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Clinical, Pathological Parameter and Transabdominal Ultrasonography in Diagnosing Chronic Pancreatitis: An Observational Study

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Abstract:

Background: *Typical clinical symptoms of chronic pancreatitis are vague and non-specific and therefore diagnostic tests are required, none of which provide absolute diagnostic certainly, especially in the early stages of disease. Ultrasonography (US) of the pancreas is challenging, given its retroperitoneal location with overlying structures and relatively small size. The quality and thereby the clinical usefulness of the pancreatic ultrasound imaging has rapidly advanced along with the technological progress.* ***Objectives:*** *In this prospective observational cohort study, our aim was to evaluate the diagnostic accuracy of features detected by a high-end transabdominal US scanner compared with the CP diagnosis defined by a diagnostic score combining clinical and imaging features, the Mayo score.* ***Results:*** *A total of 25 eligible patients who fulfilled the Mayo score, the whole pancreas could be visualized in 16 patients (64%) (Visualization score #2 in all 3 segments), and sufficient visualization for inclusion was achieved in 22 patients (88%). The pancreatic tail was the part of the pancreas most frequently incompletely visualized (07 patients, 28%). In 03 patients, visualization of the entire pancreas was inadequate to determine a US score. We performed a sub-analysis on the group with minimal change CP represented by Mayo scores 0-6 (n=22). In this group we calculated a sensitivity of 0.58 (0.37-0.79) and a specificity of 0.99 (0.93-1) for the Rosemont score.* ***Summary & Conclusion:*** *Abdominal ultrasound is a simple, non-invasive, widely available imaging tool. We found that the modality has good diagnostic accuracy and that the extent of sonographic changes is reflected by the grade of exocrine failure by the transabdominal approach. Its limitations are represented by the fact that it's highly examiner dependent and patient-dependent.*

Keywords: ***Chronic pancreatitis, Symptoms, Mayo score, Complications, Abdominal ultrasound.***

Introduction

Defined as a chronic inflammatory disease of the pancreas characterized by irreversible morphological change and typically causing pain and/or permanent loss of function. Typical clinical symptoms of chronic pancreatitis such as weight loss, pain, steatorrhea, and malnutrition are vague and non-specific and therefore diagnostic tests of pancreatic structure and function are required - none of which provide absolute diagnostic certainly, especially in the early stages of disease.[1]

Chronic pancreatitis is represented by a progressive inflammation and fibrosis of the pancreas, resulting in

permanent structural damage and loss of function. Regarding its epidemiology, incidence and prevalence worldwide varies depending on the frequency of risk factors (rates mainly paralelling alcohol consumption) and on the diagnostic method used (with higher incidence and prevalance rates where diagnosis was based on advanced imaging techniques.[2]

There is no universally accepted diagnostic gold standard for chronic pancreatitis. Transabdominal ultrasonography still is the most used first line imaging modality in the diagnostic workup of abdominal diseases. Ultrasonography is, noninvasive, widely available, inexpensive, without side effects, easy to perform, and gives first a broad overview and can localize the "region of interest" to perform detailed evaluation and eventually determine the cause of the disease. It can also reduce the use of CT, magnetic resonance pancreatography, endoscopic ultrasonography or other diagnostic methods, which are personnel-intensive and thereby costly.[3,4]

USG of the pancreas is challenging, given its retroperitoneal location with overlying structures and relatively small size. Overlying bowel gas and obesity are the most frequent limitations in trancutaneous scanning of the pancreas. US examination of the pancreas includes transverse, longitudinal and angled oblique scans. Successful visualization can often be achieved by manipulations with the transducer and is directly linked to the skill and persistence of the examiner.[5] The quality and thereby the clinical usefulness of the pancreatic ultrasound imaging has rapidly advanced along with the technological progress.

Objectives

In this prospective observational cohort study, our aim was to evaluate the diagnostic accuracy of features detected by a high-end transabdominal USG scanner compared with the Chronic Pancreatitis (CP) diagnosis defined by a diagnostic score combining clinical and imaging features, the Mayo score.

Table 1: Mayo score: Diagnostic score for chronic pancreatitis modified from Layer et al. (1994)[*6]

Pancreatic calcifications or typical histologic findings	4 points
Moderate or marked morphologic changes on ultrasonography, computed tomography or EST	3 points
Definite morphologic changes on magnetic resonance imaging	3 points
Reduced exocrine pancreatic function by EST or fecal elastase 1 level	2 point
History of acute pancreatitis or upper abdominal pain	2 points
Diabetes mellitus or impaired glucose tolerance test	1 point
EST = endoscopic. ***** The diagnosis requires 4 points.	

