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Quantitative MR Evaluation of Chronic Pancreatitis: Extracellular Volume Fraction and MR Relaxometry

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Abstract

OBJECTIVE—The purpose of this study was to determine if extracellular volume fraction and T1 mapping can be used to diagnose chronic pancreatitis (CP).

MATERIALS AND METHODS—This HIPAA-compliant study analyzed 143 consecutive patients with and without CP who underwent MR imaging between May 2016 and February 2017. Patients were selected for the study according to inclusion and exclusion criteria that considered history and clinical and laboratory findings. Eligible patients ($n = 119$) were grouped as normal ($n = 60$) or with mild ($n = 22$), moderate ($n = 27$), or severe ($n = 10$) CP on the basis of MRCP findings using the Cambridge classification as the reference standard. T1 maps were acquired in unenhanced and late contrast-enhanced phases using a 3D dual flip-angle gradient-echo sequence. All patients were imaged on the same 3-T scanner using the same imaging parameters, contrast agent, and dosage.

RESULTS—Mean extracellular volume fractions and T1 relaxation times were significantly different within the study groups (one-way ANOVA, $p < 0.001$). Using the AUC curve analysis, extracellular volume fraction of > 0.27 showed 92% sensitivity (54/59) and 77% specificity (46/60) for the diagnosis of CP (AUC = 0.90). A T1 relaxation time of > 950 ms revealed 64% sensitivity (38/59) and 88% specificity (53/60) (AUC = 0.80). Combining extracellular volume fraction and T1 mapping yielded sensitivity of 85% (50/59) and specificity of 92% (55/60) (AUC = 0.94).

CONCLUSION—Extracellular volume fraction and T1 mapping may provide quantitative metrics for determining the presence and severity of acinar cell loss and aid in the diagnosis of CP.

Keywords

extracellular volume fraction; MR relaxometry; pancreatitis; T1 mapping

Chronic pancreatitis (CP) is a progressive inflammatory disease of the pancreas, characterized by irreversible morphologic changes and gradual replacement of the acinar cells with fibrosis [1]. In the early stages of CP, the gland shows unevenly distributed fibrosis. However, in advanced CP, fibrosis may diffusely affect the entire gland [2, 3] (Figs. 1A and 1B). The morphologic changes of CP remain elusive because of a scarcity of morphologic changes on conventional radiologic and endoscopic imaging. The high risk of complications prevents biopsy of the pancreas from being a preferred option, so diagnostic evaluation often leads to an exhaustive list of costly invasive (endoscopic) and noninvasive (radiologic) imaging studies and laboratory testing [4]. Given these limitations, a reliable, preferably noninvasive imaging technique is needed for the diagnosis of CP when imaging findings are equivocal.

MRCP has become the preferred imaging modality over ERCP for evaluation of ductal abnormalities of CP [4–6]. The soft-tissue contrast provided by MRI arises principally from differences in the intrinsic relaxation properties of T1 and T2. Quantitative measurement of these parameters, also referred to as MR relaxometry, can provide information about changes in tissue characteristics. In addition to grading the ductal changes under the Cambridge classification, MRI has been shown to be sensitive for detecting parenchymal abnormalities of the CP, which often precede ductal dilatation [4, 7–10]. Alteration in the T1-weighted signal of the pancreas also correlates with pancreatic exocrine function [10–13]. This observation has been linked to the loss of acinar cells, which contain protein-rich cytoplasm that is replaced by fibrosis [14, 15]. T1 mapping measures the specific T1 relaxation time of the tissues; therefore, using the same principle, it should also be able to diagnose CP [11].

MRI techniques such as extracellular volume (ECV) fraction, DWI, and MR elastography have been used in detection of tissue fibrosis [12, 16–21]. ECV imaging has been shown to quantify myocardial fibrosis in large cohorts and is being used in clinical practice [16]. To our knowledge, usefulness of ECV imaging for the detection of pancreatic fibrosis has not been explored. Because most of the gadolinium-based contrast agents in use are extracellular during the late enhancement phase, T1 shortening of the tissues reflects their concentration in the extracellular space. On the basis of this pharmacokinetic property, ECV fraction can dichotomize tissues into their intracellular and extracellular components using T1 relaxation times obtained before and after MRI contrast enhancement (Fig. 1C).

