Magnetic Resonance Elastography and T_1 Mapping for Early Diagnosis and Classification of Chronic Pancreatitis

Min Wang, BS¹, Feng Gao, MS², Xiaoqi Wang, PhD³, Yanqing Liu, BS¹, Ruoyun Ji, BS¹, Lizhuo Cang, BS¹, and Yu Shi, MD^{1,*}

¹Department of Radiology, Shengjing Hospital of China Medical University, Shenyang, P.R. China

²Department of Pancreato-thyroidic Surgery, Shengjing Hospital of China Medical University, Shenyang, P.R. China

³Philips Healthcare, Beijing, China

Abstract

Background—Early detection and classification of chronic pancreatitis (CP) are both important and challenging.

Purpose—To investigate the diagnostic performance of MR elastography and T_1 mapping of the pancreas for different stages of CP.

Study type—Retrospective.

Subjects—Clinical and imaging records of 81 patients (from 5/2015 to 7/2017) with suspected CP were analyzed. Patients were categorized into the normal control (n=35), mild CP (n=30) and moderate/severe CP groups (n=16) according to the Cambridge classification based on concordant endoscopic retrograde cholangiopancreatography or ultrasound endoscopy findings.

Field strength/sequence—3T pancreatic MRI, which included MR elastography and T_1 mapping.

Assessment— T_1 relaxation times, pancreatic stiffness values, the main pancreatic duct (MPD) diameter and pancreatic thickness were measured in all patients.

Statistical tests—Cut-off values of T_1 relaxation times and pancreatic stiffness values for diagnosis of CP were calculated using receiver operating characteristic analysis. Associations of imaging parameters with different stages of CP were assessed using logistic regression analysis.

Results—Both T_1 relaxation times (865±220 ms vs 1075±221 ms vs 1350±139 ms) and pancreatic stiffness (1.21±0.13 kPa vs 1.50±0.15 kPa vs 1.90±0.16 kPa) differed significantly ($P < 0.001$) among the control, mild CP and moderate/severe CP groups. Pancreatic stiffness (>1.34 kPa) achieved significantly higher area under the curve (AUC) than T_1 relaxation time (>908.4

*Address reprint requests to: Y. S., MD, Department of Radiology, Shengjing Hospital, China Medical University, No. 36, Sanhao Street, Heping District, Shenyang, 110004, P.R. China. Tel.: +86 24 96615 73211; Fax: +862423929902. 18940259980@163.com.

Conflicts of interest:

Xiaoqi Wang is the employee of Philips Healthcare, but he had no control over inclusion of any data or information that might have presented a conflict of interest. There are no actual or potential conflicts of interest to declare in relation to this article. None of the other authors have conflicts of interest or any specific financial interests relevant to the subject of this manuscript.

ms) for detection of mild CP (AUC: 0.928 vs 0.751, $P = 0.011$). Pancreatic stiffness values (>1.61 kPa) also achieved significantly higher AUC than T_1 relaxation times ($>1,131.6$ ms) (AUC: 0.981 vs 0.910, $P = 0.033$) for diagnosing moderate/severe CP from the other two groups. Multiple regression analysis showed that T_1 relaxation time and stiffness were the independent factors associated with mild CP ($P = 0.025$ and <0.001 , respectively).

Data conclusion—Both MRE and T_1 mapping are promising quantitative imaging methods for evaluation of CP; MRE slightly outperformed T_1 mapping.

Keywords

MR elastography; Diagnosis; Chronic pancreatitis; T_1 mapping

Introduction

Chronic pancreatitis (CP) is characterized by progressive inflammation, pancreatic fibrosis, and impairment of both exocrine and endocrine function [1]. The diagnosis of mild CP is usually inferred from the results of conventional imaging modalities [2, 3], such as ultrasound and CT, can detect the late findings of CP but have limited value for the diagnosis of early or mild CP. Although pancreatic fluid and bicarbonate output (i.e. pancreatic function test) can be directly measured to quantify the impaired function, this assessment is invasive and time-consuming, and thus is rarely performed in clinical practice [4]. The Cambridge classification has been used since 1984 as a reference standard to diagnose and grade CP by endoscopic retrograde cholangiopancreatography (ERCP) [5]. However, the use of ERCP as a purely diagnostic tool has declined and is rarely used. The trend is likely due to the introduction of less invasive and more sensitive imaging tools that evaluate both parenchymal and ductal changes [6–8].