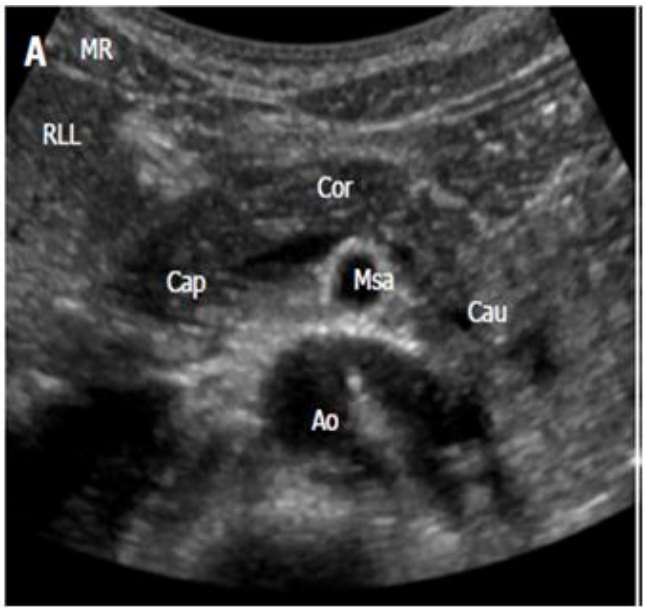
Methods & Patients

Participants: 25 eligible participants were recruited among patients referred to our outpatient clinic with suspected CP. Reasons for referral were presenting symptoms or classic CP characteristics based on previous diagnostic imaging. Patients who did not fulfil the protocol for an adequate Mayo score were not included. We excluded patients for whom US visualization of the pancreas was insufficient because of obesity, repeated overlying bowel air or other factors.

Sonographic Examination

After overnight fasting, patients were examined with US while in the supine or right lateral position, with the transverse or oblique epigastric probe in the lateral/posterior left subcostal position, complete US scanning of the pancreas was performed. The ductal and parenchymal features were recorded on a standardized form. The visibility of pancreatic head, body and tail was graded from 1 to 4 (1= good, 2= adequate, 3= poor, 4= not visible). The data were acquired from the segments of the pancreas with the best visualization.

Ethics: The study was conducted in accordance with the Helsinki Declaration (World Medical Association General Assembly 2015) and received institutional Ethics Committee approval. All patients signed an informed consent.



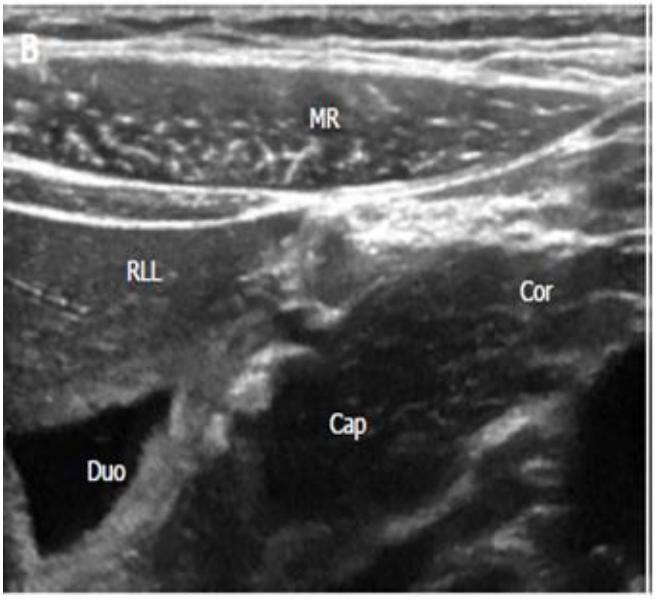


Figure 1: Pancreas and the surrounding anatomical landmarks. **A:** B-mode image (1-5 MHz); **B:** B-mode image with a 12-15 MHz transducer. Details shown with high resolution. **MR:** Musculus rectus abdominis; **RLL:** Right liver lobe; **Cap:** Caput pancreatis; **Cor:** Corpus pancreatis; **Cau**: Cauda pancreatis; **Msa:** Superior mesenteric artery; **Duo:** Duodenum; **Ao:** Aorta.

