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Review

Endoscopic Diagnostic of Chronic Pancreatitis

Aleksandar Čubranić[1], Renata Dobrila Dintinjana[2] and Nenad Vanis[3]

[1] Gastroenterology Department, Internal Clinic, Clinical Hospital Center Rijeka, Rijeka, Croatia
[2] Department of Radiotherapy and Oncology, Clinical Hospital Center Rijeka, Rijeka, Croatia
[3] Endoscopy Unit, Gastroenterology Department, University Hospital Center Sarajevo, Sarajevo, Bosnia and Herzegovina

ABSTRACT

Chronic pancreatitis is defined as a continuous inflammatory pancreatic disease, one characterized by irreversible morphological changes, often associates with pain and sometimes with the loss of endocrine and exocrine function. As a histological confirmation of chronic pancreatitis is often unavailable, the diagnosis is traditionally based on imaging methods such as computerized tomography (CT) or endoscopic retrograde cholangiopancreatography (ERCP), and recently magnetic resonance cholangiopancreatography (MRCP) as a noninvasive alternative to ERCP. Developments in the classification system of CP include the Marseille classification of 1963 which offered histopathologic criteria for CP, the Cambridge classification of 1984 which introduced imaging features of computed tomography (CT), transabdominal ultrasound (TUS) and endoscopic retrograde cholangiopancreatography (ERCP) for classification of CP as well as Rosemont classification system of 2007 which presented the endoscopic ultrasonography diagnosis of CP. Endoscopic ultrasonography (EUS) was first introduced as a diagnostic method for evaluation of pancreatic disease in 1986. It has experienced significant improvements since then and allowed for an alternative approach in diagnosing patients with pancreatic diseases. In patients with suspected pancreatic masses EUS-guided fine needle aspiration (EUS-FNA) is the best method for obtaining tissue diagnosis and differentiating CP from pancreatic carcinoma. The recent studies indicate that EUS is the method of choice when compared with other imaging methods such as ERCP because it frequently provides more accurate diagnostics. The aim of this review is to discuss the findings in endoscopic diagnostics up to the present moment and to indicate advantages, limitations and possible complications along with the current recommendations in CP diagnostics.

Key words: *chronic pancreatitis (CP), endoscopic diagnostics, endoscopic ultrasonography (EUS), endoscopic retrograde cholangiopancreatography (ERCP)*

Introduction

Chronic pancreatitis is an inflammatory process that leads to progressive irreversible damage to the exocrine and endocrine pancreatic function along with a gradual replacement with connecting tissue. The disease is easily recognized with the development of complications in its advanced stages while it's often stays unrecognized in its early and even moderate forms. Incidence of chronic pancreatitis ranges from 2 to 23 per 100 000 people per year in developed countries and prevalence is around 30/100 000. Alcoholism is the etiology in about 75% of diseased, 15% are idiopathic while the remaining causes include autoimmune and genetic factors and others related to recurrent severe acute pancreatitis and biliary obstruction. The disease most commonly occurs around 45 years of age and 75% of diseased are male[1,2].

In last couple of years chronic pancreatitis has been shown as damage of the pancreas ethiopathogenetically caused by interaction between genetic and environmental factors. In a small degree of patients the cause of the disease remains unrecognized. Patients with chronic pancreatitis usually suffer of pain in the upper abdomen, radiating under the costal edges and to the back. It is further worsened by food intake and reduced by fasting. Once 85–90% of exocrine function is lost, symptoms of malapsorption and maldigestion occur which is clinically shown as steatorrhoea, weight loss and liposoluble vitamin deficit (A,D,E,K). Endocrine insufficiency in term of diabetes usually occurs several years following exocrine deficiency. Establishing a diagnosis of chronic pancreatitis is not simple, it usually takes around 5 years and includes a well

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taken anamnesis, physical examination as well as functional pancreatic tests and imaging methods. Endoscoping techniques have an important value in diagnosis and treatment of chronic pancreatitis. Interventional endoscopy with sphincteroctomy and stent placement in the pancreatic duct has its use in treatment of complications of chronic pancreatitis, as well as the inner draining of pancreatic pseudocysts and neurolysis of celiac plexus under the guidance of endoscopic ultrasound.