Although different etiologies lead to chronic pancreatitis, pancreatic fibrosis is the common histologic finding. This fibrosis might be detected by MR techniques, such as T_1 mapping and MR elastography [9, 10]. T_1 mapping has been successfully used to assess the extent of myocardial fibrosis, and rapid acquisition in one breath-hold of T_1 mapping is currently available for abdominal evaluation [11, 12]. A prior study has reported that the T_1 relaxation time of the pancreas is greater in mild CP patients than in patients with a healthy pancreas [9]. MRE has been successfully used to stage hepatic fibrosis in patients with chronic hepatitis; even mild chronic hepatitis can be detected by MRE with high sensitivity [10]. Hence, the purpose of this study was to investigate the diagnostic performance of pancreatic stiffness, determined by MRE, and T_1 relaxation time of the pancreas, determined by T_1 mapping, for diagnosis of different stages of CP.

Materials and Methods

Population

This retrospective, Health Insurance Portability and Accountability Act–compliant study was approved by the Institutional Review Board of the local hospital. From May 2015 to July 2017, MRE was included in the routine pancreatic MR protocol for each participant with suspected pancreaticobiliary pathology. Informed consent was required to include MRE

into any patient's pancreatic MR protocol. First, we identified 219 adult patients who underwent both MRE and T_1 mapping for pancreatic evaluation. We excluded those patients with an acute episode of pancreatitis (n=37), cystic or solid pancreatic tumors (n=68), without evidence of clinical follow-up available (n=14), suboptimal image quality on T_1 maps (n=4), elastograms (n=5) or severe atrophy of the pancreatic parenchyma (n=10). Thus, 81 patients were further evaluated. Then, two gastroenterologists, with 10 years and 12 years of experience, respectively, reviewed these patients' history, ERCP or endoscopic ultrasonography (EUS) results and other imaging findings. According to the Cambridge classification, 16 patients were determined to have moderate/severe CP (mod/sev CP) based on ERCP/EUS or typical CT/MRI findings, which showed main pancreatic duct (MPD) dilation or irregularity with/without parenchymal or ductal calculi, together with clinical symptoms. Patients with normal ductal findings on ERCP (n=4) or EUS (n=31), normal serum amylase and lipase levels, and without history of acute or chronic pancreatitis together with at least a 6-month clinical follow-up, were considered as the control group (n=35). The clinical findings in the control group included choledocholithiasis (n=27), sphincter of Oddi dysfunction (n=7) and primary sclerosing cholangitis (n=1); none had with any form of pancreatitis. The diagnosis of those in the mild CP group (n=30) was based on history of consistent symptomatology (abdominal pain suspected to be of pancreatic origin), concordant ductal findings on ERCP according to the Cambridge classification [5] (n=21) or EUS findings based on the Rosemont classification [13] (n=9). Rosemont classification does not directly classify patients as having "mild CP"; therefore EUS findings were regarded as mild CP based on inhomogeneous echo texture or echogenic strands in the gland. We combined patients with equivocal or mild chronic pancreatitis into one group (mild CP group).

Imaging Technique

Patients fasted overnight for 6–8 hours prior to the MR examination. The patients first underwent clinical pancreatic MR sequences with T_1 mapping with a 3.0T Philips scanner (Philips Ingenia, Philips Healthcare, Best, the Netherlands) and then underwent MRE immediately with a 3.0T GE scanner next (Signa HDX system; GE Healthcare, Milwaukee, WI). A modified Look-Locker inversion recovery (MOLLI) 2D imaging sequence was applied for T_1 acquisition and quantification using a 5s(3s)3s sampling scheme for non-contrast enhanced application. MOLLI sequence images were obtained using a 32-channel torso coil with the following settings: 2.24 ms/1.01 ms TR/TE; 30cm FOV; 152×150 acquisition matrix; 10 mm slice thickness; 12s breath-hold duration; 20° flip angle, and 152 × 150 acquisition matrix. The MOLLI sequence was repeated 3–6 times to cover different subregions of the pancreas. MRE data were collected using a Signa Excite HD 3T GE scanner with an 8-element torso-phased array coil. Each patient was imaged using flow-compensated, multi-slice, spin-echo echo-planar-imaging (SE-EPI) pulse sequences. Axial slices were performed using 40-Hz mechanical vibrations. The mechanical vibrations were supplied by an active pneumatic driver system located outside the scanning room and were delivered to the upper abdomen centered on the xiphisternum via a plastic tube that terminated in a passive driver that transmitted the waves into the deep pancreas. The passive drivers were fastened to the upper abdomen using an elastic belt. In patients with BMI >27 kg/m², a rigid round liver driver, diameter 19 cm, was utilized with 40–50% power

