Evaluation of Ultrasound Based Point Shear Wave Elastography for Diagnosis of Inflammatory Pancreatic Diseases

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ABSTRACT

Introduction: A variety of imaging techniques exists for the diagnosis of pancreatic disorders. None of the broadly accepted diagnostic methods, uses elasticity as an indicator of tissue damage. A well-known fact is that pathological changes influence tissue stiffness and elasticity. US elastography in its different modalities has been widely used for evaluation and characterization of multiple abdominal structures. Point Shear Wave Elastography (pSWE) particularly has been reported to be highly effective in various clinical diagnostic applications. However, data on the role of pSWE in a deep-seated organ like pancreas is scarce.

Objective: To prospectively assess the diagnostic value of abdominal US elastography in the form of point shear wave elastography (pSWE) in characterizing and differentiating between normal pancreatic parenchyma and chronic pancreatitis. To establish a cut off value for the diagnosis of chronic pancreatitis. To investigate the influence of certain independent variables and the severity of pancreatitis on the acquired results.

Methods: The ultrasound based point Shear Wave Elastography (pSWE) imaging techniques were applied. A total of five measurements was obtained in each segment of the gland. The depth of region of interest (ROI) was also recorded. Design Prospective single-center study.

Results: The mean shear wave speed (SWS) values of the entire pancreatic parenchyma were 1.71m/s, 1.15m/s for the chronic pancreatitis and the normal pancreatic parenchyma respectively. With a cut off value of 1.43m/s, sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV) and accuracy (Ac) of 89.7%, 95.2%, 94.59%, 90.91% and 92.59% respectively were calculated for the diagnosis of chronic pancreatitis. Neither the independent variables researched, nor the severity of disease, defined according to the Cambridge score, proved to have statistically significant reflection on the SWS in patients with CP.

Conclusion: pSWE established considerably higher SWS in patients with chronic pancreatitis, therefore it may be successfully adopted as a diagnostic modality in patients with chronic inflammatory pancreatic disorders. External factors have minor effect on the results obtained, suggesting that the technique is highly objective. High SWS were obtained both in patients with discrete structural abnormalities (Cambridge 2) and advanced forms of pancreatitis (Cambridge 4), which points that pSWE may be utilized as differential diagnostic method in cases in which other imaging techniques provide equivocal and inconclusive results.

Keywords: Elastography, inflammatory pancreatic diseases, pancreas, ultrasound.
I. INTRODUCTION

The early diagnosis of chronic pancreatitis is a challenging goal, when understood as establishing the disease before the development of irreversible structural and functional parenchymal changes or at least before the manifestation of prominent symptoms. Diagnostic modalities used include contrast enhanced computed tomography (CECT), magnetic resonance cholangiopancreatography (MRCP), secretin-magnetic resonance cholangiopancreatography (SMRCP), ultrasound (US) B-mode, endoscopic ultrasonography (EUS), and endoscopic retrograde cholangiopancreatography (ERCP). All the techniques have variable sensitivity and specificity (Table I), with certain disadvantages.

| Imaging technique | Sensitivity (%) | Specificity (%) |
|-------------------|----------------|-----------------|
| CECT              | n/a            | n/a             |
| ERCP              | 70-80%         | 80-100%         |
| MRCP              | 88%            | 98%             |
| US                | 60-81%         | 70-97%          |
| EUS               | 80-100%        | 80-100%         |