In designing this study, we hypothesized that ECV fraction should be able to detect decreases in the ratio of pancreatic acinar cells to fibrosis in the extracellular space. The purpose of this study was to determine if ECV fraction and T1 mapping can provide quantitative metrics for pancreatic fibrosis and aid in the diagnosis of CP.

Materials and Methods

Patient Selection

This HIPAA-compliant study was approved by the institutional review board of Indiana University Hospital. Inclusion criteria were age of at least 18 years old, abdominal pain suspected to be of pancreatic origin (i.e., epigastric pain that is often constant, worsens

postprandially, and may radiate to the back [4]), CP diagnosed by a gastroenterologist, and enrollment in the pancreatic cancer screening program after referral from the surgery clinic. Patients enrolled in the pancreatic cancer screening program were being annually screened with MRCP for pancreatic cancer either because of family history of pancreatic cancer or a genetic predisposition (e.g., *BRCA*) to develop pancreatic cancer but were otherwise healthy. These patients were screened for amylase, lipase, aspartate aminotransaminase, alkaline phosphatase, carcinoembryonic antigen, cancer antigen 19–9, and C-peptide levels before enrolling in the program. Using the inclusion criteria, we consecutively selected 143 patients who presented to the gastroenterology ($n = 113$) and surgery ($n = 30$) clinics at a tertiary referral center for pancreatic diseases between May 2016 and February 2017 (Fig. 2).

Selected patients were excluded if they had imaging or laboratory evidence of acute pancreatitis (defined by the American Pancreatic Association Practice Guidelines [22] as upper abdominal pain; threefold or greater elevation of serum amylase level, lipase level, or both above the upper limit of normal; features of acute pancreatitis on cross-sectional imaging; or some combination of these factors), ERCP performed less than 30 days before MRCP, inability to receive gadolinium, or personal history of pancreatic cancer or surgery. Out of 143 patients, 24 were excluded (new diagnosis of pancreatic cancer [$n = 1$], inability to receive IV contrast material [$n = 3$], and evidence of acute pancreatitis [$n = 20$]) (Fig. 2).

Eligible patients were grouped as normal (Cambridge grade 0, $n = 60$) mild CP (Cambridge grade 2, $n = 22$), moderate CP (Cambridge grade 3, $n = 27$), or severe CP (Cambridge grade 4, $n = 10$) on the basis of MRCP ductal findings and using the Cambridge classification as the reference standard [7]. Patients with Cambridge grade 0 made up the normal group; the disease group comprised patients with Cambridge grades 2, 3, and 4 ($n = 59$). No patients had Cambridge grade 1 (i.e., equivocal). The disease group comprised patients with CP diagnosed by a gastroenterologist who had examined the patient and reviewed patient history and clinical and laboratory findings documented in the electronic medical records.

Imaging Technique

All patients were imaged with the same 3-T MR scanner (Verio, Siemens Healthcare) using the same imaging protocol. Gadobenate dimeglumine (MultiHance, Bracco Diagnostics) was administered in all patients using the standard dose of 0.1 mmol/kg.

T1 maps were acquired at unenhanced and 6-minute late enhancement phases using a dual flip-angle 3D gradient-echo technique. Fat suppression was not employed. Images were reconstructed at the MR scanner via vendor-supplied software (MapIt, Siemens Healthcare) as follows: 48 axial slices of 4-mm thickness acquired within a 19-second breath-hold with TR/TE, 3.87/1.32; flip angles, 2° and 13°; acquisition matrix, 320 × 168; and a parallel imaging (generalized auto-calibrating partially parallel acquisition, Siemens Healthcare) factor of 2. Axial breath-hold two-point Dixon T1-weighted images were acquired using TR/TE₁, 5.45/2.45; TR/TE₂, 5.45/3.675; and flip angle, 9°. The number of slices, slice thickness, FOV, and matrix size of the Dixon sequence were the same as for T1 mapping. The secretin-enhanced MRCP was performed after IV administration of 16 µg of secretin (ChiRhoStim, ChiRhoClin) via slow infusion over 1 minute. Subsequently, the pancreas was

imaged via a coronal 2D single-shot turbo spin-echo sequence (HASTE, Siemens Healthcare), repeated every 60 seconds for up to 10 minutes. Patients fasted for at least 4 hours before the MRCP. No adverse events of reaction to secretin were observed.

