EUS-based criteria for the diagnosis of chronic pancreatitis: the Rosemont classification CME

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Background: EUS is increasingly used in the diagnosis of chronic pancreatitis (CP). A number of publications in this field have used different EUS terminology, features, and criteria for CP, making it difficult to reproduce their findings and apply them in clinical practice. Moreover, traditional criteria such as the Cambridge classification for CP are arguably outdated and have lost their relevance.

Objective: Our purpose was to establish consensus-based criteria for EUS features of CP.

Design: Consensus study.

Main Outcome Measurements: Thirty-two internationally recognized endosonographers anonymously voted on terminology of EUS features, rank order, and category (major vs minor criteria). Consensus was defined as greater than two thirds agreement among participants.

Results: Major criteria for CP were (1) hyperechoic foci with shadowing and main pancreatic duct (PD) calculi and (2) lobularity with honeycombing. Minor criteria for CP were cysts, dilated ducts $\geq$3.5 mm, irregular PD contour, dilated side branches $\geq$1 mm, hyperechoic duct wall, strands, nonshadowing hyperechoic foci, and lobularity with noncontiguous lobules.

Limitation: Lack of broadly accepted reference standard.

Conclusion: In a complex disease such as CP that has no universally accepted reference standard, an EUS-based criterion for diagnosis can be determined by expert consensus opinion and the existing body of evidence. Here we present the new ''Rosemont criteria'' for the EUS diagnosis of CP. (Gastrointest Endosc 2009;69:1251-61.)

Abbreviations: BMI, body mass index; CP, chronic pancreatitis; MPD, main pancreatic duct; MRI, magnetic resonance imaging; OR, odds ratio; PD, pancreatic duct; PFT, pulmonary function test; ROC, receiver-operating characteristic curve.

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EUS imaging for chronic pancreatitis (CP) was first reported in 1986.[1,2] Since then, it has been commonly used to diagnose and assess the severity of CP. There is a lack of standardization when CP is evaluated in terms of the technique, nomenclature, and quantitative criteria used. EUS is also operator dependent, and the diagnosis of CP is based on subjective criteria associated with variability. These problems are further complicated by the absence of a reliable and validated reference standard. These limitations all serve to hinder review of existing EUS data and limit the strength of any conclusions.

To address these issues, an international consensus meeting was convened in Rosemont, Illinois (April 13-14, 2007). This meeting was attended by endosonographers from throughout North America and Japan who have expertise in the evaluation and management of CP. The conference was endorsed by the American Society for Gastrointestinal Endoscopy. The goals of the conference

were to unify the features and nomenclature of CP and to create consensus-based EUS criteria for CP.

DIAGNOSIS OF CP

CP is defined as a continuing inflammatory disease of the pancreas characterized by irreversible morphologic changes often associated with pain and sometimes with loss of exocrine or endocrine function. This definition is restrictive when the diverse clinical manifestations and natural history are considered as well as the varied etiologies of CP that have yet to be fully characterized. The diagnostic reference standard varies among institutions, with variable use and importance assigned to histologic, radiographic, and functional analyses.

Histology

Widely believed to be the reference standard, the 3 criteria for the diagnosis of CP are chronic inflammation, fibrosis, and atrophy.[3] There is no consensus among pathologists as to how much of each feature is required on a histologic specimen to firmly establish CP. Apart from the inherent difficulty in obtaining an adequate specimen, the patchy nature of CP may lead to sampling error. Autopsy studies[4,5] in elderly asymptomatic patients without a history of pancreatic disease have shown the common presence of fibrosis and atrophy in the absence of chronic pancreatitis. Thus, the accuracy of current methods for acquiring pancreatic tissue specimens and histologic review is unclear. Furthermore, the utility of using histology as the reference standard with which to compare radiographic and function testing has not been validated.

Radiographic

Pancreatic duct (PD) abnormalities seen on ERCP have a poor sensitivity for diagnosing early, or mild, CP. Pancreatography also has poor specificity, as demonstrated in a study of elderly patients without evidence of pancreatic disease.[6] Autopsy studies[7] show a high prevalence of pancreatographic abnormalities in patients without histopathologic or clinical evidence of CP. Thus, pancreatography alone does not accurately diagnose CP. MRCP with secretin stimulation may eventually replace ERCP but has similar limitations.[8] CT is fairly specific for severe disease but not sensitive for mild or moderate disease[9] and can even miss calcifications.[10]

Pancreatic function tests (secretin test)

Pancreatic function tests (PFTs) have limited utility in the diagnosis of CP because of poor patient tolerance, limited availability, and uncertain validation of test results. The diagnostic accuracy is affected by patients who have CP without pancreatic insufficiency, and conversely, pancreatic insufficiency can occur without morphologic changes. Thus, in most centers PFTs have a limited role in establishing the diagnosis of CP.[11,12]

Capsule Summary

What is already known on this topic

- Lack of standardization in EUS terminology, features, and criteria for chronic pancreatitis (CP) makes it difficult to reproduce study findings and apply them in clinical practice.

What this study adds to our knowledge

- Thirty-two international endosonographers proposed consensus-based criteria (the Rosemont criteria) for an EUS diagnostic system for CP that takes into account the existing body of evidence and the experience of experts.