CECT is the most common imaging technique used for diagnosis of CP. It has been established that structural abnormalities are present on CT in up to 93% of the patients with chronic pancreatitis [4]. However, the accuracy of the method regarding early forms of pancreatitis is unsatisfactory. Not to mention that CECT is associated with considerable radiation exposure, which makes it inconvenient for routine follow-up. MRI/smMRI is highly Sp and Se for the diagnosis of CP, since it allows evaluation of both pancreatic parenchyma and pancreatic ductal system. Unfortunately, MRI is expensive and time-consuming procedure, that requires significant expertise to interpret which makes it unsuitable for routine application. EUS shows high sensitivity and specificity, but its main disadvantage is the lack of sufficient interobserver agreement /IOA/ [5]. ERCP is both diagnostic and therapeutic for obstructive pancreatic pathology. Since the procedure is invasive and generally causes considerable postoperative complications, its usage as a diagnostic method currently is considered unjustified. US is cost-effective, repetitive, and readily available. Unfortunately, it suffers considerable limitations since it can’t always provide adequate visualization of the gland parenchyma. Its sensitivity and specificity don’t exceed 86% and 75% even in the variant of contrast enhanced US, which makes it inferior to both CT and MRI [6]. There’s a need for imaging modality which is cheap, non-invasive an easily reproducible and which at the same time enhances the diagnostic capabilities of conventional transabdominal US regarding the diagnosis of CP.

Early detection of morphological changes in the pancreatic parenchyma is crucial in the management CP. Since CP is generally defined as inflammatory cascade eventually leading to activation of the pancreatic stellate cells and development of fibrosis, undoubtedly this process would be associated with increase of the tissue stiffness [7]. Taking this fact into consideration, the diagnostic capabilities of the recently introduced US based tissue SWS measuring technologies, that differentiate tissues on the basis of their consistency, particularly point shear wave elastography, have been evaluated in this study. US elastography in its different modalities has been widely used for evaluation and characterization of multiple abdominal structures, mainly the liver. US elastography, in the form of transient elastography, pSWE, as well as real-time elastography [8]-[12] has proved reliable for evaluation of liver parenchyma. pSWE is part of the so-called dynamic methods of elastography, based on measuring the speed of generated shear waves, as an indicator of tissue stiffness [13]. Based on its physical nature, pSWE is thought to be considerably more objective than the quasistatic methods of elastography. Additionally, it allows measuring tissue stiffness in depth up to 8 cm [14], [15]. pSWE technique has been reported to be highly effective in various clinical diagnostic applications [16], [17]. However, studies on the role of pSWE in a deep-seated organ like pancreas are limited [18]-[22]. Little is known about the SWV values of normal pancreatic parenchyma and CP.

The aim of the present study is to prospectively assess the effectiveness of per-abdominal US elastography in the form of pSWE /ARFI-VTQ/ in characterizing and differentiating normal pancreas and CP.

II. MATERIALS AND METHODS

A. Study Population

Consecutive patients of chronic pancreatitis and ones who had no evidence of pancreatic disorder, admitted for diagnosis and/or treatment, at the Department of Gastroenterology at University Hospital Kaspela, Plovdiv, Bulgaria, during the period December 2020 to August 2021 were included. Patients in acute attack of chronic pancreatitis were excluded from the study.

1) Group 1

Chronic pancreatitis group Patients with imaging evidence of chronic pancreatitis, obtained through CECT and classified according to the Cambridge criteria (Cambridge II-IV) adapted for CT (Table II). Adequate visualization of the pancreatic parenchyma in conventional US B-mode. No clinical or biochemical data suggesting exacerbation of the chronic pancreatitis for at least three months prior the exam, but a history of at least three exacerbations in the past. Amylase and lipase levels lower than three times URL. The patients included in the study were followed up for at least three months after the US elastography was performed. In case establishing a definite diagnosis proved impossible, despite the imaging tests conducted, a histological examination through percutaneous Tru-cut biopsy was performed as well.