Image Analysis

Independent variables were ECV, T1 relaxation time, signal-intensity ratio (SIR) of pancreas to spleen, SIR of pancreas to paraspinal muscle, arteriovenous enhancement ratio, duodenal filling grade after secretin stimulation, and anterior-posterior diameter. Collection of data points was determined at the beginning of the study. Image analysis was performed by four radiologists with 9, 15, 16, and 21 years of experience. The two most experienced radiologists graded the MRCP findings using the Cambridge classification as the reference standard and were in complete agreement [7]. The other two radiologists were blinded to the MRCP findings and performed ROI measurements independently. Attention was given to ensure measurements avoided volume averaging from retroperitoneal fat, vessels, and dilated duct.

Extracellular Volume Fraction

ECV fraction was calculated using the following formula:

$$ECV = (1 - \text{hematocrit}) \times \frac{\Delta R1_{\text{pancreas}}}{\Delta R1_{\text{blood}}}, \quad (1)$$

where $R1_{\text{pancreas}}$ and $R1_{\text{blood}}$ are the changes in pancreatic and blood pool relaxivity, respectively, before and after contrast administration. T1 is a time constant describing the longitudinal relaxation rate, and its reciprocal ($1/T1$) is referred to as R1. When both tissues are in equilibrium, R1 is proportional to gadolinium concentration:

$$\frac{\Delta R1_{\text{pancreas}}}{\Delta R1_{\text{blood}}} = \frac{\text{Gadolinium}_{\text{pancreas}}}{\text{Gadolinium}_{\text{blood}}}. \quad (2)$$

Because the gadolinium chelates, such as gadobenate dimeglumine, are extracellular agents, the ratio of contrast agent concentrations between pancreas and blood equals the ratio of extracellular volume between the tissues:

$$\frac{\text{Gadolinium}_{\text{pancreas}}}{\text{Gadolinium}_{\text{blood}}} = \frac{ECV_{\text{pancreas}}}{ECV_{\text{blood}}}. \quad (3)$$

The ECV of the blood is defined as the fraction of the blood volume that is not composed of blood cells (i.e., the fraction composed of plasma) [17]. The plasma volume was easily calculated as:

$$ECV_{\text{blood}} = 1 - \text{hematocrit}. \quad (4)$$

The blood pool signal was measured from the aortic lumen by taking the mean ROI value of five consecutive image slices at the level of pancreas. The ECV fraction maps were generated manually using Analyze software (version 12.0, Analyze Direct).

ROI measurements for calculation of SIR of the pancreas to spleen and pancreas to paraspinal muscle were performed on axial unenhanced, T1-weighted fat-suppressed volume-interpolated breath-hold 3D gradient-echo images (VIBE, Siemens Healthcare). Fat signal fraction (FSF) of the pancreas was calculated by measuring signal intensity (SI) on the axial breath-hold two-point Dixon images using the formula [23]:

$$FSF = \frac{SI_{fat}}{SI_{fat} + SI_{water}} \quad (5)$$

Arteriovenous enhancement ratio was obtained by the ratio of signal intensity on arterial phase and 5-minute delayed contrast-enhanced VIBE images. Anterior-posterior diameter was measured perpendicular to the main pancreatic duct in the head, body, and tail on the axial opposed phase of the two-point Dixon sequence. At the pancreatic head region, measurement was obtained at the thickest pancreatic head slice lying on the right side of the superior mesenteric vein [24]. The pancreatic body was measured in the thickest portion of the gland, using the point of intersection between a vertical line along the left vertebral body margin and dorsal margin of the pancreas to the ventral margin of the pancreas. The tail of the pancreas was measured at the level of the lateral margin of the left adrenal gland. The main pancreatic duct diameter was subtracted from the diameter of the pancreas. The duodenal filling grade was assessed on the last image of the MRCP after secretin administration (grade 1, pancreatic fluid is confined to the duodenal bulb; grade 2, fluid reaches the second portion of the duodenum; grade 3, fluid reaches the third portion of the duodenum) [25]. In the Cambridge classification [7], grade 0 is considered normal and is defined as normal main duct and side branches. Grade 1 is considered equivocal and is defined as a normal main duct and fewer than three abnormal side branches. In grade 2, or mild CP, the main duct is normal but three or more side branches are abnormal. For grade 3, or moderate CP, the main duct and more than three side branches are abnormal. Finally, grade 4, or severe CP, consists of the same factors as grade 3 but with cysts larger than 10 mm, intraductal filling defects, or duct stricture.