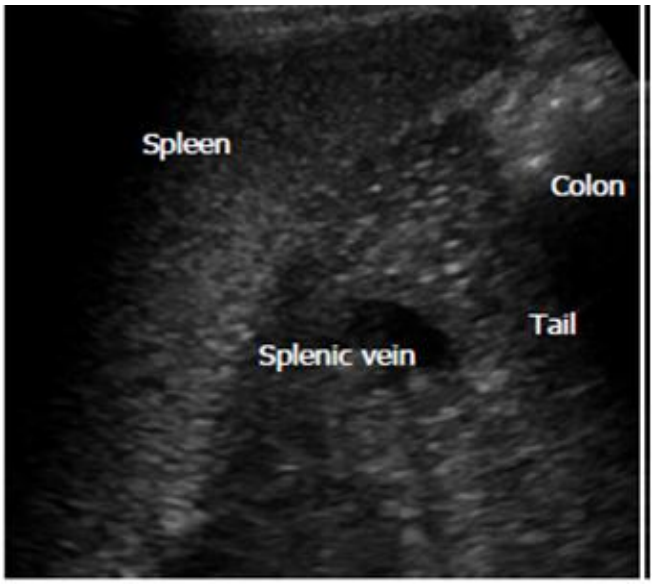


Figure 2: Left lateral side scan shows the pancreatic tail (cauda) using the spleen as acoustic window.

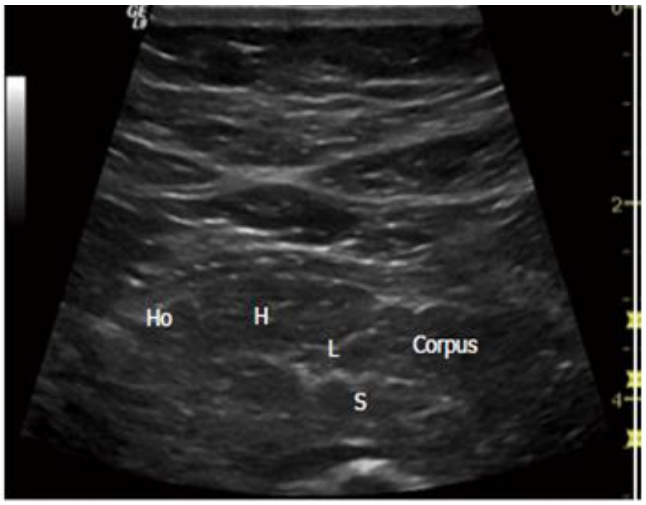


Figure 3: Early chronic pancreatitis. Typical signs in early chronic pancreatitis: lobularity (L), stranding (S), hyperechoic foci (H) and honeycombing (Ho). Pancreatic body (Corpus). This subtle changes are usually only seen in endoscopic ultrasonography.

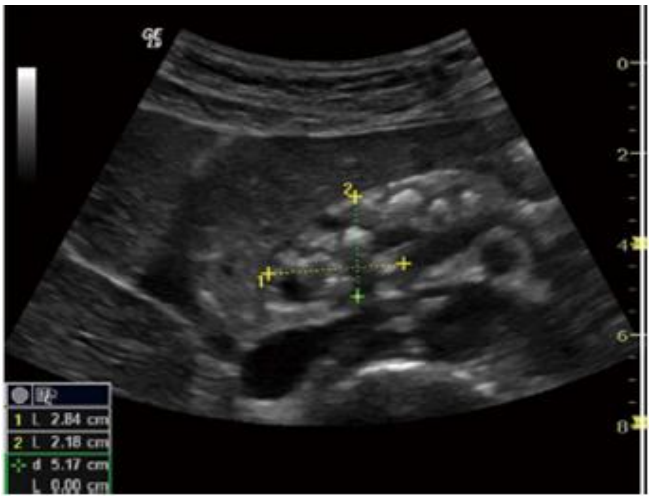


Figure 4: Advanced chronic pancreatitis. Classical signs in advanced chronic pancreatitis: main pancreatic duct dilatation in an atrophic organ with sharp, irregular contours, calcifications and small cysts. The pancreatic head is outlined.

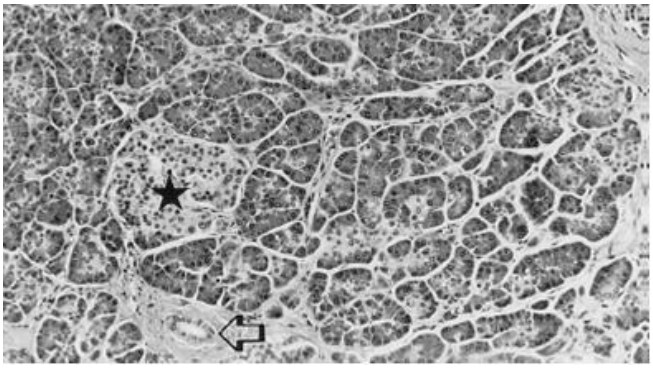


Figure 5:.Histology of chronic pancreatitis. Minimal chronic pancreatitis; Normal acini are lost and replaced by progressive fibrosis associated with fibroblast and lymphocytic infiltration. The islets (w) and intralobular pancreatic ducts (open arrows) are relatively spared.

