does not have a capsule, and PDAC easily invades beyond the pancreas, especially in an atrophied pancreas. In the present study, we measured the greatest dimension of the pancreas to clarify the maximal size of PDACs limited to the pancreas.

Materials and Methods

Patients

Tissues were obtained from 10 autopsy patients who ranged in age from 42 to 95 years (female, 3; male, 7). Autopsies were performed at the Tokyo Metropolitan Geriatric Hospital between 2014 and 2015. Patients with invasive carcinoma and/or intraductal papillary mucinous neoplasm (IPMN) that might render pancreatic size measurements difficult were excluded. This study was conducted in accordance with the principles embodied in the 2008 Declaration of Helsinki, and informed written

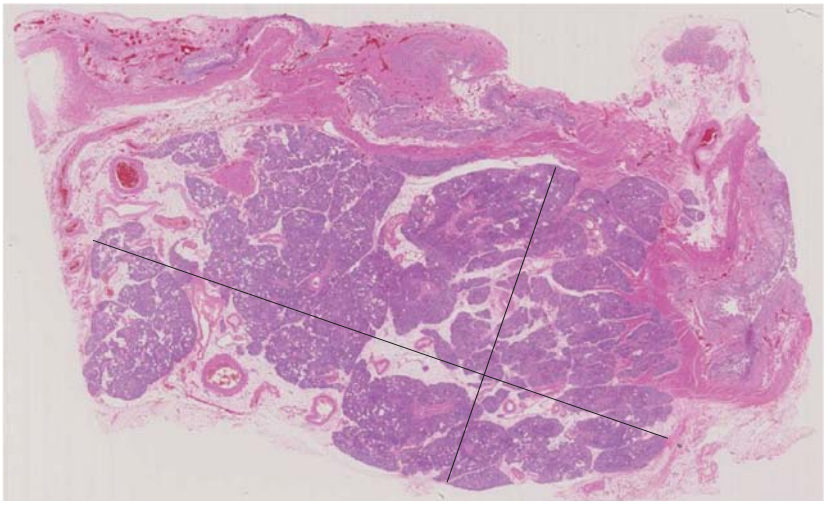

Figure 2. Representative vertical image of the pancreatic head. The black lines indicate the greatest diameter (2.43 cm) and the smallest diameter (1.33 cm).

Table 1. The greatest diameters of the pancreatic tissues and the slide numbers for which pancreatic diameters measured less than 2 cm

Age	Sex	The average greatest diameter (cm)			Number of slides from tissues with diameters less than 2 cm		
		Head	Body	Tail	Head	Body	Tail
88	M	3.48	2.16	1.64	0/6	1/7	7/9
93	M	4.18	1.75	1.92	0/3	1/3	0/4
61	M	2.57	2.30	2.08	2/5	0/3	1/3
81	F	3.60	2.07	1.99	1/5	3/6	2/4
95	F	3.06	2.77	2.25	0/5	0/3	1/3
70	M	3.16	1.94	1.94	1/7	5/8	3/8
78	F	3.11	2.59	2.31	0/5	0/3	1/4
69	M	3.17	2.36	2.01	1/5	1/4	1/2
42	M	3.89	2.55	2.23	1/8	0/5	1/5
67	M	3.55	2.29	0.93	0/2	0/1	3/3

consent for the use of tissues was obtained from the bereaved families.

Pathological examinations

The pancreas and the attached duodenum, including the papilla of Vater, were cut into 5-mm sections vertical to the main pancreatic duct. After gross examination, each slice was processed for microscopic examination. A 3-μm-thick section was cut from each paraffin-embedded tissue block, and the sections were stained with hematoxylin and eosin. All slides were captured using a virtual slide scanner (NanoZoomer 2.0-RS, Hamamatsu photonics K.K., Hamamatsu, Japan) at $\times$ 200 magnification. We measured the greatest and smallest diameters of the pancreas in each slide (Fig. 2).

Results

We measured the greatest pancreatic diameters using vertical pancreatic sections. The average greatest diameter values for the pancreatic head, body, and tail are summarized in Table 1. In all cases, the average diameter of the pancreatic head was larger than 2 cm, while the average diameters of the pancreatic body and tail were less than 2 cm in 2 and 5 cases, respectively. The slide numbers for which the greatest pancreatic diameters were less than 2 cm are summarized in Table 1. Among these, we observed 5 cases involving the pancreatic head and body and 9 cases involving the pancreatic tail.

Table 2. The smallest diameters of the pancreatic tissues and the slide numbers for which pancreatic diameters measured less than 2 cm

Age	Sex	The average smallest diameter (cm)			Number of slides from tissues with diameters less than 2 cm		
		Head	Body	Tail	Head	Body	Tail
88	M	1.24	1.13	1.08	5/6	7/7	9/9
93	M	1.72	0.96	0.89	3/3	3/3	4/4
61	M	1.34	1.33	1.14	5/5	3/3	3/3
81	F	1.46	1.40	1.51	4/5	6/6	4/4
95	F	1.71	1.05	1.13	3/5	3/3	3/3
70	M	1.53	1.00	0.98	6/7	8/8	8/8
78	F	1.73	1.03	1.02	4/5	3/3	4/4
69	M	1.86	1.12	1.37	2/5	4/4	2/2
42	M	1.60	1.32	1.16	5/8	5/5	5/5
67	M	0.84	0.95	0.69	2/2	1/1	3/3

The average smallest diameters of the pancreatic head, body, and tail were less than 2 cm in all cases (Table 2). In three cases, the average smallest diameters were less than 1 cm.

Discussion

In this study, we evaluated the entire pancreas using serial sections from 10 autopsy specimens. We found that there are many areas for which the greatest pancreatic diameter is less than 2 cm. In addition, the average smallest diameter of the pancreas was less than 2 cm in all cases, while it was less than 1 cm in 3 cases. These results indicate that as they grow, PDACs would not be limited to the pancreas, even if they measured less than 2 cm in diameter. This also suggests that small PDACs can easily invade peripancreatic tissues. Most PDACs are clinically discovered as T3 lesions[5]. Therefore, we might need to reconsider the definition of T1 PDACs. Our data suggest that truly localized PDACs must measure less than 1 cm.

Accurate tumor size and location evaluation for PDACs has been difficult because imaging methods, including CT, MRI, and ultrasonography, cannot distinguish between pancreatic tissue and peripancreatic tissue. Therefore, pathological examination sometimes find cancer invasion into the duodenal wall and peripancreatic adipose tissue, even for cases preoperatively diagnosed as T1 or T2 lesions.

Interestingly, all pancreatic tissues contained areas for which the sizes were less than 2 cm. The pancreatic neck and tail usually had smaller diameters than the head and body. Therefore, we need to evaluate tumor sizes using all pancreatic specimens to obtain accurate pathological diagnoses.

Our study has several limitations. The average patient age was 74.4 years, which is older than that of the average patient with PDAC. Most importantly, tumors grow in three-dimensional spaces. Therefore, our two-dimensional analysis has limitations. We need to evaluate tumor growth three-dimensionally using computed tomography or magnetic resonance imaging, but our analysis using pathological specimens does provide an accurate size for pancreatic tissue and distinguishes it from peripancreatic tissue.

In summary, our study evaluated the entire pancreatic parenchyma using autopsy specimens and revealed that there are pancreatic regions that measure less than 2 cm in diameter. Identifying these features may facilitate accurate tumor size, location, and tumor stage evaluation.

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