Statistical Analysis

A two-tailed probability *t* test and one-way ANOVA were used to determine differences between the four groups. ROC curve analysis was used to determine the sensitivity, specificity, and threshold values for the diagnosis of CP. The Pearson correlation coefficient was used to assess relationships between the independent variables (ECV, T1 relaxation time, SIR of pancreas to spleen, SIR of pancreas to paraspinal muscle, duodenal filling grade, and arteriovenous enhancement ratio) with the fat signal fraction and patient age. Correlation coefficients were interpreted as weak (0–0.20), moderate (0.21–0.50), substantial (0.51–0.80), or perfect (0.81–1.00) [26]. Multivariate logistic regression was used to analyze the relationship between the presence of CP and the independent variables. The

chi-square test was used to determine the distribution of sex and age in patients without and with CP. Statistical analyses were performed using MedCalc (version 17.6, MedCalc Software).

Results

The patients' age, sex, estimated glomerular filtration rate, amylase level, lipase level, hematocrit level, and other independent variables are listed in Table 1; Table 2 presents the results of statistical analysis. Patients in the normal group ($n = 60$) had a mean age of 48 years (range, 28–67 years); those in the disease group ($n = 59$) had a mean age of 59.8 years (range, 22–85 years). Distribution of patient sex ($p = 0.27$) and age ($p = 0.35$) did not differ between the normal and disease groups. Mean ECV fraction in all female patients was 0.33 (95% CI, 0.30–0.36), which is not significantly different ($p = 0.25$) than what was seen in male patients (0.36; 95% CI, 0.31–0.41). ECV fractions, T1 relaxation times, and fat signal fraction measured in the head, body, and tail of the pancreas were similar ($p = 0.53$, 0.61, and 0.30, respectively); therefore, the arithmetic mean was used in the analysis.

Quantitative Analysis

Mean T1 relaxation time and ECV fractions were statistically different between the groups (one-way ANOVA test; T1, $p < 0.001$; ECV fraction, $p < 0.001$) (Fig. 3). ECV fraction showed sensitivity of 92% (54/59), specificity of 77% (46/60), negative predictive value (NPV) of 90%, and positive predictive value (PPV) of 79% for the diagnosis of CP. T1 relaxation time showed sensitivity of 64% (38/59), specificity of 88% (53/60), NPV of 71%, and PPV of 81%. There was substantial interobserver agreement ($\kappa = 0.71$).

Logistic Regression Analysis

Multivariate logistic regression showed that ECV fraction ($p = 0.0001$), T1 mapping ($p = 0.03$), fat signal fraction ($p = 0.01$), SIR of pancreas to spleen ($p = 0.04$), and diameter in the head ($p = 0.04$) were statistically significant variables for diagnosis of CP (Table 2). Combining ECV fraction and T1 mapping showed sensitivity of 85% (50/59) and specificity of 92% (55/60) (AUC = 0.94) (Fig. 4).

Effect of Fat Signal Fraction and Age

A moderate positive correlation was found between the fat signal fraction and T1 relaxation time (Table 2; $r = 0.37$, $p = 0.003$). However, we found no statistical correlation between fat signal fraction and either ECV fraction ($r = 0.005$, $p = 0.97$) or patient age ($r = 0.24$, $p = 0.06$). There was a moderate negative correlation between age and diameter in the head ($r = -0.34$, $p = 0.009$), body ($r = -0.48$, $p = 0.0001$), and tail ($r = -0.41$, $p = 0.001$). Age showed a moderate positive correlation with T1 relaxation time ($r = 0.37$, $p = 0.003$) and a weak positive correlation with ECV fraction ($r = 0.26$, $p = 0.04$).