CLASSIFICATIONS OF CP

During the 1963 Marseille conference, histopathologic criteria for CP (fibrosis, inflammatory cells, loss of exocrine parenchyma, ductal dilation, and stones) were proposed. In 1984, the histopathologic definition was broadened by adding an obstructive variant and expanding the functional (progressive loss of function) and clinical (pain usually but not always present) components.[13] Four years later, a more comprehensive list of CP subclasses were established, differentiating between acute and chronic pancreatitis.

The 1984 Cambridge classification[14] incorporated CT, US, and pancreatographic features to classify and grade disease severity. These diagnostic modalities accurately identify patients without pancreatic pathologic conditions and those with severe CP. However, the Cambridge classification provided poor diagnostic accuracy in evaluation of patients with equivocal or early-stage disease.

The Japanese Pancreas Society distinguished 2 groups of patients, those with definite and probable CP, by use of a PFT as the reference standard.[15] The TIGAR-O classification was based on etiology: toxic, idiopathic, genetic, autoimmune, recurrent severe acute pancreatitis, or obstructive.[16]

Current diagnostic modalities are inadequate for providing a diagnosis of CP because of technical limitations, lack of standardization, interobserver variability, scarcity of certain tests, safety concerns, expense, and issues concerning test validation. The ability of the above tests to accurately, reliably, and reproducibly assess pancreatic structure and function is limited, which diminishes their utility for diagnosing and managing CP. Their utility is even more restricted in evaluation of patients with indeterminate or early-stage disease, a population in whom accurate assessment is most critical.

CRITIQUE OF THE EXISTING LITERATURE

EUS criteria for CP

There is heterogeneity within the EUS literature regarding the total number of criteria (range 5-13) assessed and the threshold number of criteria (range 1-5) required to diagnose CP (Table 1).[10,17-25] Furthermore, differences in technique (contrast, gain, and magnification), echoendoscopes (radial, linear, mechanical, and electronic), processors, and regions of the pancreas evaluated make it difficult to compare results of various investigations.

There are also differences in the way certain criteria are defined. For example, some consider a dilated main PD (MPD) to be greater than 3 mm in the pancreatic head, 2 mm in the body, and 1 mm in the tail.[17] However, in the control group of another study[18] the upper limit of MPD diameter was 3.6 mm in the head, 3 mm in the body, and 2 mm in the tail, demonstrating that use of the ''3-2-1 rule'' can lead to overdiagnosis of MPD dilation.

Although early studies considered the mere visualization of side branches as a marker of CP, they were also observed in the control group of 1 study.[19] Newer generations of echoendoscopes and processors now allow visualization of side branches in nearly all patients, which may render this criterion, at least as currently defined, obsolete. Furthermore, in another patient cohort[19] the width of side branches overlapped considerably among controls and patients with CP, suggesting that this feature also serves as an unreliable predictor of CP.

Although the overall distinction of normal from very abnormal is reasonably good, the interobserver variability for individual criteria for CP is poor. In a study of EUS recordings viewed by 11 expert endosonographers, visible side branches were ranked as the second-best predictor of CP after PD stones, yet the interobserver variability for side branches was quite poor ($\kappa = 0.18$).[26] The criterion with the highest κ value (0.61) was MPD dilation, but this finding also ranked as the least predictive of CP, thus raising questions as to the clinical utility of this feature.

Adjustment for subgroups

It is unclear whether individual criteria or the threshold number of criteria to diagnose CP should be modified within particular patient cohorts. There are emerging data showing that patient-specific features (eg, sex, age, or body mass index [BMI]) and environmental exposures (eg, alcohol, cigarettes) alter pancreatic ductal and parenchymal findings among patients with and without pancreatic disease. Therefore, the presence of certain features may require that we modify the threshold for diagnosis in certain patient cohorts to optimize diagnostic accuracy. Similarly, there is growing concern that individual criteria may provide different diagnostic accuracy among the various causes of CP.

Sex appears to be more clearly associated with EUS-related features of CP than does age. In a study[27] of 1157 consecutive patients referred for any indication, male sex was an independent predictor of CP on the basis of the presence of ≥ 5 criteria (odds ratio [OR] for male sex 1.8; 95% CI, 1.3-2.6), whereas patient age did not correlate with imaging findings. The same findings were reported in another study,[28] where a multivariate analysis among patients without evidence of pancreatic disease found that sex and not age independently predicted EUS abnormalities (OR for male sex 2.9; 95% CI, 1.2-6.8). Because there were fewer elderly female than younger female subjects in this study, there was an apparent relationship between age and EUS abnormalities on univariate analysis; this was likely due to confounding by sex. In actual practice, more criteria are often seen in older patients, especially men, that may be due to the cumulative exposure to smoking and alcohol with age.

Alcohol[29] and smoking[27] have also been associated with EUS pancreatic abnormalities. In the above study[27] of 1157 subjects, heavy alcohol ingestion (OR 5.1; 95% CI, 3.1-8.5) and heavy smoking (OR 1.7; 95% CI, 1.2-2.4) were independently associated with more EUS features of CP. Genetic studies[30] also suggest a link between PRSS1 and SPINK1 mutation, smoking, and alcohol consumption with CP. However, other than mild increases in duct size with age, there is no convincing evidence that increasing age independently leads to more criteria.

