

The importance of acoustic radiation force impulse (ARFI) elastography in the diagnosis and clinical course of acute pancreatitis

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ABSTRACT

Background/Aims: Acute pancreatitis (AP) is characterized by acute inflammation of the pancreas and it has a highly variable clinical course. The aim of our study was to evaluate the value of acoustic radiation force impulse (ARFI) elastography in the diagnosis and clinical course of AP.

Materials and Methods: Consecutive patients with a diagnosis of AP (patients group) and healthy subject (control group) were prospectively enrolled to the study. Demographic features and clinical, laboratory, and radiological data were recorded. Virtual Touch Tissue Quantification (VTQ) was used to implement ARFI elastography. The tissue elasticity is proportional to the square of the wave velocity (SWV).

Results: A total of 108 patients (age, 57±1.8 y) and 79 healthy subjects (age, 53.6±1.81 y) were included in the study. There were 100 (92.5%) edematous and 8 (7.4%) necrotizing AP. The mean SWV was significantly higher in the patient group than in the control group (2.43±0.08 vs. 1.27±0.025 m/s, p<0.001). There was not significant difference between patient and control group regarding age and gender. SWV cutoff value of 1.63 m/s was associated with 100% sensitivity and 98% specificity for the diagnosis of AP. There was not significant difference between patients with and without complications and patients with edematous and necrotizing AP regarding mean SWV value. There was also not significant correlation between mean SWV value and age, mean length of hospital stay, and mean amylase level.

Conclusion: ARFI elastography may be a feasible method for the diagnosis of AP, but it has no value for the prediction of clinical course of AP.

Keywords: Acute pancreatitis, elasticity imaging techniques, diagnosis, prognosis

INTRODUCTION

Acute pancreatitis (AP) is characterized by acute inflammation of the pancreas. It has been associated with significant morbidity, mortality, and hospitalization costs (1-4). AP has variable clinical progression. Most of patients have mild and self-limited disease, but mortality rate of patients with infected necrosis and organ failure can reach up to 30% (4). Currently, treatment is symptomatic and supportive, since there is no specific curative therapy for AP. Severe AP requires intensive treatment in the specialized tertiary centers. On admission, it is difficult to predict clinical course and development of complications. A number of scoring systems and predictive markers were defined for early prediction of clinical course, local and systemic complications, and prognosis (5). But they are insufficiently sensitive, complicated, expensive, and not available soon enough or not available at all hospitals.

Acoustic radiation force impulse (ARFI) imaging is an ultrasound-based imaging modality for the evaluation of tissue stiffness, which consists of Virtual Touch Tissue Imaging (VTI) and Virtual Touch Tissue Quantification (VTQ). The VTI technique is a qualitative method for displaying a color-coded elastogram of comparative tissue stiffness. VTQ is a quantitative method that has been used for diagnosis of chronic liver disease and space-occupying lesions in the liver, breast, and thyroid. ARFI elastography is used for the diagnosis of chronic pancreatitis, pancreatic lesions, inflammatory pancreatic disease, and AP (6-10).

The aim of this study was to determine the value of ARFI elastography in the diagnosis and the prediction of clinical course of AP.

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MATERIALS AND METHODS

Patients

Consecutive patients older than 18 y admitted to our clinic with a diagnosis of AP were enrolled to the study between January 2015 and February 2016. Among patients who were admitted more than once to our clinic, only data from the first admission were included. Diagnosis of AP was made if the patients had two of the following criteria: (an) abdominal pain characteristic of AP, (b) serum amylase and/or lipase levels three or more times the upper limit of normal, or (c) trans-abdominal ultrasound and/or a contrast-enhanced computed tomography (CECT) scan imaging within the first 7 days of hospitalization demonstrating characteristic changes of AP. For all the enrolled patients, demographic features; clinical, laboratory, and radiological data, etiology of AP; duration of hospitalization (day); presence of organ failure; local and systemic complications; interventions; and mortality were recorded.

