# An investigation of pancreatic volume by disease using pancreatic volumetry

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#### Summary

There are very few reports on pancreatic volumetry using multidetector-row computed tomography (MDCT). In the present study, we performed pancreatic volumetry for 148 patients who had undergone pancreatectomy at this institution between June 2006 and May 2011 and for 50 patients who had undergone laparoscopic cholecystectomy (LC) for cholecystolithiasis with no choledocholithiasis between January 2008 and May 2011. We then conducted a comparative investigation of pancreatic volume between the two groups.

A strong positive correlation was observed between pancreatic volume and body surface area (BSA) in the LC patients. On the basis of these results, we investigated pancreatic volume by disease using a corrected pancreatic volume that excluded BSA. The corrected pancreatic volume for patients with ordinary pancreatic cancer (invasive ductal carcinoma; IDC) was significantly smaller than that for patients with intraductal papillary mucinous neoplasm (IPMN) or bile duct cancer (BDC) and LC patients (P < 0.001). Furthermore, the corrected pancreatic volume for BDC patients was significantly larger than the volume for IPMN or LC patients. Corrected pancreatic volume is therefore useful for the differential diagnosis of tumours of the pancreatic head.

Key term: Pancreatic volumetry

#### **Background and Objectives**

Recent advances in workstations for diagnostic radiography have enabled easy and accurate construction of three-dimensional (3D) images of the blood vessels and solid organs. 3D images obtained through this process are now widely used for the preoperative simulation of surgery and liver volumetry. In particular, to cure cancers of the liver, gall bladder and pancreas, it is necessary to achieve R0 resection through surgery<sup>(1)</sup>, and, to that end, the use of 3D images to ascertain clinically accurate surgical anatomy before surgery is extremely valuable<sup>(2)</sup>.

There are very few existing reports of pancreatic

volumetry conducted using multidetectorrow thin-slice computed tomography (MDCT), indicating that only limited findings have been obtained for pancreatic volume<sup>(3-6)</sup>. In the present study, we performed pancreatic volumetry for 148 patients who had undergone pancreatectomy and 50 patients who had undergone laparoscopic cholecystectomy (LC) for cholecystolithiasis with no choledocholithiasis at our institution and investigated the parameters that influence pancreatic volume.

Concomitant pancreatitis with accompanying fibrosis and atrophy in patients with pancreatic tumours, particularly invasive ductal carcinoma (IDC), is being increasingly recognised<sup>(8-12)</sup>. The degree of pancreatic atrophy can offer a clue to the pathological characteristics of the tumour. However, till date, the nature of the changes in pancreatic volume related to pancreatic tumour or disease was not known. Here we used MDCT to conduct a comparative investigation of pancreatic volume by disease.

### **Subjects and Methods**

Fifty-three patients who had undergone LC at this institution between January 2008 and May 2011 were selected for the study. Patients who did not undergo contrast-enhanced CT because of the detection of choledocholithiasis, pancreatic lesions, cancer or renal dysfunction at the time of surgery were excluded, leaving 50 patients suitable for the investigation. Pancreatic volume was calculated using contrast-enhanced CT with a 1-mm slice thickness that was conducted immediately before surgery. A workstation (Zio station; ZIO SOFT Co., Tokyo) was used for image processing. The cross-sectional areas, calculated using free-hand tracing, were added to obtain the volume of the entire pancreas (Figure 1). The correlation of the resulting pancreatic volume with body surface area

#### Figure 1 Method of calculating pancreatic volume



Actual pancreatic volume + pancreatic duct volume + cyst volume



Pancreatic duct volume + cyst volume



Actual pancreatic volume

(BSA), height, weight, body mass index (BMI) and age was investigated using the Pearson correlation coefficient. The Mann-Whitney U test was used to assess gender differences, and P < 0.05 was considered statistically significant.

Of the 153 patients who underwent pancreatectomy at this department between June 2006 and May 2011, 148 with evaluable preoperative contrastenhanced CT scans were included in the study. The diagnoses for the patients were as follows: IDC (n = 38), intraductal papillary mucinous neoplasm (IPMN; n = 61), bile duct cancer (BDC; n = 19), carcinoma of the papilla of Vater (Vater Ca; n = 7) and others (n = 24; Table 3). The 50 patients who had undergone LC were used as a control group.

