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Effectiveness of Shear Wave Elastography in the diagnosis of acute pancreatitis on admission

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Abstract

Aim: We aimed to investigate the effectiveness of shear wave elastography (SWE) in the diagnosis of acute pancreatitis (AP). **Material and methods:** The pancreatic parenchyma of 50 patients whose clinical and laboratory findings were indicative of AP and of 70 healthy, asymptomatic volunteer participants with normal laboratory values was examined using SWE. Computed tomography was performed in all patients with AP on admission. Elastographic measurements were performed by manually drawing the contours of the pancreatic parenchyma using the free region of interest. The quantitative SWE values (meters/second [m/s], kilopascal [kPa]) of the patients and asymptomatic volunteers group were compared. **Results:** The mean SWE value of the pancreatic parenchyma was 2.60 ± 1.63 m/s in the asymptomatic volunteers and 3.48 ± 0.52 m/s in patients with AP, with a statistically significant difference ($p<0.001$, $t=-3.685$). The mean SWE value of the pancreatic parenchyma was 23.77±6.72 kPa in the asymptomatic volunteers and 45.71 ± 10.72 kPa in patients with AP, indicating a significant difference ($p<0.001$, $t=-3.685$). AP can be diagnosed with a sensitivity and specificity of 98.0% when 29.45 kPa was designated as cut-off value and with a 96.0% sensitivity and 98.3% specificity when 2.77 m/s was designated as the cut-off value. The superiority of SWE was found over B-mode US and CECT in the diagnosis of AP on admission.

Conclusion: SWE can be used as an effective imaging method with high sensitivity and specificity for the diagnosis of AP. It may be used as an important imaging method to assist in the diagnosis of AP especially when B-mode US and CECT findings are normal.

Keywords: acute pancreatitis; early diagnosis; shear wave elastography; ultrasonography

Introduction

Acute pancreatitis (AP) is characterized by inflammation of the pancreas. It is one of the most frequently encountered gastroenterological diseases, with a varying incidence between 4.9 and 73.4 cases per 100,000 worldwide [1]. According to the diagnostic criteria [2,3], patients who have 2 of the following 3 manifestations are diagnosed with AP: characteristic upper abdominal pain, elevated levels of pancreatic enzymes, and ultrasonography (US), computed tomography (CT), or magnetic resonance imaging (MRI) findings suggesting AP.

Contrast-enhanced CT (CECT) shows limited ability to detect early parenchymal changes; thus, pancreatic parenchyma can appear completely normal on CECT in patients with AP [4-6]. MRI is beneficial for the imaging of patients with iodine allergies and for evaluating the biliary tract, including the bile ducts and pancreatic duct [7]. However, the clinical use of MRI is limited because it is expensive and time-consuming. US is still the preferred first-line imaging modality used for the diagnosis of AP. Although conventional brightness (B)-mode US

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provides important information for revealing biliary etiologies of AP [7], it has a limited role in revealing early pancreatic parenchymal damage during diagnosis. Typical sonographic features of AP can be seen in a small number of patients [8]. Serum amylase and lipase levels are the most commonly requested laboratory tests used in the emergency department for the diagnosis of AP in patients admitted to the hospital with epigastric pain [9,10]. However, elevated levels are not detected in a significant number of patients with AP, which accounts for 20%, in those with conditions such as chronic pancreatitis, hypertriglyceridemia-induced pancreatitis, relapsing pancreatitis, alcoholic pancreatitis, and delayed-presentation pancreatitis [11,12].

Because early diagnosis and treatment are important in improving patient outcomes, reliable radiologic techniques are required for the diagnosis of AP on admission. Shear wave elastography (SWE) is a new imaging technology that is real-time, non-invasive, and reproducible. It allows the quantitative assessments of tissues according to their stiffness and offers information correlated to histological changes in tissues [13-15]. With SWE, the stiffness can be evaluated without any reference area; therefore, it is suitable for the diagnosis of stiffness in a variety of diseases [15]. The basic principle of SWE involves the application of a US probe that automatically produces an acoustic push pulse to generate shear waves; thus, the stiffness of the tissue is assessed based on the detected shear velocity. The propagation velocity of shear waves in tissue depends on the consistency of the tissue (i.e., slower propagation occurs through softer tissue [normal pancreas]; faster occurs through harder tissue [inflamed, stiffer pancreas]). The speed of the shear wave is measured in both meters/second (m/s) and kilopascal (kPa) [13-17]. Detection of an increase in pancreatic tissue stiffness with SWE may increase the sensitivity of B-mode US for the early diagnosis of AP.