Summary of test performance

It is difficult to determine the summary operating characteristics of EUS for CP because of the methodologic variation among studies and the lack of abroadly accepted reference standard. Figure 1 shows a receiver-operating characteristic (ROC) scatter plot for EUS in CP. Among studies without patient follow-up, Wiersema et al[18] determined by ROC curve analysis that a cutoff value of ≥ 3 features, among the 11 evaluated, provided a sensitivity of 80% and a specificity of 86%. Catalano et al[19] reported a sensitivity of 88% and a specificity of 100% when using a threshold of ≥ 3 features to diagnose CP. At this cutoff level, there was a 17% probability of having an abnormal ERCP and a 13% chance of having a positive secretin test.

Current data do not support the use of EUS-guided FNA and cytologic analysis[20] or EUS-guided Tru-cut biopsy with histologic analysis[31] because of their poor diagnostic accuracy and procedure-related risks. Using ERCP as reference standard, Hollerbach et al[20] performed EUS-FNA on 27 patients with suspected CP and noted a specificity of only 67%. In another study, by DeWitt et al,[31] on 16 patients who underwent Tru-cut biopsy, there was poor agreement ($\kappa = 0.25$) with ERCP, and 2 patients required hospitalization for a Trucut-related complication.

Studies that attempted to use a diagnostic reference standard suffer from a lack of physician blinding and a limited number of patients in whom a reference standard was available.

Hastier et al[21] assessed the prevalence of pancreatic abnormalities among patients with alcoholic liver cirrhosis,

TABLE 1. EUS features of CP used in the literature

Author	Threshold No. of criteria	Parenchymal		
		Hyperechoic foci	Hyperechoic strands	Hypoechoic lobules, foci, or areas
Wiersema et al, 1993[18]	3 or more (by ROC)	X* >3 mm		X*
Buscail et al, 1995[23]	Not reported	†	†	X
Catalano et al, 1998[19]	No criteria rules out disease; >5 criteria rules in disease; 3-5 criteria agreed with ERCP in 92%	X‡	X septa	§
Sahai et al, 1998[17]	<3 criteria rules out disease; >4 criteria rules in disease	X 1-2 mm	X	X 2-5 mm
Hastier et al, 1999[21]	1 or more	X		X
Hollerbach et al, 2001[20]	2 or more	X hyperechoic lobules	X septa	
Kahl et al, 2002[22]	1 or more	X >3 mm	X#	X
Chong et al, 2007[10]	3 or more, if no calcification	X	X	X
Conwell et al, 2007[24]	3 or more	X	X	
Stevens et al, 2007[25]	1-3, normal	X	X	
	4-5, equivocal			
	≥6, definite for CP			

X, This criterion was sought.
*Significant in multivariate analysis.
†Diffusely heterogeneous, diffusely hyperechoic, and hypertrophic were other parenchymal criteria used in this study, and heterogeneous appears to refer to hyperechoic strands and foci; echogenic duct wall was considered normal but hyperechogenic duct wall was recorded as abnormal.
‡Foci were called "calcifications" parenthetically in the article; it was not specified whether acoustic shadowing was required.
§Heterogeneous parenchyma was an additional criteria, separate from strands and foci.
||>3 mm in the head, >2 mm in the body, >1 mm in the tail.
#Hypoechoic areas surrounded by septae.

comparing EUS and ERCP in detecting pancreatic abnormalities. They noted that, after a mean follow-up of 22 months, none of the 18 subjects with alcohol-related liver cirrhosis had pancreatic disease progression by EUS, and none of the 10 with follow-up ERCP had progressed to an abnormal pancreatogram. In contrast, Kahl et al[22] showed a progression to abnormal pancreatography in all 22 patients who had a follow-up ERCP; the abnormalities on ERCP were subtle (Cambridge 1 or 2). Pungpapong et al[32] studied 99 patients with a clinical diagnosis of CP and determined by ROC analysis that using ≥4 features provided the most accurate threshold for diagnosis. However, the authors arguably used inadequate criteria to exclude the diagnosis of CP, specifically the presence of 2 negative test results (CT or magnetic resonance imaging [MRI]) obtained over a mean follow-up of at least 7 months.

MEETING DELIBERATIONS

During the initial conference breakout sessions, we focused on 4 topics, including (1) parenchymal features of CP, (2) ductal features of CP, (3) correlation of EUS imaging with histologic findings, and (4) development of an EUS diagnostic system. These topics were subsequently presented to the entire group for debate. A systematic review of the literature was performed during which we thoroughly discussed existing data, including the quality of the studies and the level of evidence. A panel of 5 experts presented a series of statements and questions to 32 internationally recognized endosonographers from North America and Japan who used digital electronic touch pads to anonymously vote on (1) the definitions and terminology of EUS features, (2) the perceived predictive value of these features and establishment of a rank order, and (3) categorization of the criteria as major versus minor. Consensus was defined as greater than two thirds agreement of participants. EUS features were categorized as major and minor criteria and were further subdivided into major A and major B because of a perceived difference in their predictive accuracy (Tables 2 and 3). Hyperechoic foci with shadowing, cysts, and ductal calculi are the 3 features that can be assessed anywhere in the gland, but the rest of the other features should be evaluated only in the body and tail of the pancreas. We should also note that the criteria were based on radial EUS imaging (Fig. 2). Use of newer radial instruments providing

TABLE 1 (*continued*)

Parenchymal			Duct criteria				
Accentuation of lobular pattern	**Irregular gland margin or increased size**	**Cyst**	**Irregular duct contour**	**Visible side branches**	**Hyperechoic duct margin**	**Dilated main duct**	**Stone**
X		X	X*	X*	X	X*	X
†		X	X	X	X†	X	X
§	X irregular margin	X	X	X "ectatic"	X	X	X
		X >2 mm	X	X	X	X‖	X
		X	X	X	X	X	X
		X	X				X
#	X increased gland size	X	X	X	X	X	X
		X	X	X	X	X	X
X		X	X	X	X	X	X
X		X	X	X	X	X	X

enhanced image resolution offers the potential to improve diagnostic accuracy and interobserver agreement. However, given that many centers now perform all pancreatic imaging solely with a linear instrument, consideration must be given to correlating these study end points with linear images as well.