Endoscopic methods

Endoscopic methods that help us in diagnostics of chronic pancreatitis are: Endoscopic ultrasound, Endoscopic retrograde cholangiopancreatography, Esophagogastroduodenoscopy

Endoscopic ultrasound in diagnosis of chronic pancreatitis

Endoscopic ultrasound was for the first time used as a diagnostic method for chronic pancreatitis in 1986[3]. Earlier publications in this field used different terminology and criteria for diagnosis of chronic pancreatitis; therefore it was challenging to use this method in everyday practice. For that reasons a consensus study has been held in Rosemont, Illinois in 2007[4]. The main goal of the study was to establish primary criteria for the use of the endoscopic ultrasound in everyday practice. 32 specialists in endosonography from North America and Japan, divided in groups by 5–6 experts, looked through available data from the literature on the endoscopic ultrasound criteria by that time. Every participant brought a definition, terminology and predictable value of parencihamal and ductal changes in chronic pancreatitis. Criteria for endoscopic ultrasound diagnosed chronic pancreatitis have been divided in major and minor, referring to their predictable value. Mentioned criteria had very good reliability KAPPA bigger then 0.7 for every change. Diagnostic system is being used regardless of patient sex, age, Body Mass Index (BMI) or drinking/smoking habits. Textual and picture review of parenchimal and ductal changes made with the endoscopic ultrasound is shown. (Tables 1, 2) (Figures 3–12).

There are lots of comparative studies between endoscopic ultrasound (EUS) and other diagnostic modalities showing bigger sensitivity and specificity of EUS in diagnosis of chronic pancreatitis. It detects early and minimal changes that cannot be shown with other diagnostic methods, thereby it has potentially replaced all of the other diagnostic modalities.

Since there are different combinations of major and minor criteria for changes shown with the EUS, Rosemont classification system divides patients with endoscopicaly visible changes for diagnosis of chronic pancreatitis in a) safe b) probable c) undetermined d) normal (no changes) for diagnosis (Tables 1–3)[5–8].

Obtained data help the potential value of EUS as a diagnostic method or to exclusion of chronic pancreatitis in selectioned patients. In a complex disease like chronic pancreatitis, where there are no universally applied standards for diagnosis, criteria obtained with EUS in the diagnosis of chronic pancreatitis can be determined as a expert opinion and became a guideline for future clinical studies, prospective studies that could include the nature of the disease, early diagnosis and a potential respond to treatment[9].

TABLE 1

PARENCHYMAL FEATURES OF CHRONIC PANCREATITIS, ACCORDING TO ROSEMONT CLASSIFICATION

Characterstic	Definition	Major criteria	Minor criteria	Range	Histological correlation
Hyperechoic foci with shadowing	Ehogenic 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
With honeycombing	Contiguous 3 lobules	Major B			
Without honeycombing	Noncontiguous lobules		Yes		
Hyperchoic foci without shadowing	Echogenic structures foci ≥2 mm in both length and width whit no shadowing		Yes	3	Unknown
Cysts	Anchoic, rounded/elliptical structures whit or whithout septations		Yes	4	Pseudocyst
	Hyperechoic lines of ≥3 mm in length in at least 2 different directions with respect to the imaged plane		Yes	5	Unknown

TABLE 2
DUCTAL CHARACTERISTICS OF CHRONIC PANCREATITIS, ACCORDING TO ROSEMONT CLASSIFICATION

Characteristic	Definition	Major criteria	Minor criteria	Range	Histological 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%		Yes	5	Ductal fibrosis

MPD = Main pancreatic duct

TABLE 3
EUS DIAGNOSIS OF CP ON THE BASIS OF CONSENSUS CRITERIA

I. Consistent whit 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 (+) ≥ 3 minor features
   c. 5 minor features
III. Indeterminate for CP
   a. 3–4 minor features, no major features
   b. major B feature alone or with <3 minor features
IV. Normal
   ≤ 2 minor features, no major features

Endoscopic retrograde cholangiopancreatography (ERCP) in diagnostics of chronic pancreatitis

ERCP is a strictly therapeutic method for some of the diseases of pancreas and billiary system, and has been replaced as a diagnostic method with the endoscopic ultrasound and magnetic resonance cholangiopancreatography (MRCP). This method mostly replaces surgery so it can be used for stones extraction from ductus choledocus with sphincerotmy and placement of endoprotesis for palliative treatment of malignant obstructions of the billiary system. Complications during the procedure are hyperamliazemy and iatrogenic pancreatitis. Complications like bleeding or colangitis are rare. Incidence of all the complications is 5–8%.

Until the invention of EUS, ERCP was a gold standard for diagnosis of chronic pancreatitis. Chronic pancreatitis was classified based on morphological changes of pancreatic ducts, that where established and defined in 1983 on a symposium in Cambridge[10,11]. The classification is based on ductal changes of the main pancreatic duct and the minor ones.