In the early period diagnosis of the AP, US and CECT are inadequate, their sensitivity and specificity are low, and it is probable that pancreatic parenchyma can appear completely normal [4,7]. There are limited studies showing that the diagnosis of the AP can be made in the early period by SWE. In these previous studies, the SWE measurements were obtained with a limited ROI, without possibility to change their dimensions [8,18]. In our study, we used the average SWE values obtained by drawing the whole of the pancreas head and body parts with the free ROI. The aim of this study was to determine the effectiveness of SWE in the diagnosis of AP using free ROI (drawing contour of pancreas) and to investigate the usefulness of SWE as a reliable radiologic technique needed for early diagnosis of the AP.

Material and methods

Fifty consecutive patients who had acute epigastric pain (i.e., the symptomatic group) admitted to the emergency department of our hospital between December 2016 and July 2017 were included in our prospective study. In this group, AP was diagnosed with at least one of the following findings accompanying epigastric pain: a) 3-fold increase in serum amylase or lipase values or b) imaging findings of AP on CECT or US. Seventy healthy volunteers were included in the control group. This group was completely asymptomatic, and B-mode sonographic imaging finding of the pancreas was normal (i.e., the asymptomatic volunteer group). The study was approved by the local research ethics committee. All patients and asymptomatic volunteers were informed of the study protocol and the requirements for the study participation, and written informed consent was obtained before the procedure.

Patients with chronic pancreatitis, necrotizing pancreatitis, malignancy, chronic liver disease, ascites, solid or cystic pancreatic mass, and pancreatitis located in the tail of the pancreas, those who were pregnant or had a history of pancreatitis, those in whom visualization of the pancreas on B-mode sonography was difficult, and those who were considered obese (body mass index [BMI] >35 kg/m^2) were excluded.

On admission, laboratory tests were performed in symptomatic patients with AP and all asymptomatic volunteers. Ranson scores were also calculated. The pancreas of all patients and asymptomatic volunteers was assessed with B-mode US and SWE imaging. All B-mode US and SWE examinations were performed by a radiologist with 12 years of experience in B-mode sonography and 2 years of experience in the SWE technique (M.S.D). B-mode US and SWE examinations were performed with a TOSHIBA Aplio 500 convex transducer (1.9-6 MHz; Toshiba Medical Systems Corporation, Tokyo, Japan).

B-mode US examination of the pancreas was performed in the supine position in transverse, longitudinal, and angled oblique scanning. When the epigastric area of the pancreatic tail could not be adequately visualized on transverse plane US, these patients were screened using the spleen as an acoustic window in the left lateral plane. Pancreatic echoes, parenchymal thickness, the pancreatic duct, and peripancreatic areas were evaluated. B-mode US was also performed to detect possible gallbladder and common bile duct stones.

The normal and abnormal US findings of the pancreas in asymptomatic volunteers and AP patients were established based on the previous published criteria [19,20]. In the AP group, increased pancreatic volume, decreased

echogenicity of the pancreatic parenchyma, heterogeneous appearance of the parenchyma, focal intrapancreatic echo changes, peripancreatic fluid, and heterogeneous echogenicity in peripancreatic fat stranding (i.e., inflammatory changes in soft tissues around the pancreas) were investigated. The presence of gallbladder stones, biliary tract stones, and bile duct dilatation was also noted.

SWE was performed after the B-mode US. During the SWE examination, elastographic images of the pancreas were obtained during a very light contact with the skin of the US probe. Each patient was examined under standard circumstances. While breathing normally, the patients were asked to inspire and then hold their breath for 5 seconds. Then, the patients were instructed to relax and continuously expire for 5 seconds until an SWE image was obtained. Consequently, these maneuvers avoided the alterations in abdominal pressure that can occur during deep inspiration and expiration. Using SWE, it is possible to select a continuous or one-shot scan. We selected the one-shot scan in order to obtain a higher image quality. During the 5 seconds required to stabilize the SWE, the images were captured and saved. Three elastographic images of the pancreas were obtained. In patients with insufficient cooperation more than three measurements were performed. Tissue stiffness elasticity measurements were performed using a color-coded map in the region of interest (ROI), which represented Young's modulus in kPa at each pixel. Tissue elasticity was characterized using a color range from dark blue (lowest stiffness) to red (highest stiffness) (0–70 kPa by default). After collecting the data, the elasticity values served as the mean stiffness (E-mean) and standard deviation (SD) in kPa and m/s. Elastic value E (kPa) is calculated using the equation $E = 3\rho(m/s)^2$. Here, m/s refers to the shear wave propagation velocity, and ρ refers to the tissue density (with approximated value in human body as 1 g/cm³) [21]. Quantitative elasticity values were measured in each patient and asymptomatic volunteer by manually drawing the contours of the entire head and corpus of the pancreas structure using the free ROI (fig 1), and the average values of three measurements were used.