amplitude [14] ; in other patients, a rectangular soft driver (19×14 cm) was utilized with 70–100% power amplitude, as previously described [15, 16]. All the drivers were developed by Mayo Clinic (Rochester, MN). The acquisition included four 22-s and one 11-s breath-holds. The imaging parameters settings were 40 Hz frequency; 1375/38.8 ms TR/TE; 32~44 cm FOV; 3 phase offsets; parallel imaging acceleration factor of 3; 96×96 acquisition matrix; 1 signal average; 32 slices; and 3.5 mm slice thickness. The pancreatic thickness was measured from axial breath-hold 2-point DIXON (mdixon) T_1 -weighted images with TE at 1.32 and 2.3 ms, (3.6 ms TR and 3.5 mm slice thickness). The diameter of the MPD was measured from T_2 -weighted images, which were acquired using 622.84 ms TR, 70.00 ms TE, and 5 mm slice thickness.

Image Analysis

Wave images were processed on the scanner automatically using the automated direct inversion algorithm (Mayo Clinic, Rochester, MN) as previous reportedly in MRE studies of the pancreas, kidney, and liver [15–18]. T_1 maps were calculated based on MOLLI images at a set of inversion recoveries (IR) with increasing TI's in each IR performed throughout one breath-hold. The T_1 maps for pancreas were read. Then, for better illustration, the T_1 maps encompassing the pancreatic parenchyma were segmented out and overlaid on the T_1 weighted images. One region of interest (ROI) was drawn separately for each subregion (head/uncinate process, body, and tail). The ROIs were drawn to encompass the largest area of pancreatic parenchyma as possible while avoiding the pancreatic border, large vessels, duct, the surrounding tissues, and retroperitoneal fat. The elastograms matching the T_1 maps were selected, as close as possible, to draw similar ROIs including pancreatic parenchyma on matching sections. Two experienced abdominal radiologists, with 3 and 5 years of experience with MRE measurement, blinded to the ERCP/EUS data, measured pancreatic stiffness, T_1 relaxation time from the head, body, and tail of the pancreas, pancreatic thickness from DIXON sequence, and MPD diameter from T_2 -weighted images. The final measurements were calculated as the mean value of the two observers after establishing the inter-observer agreement.

Statistical Analysis

The intraclass correlation coefficient (ICC) was calculated to assess inter-observer agreement for stiffness and T_1 relaxation time measurements. Continuous variables were summarized as means $\pm$ standard deviation (SD), or median with 25th and 75th percentiles of the interquartile range, as appropriate. Categorical variables were expressed as counts and percentages. The clinical characteristics of the subjects in different groups were compared using the Kruskal-Wallis test. The stiffness and T_1 relaxation time among different subregions in each group were compared using the Friedman test. Mann-Whitney U test was used for comparisons between two groups. Categorical variables (e.g. gender) were compared using Chi-squared test. Receiver operating characteristic (ROC) curve analysis was performed to determine the diagnostic accuracy of both stiffness and T_1 relaxation time for diagnosing mild CP from healthy pancreas, the presence of any CP from healthy pancreas, and mod/sev CP from normal/mild CP. The sensitivity, specificity, and accuracy with 95% confidence intervals (CI) were calculated using a cutoff value determined by maximizing sensitivity and specificity. Between-group comparisons of sensitivity,

specificity, and accuracy were based on the McNemar test. AUC comparisons were performed according to the method proposed by DeLong et al [19]. Univariate and multivariate logistic regression analyses were used to analyze the association of imaging factors, including T_1 relaxation time, stiffness, pancreatic thickness, MPD size, and demographic characteristics to the presence of mild CP and the presence of any CP (both mild and mod/sev CP vs normal pancreas). The sensitivity by MRE reached up to 100% for diagnosing mod/sev CP, making the results of the logistic regression analyses invalid, therefore, we avoid using logistic regression analyses for diagnosing mod/sev CP. ROC analyses were performed using MedCalc software (MedCalc Software, Mariakerke, Belgium). All other statistical analyses were performed using commercially available SPSS Statistics V 20.0 (IBM Corporate, New York, USA) software. $P < 0.05$ was indicative of a statistically significant difference. MPD diameter < 3 mm was considered normal, that is, nondilated. Fecal elastase-1 (FE-1) < 200 $\mu\text{g/g}$ was considered normal [20].