Parenchymal features of CP

Hyperechoic foci with postacoustic shadowing was considered a major A criterion (Table 2). This feature is defined as the presence of echogenic structures ≥ 2 mm in length and width that produce a shadow (Fig. 3). At least 3 of these structures are needed for the feature to be considered a marker of CP. However, pathology studies reveal that calcification located distant from the MPD may actually be located in terminal duct branches, leading to the false assumption of a parenchymal-based process. This feature was felt to be highly predictive of CP and, therefore, needed fewer supporting secondary features to establish a diagnosis of CP.

The presence of specular reflectors creates image artifacts that may be falsely interpreted as features indicative of CP. The point was emphasized that scanning must be conducted in a manner that considers the orientation of viewed structures, and the resulting angle of insonation, when interpreting features of CP.[33]

Lobularity was defined endosonographically as well-circumscribed, ≥ 5 mm structures with rims that are hyperechoic relative to the echogenicity of its central areas (Fig. 4). At least 3 lobules in the body or tail are necessary for the feature to be considered present. When at least 3 of the lobules are contiguous, the feature is termed "honeycombing" lobularity and is then considered a major B criterion, whereas 3 or more noncontiguous lobules are felt to represent a minor criterion. Honeycombing lobularity is felt to be strongly suggestive of a pathologic condition. Although these lobules do not correspond to microscopic pancreatic lobules, which are too small to be visualized by EUS, they likely represent compartmentalization of the pancreas into segments by fibrotic strands. No distinction was made regarding the location of lobules, either central (periductal) or peripheral (near the gland border) and in their predictive value for CP. Because of the relatively hypoechoic appearance of the pancreatic head, the group recommended that lobularity should only be assessed within the pancreatic body and tail.

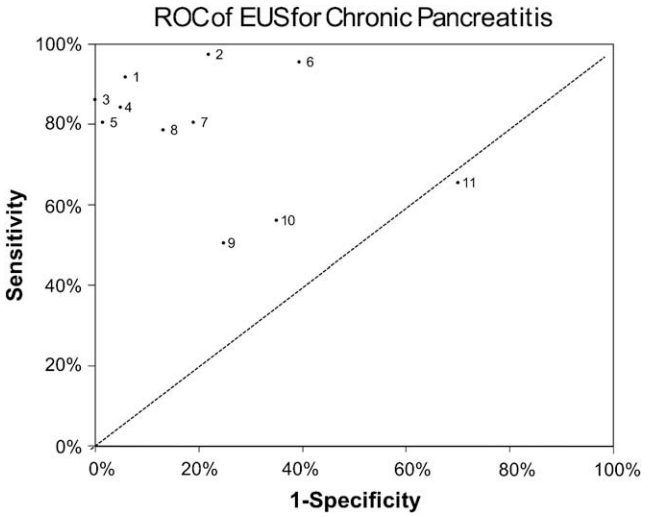

Figure 1. ROC curve for EUS in CP data, representing a summary measure of test performance. Those near the diagonal dotted lines have little or no discriminatory value. *1,* Pungpapong et al,[32] 2007, >3 criteria; *2,* Kahl et al,[22] 2002, >0 criteria vs second ERCP; *3,* Buscail et al,[23] 1995; *4,* Catalano et al,[19] 1998, >0 criteria versus ERCP; *5,* Catalano et al,[19] 1998, >0 criteria versus ERCP and pancreatic function test; *6,* Hollerbach et al,[20] 2001, >1 criteria; *7,* Chong et al,[10] 2007, >2 criteria if no stones; *8,* Wiersema et al,[18] 1993, >2 criteria versus ERCP and pancreatic function test; *9,* Hollerbach et al,[20] 2001, >1 criteria versus pancreatic function test; *10,* Chowdhury et al,[34] 2005, >3 criteria versus pancreatic function test; *11,* Wiersema et al,[18] 1993, >2 criteria versus pancreatic function test.

The presence of hyperechoic, nonshadowing foci was felt to represent a minor criterion of CP. These are defined as echogenic structures ≥3 mm in both length and width with no shadowing (Fig. 5). At least 3 of these structures are needed for the feature to be considered abnormal. Experts felt it was important to optimize the focal point of ultrasonographic imaging, again to avoid artifacts.