After US examination, CECT was performed with a 64-detector row CT scanner (Brilliance CT system; Philips Healthcare, Cleveland, OH) without oral contrast agent in AP group, within the first 72 hours of admission. All patients received intravenous nonionic contrast medium (2 mL/kg; flow rate 3 mL/sec). Images were obtained with a 2-mm slice thickness. CT scans were reviewed on a CT workstation (Philips Extended Brilliance Workspace; Philips Healthcare) by two radiologists (7 years of experience [MS] and 6 years' experience [SA] in abdominal CT) who were blinded to the laboratory data and clinical course. The CT criteria for AP were as follows: an increase in the size of the pancreas, shaggy and irregular pancreatic contours, peripancreatic edema and fluid, hypo-enhancing heterogeneous parenchyma, and/or pancreatic necrosis. CT severity index (CTSI) was also calculated.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS, version 24, SPSS Inc., Chicago, IL, USA) program was used to perform the statistical analyses. The Kolmogorov–Smirnov test was used to test the normal distribution of continuous variables. Primarily, defini-

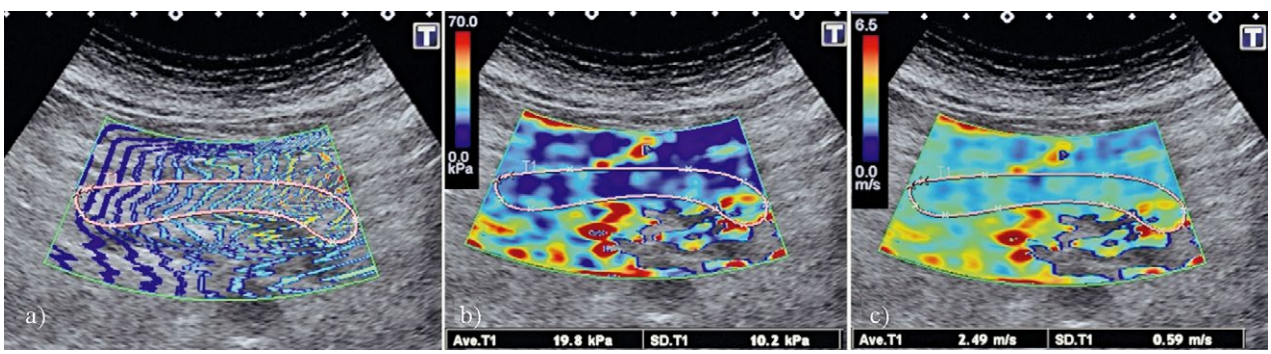

Fig 1. A 34-year-old asymptomatic woman with a normal pancreas. Quantitative elasticity values were measured by manually drawing the contours of the entire head and corpus of the pancreas structure, on the propagation mode, in the longest longitudinal plane, using the free ROI (a). The mean quantitative elasticity values were measured as 19.8 kPa (b) and 2.49 m/s (c).

Table I. The mean SWE values of the pancreatic parenchyma in patients with acute pancreatitis and asymptomatic volunteers

	Asymptomatic volunteers	**Patients with acute pancreatitis**	**p**
mean SWE (kPa)	23.77±6.72 (ranged 13.0-44.00)	45.71±10.72 (ranged 19.60-70.70)	p<0.001
mean SWE (m/s)	2.40±0.37 (ranged 1.58-3.26)	3.48±0.52 (ranged 2.40- .98)	p<0.001

tive statistics related to the variables were evaluated. Descriptive statistics were expressed as the mean, SD, frequency, and percentile. Student's *t*-test and the chi-square test were used to evaluate the differences between the two groups. Pearson correlation analysis was used to compare the SWE values, Ranson scores, and CTSI. A p-value of less than 0.05 was considered statistically significant. Receiver operating characteristic (ROC) curve analysis was used to determine the best cut-off value and associated sensitivity and specificity for the SWE values of the patients with AP and asymptomatic volunteers.