Results

The patients' demographic and clinical characteristics are shown in Table 1. These three groups had similar gender distribution ($P = 0.720$), BMI ($P = 0.162$), age ($P = 0.453$), serum amylase ($P = 0.115$), and lipase levels ($P = 0.171$). The mean MPD diameter in the control group was narrower (2.47 ± 0.56 mm) than in the mild CP group (2.94 ± 0.51 mm) ($P = 0.002$) and mod/sev CP group (5.17 ± 2.30 mm) ($P < 0.001$). Pancreatic thickness was slightly greater in the control group (19.2 ± 4.2 mm) than in the mild CP group (18.2 ± 3.5 mm) ($P = 0.305$) and mod/sev CP group (16.2 ± 4.3 mm) ($P = 0.015$). FE-1 in the mod/sev CP group was significantly lower (121 ± 100 $\mu\text{g/g}$) than in the control group (312 ± 156 $\mu\text{g/g}$) ($P < 0.001$) and mild CP group (285 ± 164 $\mu\text{g/g}$) ($P = 0.001$). FE-1 did not differ between the mild CP and control groups ($P = 0.418$).

Correlation of T_1 Relaxation Time and Pancreatic Stiffness with CP Category

Three representative figures for normal pancreas, mild CP and moderate CP cases are shown Fig. 1–3, respectively. The corresponding wave images are shown in Fig. 4. The distribution of pancreatic stiffness and T_1 relaxation times are shown in Table 2, Fig. 5 and 6. The mean pancreatic stiffness values and T_1 relaxation times were significantly different (both $P < 0.001$) among the study groups. Both the pancreatic stiffness and the T_1 relaxation times were consistent among the different pancreatic subregions in all the CP and control groups (all $P > 0.05$). Thus, the mean values of the three subregions for each patient were used for all calculations and statistical comparisons. Excellent inter-observer agreement was observed for stiffness measurements (ICC = 0.93; 95% CI: 0.90–0.96), and for T_1 relaxation time measurements (ICC = 0.94; 95% CI: 0.91–0.96).

AUC Analysis for Diagnosis of Chronic Pancreatitis

MRE (pancreatic stiffness > 1.34 kPa) achieved significantly better diagnostic performance for distinguishing mild CP from normal pancreas than did T_1 mapping (T_1 relaxation time > 908.4 ms) (AUC: 0.928 vs 0.751, $P = 0.011$). Although MRE had slightly greater sensitivity (83.3% vs 80.0%, $P = 1.000$), specificity (85.7% vs 68.6%, $P = 0.109$), and accuracy (84.6% vs 73.8%, $P = 0.167$), none of these comparisons reached statistical

significance (Table 3 and Fig. 7A). For diagnosing the presence of any CP, pancreatic stiffness (>1.34 kPa) also achieved better diagnostic performance than did T_1 mapping (>908.4 ms) (AUC: 0.953 vs 0.822, $P=0.009$). For distinguishing mod/sev pancreatitis from normal pancreas or mild CP, pancreatic stiffness (>1.61 kPa) also achieved better diagnostic performance than did T_1 mapping ($>1,131.6$ ms) (AUC: 0.981 vs 0.910, $P=0.033$) (Table 3, Fig. 7 B and C).

Multiple Regression Analysis for Diagnosis of Chronic Pancreatitis

In the univariate analysis of the diagnoses of mild CP versus normal pancreas, the MPD diameter was significantly associated with mild CP ($P=0.025$), but did not reach statistical significance in the multivariate analysis ($P=0.136$). In multivariate regression analysis, T_1 relaxation time and stiffness were independently associated with the diagnosis of mild CP ($P=0.025$ and <0.001 , respectively), as shown by Table 4.

In the univariate analysis of the diagnosis of any CP (mild or mod/sev) versus normal pancreas, MPD, thickness and FE-1 were significantly associated with any CP ($P<0.001$, 0.011 and 0.045, respectively), but did not reach statistical significance in the multivariate analysis ($P=0.067$, 0.823 and 0.284, respectively). In multivariate regression analysis, T_1 relaxation time and stiffness were the variables independently associated with the presence of any CP ($P=0.024$ and <0.001 , respectively), as shown by Table 5.