Type of AP, organ failure, and local complications were defined according to Revised Atlanta Classification (11). Organ failure was assessed during the first 7 days of hospitalizations on the basis of the most extreme laboratory value or clinical measurement in each 24-h period. Transient organ failure was defined as duration lasting 48 h or less, whereas persistent organ failure was greater than 48 h. Percutaneous and endoscopic drainage of fluid collection, surgical, and endoscopic necrosectomy were defined as interventions. No interventions were performed in the conservative management group. Patients without organ failure or complications were followed until 2 weeks after discharge and those with organ failure and/or complications were followed until complete recovery or death.

All patients underwent trans-abdominal ultrasonography (USG) examination during admission to our clinic. Patients who have ongoing severe abdominal pain for 72 h after admission and/or patients who have peripancreatic and intra-abdominal fluid collection during initial USG examination underwent CECT examination. All patients who did not have CECT examination underwent control USG examination 2 weeks after discharge for excluding the development of possible local complications after initial USG. USG and/or CECT examination were performed repeatedly in patients with necrotizing AP and complications when it is necessary. Radiological imaging was reviewed by an experienced abdominal radiologists.

Patients who had only USG examination were presumed to have edematous AP and no local complications. AP was considered to be associated with alcohol if the patient consumed five or more alcoholic drinks per day. Necrosis was defined as lack of enhancement of pancreatic parenchyma and/or heterogeneous and non-liquid density of varying degrees on CECT. Infected necrosis was defined as any infection of necrotic pancreatic parenchyma or peripancreatic collections. Confirmation of infected necrosis was done by CECT evidence of free air within the necrotic collections or by culture of percutaneous fine-needle aspirates or aspiration of pus.

Control group

Healthy adult subjects were included in the control group during study period. Control group was composed of patients who were evaluated in our outpatients clinic for annual check-up and our hospital staff. Subjects were excluded from the control group if they had a history acute or chronic pancreatitis and pancreatic surgery or obesity (body mass index >30 kg/m²). All subjects had normal vital signs, routine blood and urine tests, blood electrolytes, lipase and amylase levels, electrocardiographic findings, hepatic and renal function test results, and pancreatic trans-abdominal B-mode sonographic findings.

ARFI elastography

An ACUSON S2000 ultrasound system (Siemens Medical Solutions) and a 1- to 4- MHz convex probe were used to obtain B-mode sonograms and ARFI elastogram. B-mode sonograms and ARFI elastography were performed by a radiologist (C.G.) who was experienced in B-mode sonograms and in the ARFI technique. VTI and VTQ were used to implement ARFI elastography. Details of the technical description and examination procedure have been previously described in our study (10). After conventional B-mode pancreatic ultrasonography, region of interest at a size of 1-cm axial by 6-mm width was set in the tail, body, and head of pancreas, obtaining three measurements of SWV in each part of the pancreas. Total nine measurements of SWV were averaged and used in the analysis. ARFI elastography examination was performed in the 24 h after admission to our clinic and it was not repeated during clinical follow-up.

Our study protocol was prepared according to the ethical guidelines of Helsinki Declaration and was approved by the Ethics Review Board of Dicle University School of Medicine.

Statistical analysis

Descriptive statistic was used for numerical and non-numerical values. Results are expressed as mean±standard error (SE) (range) or number (proportion) of patients. Student T test and Mann-Whitney U test were used for comparison of numerical values. Chi-square test was used for comparison of non-numerical values. The correlation between two numerical values was tested by Pearson and Spearman tests. p values were considered statistically significant at $p \leq 0.05$. Receiver operating characteristic curve analysis was used to determine the cutoff point and associated sensitivity and specificity for the SWV values that were obtained from the patient and control groups.

RESULTS

A total of 148 patients with AP were admitted to our clinic during study period. A total of 40 patients were excluded from the study. The reasons for exclusion of these patients were recurrent AP in eight patients and non-availability of elastography (not performed) owing to absence of operator during admission of patients in 32 patients. A total of 108 patients (age, 57 ± 1.8 y (range, 19-90 y), 44 men and 64 women) were included in the study. Table 1 shows the laboratory findings, and Table 2 shows the clinical features of patients group. The etiology of AP was gallstones in 79 (73%) patients, idiopathic in 24 (22%), and hypertriglyceridemia in 5 (4.6%) patients. As expected, patients with biliary AP had high serum transaminase level, and patients with AP caused by hypertriglyceridemia had high triglyceride and relatively low amylase level (data not shown). Mean SWV was 2.43 ± 0.08 m/s (range, 1.57-4.50 m/s) in the patient group.