Results

The symptomatic group included 29 males (58%), age range 18-84 years (mean age 52.86±18.96 years), and the asymptomatic volunteers group included 33 males (47.1%), age range 18-81 years (mean age 50.28±16.85 years). There were no statistically significant differences between the two groups regarding age, gender, and BMI ($p>0.05$).

The mean SWE values of the pancreatic parenchyma in patients with AP and asymptomatic volunteers are summarized in table I. There was a statistically significant difference with respect to SWE values between the two groups ($p<0.001$).

The cut-off values of SWE for AP sensitivity and specificity are shown in table II. ROC curve analysis of SWE values of AP is shown in figure 2.

Biliary pancreatitis was diagnosed in 18 patients (36%). In these patients, a gallbladder stone or common bile duct stone was detected.

At admission of the 50 patients with AP only 22 had US findings supporting AP. In 10 of the 28 patients with normal US pancreas, CECT found modifications specific for AP. In the rest of 18 patients, the diagnosis of AP was established based on clinical and laboratory findings. The average SWE values in the group of AP patients with normal US and CECT patients were 3.28±0.38 m/s and 41.67±9.65 kPa significant higher comparing with the normal group ($p<0.001$) (fig 3).

On CECT, findings that supported AP were present in 32 patients (diffuse interstitial edematous AP in 26 patients and focal interstitial AP in 6 patients). The SWE numerical values of the 6 patients with focal interstitial AP were 3.58±0.62 m/s and 45.55±10.04 kPa (fig 4). There was less than a threefold increase in amylase and lipase values on admission in 2 of the symptomatic patients, findings that supported AP were observed on CECT. In these 2 patients, the mean SWE values were 2.88 m/s and 31.2 kPa. Regarding the cut-off values determined, SWE could diagnose AP on admission in these patients with focal interstitial AP and normo-amylasemic patients.

The mean Ranson score and mean CTSI were 2.46±1.76 and 1.4±1.45, respectively, in the AP group. There was a significant correlation between SWE values measured in kPa and CTSI ($r=0.310$, $p=0.028$). No correlations were found between the SWE values measurement in m/s and the Ranson score ($r=-0.026$, $p=0.858$),

Table II. The cut-off values of SWE (m/s and kPa) for acute pancreatitis sensitivity and specificity

Cut-off value	Sensitivity (%)	Specificity (%)
29.45 kPa	98.0	98.0
2.77 m/s	96.0	98.3

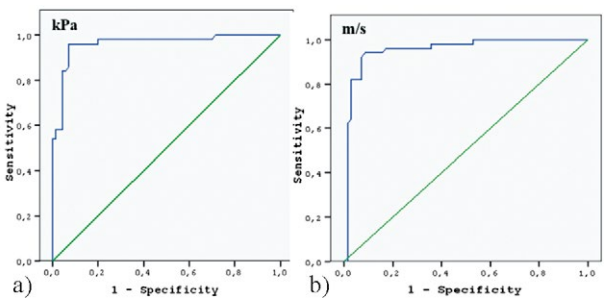

Fig 2. The ROC curve analysis of SWE values of acute pancreatitis and the best cut of value for kPa (a, b) and m/s (c, d).

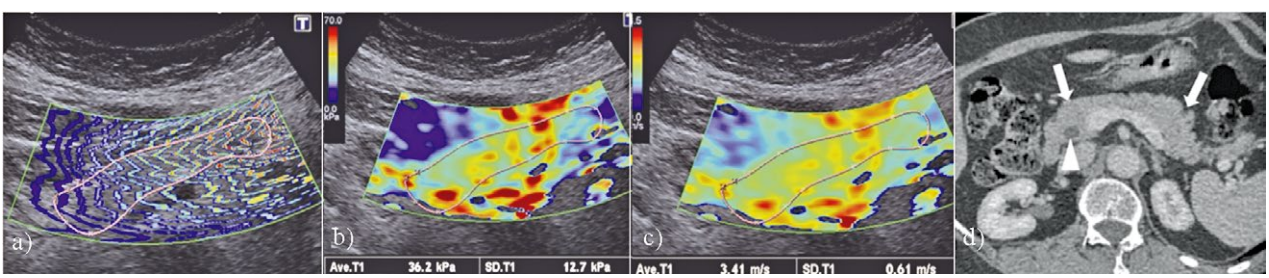

Fig 3. A 60-year-old symptomatic woman with biliary acute pancreatitis (characteristic upper abdominal pain and more than a threefold increase in serum amylase and lipase values on admission) and normal B-mode ultrasonography and contrast enhanced computed tomography: a) quantitative elasticity measurement; the mean quantitative elasticity values were increased – 36.2 kPa (b) and 3,41 m/s (c). Dilatation (arrow head) and a milimetric stone in the distal end of common bile duct was found (d).