Discussion

Quantitative MRI offers potential advantages over conventional qualitative imaging, including simplicity of analysis, quantitative and population-based comparisons, and more

direct interpretation of detected changes. In this study, we evaluated the ability of ECV imaging to detect increasing ECV as an indicator of pancreatic fibrosis and T1 mapping to detect loss of acinar cells, which contain protein-rich cytoplasm. Our results showed that ECV fraction could differentiate patients in the normal and disease groups with 92% sensitivity (54/59) and 77% specificity (46/60). T1 mapping showed sensitivity of 64% (38/59) and specificity of 88% (53/60) (Fig. 5). Combining ECV fraction and T1 mapping by logistic regression maintained specificity at 92% (55/60) and improved sensitivity to 86% (50/59) (AUC, 0.94).

Sensitivity and specificity of ECV fraction and T1 mapping were superior to T1-weighted SIR of pancreas to either spleen or paraspinal muscle, duodenal filling after secretin stimulation, and arteriovenous enhancement ratio of the pancreas. Sensitivity and specificity were also higher than in published studies that examined qualitative imaging criteria of CP using multiple qualitative MRCP findings, DWI to detect pancreatic fibrosis, T1-weighted SIR of the pancreas to paraspinal muscle correlated with histopathology, and grading of duodenal filling to detect the decreased exocrine fluid volume of the pancreas [12, 19, 25, 27, 28]. Prior studies often reported difficulty in assessing the severity of CP. For example, DWI was unable to differentiate mild from severe CP [19]. However, pairwise comparison in our study showed that mean ECV fractions were significantly different enough in normal (0.26), mild (0.38), moderate (0.42), and severe CP (0.51) groups to allow staging of severity as well.

Because ECV fraction and MR relaxometry to our knowledge have not been studied to diagnose CP, correlation analysis was performed to explore the relationship with the patient's age, sex, and pancreatic fat signal fraction. ECV fraction and T1 relaxation times were not statistically different between the sexes. Age of the patients in the normal group showed a weak positive correlation with the ECV fraction and a moderate positive correlation with the T1 relaxation time. Patients with CP had a slightly higher pancreatic fat fraction (10.6%) than those without CP (6.9%). Similar positive correlations were seen between the T1 relaxation times and fat fraction in both the normal and CP groups ($r = 0.37$ and 0.35 , respectively). However, a significantly high degree of pancreatic fat signal could alter the true parenchymal signal by lowering the mean T1 relaxation time. Increasing pancreatic fat fraction did not influence ECV fraction ($r = 0.001$), so ECV fraction might be a better test than T1 mapping because of its insensitivity to the signal changes from infiltrating fat.

Several studies have shown correlation of decreased T1-weighted signal of the pancreas to the loss of cytoplasmic proteinaceous content of acinar cells [10–12, 14]. A recent study using T1-weighted gradient-echo imaging reported a strong positive correlation between the T1-weighted SIR and pancreatic exocrine function as determined by pancreatic function testing [10]. T1-weighted SIR has also detected pancreatic exocrine dysfunction in patients with no ductal abnormalities, suggesting that T1-weighted SIR might be a sensitive marker of early CP [10]. However, limitations exist in conventional T1-weighted imaging in which the tissue contrast depends on multiple factors including acquisition parameters, receiver coil geometry, and sensitivity and signal amplifier gains. Variation in signal intensity is commonly observed through the choice of pulse sequence and manipulation of acquisition

parameters (e.g., flip angle, TE, TR, inversion time). These limitations preclude any direct comparisons of intensity values across subjects, time points, or imaging centers. As a quantitative imaging technique, T1 mapping measures the specific T1 relaxation time of tissues, can facilitate improved characterization of tissue, and can enhance image tissue contrast [29]. Further, the quantitative nature of the data allows ready comparison across longitudinal time points and against population-derived norms, as well as permitting more meaningful interpretation of intensity changes. These advantages might explain the superior sensitivity and specificity of T1 mapping and ECV fraction in our study and better definition of the disease severity based on the Cambridge classification. Additionally, with recently introduced fast pulse sequences, T1 mapping takes less time to perform compared with other imaging techniques such as DWI or secretin-stimulated MRCP. Another factor that could influence the T1 mapping and ECV fraction would be pancreatic edema, so we excluded patients with edema.