Discussion

We investigated the value of both MR elastography (MRE) and T_1 mapping for diagnosing CP. In this study, both MRE and T_1 mapping achieved good diagnostic performance for diagnosing different stages of CP; MRE slightly outperformed T_1 mapping. In multivariate analysis, both pancreatic stiffness and T_1 relaxation time were independent predictors for the diagnosis of mild and of any CP.

CP leads to irreversible parenchymal and ductal changes in the pancreas. In a recent systemic review [21], EUS and ERCP outperformed all other imaging modalities for diagnosing CP. However, EUS and ERCP are invasive techniques; furthermore, diagnostic ERCP has been largely replaced by EUS [22, 23] and non-invasive imaging modalities. Both clinicians and radiologists have accepted noninvasive imaging to evaluate pancreatic parenchyma and pancreatic ducts [6, 7, 24, 25]. In patients with moderate or severe CP, irregularities and dilatations of the MPD and side branches on CT/MR imaging and typical clinical symptoms are expected; hence moderate or severe CP is usually easily diagnosed. In our study, both MRE and T_1 mapping also achieved very high diagnostic performance (both AUC >0.9 and sensitivity $>90\%$) for distinguishing moderate/severe CP from normal/mild CP. However, in patients with mild CP, findings using conventional imaging may be subtle or even absent [4]. Consequently, those imaging techniques are insensitive for the diagnosis of mild CP.

Previous studies showed that ultrasound elastography can provide relevant information about tissue stiffness and thus may aid the diagnosis of CP [26–29]. Quantitative EUS elastography (EUS-EG) evaluation, including strain ratio and histogram analysis, has been

reported to achieve relatively high AUC values for the presence of CP (0.86 and 0.91) [30–33], which are lower than that achieved by MRE in our study (0.953), but higher than those achieved by T_1 mapping (0.822). EUS-EG only measures theoretically relative elasticity in ROIs, rather than absolute values of stiffness. Moreover, EUS-EG is a subjective and invasive method, EUS-EG images are markedly affected by the size of ROI and the level applied to the pancreas, and the ROI setting of the strain ratio cannot include the entire pancreatic parenchyma. On the other hand, MRE is objective, non-invasive, and produces the entire pancreatic stiffness map. Individual values of each separate subregion can be analyzed. Hence, MRE has the potential to detect heterogeneous changes of CP in different regions. The newly emerged shear wave elastography (SW-EG), measuring the Young's modulus [28], was also recently used to diagnose CP. However, SW-EG uses US, the probe is more distant from the pancreas compared to EUS, which reduces the resolution of the pancreas image, particularly when large area of gastrointestinal gas or liquid component (e.g. large vessels, stomach) are present, because the shear waves are easily refracted and reflected. In this study, MRE propagated good waves across the entire upper abdomen, the technical failure of wave data was only reported in 5 of 219 cases. We found that the MRE-based stiffness was very sensitive to detect mild CP, showing higher sensitivity (83.3% vs 77.1%) and specificity (85.7 vs 64.9%) than that reported by SW-EG (normal and indeterminate CP vs consistent with CP and suggestive of CP) [28]. Mild CP directly alters the mechanical properties of pancreatic tissue. The histological changes of CP, histological fibrosis, inflammation and changes of the cellular density, lead to increased stiffness detected by MRE, prior to the signal changes detectable by conventional MR imaging. The mean numerical stiffness values (shear modulus) of normal pancreas and mild CP were 1.21 kPa and 1.50 kPa, respectively, whereas the Young's moduli in EUS studies were 3.5 kPa and approximately 5–7 kPa, respectively. Based on elasticity theories, the Young's modulus of soft biological tissues is nearly three times as great as shear modulus [17], which might partially explain these differences.

T_1 mapping quantitatively measures the T_1 relaxation time of the target organ. Similar to stiffness, T_1 relaxation time is also a tissue-specific property and independent of imaging parameters. Both stiffness and T_1 relaxation times should be interchangeable across MRI machines, vendors and magnet strength. T_1 mapping has been successfully used in a number of cardiac diseases including myocardial fibrosis and myocardial deposition diseases. Tirkes et al first compared T_1 relaxation times between a control (mean=797 ms) and mild CP group (mean=1099 ms), which were similar to our results (mean=865 ms and 1075 ms, respectively). A T_1 relaxation time (>900 ms) was 80% sensitive and 69% specific for the diagnosis of mild CP in Tirkes' study, which was also consistent with our results. Our study further proved that the performance of MRE was slightly better than T_1 mapping for diagnosis of mild CP. MRE was more specific than T_1 mapping (85.7% vs 68.6%), with similar sensitivity (83.3% vs 80.0%). In Tirkes' study [34], combining extracellular volume fraction with T_1 mapping yielded a high AUC, 0.94, for diagnosing the presence of CP, which is very similar to our results using MRE (0.953). Compared with secretin-enhanced MRCP, which adds several minutes of imaging time and significant cost, both MRE and T_1 mapping acquisition are simple, fast and free of intravenous injection of secretin and should

