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Is the size of the pancreas useful in diagnosing chronic pancreatitis? An ultrasound based, retrospective study

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ABSTRACT

Background/Objectives: According to the widely accepted "Cambridge Classification", one of the morphological criteria for chronic pancreatitis (CP) is enlargement of the pancreas. Increased size seems to be an obvious feature of an inflammatory disease. However, it has never been validated so far, if CP is indeed accompanied by significant enlargement of the pancreas.
Methods: In this retrospective study, reference values for the size of the pancreas (head, body and tail measured in the transverse plane by transabdominal ultrasound) were established from 921 patients without pancreatic disease. Measurements were performed by a single investigator. Subsequently, the size of the pancreas from 72 patients with CP was compared to age- and sex-matched controls.
Results: Calculating the 5th and 95th percentile, reference values of the pancreatic size were as follows: head 1.5–3.1 cm (mean: 2.2); body 0.6–1.6 cm (mean: 1.1); tail 1.4–3.0 cm (mean: 2.1). The size of the pancreas correlated significantly with body height, weight and body mass index. Patients with CP had only a slightly but statistically significantly larger pancreas than controls. Mean values from the CP group were still between the 5th and 95th percentile of matched controls.
Conclusions: Although the pancreas from patients with CP was statistically significantly larger compared to controls, the difference was only marginally. According to these data, it is at least questionable if pancreatic size is a helpful parameter for sonographic evaluation to discriminate chronic pancreatitis from healthy pancreas.

1. Introduction

Imaging techniques such as transabdominal ultrasound, endoscopic ultrasound (EUS) computed tomography (CT) and magnet resonance imaging (MRI) are crucial for the diagnosis and follow-up of patients with chronic pancreatitis (CP). The initial diagnosis of CP can be sometimes challenging due to the non-uniform clinical manifestation and the lack of disease defining laboratory tests. At the beginning of the disease, some patients present with typical chronic upper abdominal pain with belt-shaped radiation, others suffer from pain only during acute attacks or following complications such as pseudocysts or calcifications and some patients present with asymptomatic disease, diagnosed as an incidental finding [1]. Pancreatic enzymes such as lipase and amylase are typically only elevated in the serum during acute attacks of chronic pancreatitis and do not discriminate between a single episode of acute pancreatitis and repeated exacerbations of CP. Exocrine function tests are also not helpful at early stages of the disease since exocrine insufficiency is a symptom of advanced CP [2].

After initial diagnosis, patients with chronic pancreatitis (CP) frequently need imaging examinations of the pancreas during follow-up of the disease. Acute attacks or pain exacerbations require prompt evaluation in order to diagnose complications such as duct obstruction or large pseudocysts early.

Morphologic evaluation of the pancreas is therefore pivotal for the establishment of the diagnosis and for follow-up of the disease. Parenchymal heterogeneity, irregular organ contour, calcifications,

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duct irregularities, duct enlargement and pseudocysts are typical signs of chronic pancreatitis [3].

For both situations, initial diagnosis and follow-up of chronic pancreatitis, transabdominal ultrasound, CT, MRI and endoscopic ultrasound are frequently used techniques. Although the accuracy of transabdominal ultrasound is lower compared to the other imaging modalities [4], it is still commonly used since it is easy accessible, fast, cheap and without adverse effects such as radiation exposure. It is therefore widely accepted that in clinical practice transabdominal ultrasound is the first diagnostic step when CP is suspected [5].

The typical morphological features of CP were first described in the "Cambridge-classification" in 1984 [3]. The Cambridge classification was the result of a workshop of "an international group of doctors interested in pancreatic disease". Thus, the definitions and recommendations of the Cambridge classification are only an expert opinion without systematic critical appraisal. Although the Cambridge classification has been widely used and is still recommended in recent publications [6] or national guidelines [5], some of the definitions have never been subjected to a systematic examination.

One criterion for the image grading of CP in the Cambridge classification is enlargement of the gland. At first sight it seems comprehensible that inflammation and calcification of the pancreas is accompanied by gland enlargement. However, determination of pancreatic enlargement is difficult since reliable and commonly accepted reference values of healthy controls are not available. Many of the studies investigating normal pancreatic size by ultrasound are underpowered and the results of these studies are controversial [7–17]. In addition, pancreatic size was measured in various planes making it difficult to compare the studies [18].