Pancreatic volume was calculated in the same manner as described above. Furthermore, the volume of tumours and cysts and expanded pancreatic duct volume were subtracted to accurately calculate the actual pancreatic volume (Figure 1). A comparison of pancreatic volume was conducted on the basis of the investigation of the 50 LC patients using a corrected pancreatic

#### Table 1 Background of the LC patients

Total number	50 (M:F 25:25)						
Gender	M 85.3ml: F 66.3ml						
Age	$60.8~{ m yrs}\pm14.3$						
Weight	$61.8~{ m kg}\pm11.8$						
Height	$160.2~\mathrm{cm}\pm9.2$						
BMI	$23.9\pm3.3$						
BSA	$1.6~\mathrm{m2}\pm0.19$						

# Table 2 Correlation between each parameter and pancreatic volume in LC patients

Gender	p<0.001
Age	r=-0.22 p=0.11
Weight	r-=0.536 p<0.001
Height	r=0.583 p<0.001
BMI	r=0.26 p=0.06
BSA	r-=0.586 p<0.001

volume that excluded BSA, enabling a comparative investigation of the corrected pancreatic volume by disease. Testing was conducted using the Mann-Whitney U test, and P < 0.05 was considered statistically significant.

### Results

The average pancreatic volume for the 50 LC patients was 75.7  $\pm$  21.8 mL. Preoperative complications included diabetes in 1 patient, oral treatment for hypertension in 16 and oral treatment for hyperlipidaemia in 5. The mean values and standard deviations for age, height, weight, BSA and BMI were 60.8  $\pm$  14.3 years, 160.2  $\pm$  9.2 cm, 61.8  $\pm$  11.8 kg, 1.60  $\pm$  0.19 m<sup>2</sup> and 23.9  $\pm$  3.27 kg/m<sup>2</sup>, respectively (Table 1). The correlation with pancreatic volume was confirmed for each parameter (Table 2) as follows: age, r = -0.22,



Figure 2 Correlation between pancreatic volume and BSA

P = 0.11; height, r = 0.583, P < 0.001; weight, r = 0.536, P < 0.001; BSA, r = 0.586, P < 0.001 and BMI, r = 0.26, P = 0.06. The strongest correlation was observed for BSA, which showed a strong positive correlation (Figure 2). With regard to age and BMI, the correlation was confirmed by the corrected pancreatic volume obtained by dividing the pancreatic volume with BSA. The relationships of age and BMI with corrected pancreatic volume were not significant as follows: r = -0.09, P = 0.53 and r = 0.06, P = 0.67, respectively. Between the genders, the correlation was stronger for males (P < 0.001). However, when corrected pancreatic volume was used, no significant gender difference was observed (P = 0.07).

Pancreatic volume by disease was calculated using a corrected pancreatic volume that excluded BSA. The average corrected pancreatic volumes for the patients who underwent pancreatectomy and the LC patients were 43.2  $\pm$  13.3 mL/m<sup>2</sup> and 46.1  $\pm$ 10.8 mL/m<sup>2</sup>, respectively. The corrected pancreatic volume was compared by disease for the patients who underwent pancreatectomy. The average corrected pancreatic volume for the 38 IDC patients was 35.6  $\pm$  12.2 mL/m<sup>2</sup>. Of these, the average corrected pancreatic volume for the 20 patients who underwent pancreatic duodenectomy was 34.0  $\pm$  13.5 mL/m<sup>2</sup>, while that for the 18 patients who underwent distal pancreatectomy was 37.5  $\pm$  10.5

Table 3	Background	l of pat	tients wh	io und	erwent	pancreatectomy
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Total number	148	
M:F	96:52	
Average age	66.8 years	
Disease	Invasive ductal carcinoma (IDC), $n = 38$ Intraductal papillary mucinous neoplasm (IPMN), $n = 61$ Intraductal papillary mucinous adenoma (IPMA), $n = 43$ Intraductal papillary mucinous adenocarcinoma (IPMC), $n = 18$ Bile duct cancer (BDC), $n = 18$ Carcinoma of the papilla of Vater (Vater Ca), $n = 7$ Neuroendocrine tumour, $n = 5$ Mucinous cystic tumour (MCN), $n = 4$ Serous cystic neoplasm (SCN), $n = 3$	Acinar cell carcinoma, $n = 2$ Pancreatic pseudocyst, $n = 2$ Splenic artery aneurysm, $n = 1$ Solid pseudopapillary tumour (SPT), $n = 1$ Retention cyst, $n = 1$ Myxosarcoma, $n = 1$ Gall-bladder cancer, $n = 1$ Stomach cancer, $n = 1$ Chronic pancreatitis, $n = 1$ Arteriovenous malformation, $n = 1$
Type of surgery	Pancreaticoduodenectomy (PD), n = 84 Distal pancreatectomy with splenectomy (DPS), n = 50 Spleen-preserving distal pancreatectomy (SpDP), n = 14	

 $mL/m^2$ . The difference between the patients who underwent pancreaticoduodenectomy and those who underwent distal pancreatectomy was not significant (P = 0.32).