be added to clinical imaging protocols. In those centers when MRE hardware is not available, T_1 mapping can provide an alternative choice with reasonable diagnostic accuracy.

Our study has several limitations. First, this is a retrospective study with relatively small subject numbers. Secondly, the diagnosis of CP was not confirmed histologically. The criteria for CP used in this study, particularly EUS criteria, are known to be subjective and not very sensitive for the detection of early CP. Third, MRE has lower resolution than standard MRI pulse sequences. MRE and T_1 mapping might not be suitable for detection of severe CP that is more likely to have severe pancreatic atrophy. To control this potential bias, such patients were excluded from this study. We believe that the practical importance of this limitation is mitigated because the diagnosis of severe CP is usually easy and is not likely to require stiffness/ T_1 measurements. Fourth, we did not evaluate other MR sequences, such as DWI imaging, which might also be useful for CP diagnosis.

In conclusion, both MRE and T_1 mapping are fast, cost-effective, and promising MR methods for diagnosing CP; MRE slightly outperformed T_1 mapping. Although these methods cannot substitute for EUS or ERCP to detect ductal changes, they offer quantitative measurements of early parenchymal changes. Therefore, these techniques can provide very valuable supplementary information and screening for suspected CP. In practice, patients referred with typical abdominal pain who are being evaluated for CP may undergo MRCP/EUS combined with T_1 mapping/MRE to assess for both morphological and mechanical changes, thereby optimizing the detection of minimal changes in CP.

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Figure 1. Pancreatic images from a 24-year healthy female volunteer. T_1 mapping image (A), MRE magnitude image (B), ERCP image (C), and elastogram (D) at 40 Hz. The pancreatic T_1 relaxation time and stiffness value on the elastogram (outlined in white dotted line) were 758 ± 43 ms and 1.18 ± 0.23 kPa, respectively.

Figure 2.

Images from a 46-year female with mild CP. T_1 mapping image (A), MRE magnitude image (B), ERCP image (C), and elastogram (D) at 40 Hz for the pancreas. The pancreatic T_1 relaxation time (1344 ± 103 ms) and stiffness (1.53 ± 0.34 kPa) value on the elastogram (outlined in white dotted line) were both greater than normal.

Figure 3.

Images from a 52-year male with moderate CP. T_1 mapping image (A), magnitude image (B), ERCP image (C), and elastogram (D) at 40 Hz for the pancreas. The pancreatic T_1 relaxation time (1544 ± 87 ms) and stiffness (1.81 ± 0.27 kPa) value on the elastogram (outlined in white dotted line) were both greater than normal and mild group.

Figure 4. Representative pancreatic magnitude images (left) and wave images of the x, y, and z (from left to right) components of the vector displacement field generated by MRE. Images were obtained from a 24-year healthy female volunteer (upper row), a 46-year female with mild CP (middle row) and 52-year male with moderate CP (lower row) corresponding to Fig 1, 2 and 3, respectively.

Figure 5.

Box plot of pancreatic stiffness in the control (mean = 1.21 kPa, 95% CI: 1.17–1.26), mild CP group (mean = 1.50 kPa, 95% CI: 1.44–1.56) and mod/sev CP (mean = 1.90 kPa, 95% CI: 1.81–1.98). The stiffness of the pancreas in the mod/sev CP and mild CP group were significantly greater than normal group (both $P < 0.001$).

Figure 6.

Box plot of pancreatic T_1 relaxation times in the control (mean = 865 ms, 95% CI: 789–940) and mild CP group (mean = 1075 ms, 95% CI: 993–1158) and mod/sev CP (mean = 1350 ms, 95% CI: 1276–1423). The mean T_1 relaxation time of the pancreas in the mild CP and mod/sev CP group were significantly greater than normal group ($P=0.001$ and <0.001 , respectively).

Figure 7.