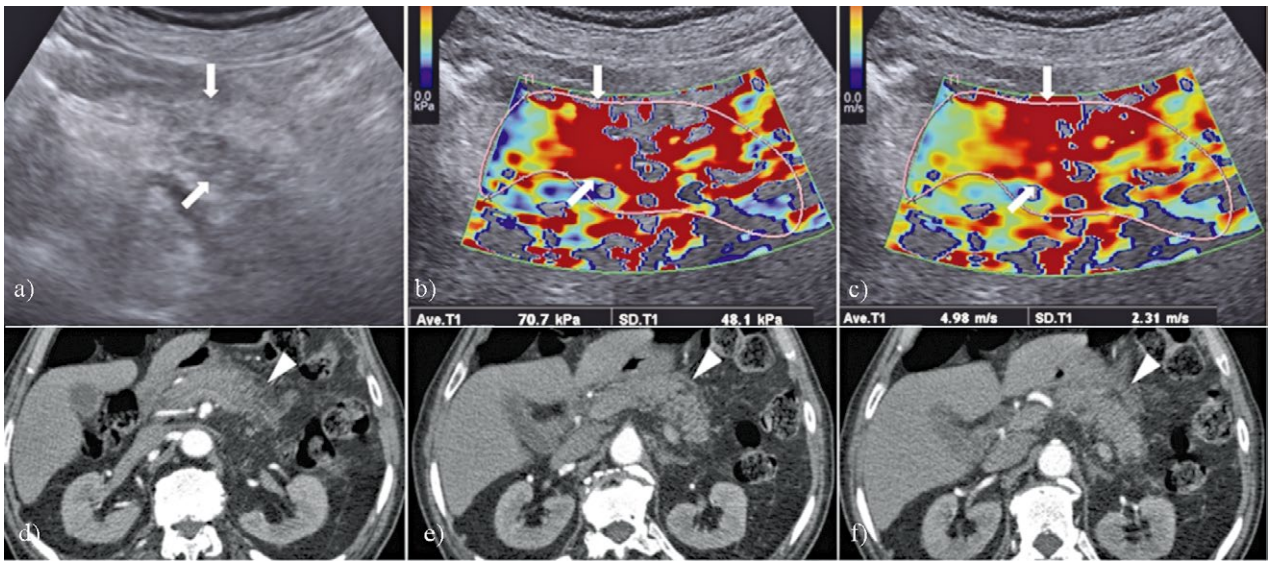

Fig 4. A 80-year-old symptomatic man with acute focal interstitial edematous pancreatitis. On B-mode ultrasound examination observed focal hypoechoic areas (arrows) in the pancreatic corpus (a). Quantitative elasticity values was increased: (70.7 kPa (b) and 4,98 m/s (c). On contrast enhanced computed tomography in the axial plane (d, e, f) there was a slight increase in the size of the pancreas, shaggy and irregular pancreatic contours, peripancreatic edema and fluid (arrow head).

SWE values measurement in m/s and CTSI (r=0.219, p=0.127), and the SWE values measurement in kPa and the Ranson score (r=-0.027, p=0.852).

Discussions

The early diagnosis of morphologic changes in the pancreas parenchyma is important in the management of AP. Abdominal imaging may be useful in detecting AP in patients with atypical presentations [3,22]. Contributions of B-mode US are generally limited in demonstrating AP, with sensitivity of B-mode US having been reported as 50% in diagnosing AP [23,24]. As the sensitivity of B-mode US in detecting AP is low, CECT is generally preferred [25]. However, CECT has limited ability to evidence the inflammatory parenchymal changes occurring during the early period of AP, and the CECT findings on admission may be completely normal in 30–40% of patients [4-6]. It is believed that many normo-amylasemic patients with AP confined to the mild-to-moderate clinical group may be overlooked or misdiagnosed because the pancreatic parenchyma is visualized as normal on B-mode US and CECT examinations [18,26].