Results

Table 2: Demographic data, laboratory results among study participants

Characteristics	Chronic pancreatitis (n= 25)	Reference Range
Age [mean, range]	54 (29-78) years	-
Male : Female	11/14 [0.79:1]	-
Body mass index	23.8 (20.4–27.2)	-
Smokers, including ex-smokers	9/25 [36%]	-
Alcoholics, including ex- alcoholics	7/25[28%]	-
HbA1c, %	6.2 (5.5–6.8)	-
Glucose	97 ± 22	63-108 mg/dL
Serum amylase	152 ± 75	30-150 U/L
Serum lipase	267 ± 178	20-250 U/L
Alanine aminotransferase	37 ± 21	5-55 U/L
Alkaline phosphatase	72 ± 29	20-110 U/L
Fecal elastase	165 ± 47	16–458 µg/g
Triglycerides	109 ± 67	35-155 mg/dL

Faecal elastase 1 was analyzed with a commercial monoclonal analysis kit. A fecal elastase 1 level, 200 mg/mg was considered pathologic (Loser et al. 1996).7 Pain in abdomen 19 (76%) is most common complaint in clinical scenario of chornic pancreatitis. Vomiting 13 (52%) is second most common complaint in present study followed by fever 11 (44%) and least common is weight loss 4 (16%).

Table 3: USG diagnosis of lesions in chronic pancreatitis subjects [n=25]

Obscured	3 (12%)
Normal	0
Edematous pancreatitis	7 (28%)
Acute on chronic pancreatitis	4 (16%)
Chronic pancreatitis with peri-pancreatic fluid collection	8 (32%)
Chronic pancreatitis with pseudocyst	3 (12%)
Total	25 (100%)

A total of 25 eligible patients who fulfilled the Mayo score, the whole pancreas could be visualized in 16 patients (64%) (visualization score #2 in all 3 segments), and sufficient visualization for inclusion was achieved in 22 patients (88%). The pancreatic tail was the part of the pancreas most frequently incompletely visualized (07 patients, 28%). In 03 patients, visualization of the entire pancreas was inadequate to determine a US score. We performed a sub-analysis on the group with minimal change CP represented by Mayo scores 0-6 (n=22). In this group we calculated a sensitivity of 0.58 (0.37-0.79) and a specificity of 0.99 (0.93-1).

Visualization of calcifications and cysts by USG:

We calculated inter-rater agreement between US and CT for calcifications and cysts. The calculation was performed on the subgroup of 17 patients for whom CT scans were available. US and CT detection of calcifications were in almost perfect agreement (k= 0.92). Agreement between US detection and CT detection of cysts was substantial (g= 0.69). It was deducted that CT was better evaluating the factors of parenchyma, MPD, calcification, pseudocyst collection, ascites, pleural effusion, necrosis, complications and adjacent areas of the pancreas in comparison to USG and helped in better to determine the pathological process of pancreas and surrounding extent and involvement.

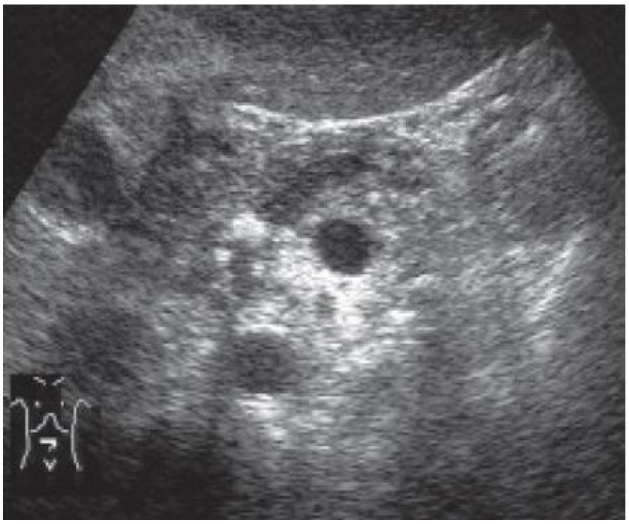


Figure 6: Intraductal pancreatic calcifications

Contribution of USG to the diagnosis of chronic pancreatitis and its complications