A: Results of ROC curve analysis for T_1 relaxation time and stiffness as criteria for diagnosis of mild CP. T_1 relaxation time: Threshold value of 908.4 ms was 80.0% sensitive (95% CI: 61.4%–92.3%) and 68.6% specific (95% CI: 50.7%–83.1%) for the diagnosis of mild CP (AUC = 0.751). Stiffness: threshold value of 1.34 kPa was 83.3% sensitive (95% CI: 65.3%–94.4%) and 85.7% specific (95% CI: 69.7%–95.2%) for the diagnosis of mild CP (AUC = 0.928). B: Results of ROC curve analysis for T_1 relaxation time and stiffness as criteria for diagnosis of mod/sev CP. T_1 relaxation time: Threshold value of 1,131.6 ms was 93.8% sensitive (95% CI: 69.8% – 99.8%) and 75.4% specific (95% CI: 63.1 – 85.2%) for the diagnosis of mod/sev CP (AUC = 0.910). Stiffness: threshold value of 1.61 kPa was 100.0% sensitive (95% CI: 79.4%–100.0%) and 87.7% specific (95% CI: 77.2%–94.5%) for the diagnosis of mod/sev CP (AUC = 0.981). C: Results of ROC curve analysis for T_1 relaxation time and stiffness as criteria for diagnosis of CP. T_1 relaxation time: Threshold value of 908.4 ms was 87.0% sensitive (95% CI: 73.7%–95.1%) and 68.6% specific (95% CI: 50.7%–83.1%) for the diagnosis of mod/sev CP (AUC = 0.822). Stiffness: threshold value of 1.34 kPa was 89.1% sensitive (95% CI: 76.4%–96.4%) and 85.7% specific (95% CI: 69.7%–95.2%) for the diagnosis of mod/sev CP (AUC = 0.953).

Table 1

Demographic and Clinical Characteristics of Controls and Two Chronic Pancreatitis (CP) Groups

	Control (n=35)	Mild CP (n=30)	Mod/Sev CP(n=16)
Age (years)	52 (Range:21–82)	56 (Range:33–81)	57 (Range:37–78)
Gender (F:M)	21:14	15:15	9:7
BMI (Kg/M ²)	23.0 (SD:2.5)	23.7 (SD:2.7)	22.3 (SD:2.9)
Lipase level (U/L)	68(50–82) *	81(56–104) *	86(62–110) *
Amylase level (U/L)	37(SD:11)	42(SD:13)	50(SD:22)
FE-1 (µg/g)	312(SD:156)	285(SD:164)	121(SD:100)
MPD (mm)	2.47(SD:0.56)	2.94(SD:0.51)	5.17(SD:2.30)
Thickness (mm)	19.2(SD:4.2)	18.2(SD:3.5)	16.2(SD:4.3)

BMI = body-mass index, SD = standard deviation, MPD = main pancreatic duct, FE-1 = Fecal elastase-1

* median with 25th and 75th percentiles, Mod/Sev = Moderate/Severe.

Table 2
 T_1 Relaxation Times and Stiffness of the Pancreas of Controls and Two Chronic Pancreatitis (CP) Groups

	T_1 relaxation time (ms)				Stiffness (kPa)			
	Control	Mild CP	Mod/Sev CP P(n=16)	P [#]	Control	Mild CP	Mod/Sev CP P(n=16)	P [#]
Mean	865 (220)	1075 (221)	1350 (139)	<0.001	1.21 (0.13)	1.50 (0.15)	1.90 (0.16)	<0.001
Head	844 (216)	1051 (190)	1317 (149)	<0.001	1.18 (0.18)	1.48 (0.18)	1.85 (0.16)	<0.001
Body	884 (242)	1119 (260)	1373 (124)	<0.001	1.23 (0.16)	1.53 (0.18)	1.94 (0.16)	<0.001
Tail	866 (266)	1055 (284)	1358 (154)	<0.001	1.22 (0.15)	1.49 (0.18)	1.91 (0.17)	<0.001
P [*]	0.814	0.452	0.489		0.698	0.736	0.287	

Data are expressed as mean (standard deviation)

* P was calculated by using the Friedman test, denoting differences of the characteristics among different subregions in each group

P was calculated by using the Kruskal-Wallis test, denoting differences of characteristics among different groups.