Based on ERCP chronic pancreatitis is divided in 5 stages:

Stage I – normal view of pancreotogram
Stage II – questionable finding, <3 changes in side ducts are shown
Stage III – mild chronic pancreatitis, 3 or more side ducts are changed
Stage IV – medium severe chronic pancreatitis, >3 side ducts are changed as well as the main duct
Stage V – severe chronic pancreatitis – all of the above plus 1 or more of following changes: dilatation of the main duct for more than 10mm, intraductal defect of loading, ductal strictures[12].

Esophagogastroduodenoscopy (EGDS) in diagnosis of chronic pancreatitis

EGDS enables quick diagnosis and therapy of many diseases of the upper gastro intestinal system (esophagus, stomach, duodenum and patomorphological changes of this organs, it enables cytological and patohistological diagnosis). One of the indications for endoscopy of the upper GI tract is collecting the samples of duodenum and jejunum as well as their content as a part of the functional tests of pancreas. During the EGDS pathomorphological changes of the mucosa in bulbus duodeni and descending part of duodenum can be seen in a patient with the chronic inflammatory changes of pancreas. Some patomorphological changes of duodenum during the EGDS can suggest chronic pancreatitis (Figures 1, 2).

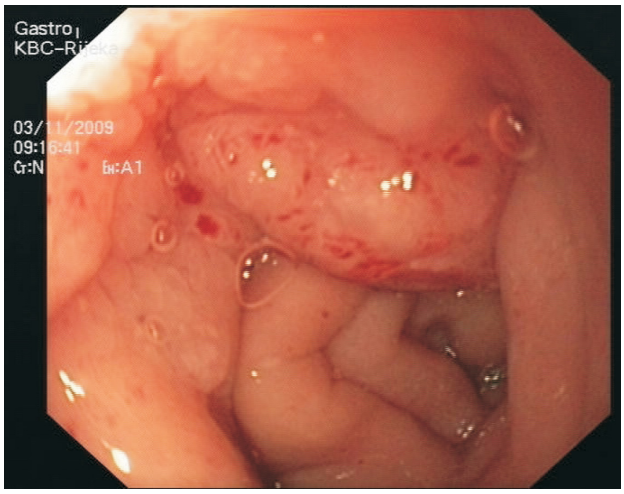

Fig. 1. Benign duodenal stenosis in chronic pancreatitis.

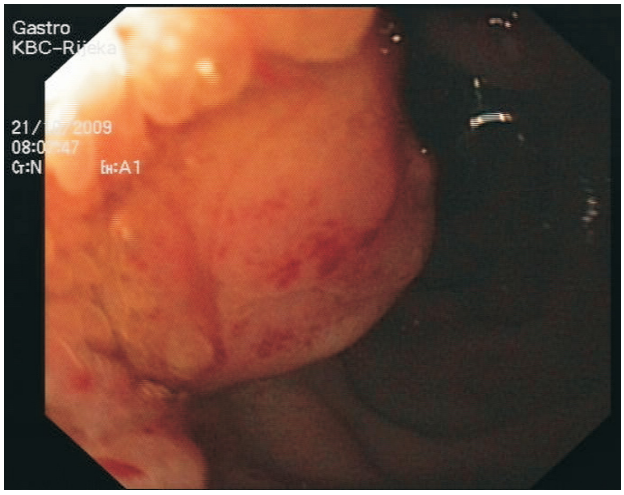

Fig. 2. Benign duodenal stenosis in chronic pancreatitis.

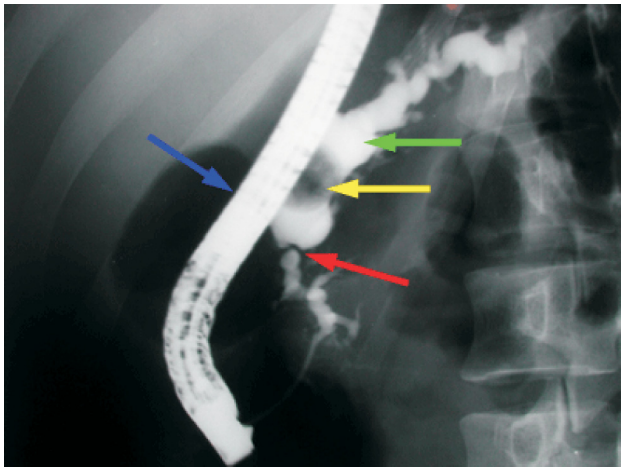

Fig. 3. ERCP display severe chronic pancreatitis (arrows show concretions and stricture).