The average corrected pancreatic volume for the IPMN patients was 45.0  $\pm$  13.3 mL/m<sup>2</sup>. Of these, the average corrected pancreatic volume for the 33 patients who underwent pancreaticoduodenectomy was 48.5  $\pm$  15.7 mL/m<sup>2</sup>, while that for the 28 patients who underwent distal pancreatectomy was 42.3  $\pm$  8.8 mL/m<sup>2</sup>, with no significant difference (P = - 0.10).

The average corrected pancreatic volumes for the BDC and Vater Ca patients were  $52.3 \pm 9.3 \text{ mL/m}^2$  and  $50.8 \pm 1.8 \text{ mL/m}^2$ , respectively (Table 4).

The corrected pancreatic volume for the IDC patients was significantly smaller than that for the IPMN, BDC and LC patients (P < 0.001). The corrected pancreatic volume for the BDC patients was significantly larger than that for the LC and IPMN patients (P < 0.05; Figure 3).

#### Discussion

Till date, there have been very few detailed investigations of pancreatic volume. Djuric-Stefanovic et al. used the same MDCT method as used in the present study to conduct volumetry of the normal pancreas and reported that pancreatic

volume was correlated with gender, craniocaudal diameter of the pancreas and transverse diameter of the first lumbar vertebra; however, it was not correlated with age<sup>(4)</sup>. Shirakawa et al. investigated the rate of pancreatectomy using MDCT and reported that it was possible to predict the onset of diabetes following distal pancreatectomy<sup>(5)</sup>. Goda et al. and Sakata et al. also reported a correlation between pancreatic volume and endocrine function using pancreatic volumetry<sup>(6,7)</sup>. Goda et al. claimed that pancreatic volume is strongly correlated with BSA and used a corrected value excluding BSA to compare pancreatic volume using the same method used in the present study. With regard to volumetry of other organs, Urata et al. have reported a standard liver volume<sup>(13)</sup>, and Kaneko et al. have investigated the volume of the spleen<sup>(14)</sup>. In the present study, we used a 1-mm slice MDCT image to conduct precise pancreatic volumetry. We investigated the normal pancreas and identified the parameters influencing pancreatic volume. To



Figure 3 Corrected pancreatic volume by disease

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		Number of patients	Average value ml/m <sup>2</sup>	Median value ml/m <sup>2</sup>	Standard deviation
LC		50	46.1	44.3	$\pm 10.8$
All pancreatic diseases		148	43.2	42.6	$\pm 13.3$
IDC	Total	38	35.6	34.2	$\pm 12.2$
	PD	20	34.0	33.3	$\pm 13.5$
	DP	18	37.5	35.6	$\pm 10.5$
IPMN	Total	61	45.0	43.1	$\pm 13.3$
	PD	33	48.5	44.3	$\pm 15.7$
	DP	28	42.3	42.5	$\pm 8.8$
BDC		18	52.3	53.1	$\pm 9.3$
Vater Ca		7	50.8	44.5	$\pm 18$
Other pancreatic disease		24	41.2	39.9	$\pm 10.8$

our knowledge, this is the first report on changes in pancreatic volume in patients with pancreatic disease.

First, we conducted volumetry under the supposition that the pancreas of a patient with choledocystolithiasis in the absence of cholecystolithiasis was representative of a normal pancreas. We then investigated the correlation between pancreatic volume and BSA, height, weight, BMI and age. Pancreatic volume showed a positive correlation with BSA, height and weight, with the strongest correlation between pancreatic volume and BSA. In short, we considered that pancreatic volume increases with body size. However, no significant correlation was observed with BMI or age, and there was no obesity-induced swelling or ageing-induced atrophy. Therefore, to eliminate the effects of differences in body size when comparing pancreatic volume, we deemed it appropriate to correct the volume for BSA. The comparisons in this study were therefore conducted using a corrected pancreatic volume that excluded BSA.