Secretin has been used to stimulate the pancreas and assess the amount of excreted pancreatic juice during endoscopic studies and MRCP. Sensitivity and specificity of reduced duodenal filling (i.e., grade 1 or 2) for assessment of pancreatic exocrine insufficiency were reported to be 72% and 87%, respectively [25]. Our study showed that grading of duodenal filling has only 13% sensitivity but 100% specificity for the diagnosis of CP, which is concordant with a recently published study [10]. The low sensitivity and excellent specificity might be the result of preservation of pancreatic juice production until the late stages of CP.

A variety of T1 mapping sequences are in clinical use, but very few are offered for the abdominal imaging by the MRI vendors. In this study, we used a dual flip-angle gradient-echo sequence with 3D acquisition, which is suitable for abdominal imaging because it acquires volumetric T1 maps of the abdomen in a single breath-hold. In comparison, a Look-Locker T1 mapping sequence, which does not offer 3D acquisition, can acquire three images of the pancreas within one breath-hold. Although the dual flip-angle technique is faster than other T1 mapping techniques, it is also sensitive to B1+ field inhomogeneity encountered over a large FOV, especially at higher magnetic field strengths [30]. Therefore, incorporating B1+ correction should be considered in future studies using a dual flip-angle technique.

It is important to use standard imaging parameters for ECV fraction imaging. Different physiologic and imaging parameters (e.g., estimated glomerular filtration rate, contrast agent dose, delay) and different relaxivity properties of gadolinium-based contrast agents can cause variability in measured T1 relaxation times [31, 32]. To avoid influence of these factors, the same contrast agent, dosage, delay, and imaging protocol were used for all patients in this study.

In summary, our study showed that ECV fraction and tissue relaxometry information provided by T1 mapping can provide quantitative metrics for determining the presence and severity of acinar cell loss and fibrosis and aid in the diagnosis of CP. Including these quantitative imaging techniques as part of the routine MRCP evaluation can help radiologists by increasing sensitivity and specificity in evaluation of CP. Our study is the first to our knowledge to explore the potential benefit of these new imaging techniques. Prospective

studies should be performed to validate these results using histopathologic correlation, different T1 mapping sequences, and MR scanners from different vendors.

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Fig. 1.

Histopathology of chronic pancreatitis (CP). Histologic hallmarks of CP are fibrosis, chronic inflammation, and loss of acinar cells.

A, Photomicrograph (H and E, $\times 400$) of mild CP shows perilobular (*thick arrow*) and intralobular (*thin arrow*) fibrosis. Most of pancreatic acinar cells (G) are still intact.

B, Photomicrograph (H and E, $\times 200$) shows amount of peri- and intralobular fibrosis (F) becomes more widespread as disease progresses, replacing normal acinar tissue (G).

Nonstaining oval areas (*arrow*) indicate autodigestive fatty tissue necrosis.

C, Illustration shows normal and increased extracellular space from fibrosis before (*top*) and after (*bottom*) enhancement with gadolinium. Normal pancreas is shown on left; chronic pancreatitis is shown on right. As amount of pancreatic fibrosis increases, lower T1 relaxation time is expected because of higher concentration of gadolinium (GD) in extracellular space. Extracellular volume imaging exploits this property of gadolinium-based contrast agents to calculate extracellular volume fraction of tissues. PD = pancreatic duct. (© Trustees of Indiana University)

Fig. 2.
Patient selection algorithm.

Fig. 3.

Bar graphs of mean extracellular volume (ECV) fraction and T1 relaxation time showing differences among study groups. Vertical lines and whiskers indicate 95% CIs. Normal = Cambridge grade 0; mild chronic pancreatitis (CP) = Cambridge grade 2; moderate CP = Cambridge grade 3; severe CP = Cambridge grade 4.

