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Utility of virtual touch quantification in the diagnosis of pancreatic ductal adenocarcinoma

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ABSTRACT

This study aimed to compare the tissue stiffness of pancreatic ductal adenocarcinoma (PDAC) with that of pancreatic parenchyma using virtual touch quantification (VTQ). SWV was measured in 34 PDAC lesions and in pancreatic parenchyma of both controls and patients.

SWVs in PDAC lesions were significantly higher than in pancreatic parenchyma in both healthy controls and in patients with PDAC. The area under the ROC for diagnosis of PDAC was 0.94 for pancreatic parenchyma in healthy controls, and 0.85 for pancreatic parenchyma in patients with PDAC.

VTQ can provide a useful and additional information for diagnosis of PDAC.

1. Introduction

Pancreatic ductal adenocarcinoma (PDAC) is diagnosed by imaging modalities such as ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI). US is often used as the first modality because of its low invasiveness and low cost. US findings of PDAC show a hypo- or mixed echogenicity lesion with an irregular border. Differentiation of PDAC from other pancreatic neoplasms or chronic pancreatitis, and especially from mass-forming chronic pancreatitis, may not be easy. Virtual touch quantification (VTQ) is a method that uses US to assess the elastic properties of tissue. VTQ estimates the shear wave velocity (SWV) to evaluate tissue stiffness [1]. VTQ is integrated into US apparatus and provides information about tissue stiffness additional to conventional US findings. Briefly, a small localized displacement in the target tissue is generated by a duration push pulse transmitted from the transducer. The velocity of the shear wave by the tissue displacement is quantitatively measured with US. High tissue stiffness results in an increase of SWV. The square of the SWV is considered to have a linear correlation with the stiffness of an elastic material [2]. Since VTQ does not use external compression, image acquisition is less affected by the operator's technical factors, including the degree of pressure of the probe, than strain imaging and allows quantitative measurement of tissue characteristics, including elasticity and speed. High reproducibility is another advantage of VTQ [3]. In recent studies, the usefulness of VTQ in the diagnosis of malignant tumors has been reported in several organs such as the liver, breast, thyroid, and prostate [4–8].

PDAC is a firm mass, owing to the presence of fibrosis and a marked desmoplastic reaction [9]; therefore, PDAC is stiffer than extra-lesional pancreatic parenchyma. The stiffness of deep tissue, such as the pancreas, can also be measured by VTQ. To date, only one study has reported the usefulness of VTQ for the differential diagnosis of benign and malignant solid pancreatic lesions [10].

SWV as a tissue stiffness indicator may be helpful in the diagnosis of PDAC. The aim of the present study was to measure the SWV of PDAC and background pancreatic parenchyma and to investigate the performance of SWV in diagnosing PDAC.

2. Subjects and methods

Thirty-six patients with PDAC and 19 healthy controls were prospectively enrolled between September 2012 and March 2015 at our hospital. The diagnosis of PDAC was based on pathological diagnosis via endoscopic ultrasound fine needle aspiration (EUS-FNA), pancreatic juice cytology, or surgical specimen. The study protocol was approved by the ethics committee of the University of Tottori (No. 2314). Written informed consent was obtained from all participating subjects.

Abbreviation: (VTQ), virtual touch quantification; (SWV), shear wave velocity; (PDAC), pancreatic ductal adenocarcinoma; (ROC), receiver operating characteristic; (US), ultrasonography; (CT), computed tomography; (MRI), magnetic resonance imaging; (EUS-FNA), endoscopic ultrasound fine needle aspiration; (ROI), region of interest.

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Measurements of SWV were performed using the ACUSON S2000™ (Siemens, Erlangen, Germany). A region of interest (ROI) at a size of 10 mm axial by 6 mm width was set in the head, body, and tail of the pancreas and in the pancreatic mass without any vessels or biliary structures (Fig. 1). SWV was measured five times each in the ROI of the lesion and the pancreatic parenchyma. The average value was calculated from three values excluding the maximum and minimum values. The coefficient of variation was 9.8% for SWV.

3. Statistical analysis

The statistical analysis was performed using StatFlex ver. 6.0 for Windows (Artech Co., Ltd., Osaka, Japan). Categorical variables were compared using the chi-square test. Continuous variables were compared using the Mann-Whitney U-test. Comparisons of the SWV among PDAC, background pancreatic parenchyma in patients with PDAC and pancreatic parenchyma in healthy controls were performed using the Kruskal-Wallis test and Dunn test as post hoc analysis. All values are expressed as means ± standard deviation or medians with interquartile ranges. $p < 0.05$ was considered significant. The diagnostic performance of VTQ was assessed using receiver-operating characteristic (ROC) curve analysis. Optimal cut-off values for SWV of the pancreas were chosen according to the Youden index [11]. Similarly, the sensitivity, specificity, positive predictive value, and negative predictive value were computed for these cut-off values.

4. Results

The background characteristics of the 36 patients with PDAC and 19 healthy controls are shown in Table 1. The proportion of men was significantly higher in the healthy controls than in the patients with PDAC. Three patients with PDAC (8%) and five healthy controls (26%) had a daily alcohol intake of more than 60 g over the past five years. No subjects had chronic pancreatitis. There were no significant differences in age, body mass index, alcohol intake, smoking history, and the prevalence of diabetes mellitus, hypertension, and dyslipidemia between the patients with PDAC and the healthy controls.

In the patients with PDAC, there were 20 cases in the head, 10 cases in the body, and 6 cases in the tail. In 2 cases of pancreatic head ductal adenocarcinoma, the lesions could not be detected by conventional B-mode US, resulting in SWV being evaluated in 34 PDAC lesions.