Figure 7: Large caudal pancreatic cyst

Discussion

Defined as a chronic inflammatory disease of the pancreas characterized by irreversible morphological change and typically causing pain and/or permanent loss of function,[1] chronic pancreatitis is beset by destruction of healthy pancreatic tissue and the development of fibrous scar tissue. Gradual loss of exocrine and endocrine function ensues with clinical manifestations such as steatorrhea, abdominal pain, and diabetes. Current treatments can only provide temporary pain relief and manage complications, but are unable to halt or slow the advance of this disease.[8]

In some patients, chronic pancreatitis can be entirely silent, and in presentation patients may present with the sequelae of exocrine or endocrine insufficiency: steatorrhea, weight loss and diabetes. Less common initial presentations include biliary obstruction with recurrent episodes of mild jaundice, cholangitis, or vague attacks of indigestion. Obstruction of the splenic vein by an inflamed tail of the pancreas can lead to left-sided portal hypertension, gastric varices and GI bleeding. Chronic pancreatitis and pancreatic cancer may present in a similar manner, making it difficult to distinguish between them.[9]

There is no universally accepted diagnostic gold standard for chronic pancreatitis. While no one radiological, clinical or endoscopic tool can definitively diagnose this disease; there is an array of diagnostic instruments, which fall into four broad categories. Histology Histological features of chronic pancreatitis include parenchymal fibrosis, acinar atrophy, ductal distortion, and intraductal calcification.[10,11] Histological diagnosis is limited by a lack of consensus around grading for chronic pancreatitis. Whilst histology is the most specific method of diagnosis, however it is rarely available and therefore proxy testing is required.

The diagnostic tool specifies that 2 of the following 4 items be present: repeated upper abdominal pain, abnormal pancreatic enzyme levels (serum or urine), abnormal pancreatic function, and on-going heavy alcohol ingestion (of > 80 g pure ethanol per day). These items, along with characteristic early findings by EUS imaging are said to be indicative of early chronic pancreatitis. According to this tool, more than 2 of the following EUS criteria are required for diagnosis (as well as at least one from the first 4 criteria: (1) lobulating with honeycombing; (2) lobulating without honeycombing; (3) hyperechoic foci with stranding; (4) stranding; (5) cysts; (6) dilated side branches; and (7) hyperechoic MPD margin. More recently, reports of the Tissue Harmonic Echo mode on EUS have suggested that these modes can reveal details of abnormalities of early chronic pancreatitis and might therefore contribute to a definite diagnosis in the early stages of disease.[11,12]

In a US examination of the pancreas the echotexture, the size of the gland including the main pancreatic duct (MPD), and anatomical landmarks of the pancreas should be evaluated. The echotexture in a normal pancreas is isoechogenic or hyperechogenic compared to the healthy liver.[13] Frequently, the echogenicity of pancreas is increasing with age. Orientational antero-posterior dimensions of the pancreas are: the head (2.5 cm), body (1.5 cm), tail (3.5 cm) and the pancreatic duct (< 2.5 mm). Fatty replacement (lipomatosis) of the pancreatic gland and decrease in size is common with increasing age but can also be found in patients with cystic fibrosis, CP, some types of diabetes and other diseases.[14,15,16]

Abdominal ultrasound is a simple, non-invasive, widely available imaging tool. Its limitations are represented by the fact that it's highly examinerdependent and patient-dependent (excessive adipose tissue, history of upper GI tract surgery or overlying gas can lead to a poor view of the pancreas). Examination is done using a convex probe, with a frequency of 3.5-5 Mhz, using epigastric and left subcostal approaches. To optimise visualisation of the pancreas, some recommend drinking 500 ml of water before the examination, to make the stomach an acoustic window. Ultrasound can show atrophy/enlargement of the pancreas, inhomogenous echostructure (by hyperechoic areas corresponding to fibrosis), irregular gland border, pancreatic duct changes (dilatation, irregularity or stones), cysts and pseudocysts. US has a sensitivity of 60-70% and specificity of 80-90% in diagnosing chronic pancreatitis3. Although its role in positive diagnosis is limited, US is very useful in follow-up: it can assess position of intraductal or pseudocystogastric stent and it can evaluate the efficacy of extracorporeal lithotripsy by showing the disappearance of stones and reduction in pancreatic duct diameter.[15,16]

Study limitations

- A study on USG is operator dependent.
- The examinations were performed by operators blinded to earlier history and radiologic imaging.

- Blinding to patient appearance and communication during the procedure was not feasible.
- Blinding biases may exist.
- Single centre study
- Small sample size

Conclusion

Abdominal ultrasound is a simple, non-invasive, widely available imaging tool. We found that the modality has good diagnostic accuracy and that the extent of sonographic changes is reflected by the grade of exocrine failure by the transabdominal approach. Its limitations are represented by the fact that it's highly examiner dependent and patient-dependent.

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