A total of 100 (92.5%) patients were accepted as edematous AP and 8 (7.4%) were accepted as necrotizing AP. A total of 77 patients were followed by only USG examination. All those patients had edematous pancreatitis and did not have any complications during clinical follow-up. CECT was performed in 31 patients. Pancreatic and/or peripancreatic necrosis were identified in eight (7.4%) patients. Necrosis was containing more than 50% of pancreas three patients, between 30% and 50% in two patients, and less than 30% in three patients. Local complications were developed in 16 patients. Acute fluid collection was identified in 10 patients with edematous AP. Complete resolution was observed in eight of them and pseudocyst was developed in two patients. Acute necrotic collection was observed in six patients, and acute

Table 1. Laboratory features of patients with acute pancreatitis during admission to our clinic

Parameter	Mean±SE (range)
Amylase (U/L)	1670±110 (341-3010)
Lipase (U/L)	562±69 (14-1662)
ALT (U/L)	227±27 (7-1064)
AST (U/L)	235±28 (13-1257)
ALP (U/L)	209±26 (25-1263)
GGT (U/L)	430±45 (15-1543)
Total bilirubin (mg/dL)	2.27±0.29 (0.1-12)
BUN mg/dL)	35±2.05 (13-90)
Creatinin (mg/dL)	0.79±0.04 (0.3-3.3)
Albumin (g/dL)	3.5±0.07 (2-5)
Glucose (mg/dL)	149±9.35 (74-412)
LDH (U/L)	460±30 (110-1391)
Triglyceride (mg/dL)	268±136 (31-8000)
Calcium (mg/dL)	8.7±0.11 (4.5-10)
Hemoglobin (g/dL)	13.5±0.18 (10.8-17.2)
WBC (n/mm ³)	13.510±4150(4.500-26.100)

ALT: alanin aminotransferase; AST: aspartat aminotransferase; ALP: alkaline phosphatase; GGT gama-glutamyl transferase; BUN: blood urea nitrogen; LDH: lactate dehydrogenase; WBC: white blood cell

Table 2. Clinical features of patients

	No of patients (%)
Type of acute pancreatitis	
Oedematous	100 (92.5)
Necrotizing	8 (7.4)
Local complications	
Acute fluid collection	10 (9.2)
Pseudocysts	2 (1.8)
Acute necrotic collection	6 (5.7)
Walled-off necrosis	6 (5.7)
Organ failure	
Single	4 (3.7)
Multiple	1 (0.9)
Transient	3 (2.7)
Persistent	2 (1.8)
Etiology	
Gallstones	79 (73.1)
Idiopathic	24 (22.2)
Hypertriglyceridemia	5 (4.6)
Outcomes of patients	
Duration of hospital stay (days)	7.5±0.5
In hospital death	1 (0.9)

necrotic collection was progressed to walled-off necrosis in all these patients. Ultrasound-guided percutaneous drainage was performed in three patients with walled-off necrosis. Organ failure was developed in five patients: three patients had single and transient organ failure (renal failure in all), one patient had single and permanent organ failure (renal), and one patient had multiple and permanent organ failure. A female patient with necrotizing AP induced by hypertriglyceridemia and multiple and permanent organ failure died on the seventh day of hospital admission.