A, ECV fractions of normal and three CP groups. Intergroup comparison (ANOVA) showed statistically significant difference between ECV fraction of each group ($p < 0.001$). Pairwise comparison showed that mean ECVs of all groups were statistically different ($p < 0.05$).

B, Mean T1 relaxation times of normal and three CP groups. Mean T1 relaxation time of normal and severe CP groups were statistically different from all other groups. However, mild and moderate CP groups are similar.

Fig. 4.

Comparison of ROC curves of different imaging variables used in this study for diagnosis of chronic pancreatitis. Best diagnostic performance was achieved by combining extracellular volume (ECV) fraction and T1 relaxation time (*red curve*) using logistic regression (0.94). AUC of individual variables were ECV, 0.90; T1 relaxation time, 0.80; anterior-posterior diameter in head (APD head), 0.70; arteriovenous enhancement ratio (AVR), 0.63; and signal-intensity ratio of pancreas to spleen (SIR P/S), 0.65.

Fig. 5.

Quantitative imaging of pancreas.

A, Axial quantitative extracellular volume (ECV) map in 67-year-old woman who was enrolled in pancreatic cancer screening program because of genetic susceptibility to breast cancer. Each pixel represents ECV fraction calculated by formula on scale of 0.0–1.0.

MRCP was performed as annual screening test and showed no evidence of chronic pancreatitis (CP). Mean ECV fraction was 0.23. Border of pancreas is shown by white line.

B, Axial quantitative ECV color map of pancreas in 47-year-old woman with history of pancreas divisum and repeated episodes of CP. Pancreas shows diffusely higher ECV fractions (mean, 0.49) compared with **A**.

C, Unenhanced axial T1 mapping of pancreas in 55-year-old woman with family history of pancreatic cancer. MRCP was performed as annual screening and did not show evidence of CP or pancreatic cancer. T1 relaxation times were low throughout parenchyma, as indicated by blue color tones. Mean relaxation time of pancreas was 850 ms.

D, Unenhanced axial T1 mapping of pancreas in 41-year-old woman with history of CP. Pancreas shows higher T1 relaxation times, as represented by turquoise and green tones. Mean T1 relaxation time was 1378 ms.

TABLE 1

Summary of Results

Characteristic	Patient Group				p
	Normal	Mild CP	Moderate CP	Severe CP	
No. of patients	60	22	27	10	
Sex					0.27 ^a
Female	16	17	17	6	
Male	10	5	10	4	
Age (y) (range)	48 (28–67)	63 (40–83)	63 (40–83)	58 (22–85)	0.35 ^a
Laboratory findings ^b					
Hematocrit (%)	41 (38–45)	39 (35–45)	39 (35–45)	39 (34–50)	0.50
eGFR (mL/min/1.73 m ²)	73 (50–89)	70 (50–87)	70 (50–87)	59 (47–83)	0.59
Amylase level (U/L) ^c	59 (31–225)	50 (13–156)	50 (13–156)	66 (13–214)	0.24
Lipase level (U/L) ^d	96 (11–359)	74 (11–471)	74 (11–471)	120 (7–124)	0.14
ECV fraction	0.26 (0.24–0.28)	0.38 (0.33–0.43)	0.42 (0.39–0.46)	0.51 (0.47–0.56)	< 0.001
Imaging findings ^b					
T1 relaxation time (ms)	743 (690–797)	1055 (922–1187)	1064 (919–1209)	1242 (1085–1400)	< 0.001
Diameter (mm) ^e	24 (23–25)	21 (18–22)	19 (17–21)	18 (13–22)	< 0.001
Fat signal fraction	0.07 (0.06–0.07)	0.11 (0.08–0.14)	0.10 (0.09–0.12)	0.10 (0.07–0.13)	0.00
Signal-intensity ratio					
Pancreas to spleen	1.04 (1.00–1.08)	0.99 (0.92–1.07)	0.96 (0.90–1.03)	0.91 (0.83–0.99)	0.02
Pancreas to paraspinal muscle	1.28 (1.23–1.34)	1.30 (1.20–1.40)	1.24 (1.14–1.35)	1.16 (1.05–1.26)	0.09
Arteriovenous enhancement ratio	1.80 (1.05–2.55)	1.25 (0.42–2.07)	1.19 (0.16–2.57)	0.98 (0.30–1.66)	0.09
Duodenal filling grade ^f					0.06
1	0/40 (0)	0/21 (0)	1/22 (4)	2/9 (22)	
2	0/40 (0)	0/21 (0)	1/22 (4)	1/9 (11)	
3	29/40 (73)	14/21 (67)	15/22 (68)	6/9 (67)	
4	11/40 (27)	7/21 (33)	5/22 (23)	0/9 (0)	

Note—CP = chronic pancreatitis, eGFR = estimated glomerular filtration rate, ECV = extracellular volume.