When the diagnosis of AP is made early and treatment is subsequently initiated, it is of great benefit to patients. Therefore, reliable radiologic techniques are necessary for early detection of AP, especially in groups of patients with normal B-mode US, CECT findings, atypical abdominal pain, and normoamylasemic AP on admission. We determined that the SWE values were significantly higher in the patient group diagnosed with AP than those in the asymptomatic volunteer group. Early period diagnosis of AP was achieved with US in 44% of the patients, and with CECT in 68%. Our results demonstrate a high success rate (over 96.0% sensitivity and specificity) of SWE for diagnosing AP and the superiority of this method over B-mode US and CECT. When SWE is combined with B-mode US, a typical first-line modality with low sensitivity in the diagnosis of AP, AP may be diagnosed with high sensitivity and specificity during its early onset.

In the literature, there are limited studies regarding the use of SWE in the diagnosis of AP. Göya et al reported that SWE differentiates AP from normal parenchyma with 100% sensitivity and 98% specificity when the cut-off value was determined as 1.63 m/s [8]. Mateen et al reported that the mean SWE value of normal peripancreatic soft tissue was approximately 1 m/s; however, if the mean SWE value of peripancreatic soft tissue was higher than 2.2 m/s, it was suggestive of AP [27]. In another study, no significant differences were determined in SWE values that were obtained for the patient group with AP and the asymptomatic volunteers group [28]. In these studies in the literature [8,28,29], only the m/s SWE numerical values were stated. Since both the m/s and kPa SWE values could be obtained using our US device, we measured both. We found a significant difference between the patients with AP and asymptomatic volunteers in both SWE numerical values, so we thought this finding improved the reliability of our results and

measurement technique. We found the mean SWE values in asymptomatic volunteers 23.77±6.72 kPa, 2.40±0.37 m/s and in patients with AP 45.71±10.72 kPa, 3.48± 0.52 m/s. According to our results the best cut-off values for diagnosing AP were 29.45 kPa and 2.77 m/s. The previous published SWE measurements were obtained from areas with a limited ROI in the shape of small squares whose sizes could not be changed, generally from the head, body, and tail [8,27-29]. The SWE values may considerably vary by using small squares ROI. We obtained higher SWE values because we used the average SWE values obtained by drawing the whole of the pancreas head and body parts with the free ROI. We think that, in comparison to other measurement techniques, ours is more reliable, because we obtained an average SWE value. Another reason for the higher values of SWE in our study compared to previous studies may be due to the different devices being used.

AP is divided into two subtypes: interstitial edematous and necrotizing pancreatitis. The majority (90–95%) of patients with AP have interstitial edematous pancreatitis, which responds rapidly to conservative treatment. In interstitial edematous pancreatitis, generally diffuse, focal infiltration occurs rarely in the pancreas because of inflammatory edema [2]. We think that, in comparison to other methods, the measurement method we used in this study may be more applicable in cases involving diffuse forms of interstitial edematous pancreatitis, which constitute the majority of AP cases. Also average SWE values were higher in 6 patients with focal interstitial pancreatitis findings in the pancreas head or body part on CECT than the values in the asymptomatic volunteers group. As diffuse and focal interstitial AP were diagnosed using the SWE, numerical values obtained from the whole pancreas parenchyma (affected or unaffected) can be used reliably. However, in patients with necrotizing pancreatitis, who constitute a small percentage of AP cases (5–10%), tissue losses appear to be caused by necrosis [2]. For this reason, lower SWE values are obtained [8]. Therefore, we did not include patients who were diagnosed with necrotizing pancreatitis on CECT.

It has been reported in many studies that CTSI is a more sensitive predictor than Ranson score in terms of showing the severity of AP [31]. According to our results, no correlation was found between m/s and the Ranson score, m/s and CTSI, and kPa and the Ranson score. However, we found a significant correlation between kPa and CTSI; therefore, it is possible to use the kPa values together with SWE in evaluating the severity of AP.

Our study has several limitations. For example, the quality of the images obtained with SWE depends on the operator's abilities. Furthermore, we only examined the pancreatic head and corpus because of the difficulty in visualizing the pancreatic tail in the absence of transducer compression. As necrotizing pancreatitis reduced the SWE values [8], we did not include it in our study. The relationship between SWE values and the severity of pancreatitis was not assessed in terms of morbidity and mortality. The pancreas is located deep inside the body in obese patients, SWE cannot be performed and also visualization of the pancreas on B-mode sonography was difficult without applying pressure by transducer, therefore we exclued patiens with BMI greater than 35.

Conclusion

SWE is an effective and reliable imaging method with excellent sensitivity and specificity values for the early diagnosis of AP. It may be used especially in patients who are normoamylasemic and who present with atypical abdominal pain as an important imaging method to assist in the diagnosis of AP when B-mode US and CECT findings are normal.

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Conflict of interest: none.

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