2) Group 2

Normal pancreatic parenchyma group Patients that had neither personal nor family history of pancreatic disorders. Increased alcohol consumption (>20 g pure alcohol/d) and consumption of drugs known to induce pancreatitis were considered exclusion criteria. Patients with diabetes, gall bladder stones, surgical interventions in the upper abdomen were considered ineligible for the study as well. All the patients included had normal amylase and lipase levels on
admission and US B-mode evidence of normal pancreatic parenchyma-homogenous structure, smooth contours, iso- or slightly hypechoic parenchyma compared to the liver, normal size of the gland-25-30 mm in the head, 18 mm in the body, 25-30 mm in the tail, non-dilated main pancreatic duct (up to 2 mm in the body). A chief requirement was adequate visualization of the pancreas in conventional B-mode. Age, body mass index (BMI) and smoking were not considered exclusion criteria.

| Cambridge Criteria | Normal pancreatic parenchyma |
|--------------------|-----------------------------|
| Cambridge 0/Normal | The establishment of CP through CT/MRI is impossible |
| Cambridge 1/Unclear | Two or more of the following: MPD varying between 2-4mm in body region, mild enlargement of the pancreas, heterogeneous structure of the parenchyma, small cystic lesions (<10mm), irregular ductal contour, pathological side branches >3 |
| Cambridge 2/Mild pancreatitis | As 2 + MPD > 4 mm |
| Cambridge 3/Moderate pancreatitis | As 2 or 3 + one of the following – cystic lesions >10 mm, calcifications in the parenchyma, ductal calcifications, ductal strictures, deformation of the MPD |
| Cambridge 4/Severe pancreatitis | As 2 + MPD > 4 mm |

3) Characteristics of the Study Population
A total number of 53 patients were included in the study. The mean age of the patients was 69.52±14.48 years (ranging from 21 to 79 years) (male: female ratio, 17:8) and ranged from 36-77 years in age (mean± SD, 58.92±15.6 years). The Normal Pancreatic Parenchyma group had 28 patients (male: female ratio, 10:18) belonging to the age group of 21-79 years (mean± SD, 49.79±23.036 years). The frequency of male patients was different among the 2 groups, however the difference was statistically insignificant (p=0.05): it was higher in the CP group. Age too was different among the 2 groups, however the difference was not statistically significant (p=) as well: it was higher in the chronic pancreatitis groups.

4) Patient Preparation for Imaging and Investigation
All the patients are required to observe at least six hours of fasting and to be at rest for at least ten minutes prior to examination. The examination begins as a conventional US B-mode abdominal scan. For a successful examination the pancreatic parenchyma should be adequately presented. The conventional ultrasound includes evaluation of the size and structure of the pancreas, the presence of focal lesions, calcifications, peripancreatic effusion. The ductal system is observed as well. Additionally the other abdominal organs are evaluated as well, looking for metastatic disease or complications. For examination, the patient is required to lie down still in supine position. The upper abdominal transverse B-mode scan is done placing the transducer in the epigastrium. The probe is angled to locate the celiac trunk. A key landmark is the splenic vein, which is located by angling the probe further and sliding it in the caudal direction. In this position of the probe the body of the pancreas is well visualized. The scanning technique is adapted to the organ. The head of the pancreas is directed downwards and to the right. The tail is directed upwards and to the left. pSWE is performed in each segment of the pancreas. Before each measurement the patient is asked to relax and hold breath in expiration, aiming to exclude whatever artefacts, though theoretically those are removed automatically. At least five adequate measurements are made in each region and the mean shear wave velocity (SWV) value is considered. The depth of region of interest /ROI/ is also recorded.

5) Ultrasound System
We used ultrasound system Siemens Acuson S2000, with 6C1 HD transducer 1.5-6 Mhz, with VTQ-virtual touch quantification software. It uses point shear wave elastography where ARFI /acoustic radiation force impulse/ and SWE are combined. The maximal shear wave speed measured was 4.95 m/s. Unsuccessful results were registered as X,XX m/s.