The fourth parenchymal feature of CP is cysts. Although cysts are one of the most recognizable and intraobserver-reproducible features, it was felt to be a minor criterion. Cysts were defined as anechoic, rounded/elliptic structures that should measure ≥2 mm in short axis (Fig. 6). The panel felt that all cysts should be evaluated as a potential feature of CP regardless of their location within the pancreas. The relatively low predictive value of cysts was thought to result from the broad differential that may include pseudocysts (associated with acute or chronic pancreatitis), or prominent cystic-appearing dilation of side branches seen with CP, but also obstructive processes. Cysts may also represent primary cystic neoplasias, secondary cysts, or cystic degeneration of solid tumors. Although characteristic features have been described for many types of cysts, the tremendous overlap in appearance diminishes the diagnostic accuracy of imaging alone. The panel felt it important to fully characterize the appearance of cysts and surrounding structures.

A fifth and final parenchymal feature of CP described was stranding. This also was felt to be of poor specificity, so therefore it was classified as a minor criterion of CP. By definition, strands are hyperechoic lines ≥3 mm in length seen in at least 2 different directions with respect to the imaged plane (Fig. 7). This strict definition was felt to reduce the presence of artifacts commonly labeled as strands. At least 3 strands were considered necessary to be considered indicative of CP. Stranding should be evaluated in the body and tail and the ventral pancreas. It is a nonspecific finding if it is present in both dorsal and ventral pancreas, but not if found in the ventral pancreas alone.

Ductal features of CP

Table 3 shows the presumed ductal features of CP and their corresponding definitions. The panel felt that the presence of MPD calculi should be noted regardless of their location within the pancreas but that other ductal features should be assessed only in the body and tail of the pancreas. MPD calculi, defined as echogenic structures with acoustic shadowing, is the most predictive of CP and deemed a major A criterion (Fig. 8).

The rest of the ductal features of CP are considered minor criteria. There was consensus among the group regarding the difficulty and subjectivity when defining an ''irregular main pancreatic duct'' and ''dilated side branches.'' However, in keeping with the generally recognized definitions, an irregular MPD contour was defined as a main duct that was uneven and ectatic in its course (Fig. 9). Dilated side branches were defined by the presence of 3 or more tubular anechoic structures each measuring >1 mm in width and communicating with the MPD (Fig. 10). There was consensus that these 2 criteria should be assessed only from the pancreatic body and tail.

Although there is no consensus among published reports, the group concluded that when the MPD diameter is ≥3.5 mm within the pancreatic body or >1.5 mm within the tail, then the duct is considered dilated (Fig. 10). It is ideal in this situation to use newer-generation electronic radial EUS, which can measure accurately structures as small as 0.1 mm. Normally there should be a gradual decrease in the MPD diameter from the pancreatic head to the tail. Lack of tapering increases the likelihood of an abnormal MPD when the diameter is borderline dilated. A hyperechoic MPD margin was defined as a relatively hyperechoic duct wall found in greater than 50% of the entire MPD in the body and tail (Fig. 11). When imaged in a parallel or perpendicular orientation, *both* proximal and distal MPD borders must be hyperechoic to distinguish it from specular reflector[28] artifacts.

Correlation of EUS imaging with histologic findings

It is difficult to correlate macroscopic EUS features of CP with histologic features. Although Japanese authors

TABLE 2. Consensus-based parenchymal features of CP

Feature	Definition	Major criteria	Minor criteria	Rank	Histologic correlation
Hyperechoic foci with shadowing	Echogenic structures ≥2 mm in length and width that shadow	Major A		1	Parenchymal-based calcifications
Lobularity	Well-circumscribed, ≥5 mm structures with enhancing rim and relatively echo-poor center			2	Unknown
A. With honeycombing	Contiguous ≥3 lobules	Major B			
B. Without honeycombing	Noncontiguous lobules		Yes		
Hyperchoic foci without shadowing	Echogenic structures foci ≥2 mm in both length and width with no shadowing		Yes	3	Unknown
Cysts	Anechoic, rounded/elliptical structures with or without septations		Yes	4	Pseudocyst
Stranding	Hyperechoic lines of ≥3 mm in length in at least 2 different directions with respect to the imaged plane		Yes	5	Unknown

Attendees ranked these features according to predictive value (1 = highest predictor) with an electronic key pad.

TABLE 3. Consensus-based ductal features of CP

Feature	Definition	Major criteria	Minor criteria	Rank	Histologic correlation
MPD calculi	Echogenic structure(s) within MPD with acoustic shadowing	Major A		1	Stones
Irregular MPD contour	Uneven or irregular outline and ectatic course		Yes	2	Unknown
Dilated side branches	3 or more tubular anechoic structures each measuring ≥1 mm in width, budding from the MPD		Yes	3	Side-branch ectasia
MPD dilation	≥3.5-mm body or >1.5-mm tail		Yes	4	MPD dilation
Hyperechoic MPD margin	Echogenic, distinct structure greater than 50% of entire MPD in the body and tail		Yes	5	Ductal fibrosis

stress the importance of perilobular and interlobular fibrosis in the diagnosis of CP, endoscopic methods of tissue procurement primarily demonstrate only intralobular fibrosis. Although bands of interlobular fibrosis may be contained within core biopsy specimens, the limited sample size makes it difficult to verify the presence and relationship to surrounding structures. Furthermore, proposed histologic features of CP remain controversial even when surgical specimens are assessed. The limited size of FNA and core biopsy specimens further complicates this debate. Thus, at this time we are not incorporating cytologic or histologic features of samples obtained by EUS-guided FNA or EUS-guided Tru-cut biopsy into the criteria. We instead have proposed a correlate between EUS features and pathologic findings based on expert opinion yet understand the limitations of doing so.