Table 3 shows characteristics of patients with and without complications. There was not statistically significant difference between patients with and without complications regarding mean SWV value and amylase level. Patients with complications were younger than patients without complication (40.7 ± 4.5 vs. 60.2 ± 1.8 y, $p<0.001$), and mean length of hospital stay was longer in patients with complication than in patients without complications (12.3 ± 1.5 vs. 6.5 ± 0.2 d, $p<0.001$). There was not statistically significant correlation between mean SWV value and age ($p=0.352$, $r=0.090$), mean length of hospital stay ($p=0.597$, $r=0.52$), mean amylase level ($p=0.318$, $r=0.97$), and mean white blood cell count ($p=0.054$, $r=0.194$). There was not significant difference between patients

Table 3. Characteristics of patients with and without complications

Parameter	Complication (+) (n=16) (mean±SD)	Complication (-) (n=92) (mean±SD)	p
Age (year)	40.7±4.5	60.2±1.8	<0.001
Duration of hospital stay (day)	12.3±1.5	6.5±0.2	<0.001
Amylase (U/L)	1456±213	1700±84	0.386
SWV (m/s)	2.70±0.247	2.36±0.63	0.151

SWV: square of the wave velocity

Table 4. Comparison of the patients and the control group

Parameter	Acute pancreatitis (n=108)	Control (n=78)	p
Age (year) (mean±SD)	57.8±1.82	53.6±1.81	0.101
Gender (Male/female)	44/64	33/45	0.503
SWV (m/s) (mean±SD)	2.40±0.063	1.27±0.025	<0.001

SWV: square of the wave velocity

with edematous and necrotizing AP regarding mean SWV value (2.80 ± 0.354 vs. 2.39 ± 0.063 m/s, $p=0.361$).

A total of 79 healthy persons (age, 53.6 ± 1.81 y (range, 21-82 y), 33 men and 46 women) were included in the study. Mean SWV in control group was 1.27 ± 0.025 m/s (range, 0.6-1.63 m/s).

Table 4 shows some features of patient and control groups. There was not statistically significant difference between patient and control group regarding age ($p=0.102$) and gender ($p=0.503$). The mean SWV of patients group was significantly higher than mean SWV value of the control group (2.43 ± 0.08 vs. 1.27 ± 0.025 m/s, $p<0.001$). SWV cutoff value of 1.63 m/s was associated with 100% sensitivity and 98% specificity for the diagnosis of AP.

DISCUSSION

In this prospective study, we evaluated the feasibility of ARFI technique in the diagnosis and prediction of clinical course of AP. We have found that ARFI technique has a high sensitivity and high specificity for the diagnosis of AP, but it cannot differentiate between edematous and necrotizing AP and it does not have any predictive value for the clinical course of AP.

Abdominal ultrasonography, CECT, magnetic resonance imaging (MRI), magnetic resonance cholangiopancreatography (MRCP), endoscopic ultrasonography (EUS), and endoscopic retrograde cholangiopancreatography (ERCP) have been used for the diagnosis of AP. All these diagnostic modalities have some advantages and disadvantages for the detection of AP and local complications (1). CECT is highly sensitive for detection of pancreatic and peripancreatic necrosis and local complication such as intra-abdominal fluid collection, walled-off necrosis, infected necrosis, and vascular thrombosis. Radiation-free MRI and MRCP can be time-consuming and expensive. MRI is not recommended for routine examinations of pancreas (12). Since EUS and ERCP are invasive, expensive, and have some complications, these procedures should be used for selected patients with AP. Compared to these diagnostic modalities, US imaging has distinct advantages in terms of ease of use, low cost, and lack of radiation. We found high sensitivity and specificity of ARFI in the diagnosis of AP. But this technique has some limitation in the diagnosis of AP. For example, difficult pancreatic examination in obese, thick/muscular, and

in non-cooperated patients, as well as in patients with abnormal localized and small pancreas and the presence of large-volume peripancreatic fluid collection are some of the limitations. The presence of large-volume air in gastrointestinal tract and pulsations from abdominal aorta and mesenteric and celiac arteries may interfere with measurement of elasticity by ARFI. Although AP is usually acute diffuse inflammation of pancreatic tissue, inflammation in pancreatic tissue in some patients with AP may be patchy or segmental. Acute segmental inflammation usually localized to the head of pancreas and occurs with gallstones (10,13,14). The severity of inflammation in the pancreatic tissue changes during clinical course. There is no information regarding the most reliable time for performing elastography for AP in the literature. Therefore, examination time after onset of AP and examined segment of pancreas by ARFI may change the SWV value. We measured tissue elasticity by ARFI within 24 h after admission to clinic but did not measure SWV in peripancreatic tissue. The measurement of tissue elasticity only at the beginning of illness and measurement of segmental pancreatic parenchymal elasticity are important drawbacks of ARFI technique.