^g Chi-square test using normal and disease groups.
^h Values are means with 95% CI in parentheses.
ⁱ Normal range is 20–85 U/L.
^j Normal range is 0–160 U/L.
^k Diameter of the pancreas is different in the head, body, and tail ($p < 0.001$). Therefore, we analyzed diameter in the head, body, and tail individually. All three segments of the pancreas showed statistically significant difference between the cohorts ($p < 0.001$).
^l Values in parentheses are percentages. Secretin was not given in all patients.

TABLE 2

Statistical Analysis of the Independent Variables

Statistical Test	ECV Fraction	T1 Mapping	Diameter (mm)			FSF	Signal-Intensity Ratio		AVR	DF
			Head	Body	Tail		Pancreas to Spleen	Pancreas to Paraspinal Muscle		
One-way ANOVA ^a	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.02	0.09	0.09	0.06
Diagnostic performance										
Criteria ^b	> 0.27	> 950 ms	< 23	< 18	< 18	> 0.07	< 1.00	< 1.18	< 0.66	2
Sensitivity (%)	92 (54/59)	64 (38/59)	37 (22/59)	54 (32/59)	64 (38/59)	71 (42/59)	58 (34/59)	51 (30/59)	51 (30/59)	13 (5/40)
Specificity (%)	77 (46/60)	88 (53/60)	95 (57/60)	90 (54/60)	83 (50/60)	65 (39/60)	75 (45/60)	73 (44/60)	75 (45/60)	100 (40/40)
AUC	0.90	0.80	0.70	0.73	0.74	0.75	0.65	0.55	0.63	0.57
PPV (%)	79	81	88	76	72	67	68	65	65	100
NPV (%)	90	71	60	65	69	69	64	60	68	54
Correlation (<i>r</i>) ^c										
With FSF	0.001	0.38	0.07	0.10	-0.01	NA	0.12	0.07	-0.02	0.36
With age	0.26	0.37	-0.34	-0.48	-0.41	0.24	-0.05	-0.07	-0.18	-0.12
Tukey-Kramer pairwise comparison ^d										
Normal (a)	b, c, d	b, c, d	b, c, d	b, c, d	c, d	b, c	NA	NA	NA	d
CP										
Mild (b)	a, c, d	a, d	a	a	NA	A	NA	NA	NA	d
Moderate (c)	a, b, d	a, d	a	a	a	A	NA	NA	NA	d
Severe (d)	a, b, c	a, b, c	a	a	a	NA	NA	NA	NA	a, b, c
Multivariate logistic regression (<i>p</i>) ^e	0.0001	0.03	0.04	0.78	0.76	0.01	0.04	0.12	0.10	0.06

Note—ECV = extracellular volume, FSF = fat signal fraction, AVR = arteriovenous enhancement ratio, DF = duodenal filling grade, PPV = positive predictive value, NPV = negative predictive value, CP = chronic pancreatitis. NA = not applicable.

^aOne-way ANOVA test was used to determine if the values in each group were statistically different from each other.

^bYouden index was used to determine the threshold value of criteria.

^cNo disease group (normal) was used to analyze the natural relationship of the independent variables with age of the patient and FSF of the pancreas.

^dTukey-Kramer pairwise comparison test was used to compare means of each group. Statistical significance was set at $p < 0.05$.

Multiple logistic regression analysis shows the effect of each variable for the diagnosis of CP. A p value < 0.05 was considered statistically significant. Using the logistic regression analyses, ECV fraction and T1 mapping were combined and diagnostic performance was compared with individual variables, as seen in Figure 4.

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