In the early stages of alcohol-related CP, small, fine septations normally seen within the parenchyma become thicker, with areas of fibrosis near the septations. A prominent PD may also be seen. In more advanced disease the septations

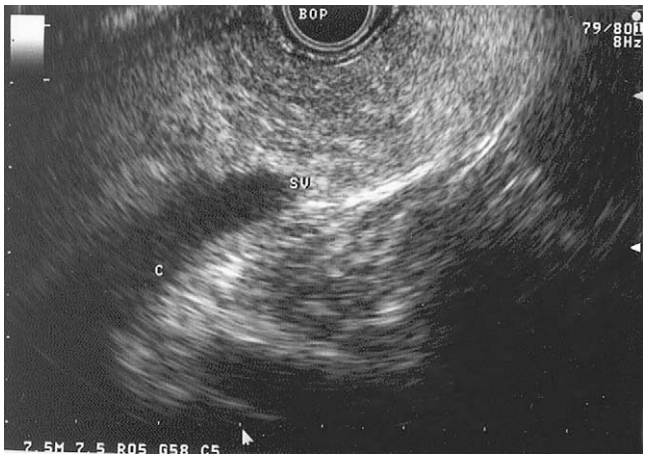

Figure 2. Normal body of pancreas, finely granular, mixed echogenic parenchyma. *SV,* Splenic vein; *c,* confluence.

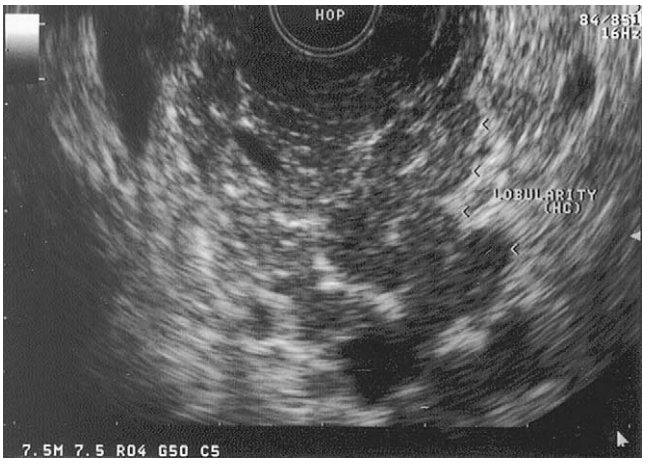

Figure 4. Pancreatic parenchyma demonstrating honeycombing lobularity.

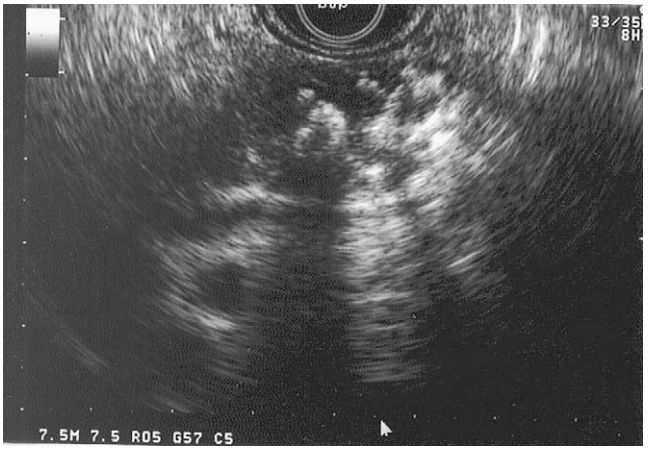

Figure 3. Hyperechoic foci with shadowing within the parenchyma.

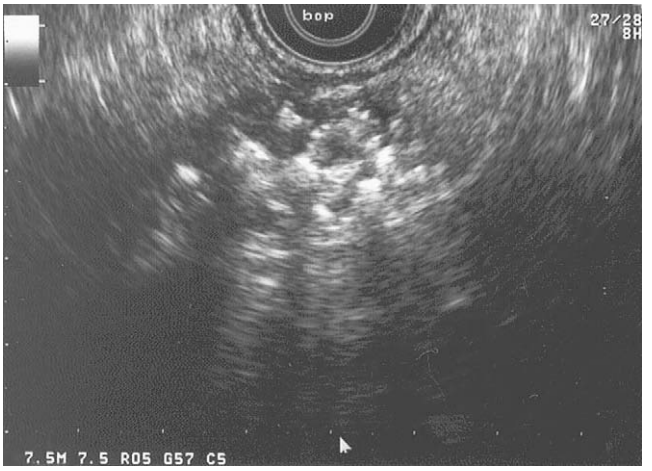

Figure 5. Nonshadowing hyperechoic foci within the parenchyma.

become thicker, accompanied by an irregular and dilated MPD, parenchymal atrophy, and focal fatty changes.

The final stage is characterized by a diffusely dilated PD, hyperechoic foci, thick septations, and lobularity. We propose that the presence of multiple hyperechoic bands encircling areas of the parenchyma represents fibrosis. These bands do not represent lobules histologically and do not correspond perfectly to physiologic units within the pancreas but instead represent areas that have been separated by bands of fibrosis. As these bands get larger, more discrete findings become evident on EUS. Akin to cirrhosis of the liver, these findings could be focal, diffuse, or multifocal.