Conclusion

Chronic pancreatitis is a clearly defined disease, but unfortunately, insufficiently classifies disease, which prevents us to start with the early treatment and prevention. Histopathological verifications and classification of chronic pancreatitis are necessary for the retroperitoneal localization, but the tissue obtained with the minimal invasive procedure isn't always adequate. As a consequence lot of the classification of the disease is not based on the tissue changes, but as a basis for diagnosis, treatment and studies, imaging methods are used. In advanced disease morphological changes are clearly shown with methods like ultrasound, endoscopic ultrasound, CT, MRCP, ERCP. This imaging modalities are suboptimal (except for the EUS) in detection of early and minimal changes in chronic pancreatitis.

Where is endoscopy today in diagnosis of chronic pancreatitis? EGDS can raise a suspicion on chronic pancreatitis, but it is not the method of choice for diagnosis. ERCP was a golden standard for diagnosis of chronic pancreatitis. Knowing that ERCP chows only ductal changes, but not the parenchimal, and having in mind all possible complications, ERCP is today a method used only in therapeutical purposes. Today's role of ERCP in chronic pancreatitis lies in placement of endoprotesis in an obstructive type of pancreatitis.

Technical development of EUS enabled a new approach in classification and diagnosis of chronic pancreatitis. Where there is a clinical doubt that there has been a developed carcinoma in chronically changed tissue of pancreas, EUS-FNA for obtaining cytological material can be done. Endoscopic ultrasound is by the time, not broadly used method, outside the big hospital centers, because it requires high expertise for handling and interpretation of the obtained pictures. Other available imaging methods (CT, UTZ, MRCP) are being used for the patients with the suspected chronic pancreatitis. There is a question if the minimal changes shown by the EUS should be treated? For this time, only the patients with the symptoms should be treated. Rosemont classification sets a base for further prospective studies that would include the nature of the disease, potential response to early treatment, prevention of the progression of the disease and its complications. Therefore, it is not important only to early diagnose the disease, but also to start with the treatment as early as possible.

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A. Čubranić

Gastroenterology Department, Internal Clinic, Clinical Hospital Center Rijeka, Krešimirova 42, 51 000 Rijeka, Croatia
e-mail: acubrani@yahoo.com

ENDOSKOPSKA DIJAGNOSTIKA KRONIČNOG PANKREATITISA

S A Ž E T A K

Kronični pankreatitis definiramo kao kontinuiranu uplanu bolest gušterače, koju karakteriziraju ireverzibilne morfološke promjene, često se povezuje s boli te ponekad s gubitkom endokrine i egzokrine funkcije. Histološku potvrda kroničnog pankreatitisa ćesto nije moguća, stoga se dijagnoza tradicioinalno temeni na slikovnim metodama poput CT-a ili ERCP-a, te od nedavno MRCP-a kao neinvazivne alternative ERCP-u. Razvoj sustava klasifikacije kroničnog pankreatitisa uključuje klasifikaciju iz Marseillea iz 1963 koja je ustanovila histopatološke kriterije, te klasifikaciju iz Cambridgea koja je u klasifikaciju uvela CT, transabdominalni ultrazvuk, ERCP. Rosemont sustav klasifikacije iz 2007 uključila je još i endoskopsku ultrasonografiju (EUS) u dijagnozu kroničnog pankreatitisa. EUS se kao dijagnostička metoda po prvi puta javila u evaluaciji kroničnog pankreatitisa 1986. godine. Od tada je došlo do mnogih poboljšanja te nam danas omogućuje alternativni pristup u dijagnostici pacijenata sa kroničnim pankreatitisom. Kako bi se dijagnosticirali i razlikovali kronični pankreatitis i karcinom pankreasa kao najbolja metoda za uzorak tkiva nameće se EUS navođena aspiracija finom iglom (EUS-guided fine needle aspiration). Nedavne su studije pokazale kako je EUS metoda izbora u usporedbi sa ostalim slikovnim metodama kao što je ERCP jer češće daje točniju dijagnostiku. Cilj ovog preglednog rada je raspraviti nalaze endoskopske dijagnostike do danas, kako bi se razjasnile prednosti, limitacije i moguće komplikacije zajedno sa trenutnim preporukama u dijagnostici kroničnog pankreatitisa.