Table 3Diagnostic Performance of T_1 Relaxation Time and Stiffness for Diagnosing Different Grades of Chronic Pancreatitis (CP)

Parameters	Grade of CP	Cut-off	AUC [% (95%CI)]	Sensitivity [% (95%CI)]	Specificity [% (95%CI)]	PPV [% (95%CI)]	NPV [% (95%CI)]
T_1 relaxation time (ms)	Normal vs Mild CP	>908.4	0.751 (0.629–0.874)	80.0 (61.4–92.3)	68.6 (50.7–83.1)	68.6 (50.7–83.1)	80.0 (61.4–92.3)
Stiffness (kPa)		>1.34	0.928 (0.871–0.985)	83.3 (65.3–94.4)	85.7 (69.7–95.2)	83.3 (65.3–94.4)	85.7 (69.7–95.2)
T_1 relaxation time (ms)	Normal vs Any CP	>908.4	0.822 (0.729–0.916)	87.0 (73.7–95.1)	68.6 (50.7–83.1)	78.4 (64.7–88.7)	80.0 (61.4–92.3)
Stiffness (kPa)		>1.34	0.953 (0.914–0.991)	89.1 (76.4–96.4)	85.7 (69.7–95.2)	89.1 (76.4–96.4)	85.7 (69.7–95.2)
T_1 relaxation time (ms)	Normal/Mild CP vs Mod/Sev CP	>1131.6	0.910 (0.862–0.984)	93.8 (69.8–99.8)	75.4 (63.1–85.2)	48.4 (30.2–66.9)	98.0 (89.4–99.9)
Stiffness (kPa)		>1.61	0.981 (0.957–1.000)	100.0 (79.4–100.0)	87.7 (77.2–94.5)	66.7 (44.7–84.4)	100.0 (93.7–100.0)

AUC = Area under curve, PPV = Positive predictive value, NPV = Negative predictive value, Mod/Sev = moderate and severe.

Table 4

Univariate and Multivariate Analysis for the Occurrence of Mild CP

Variable	Univariate analysis		Multivariate analysis	
	Odds ratio (95%CI)	P	Odds ratio(95%CI)	P
MPD diameter(>3mm)	3.50(1.17–10.47)	0.025	3.45(0.68–17.54)	0.136
T_1 relaxation time(>908.4ms)	8.73(2.78–27.41)	<0.001	5.41 (1.24–23.58)	0.025
Stiffness(>1.34kPa)	30.00(7.79–115.54)	<0.001	21.00 (4.88–90.27)	<0.001
Age(>61years)	2.80(0.89–8.84)	0.080	---	---
Gender(Female)	0.67(0.25–1.79)	0.667	---	---
BMI(>24.95Kg/M ²)	3.32 (0.90–12.21)	0.071	---	---
Lipase level (>101.3U/L)	3.88(0.93–16.27)	0.064	---	---
Amylase level (>34.0U/L)	2.77(0.94–8.12)	0.064	---	---
FE-1 (<200µg/g)	1.44(0.49–4.22)	0.502	---	---
Thickness(16.41mm)	2.58(0.89–7.52)	0.082	---	---

The values in bold denote statistical significance, BMI = body-mass index, MPD = main pancreatic duct, FE-1 = Fecal elastase-1.

Table 5

Univariate and Multivariate Analysis for the Occurrence of CP

Variable	Univariate analysis		Multivariate analysis	
	Odds ratio (95%CI)	P	Odds ratio(95%CI)	P
MPD diameter (>3mm)	6.22(2.25–17.22)	<0.001	4.49(0.90–22.35)	0.067
T ₁ relaxation time(>908.4ms)	14.55(4.77–44.40)	<0.001	5.69(1.26–25.64)	0.024
Stiffness(>1.34kPa)	49.20(13.06–185.29)	<0.001	26.15(5.66–120.92)	<0.001
Age(>61years)	2.58(0.89–7.50)	0.082	---	---
Gender(Female)	0.67(0.27–1.62)	0.372	---	---
BMI(>24.95Kg/M ²)	2.74(0.80–9.38)	0.109	---	---
Lipase level(>62.5U/L)	2.45(0.99–6.07)	0.052	---	---
Amylase level(>38.0U/L)	2.41(0.98–5.93)	0.057	---	---
FE-1 (<200µg/g)	2.65(1.02–6.87)	0.045	2.52(0.47–13.71)	0.284
Thickness(16.92mm)	3.44(1.32–8.93)	0.011	1.20(0.24–5.99)	0.823

The values in bold denote statistical significance, BMI = body-mass index, MPD = main pancreatic duct, FE-1 = Fecal elastase-1.