Caudal pancreatic atrophy is a phenomenon that is frequently observed in patients with pancreatic cancer<sup>(7-11)</sup>; therefore, the presence of pancreatic atrophy suggests the possible presence of pancreatic cancer. However, till date, there are no studies that compare pancreatic volume in patients with the volume of a normal pancreas; therefore, the degree of atrophy is difficult to determine. In the present study, the corrected pancreatic volume for IDC patients was significantly smaller than that for BDC, IPMN and LC patients, indicating pancreatic atrophy. We therefore succeeded in confirming the presence of pancreatic atrophy in IDC patients. The mechanism underlying pancreatic atrophy in IDC is thought to be obstructive pancreatitis caused by blockage of the main pancreatic duct<sup>(8-</sup> <sup>12)</sup>. However, there are few reports on the degree of atrophy related to obstructive pancreatitis that is determined by CT. Because the extent of atrophy in IDC of the pancreatic head is potentially greater than that in patients with IDC of the pancreatic

tail, we anticipated a smaller volume in patients with IDC of the pancreatic head. However, no significant difference was observed in the corrected pancreatic volume between IDC patients who had undergone pancreaticoduodenectomy and those who had undergone distal pancreatectomy. Pancreatic atrophy in IDC may therefore extend to the entire pancreas.

Furthermore, the corrected pancreatic volume for BDC patients was significantly larger than that for LC or IPMN patients. This was thought to be a result of pancreatic swelling. There are no reports of pancreatic volume in patients with inferior bile duct cancer, and the mechanism underlying pancreatic swelling remains unclear. Bile congestion secondary to biliary obstruction and the accompanying metabolic abnormalities may have an influence.

In patients with tumours of the pancreatic head, it is often difficult to differentiate between invasive ductal carcinoma and pancreatic tumours. In these patients, the degree of pancreatic atrophy can help with the diagnosis. In particular, we believe that this method can be useful to differentiate tumours of the pancreas from inferior bile duct cancer.

## Conclusions

Pancreatic volume is correlated with body size, but not with age or obesity. Corrected pancreatic volume is useful for the differential diagnosis of tumours of the pancreatic head.

- Kimura W: Strategies for the treatment of invasive ductal carcinoma of the pancreas and how to achieve zero mortality for pancreaticoduodenectomy. J hepatobiliary pancreat surg 15: 270-277, 2008.
- Kimura W: Surgical anatomy of the pancreas for limited resection. J hepatobiliary pancreat surg 7: 473-479, 2000.
- 3. Aimoto T, Uchida E, Nakamura Y, et al: Multicentric pancreatic intraepithelial neoplasias (PanINs) presenting with the clinical features of chronic pancreatitis. J Hepatobiliary Pancreat Surg 15: 549-553, 2008.

- 4. Djuric-Stefanovic A, Masulovic D, Kostic J, Randjic K, Saranovic D: CT volumetry of normal pancreas: correlation with the pancreatic diameters measurable by the cross-sectional imaging, and relationship with the gender, age, and body constitution. Surg Radiol Anat 34: 811-817, 2012. doi: 10. 1007/s00276-012-0962-7. Epub 2012 Mar 21.
- 5. Shirakawa S, Matsumoto I, Toyama H, Shinzeki M, Ajiki T, Fukumoto T, Ku Y. J: Pancreatic volumetric assessment as a predictor of new-onset diabetes following distal pancreatectomy. Gastrointest Surg 16: 2212-2219, 2012. doi: 10.1007/s11605-012-2039-7. Epub 2012 Sep 28.
- 6. Sakata N, Egawa S, Rikiyama T, et al: Computed tomography reflected endocrine function of the pancreas. J Gastrointest Surg 15: 525-532, 2011.
- Goda K, Sasaki E, Nagata K, et al: Pancreatic volume in type 1 and type 2 diabetes mellitus. Acta Diabetol 38: 145-149, 2001.
- Etemad B, Whitcomb DC: Chronic pancreatitis: diagnosis, classification, and new genetic developments. Gastroenterology 120: 682-707, 2001.
- Watanabe S, Nagashio Y, Asaumi H, et al: Pressure activates rat pancreatic stellate cells. Am J Physiol Gastrointest Liver Physiol 287: G1175-1181, 2004.
- Yamamoto M, Otani M, Otsuki M: A new model of chronic pancreatitis in rats. Am J Physiol Gastrointest Liver Physiol 291: G700-708, 2006.
- Asaumi H, Watanabe S, Taguchi M et al: Externally applied pressure activates pancreatic stellate cells through the generation of intracellular reactive oxygen species. Am J Physiol Gastroin- test Liver Physiol 293: G972-978, 2007.
- Urata K, Kawasaki S, Matsunami H, et al: Calculation of child and adult standard liver volume for liver transplantation. Hepatology 21: 1317-1321, 1995.
- Kaneko J, Sugawara Y, Matsui Y, et al: Spleen size of live donors for liver transplantation. Surg Radiol Anat 30: 515-518, 2008.