ARFI elastography was used for the diagnosis of AP, chronic pancreatitis, and pancreatic cancer and for benign pancreatic lesions (6-10). Mateen et al. (8) have reported significantly higher SWV value in patients with AP than in healthy control (3.28 vs. 1.28 m/s, $p < 0.001$) and those with chronic pancreatitis (3.28 vs. 1.24, $p < 0.001$). Yashima et al. (6) have reported that SWV value in patients with chronic pancreatitis was significantly higher than that in healthy volunteers in head, body, and tail of the pancreas. Park et al. (7) have investigated ARFI elastography for the diagnosis of focal solid pancreatic lesions including 8 benign and 19 malignant lesions. They have not found significant differences between malignant and benign lesions regarding SWV value (3.3 vs. 2.4 m/s, $p = 0.101$) (7). In our previous study, we found significantly higher SWV in patients with AP than in healthy control (2.14 vs. 1.17 m/s, $p < 0.001$) (10). But Xie et al. (9) did not find significant difference between patients with AP and healthy control regarding SWV. We found that ARFI elastography is a reliable method for the diagnosis of AP, but it cannot differentiate between edematous and necrotizing AP.

Pancreatic and/or peripancreatic necrosis develop in about 5% to 10% patients with AP. Necrotizing AP usu-

ally manifests as necrosis involving both the pancreas and peripancreatic fat tissue and less commonly as necrosis of only the peripancreatic fat tissue. The findings of impaired pancreatic perfusion and necrosis evolve in a few days (5,15-17). At the beginning of the necrotizing AP, CECT may show patchy pattern perfusion in the pancreas, with variable attenuation. One week after the onset of AP, a non-enhancing area of pancreatic parenchyma in CECT examination should be considered as necrosis (3,18). Because of radiation exposure and potentially aggravation effect of contrast agent on pancreatic inflammation during 48 and 72 h after symptom onset, routine CECT examination is not recommended for all patients with AP except patients who are presumed to have necrotizing AP and/or any local complications (15). We performed initial CECT examination 72 h after admission to the clinic for detection of pancreatic and peripancreatic necrosis. We excluded the presence of possible local complications by control USG examination and complete clinical and laboratory improvement in patients who underwent only USG examination.

Although the diagnosis of AP, with the aid of typical clinical symptoms and signs, elevated serum amylase, lipase level, and/or radiological findings are relatively easy to confirm in almost all patients, it is difficult to anticipate the clinical course of patients with AP. AP has a variable clinical course. Complete recovery without permanent organ dysfunction occurs in most of patients with AP. But the mortality rate of patients with infected necrosis can reach up to 30% (19-21). Patients with non-complicated edematous AP can be treated in local hospitals, but patients with complicated necrotizing AP should be timely transferred to experienced reference centers (22). It has been shown that the early diagnosis of severe AP and adequate intensive therapy can decrease the mortality of AP (4). Several laboratory and clinical predictive markers and scoring systems were used in the clinical practice for early anticipation of clinical course and prognosis. Several scoring algorithms and classification systems were used for the classification of AP (1). We did not find any studies in the literature about ARFI elastography technique and the clinical course of AP. In this study, we used ARFI technique for the diagnosis and prediction of clinical course, development of complication, and mortality of AP. We found that ARFI technique is a reliable method for the diagnosis of AP, but it has no predictive value for the development of necrosis, local and systemic complication, and mortality in AP.

Our patients were divided into complicated and non-complicated AP group and edematous and necrotizing AP group on the basis of US and/or CECT findings. This may lead to some errors because fluid collection may be easily missed during US examination and necrotizing cases may have silent clinics and grouped as non-complicated AP. This is an important limitation of our study.

In conclusion, ARFI elastography may be a feasible method for the diagnosis of AP, but it is not seen as valuable method for differentiating between edematous and necrotizing AP and for the prediction of clinical course of AP.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of the Dicle University School of Medicine.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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