There were no significant differences in SWV among the three sites of pancreatic parenchyma in the healthy controls (head: 1.06 ± 0.13 m/s, body: 1.11 ± 0.12 m/s, tail: 1.08 ± 0.19 m/s). Similarly, there were no significant differences in SWV among the three sites of pancreatic parenchyma in the patients with PDAC (head: 1.30 ± 0.44 m/s, body: 1.49 ± 0.70 m/s, tail: 1.25 ± 0.46 m/s). The parenchymal SWVs of pancreatic body in the patients with PDAC were significantly higher than in the healthy controls.

Table 1
Background characteristics of healthy controls and patients with pancreatic ductal adenocarcinoma.

	Controls (n = 19)	Pancreatic ductal adenocarcinoma (n = 36)	*p* value
Gender-male, n (%)	15 (79)	17 (47)	0.02
Age, years	63.3 [29, 84]	70.2 [40, 83]	0.14
BMI, kg/m^2	22.0 [17.0, 27.0]	22.0 [13.8, 31.9]	0.93
Alcohol, n (%)	5 (26)	3 (8)	0.11
Smoking, n (%)	4 (21)	11 (31)	0.45
Diabetes mellitus, n (%)	2 (11)	9 (25)	0.30
Hypertension, n (%)	9 (50)	16 (55)	0.96
Dyslipidemia, n (%)	2 (11)	11 (31)	0.10
Chronic pancreatitis, n (%)	0	0	
Location of lesion, n		head:body:tail = 20:10:6	
Diameter of lesion, mm		34.1 [10, 96]	

BMI body mass index, *Alcohol* ethanol intake 60 g/day for more than 5 years, *Smoking* Brinkman Index ≧ 600.

SWVs of body and tail parenchyma were compared between the 20 patients with pancreatic head ductal adenocarcinoma and the healthy controls to investigate the effects of tumor-concomitant pancreatitis. The mean SWV of the body parenchyma in the 20 patients with pancreatic head ductal adenocarcinoma (body: 1.71 ± 0.86 m/s) was significantly higher than that of the healthy controls (body: 1.11 ± 0.12 m/s, $p < 0.001$). The mean SWV of the tail parenchyma in the 20 patients with pancreatic head ductal adenocarcinoma (tail: 1.33 ± 0.56 m/s) was higher than that in the healthy controls (tail: 1.08 ± 0.19 m/s), although the difference was not statistically significant ($p = 0.23$).

The SWVs of the pancreatic tumors were significantly different from the pancreatic parenchyma in both patients with PDAC and healthy controls using the Kruskal-Wallis test ($p < 0.0001$) (Fig. 2). The SWV of PDAC (2.34 ± 0.95 m/s) was significantly higher than that of pancreatic parenchyma in healthy controls (1.08 ± 0.15 m/s, $p < 0.001$) and that of pancreatic parenchyma in patients with PDAC (1.34 ± 0.55 m/s, $p < 0.001$). The SWV in the tumors in each location in the pancreas was significantly different among three groups (head: $p < 0.0001$, body: $p = 0.00023$, tail: $p = 0.0044$). The SWV of PDAC in each part (head: 2.62 ± 0.97 m/s, body: 2.09 ± 0.83 m/s, tail: 1.95 ± 0.96 m/s) was also significantly higher than that of pancreatic parenchyma in healthy controls (head: 1.06 ± 0.13 m/s, $p < 0.01$, body: 1.11 ± 0.12 m/s, $p < 0.01$, tail: 1.08 ± 0.19 m/s, $p < 0.01$) and of pancreatic parenchyma in patients with PDAC (head: 1.30 ± 0.44 m/s, $p < 0.01$, body: 1.49 ± 0.70 m/s, $p < 0.01$, tail: 1.25 ± 0.46 m/s, $p < 0.05$).

The ROC curves for SWV showed an AUROC value of 0.94 between PDAC and pancreatic parenchyma in healthy controls, and an AUROC value of 0.85 between PDAC and parenchyma in patients with PDAC

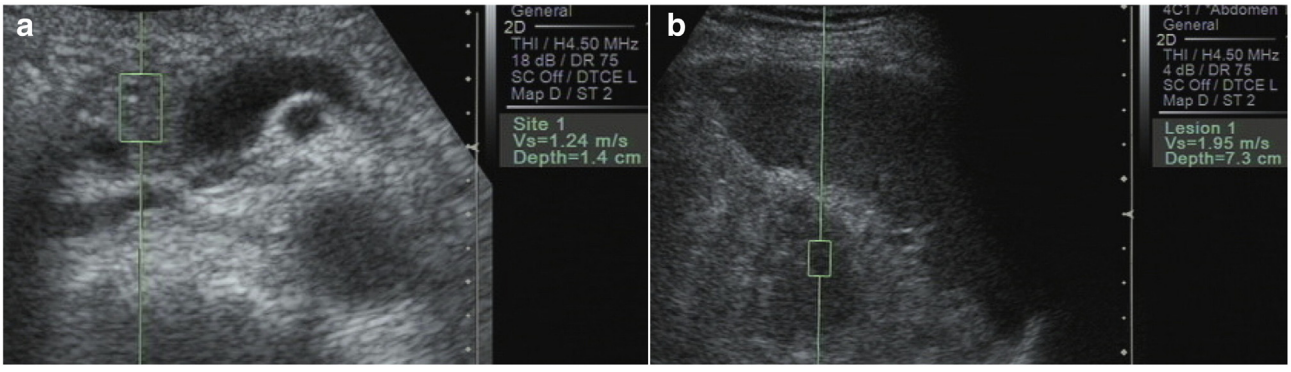

Fig. 1. Measurements of shear wave velocity with virtual touch quantification. (a) Shear wave velocity was measured in pancreatic parenchyma in healthy controls. (b) Shear wave velocity was measured in pancreatic ductal adenocarcinoma.