III. STATISTICAL ANALYSIS
Statistical analysis data obtained from the patients was collected in a Microsoft Excel file. The statistical analysis of the data was carried out using the Statistical Package for Social Sciences (SPSSS) (24th Version)/36/. The mean values of age were compared among the groups by using the one-way analysis of variance (ANOVA) and the simple contrast was applied in order to compare them. For a statistical study of quantitative variables, the mean and standard deviations were calculated. To assess the correlation between scale variables bivariate analysis (Pearson’s correlation) was performed. The correlation between nominal variable was investigated through Chi-square analysis. The diagnostic performances of pancreatic stiffness measurements were assessed by using the area under the receiver operating curve (AUROC). ROC curve was thus built for the detection of chronic pancreatitis. Optimal cut off values were chosen to maximize the sum of sensitivity (Se) and specificity (Sp). Positive predictive values (PPV), negative predictive values (NPV), accuracy were also assessed. We calculated 95% confidence intervals (CI) of the AUROC curves to compare their predictive values.

IV. RESULTS

A. Group 1: Chronic Pancreatitis Group
SWV values of the pancreatic parenchyma were calculated-0.920-2.110 m/s (mean 1.668±0.33 m/s), 1.010-2.174 m/s (mean 1.744±0.35 m/s) and 1.356-2.266 m/s (1.733±0.28 m/s) in the head, body and tail of the pancreas respectively. There was strong positive and statistically significant correlation (r>0.5; p<0.05) between the results obtained in different parts of the gland, therefore a mean SWV value for the entire pancreatic parenchyma was calculated between 0.920-2.266 m/s (mean± SD 1.712±0.284 m/s).

| Segment | Min. | Max. | Mean± SD |
|---------|------|------|----------|
| Head    | 0.920 m/s | 2.110 m/s | 1.668±0.33 m/s |
| Body    | 1.010 m/s | 2.174 m/s | 1.744±0.35 m/s |
| Tail    | 1.356 m/s | 2.266 m/s | 1.733±0.28 m/s |
| Entire pancreas | 0.920 m/s | 2.266 m/s | 1.712±0.284 m/s |

(p<0.05, r>0.5)
In order to investigate the influence of certain independent variables on the results, the correlations between the SWV and BMI, depth of ROI and Cambridge score were researched. The depth of measurement varied between 2.720 and 8.00 cm (mean 4.832±1.358 cm). The correlation between SWV and depth of measurement proved insignificant (p=0.883). Regarding the BMI it ranged 18.230-29.410 kg/m² (mean 22.967±3.422 kg/m²). Its correlation to SWV was found insignificant as well (p=0.433). Correlation to the Cambridge score was found neither for the head (p=0.355), nor for the body (p=0.299) or tail (p=0.959) the pancreas.

B. Group 2: Normal Pancreatic Parenchyma Group

The mean± SD values were calculated for the head, body, and tail of the pancreas. Since statistically significant strong positive correlation was found between the segments of the pancreas, mean±SD value for the entire parenchyma was calculated.

| TABLE IV: SHEAR WAVE SPEED VALUES IN HEALTHY PANCREATIC PARENCHYMA |
|-----------------|------|------|-----------------|
| Segment         | Min. | Max. | Mean± SD        |
| Head            | 0.802 m/s | 1.422 m/s | 1.118±0.201 m/s |
| Body            | 0.908 m/s | 1.216 m/s | 1.226±0.306 m/s |
| Tail            | 0.706 m/s | 1.420 m/s | 1.098±0.214 m/s |
| Entire pancreas | 0.706 m/s | 2.146 m/s | 1.147±0.253 m/s |

(p=0.05; r=0.5)

To establish the diagnostic performance of the pSWE in differentiating normal parenchyma and CP, a cut-off value for the diagnosis of CP was calculated. The sensitivity, specificity, positive predictive value /PPV/, negative predictive value /NPV/ and accuracy of the test were also calculated for each segment of the gland and for the entire parenchyma as follows:

| TABLE V: DIAGNOSTIC CAPABILITIES OF pSWE FOR EVALUATION CHRONIC PANCREATITIS |
|-----------------|-----------------|------|------|-----------------|
| Segment         | Cut-off         | AUROC | Sensitivity | Specificity | PPV | NPV |
| Head            | 1.34 m/s        | 0.934 | 92.3% | 92.9% | 92.31% | 92.86% |
| Body            | 1.42 m/s        | 0.868 | 92.3% | 85.7% | 92.31% | 85.71% |
| Tail            | 1.43 m/s        | 0.986 | 92.3% | 100%  | 100%  | 93.33% |
| Entire p.       | 1.43 m/s        | 0.928 | 89.7% | 95.2% | 94.59% | 90.91% |