Development of an EUS diagnostic system for CP

The underlying goal of this conference was to develop initial consensus regarding the definition, utility, and applicability of conventional CP criteria. We recognize that the results of our deliberations do not provide validation of our recommendations. However, we also believe they represent an improvement over the current means of EUS diagnosis, which assigns equal importance to each criterion. We intend to apply these criteria in a manner that provides easy and reproducible means of EUS diagnosis and grading of CP so that they may be used to help guide patient care and future study design. Of note, the experts reviewed each EUS feature with its corresponding definition and observed a κ value for interobserver reliability of >0.7 for each feature. This good level of reliability was achieved after an extensive review of the literature followed by deliberation among the participants.

The diagnostic system should be applied independent of a patient's sex, age, BMI, alcohol and tobacco use, and other clinical variables, recognizing that some of these factors lead to a higher likelihood of pathologic conditions. The purpose of categorizing EUS features of CP as major and minor was based on the premise that not all features have the same positive predictive value or reliability. Major criteria were divided into major A (hyperechoic foci with shadowing and MPD calculi) and major B (lobularity, honeycombing type). Minor criteria included (1)

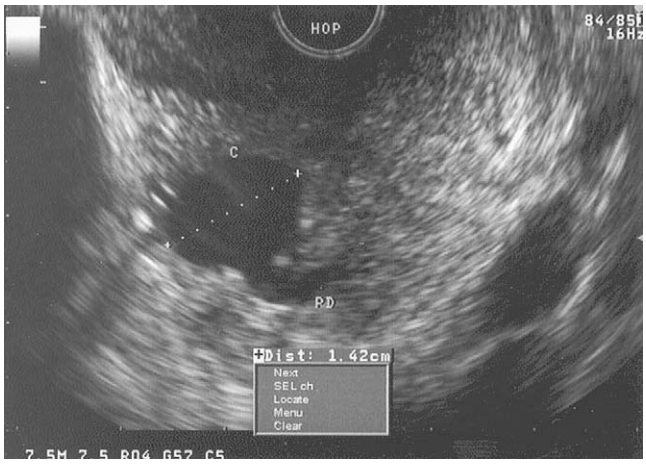

Figure 6. Pancreatic cyst *(c)* measuring 1.4 cm, communicating with the PD.

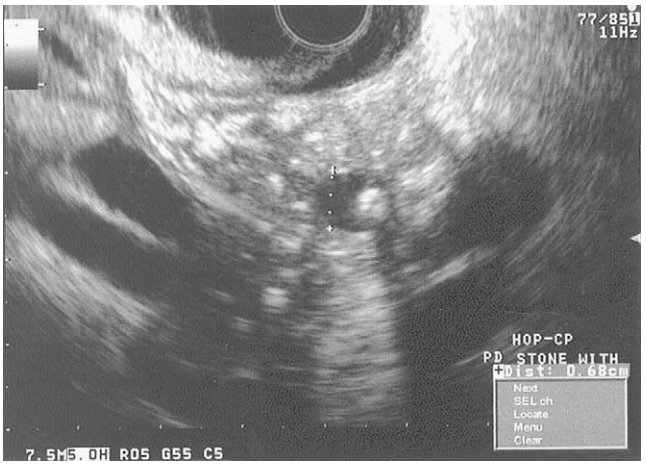

Figure 8. Dilated pancreatic duct (0.68 cm) with MPD calculi with shadowing.

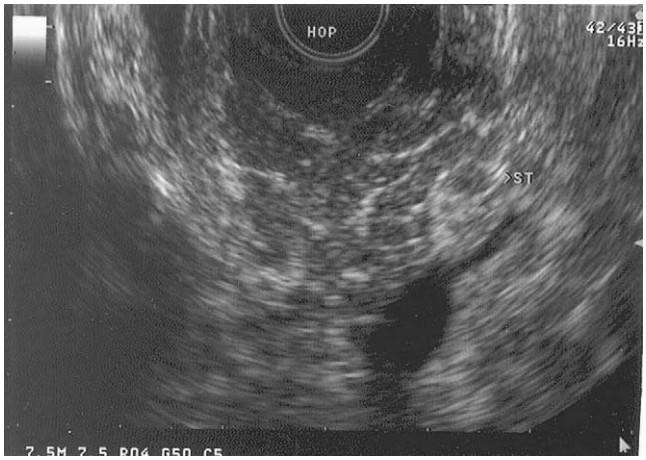

Figure 7. Pancreatic parenchyma with stranding (hyperechoic lines >3 mm in multiple directions).

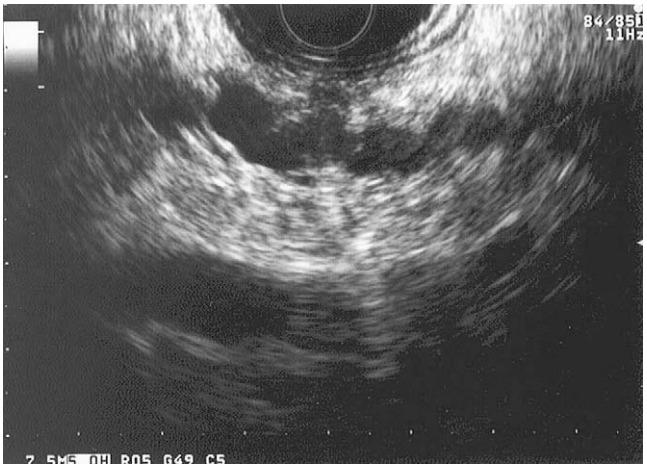

Figure 9. Dilated PD with marked contour irregularity.

cysts, (2) dilated MPD, (3) irregular MPD contour, (4) dilated side branches, (5) hyperechoic duct wall, (6) strands, (7) hyperechoic foci (nonshadowing), and (8) nonhoneycombing lobularity (noncontiguous lobules).