The issue of pancreatic size in patients suffering from CP was only addressed by one study, published in 1984 [19]. In this study, patients with cystic fibrosis were used "as a model for CP" which is at least problematic since cystic fibrosis most frequently presents with exocrine pancreatic insufficiency (accompanied by pancreatic atrophy) and only occasionally with signs of CP [20]. The results can therefore not be transferred to CP of other etiology. Furthermore, the study was substantially underpowered with 16 patients and controls each. In this study, pancreatic size did not differ in patients and controls and the measurement was therefore rated as not helpful.

The aim of this retrospective study was to determine whether pancreatic size differs significantly in patients with CP. In order to have a reliable control group, we first established reference values from 921 patients without any pancreatic disease.

2. Methods

2.1. Study design

Ultrasound measurements for this study were conducted between June 2009 and September 2010 in the internal ultrasound unit of a German university hospital (Klinikum rechts der Isar, Technische Universität München). The majority of the cohort of this study was previously used in another study (Treiber et al., submitted). In this publication, we prospectively analyzed kidney size. By analyzing the ultrasound reports from these patients, we retrospectively collected measurements of pancreatic size and anthropometric data. Additionally, patients suffering from chronic pancreatitis who received ultrasound during the same period were enrolled. The study was approved by the institution's ethic committee (Ethikkommission der Fakultät für Medizin, Technische Universität München, project number 2735/10).

2.2. Patients

Altogether, 1109 patients were enrolled in this study (551 female, 558 male). According to the exclusion criteria, 116 patients were excluded (42 female, 74 male), 19 with acute pancreatitis, 5 with pancreatic carcinoma, 8 with pancreatic surgery in the past, 19 with various other conditions such as cystic lesions, IPMNs or other tumors of unknown dignity, and 65 with completely invisible pancreas because of meteorism. Patients with no history of pancreatic disease and no apparent sonographic signs of any pancreatic disorder (n = 921; female: 478, male: 443) were used to determine normal values for the size of the pancreas. Patients characteristics are shown in Table 1.

Patients with known chronic pancreatitis (n = 72, female: 31, male: 41) were then compared to healthy controls. The diagnosis of CP was based on two or more of the following criteria: presence of recurrent pancreatitis, radiological findings such as pancreatic calcifications and/or pancreatic ductal irregularities and/or pathological sonographic findings. From these patients, 44 had alcoholic CP, 13 idiopathic disease, 1 had drug induced pancreatitis, 1 hyperparathyroidism, 2 had CP related to pancreas divisum and in 11 cases there were no information regarding the etiology in the records. In this retrospective study, we were able to find sufficient information concerning disease activity (CP with/without acute episode) from 70 CP patients (97%) enrolled in our study. 17 patients (24%) had an acute episode of CP, whereas 53 of the patients (76%) had chronic disease without an acute episode. Data on the time of initial diagnosis was available from 61 patients (85% of the cohort). The mean duration from the initial diagnosis to the ultrasound investigation was 4.4 years (standard deviation: 6.4). Nine patients had the initial diagnosis of CP at the time of the ultrasound investigation.

Because of the observed gender-related difference in control subjects, the disproportionateness of female and male patients with CP and the advanced mean age in the CP group, we used matched pairs to analyze the size differences between patients with CP and controls. For each patient with CP, 3 age- and sex-matched patients from the control group were selected and these

Table 1
Patients characteristics from healthy controls. Anthropometric data and lipase levels were not available from all patients.

Included patients without pancreatic disease (n)	♀ 478 **mean; SD**	♂ 443 **mean; SD**	♀ + ♂ 921 **mean; SD**
Age	39.6; 13.1	41.4; 11.9	40.5; 12.6
Body height (cm)	165.6; 6.7	177.2; 11.2	171.4; 10.9
(Number of patients)	(135)	(133)	(268)
Body weight (kg)	62.5; 12.5	78.7; 15.9	70.6; 16.5
(Number of patients)	(134)	(133)	(267)
BMI (kg/m^2)	22.8; 4.4	24.6; 4.0	23.7; 4.3
(Number of patients)	(133)	(132)	(265)
Lipase (Reference values: 13–60 U/l)	36.5; 14.6	45.0; 50.3	40.3; 35.8
(Number of patients)	(155)	(127)	(282)

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