To summarize, mean values of 1.71 m/s and 1.15 m/s for the CP and normal pancreatic parenchyma respectively, were established. With a cut-off value of 1.43 m/s, we calculated Se-89.7%, Sp-95.2%, PPV-94.59%, NPV-90.91% and Ac-92.59% of pSWE for the diagnosis of CP.

The data presented shows that the study has high sensitivity and specificity values, which means that the test methodology has very good demarcation capabilities and can serve to differentiate between groups of individuals with normal pancreatic parenchyma and chronic pancreatitis. The same applies to the positive and negative predictive values.

V. DISCUSSION

ARFI technology has been reported to be useful in describing parenchymal stiffness in various abdominal organs [17]. Reference [18] were the first to apply transabdominal US pSWE on the pancreas, as they diagnosed pancreatic cystadenoma, which mimicked a solid neoplasm at conventional imaging (US and CT), as cystic at pSWE. Reference [19] were the first to prove that a routine observation of all parts of the pancreatic parenchyma, using pSWE, is possible. They identified a cut-off value of 1.40 m/s for the diagnosis of chronic pancreatitis. They also stated that the depth of ROI is the only external factor to influence the SWV value (>4.2 cm) [19]. Reference [21] conducted one of the very few studies to identify the performance of pSWE for the diagnosis of chronic pancreatitis. They established a mean value of 1.57 m/s for the SWS of the pancreatic parenchyma in patients with CP. With a cut-off value of 1.40 m/s they calculated 70% accuracy of the pSWE [22].

In our study we calculated mean SWS values for both normal pancreatic parenchyma and chronic pancreatitis. For the normal pancreas we established mean SWS values of 1.118 m/s, 1.226 m/s, 1.098 m/s and 1.147 m/s for the head, body, tail and entire pancreas respectively. Those results are close to the ones obtained by [20] and [21]. Regarding CP SWS values of 1.668 m/s, 1.744 m/s, 1.733 m/s and 1.712 m/s respectively for the head, body, tail and entire pancreas were calculated. Those results seem higher than the ones established in the [22], however it’s worth clarifying that in the study mentioned, patients with advanced forms of pancreatitis and local complications were excluded from the analysis.

In order to evaluate the influence of certain independent variables on SWS, the correlation between BMI, depth of ROI and Cambridge score and SWS values was researched. No statistically significant correlation was found, suggesting that external factors have minor impact on the results of pSWE. Additionally, those results point that pSWE might be considered equally informative in both early and advanced forms of CP.

The diagnostic performance of the method was researched using an area under the receiver operating curve /AUROC/. A cut-off value of 1.43 m/s was established for the diagnosis of CP. Similar cut-off value was identified by [19] and [22]. The Se, Sp, NPV, PPV and accuracy of the method were calculated as 89.7%, 95.2%, 90.91%, 94.59% and 92.59% respectively.

Those results are considerably higher than the ones of conventional B-mode US, which suggests that pSWE could be routinely used to enhance the diagnostic capabilities of conventional US regarding the diagnosis of CP, of course within its limitations related mainly to inadequate presentation of the gland.

VI. CONCLUSION

The study concludes that pSWE imaging technique may be successfully adopted in order to diagnose chronic pancreatitis. It may be used as a fast, repetitive and cost-effective method for differential diagnosis between normal pancreatic parenchyma and chronic pancreatitis.
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