Traditionally, the EUS diagnosis of CP has been established after a predetermined threshold of features has been reached. Some authors require a minimum of 2, whereas others require a minimum of 5 features. Clearly, the higher the threshold, the higher the specificity (low sensitivity), whereas the lower the preset threshold, the lower the specificity (high sensitivity). EUS examinations noting a number of features equal to the ROC-derived best cutoff value are considered indeterminate (Fig. 1).

A summary of the consensus opinion of EUS diagnosis of CP is presented in Table 4. First, examinations ''consistent with CP'' are achieved by (1) 1 major A feature and $\geq$3 minor features, (2) 1 major A and major B, or (3) 2 major A features. Second, examinations ''suggestive of CP'' are achieved by (1) 1 major A and <3 minor features, (2) major B and $\geq$3 minor features, or (3) any 5 or more minor features. Third, examinations ''indeterminate for CP'' are achieved by (1) >2 minor features, <5 minor features without major features or (2) major B feature alone or with <3 minor features. Last, ''normal''results are achieved by $\leq$2 minor features. This last category excludes features such as cysts, dilated MPD and side branches, hyperechoic nonshadowing foci, and major features.

CONCLUSION

The available data support the potential value of EUS as a tool to diagnose or exclude CP in appropriately selected patients. However, confusion exists regarding the proper use of the EUS criteria for CP.

We present consensus-based criteria for an EUS diagnostic system for CP that takes into account the existing body of evidence and the experience of experts. To

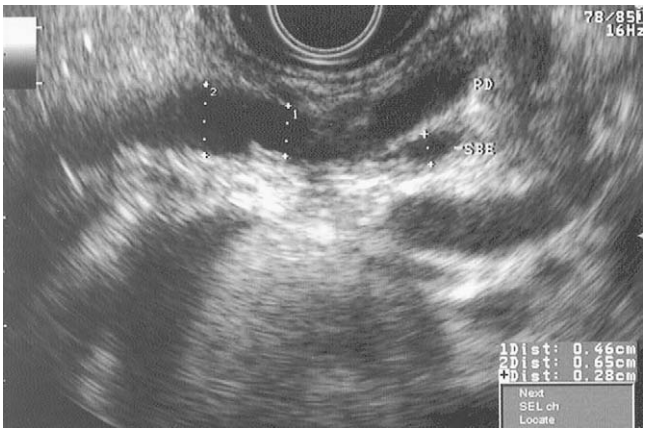

Figure 10. EUS image demonstrating a dilated PD measuring 0.65 cm with side-branch ectasia measuring 0.28 cm.

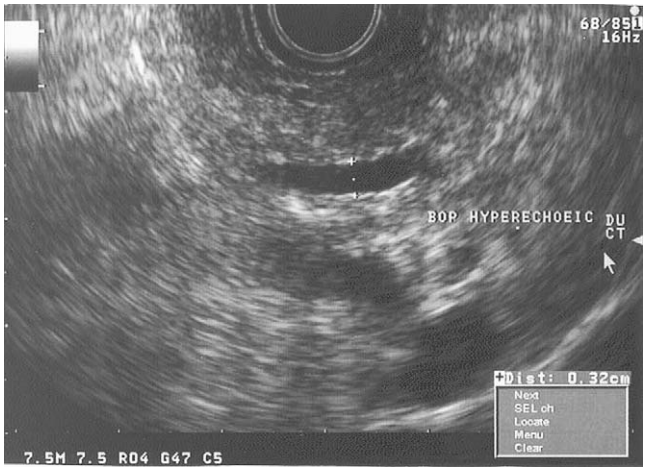

Figure 11. PD demonstrating hyperechoic borders.

promote standardization in practice and reproducibility of future research endeavors, there is a need to make these EUS images of the various features of CP available for review in a Web-based open forum where endosonographers from around the world can view the images, exchange ideas with their colleagues, and hopefully incorporate them into their practice.

TABLE 4. EUS diagnosis of CP on the basis of consensus criteria*

I. Consistent with CP
A. 1 major A feature (+) ≥3 minor features
B. 1 major A feature (+) major B feature
C. 2 major A features
II. Suggestive of CP†
A. 1 major A feature (+) <3 minor features
B. 1 major B feature (+) ≥3 minor features
C. ≥5 minor features (any)
III. Indeterminate for CP†
A. 3 to 4 minor features, no major features
B. major B feature alone or with <3 minor features
IV. Normal
≤2 minor‡ features, no major features

*EUS diagnosis of CP should be made in the appropriate clinical setting.
†Diagnosis requires confirmation by additional imaging study (ERCP, CT, MRI, or PFT).
‡Excludes cysts, dilated MPD, hyperechoic nonshadowing foci, dilated side branch.

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