Endoscopy

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Current Developments in Diagnostic and Therapeutic Endoscopy

Section Editor: John Baillie, MB ChB, FRCP

The Role of EUS in the Investigation of Abdominal Pain of Possible Pancreatic Origin

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G&H What symptoms are usually associated with abdominal pain of possible pancreatic origin?

JC The symptoms of abdominal pain secondary to noncalcific chronic pancreatitis, also known as early chronic pancreatitis, are not very specific and often overlap with those of other diseases. The most common symptom is epigastric pain often worsened by eating, usually radiating to the back. Occasionally, patients will have nausea and vomiting as well. Patients with very advanced chronic pancreatitis may develop diabetes or maldigestive diarrhea (steatorrhea), in which the pancreas is so damaged that it is unable to produce pancreatic enzymes to aid in the digestion of food.

G&H How is this condition differentiated from or related to other gastrointestinal diseases?

JC Several gastrointestinal diseases share the nonspecific symptoms of noncalcific chronic pancreatitis mentioned above. For example, patients with biliary colic, pain due to biliary or gallstone disease, or infection of the biliary tree can often present with the same type of postprandial epigastric pain, radiating to the back and to the right side and worsening with ingestion of fatty foods as well. Patients with gastroparesis also experience similar symptoms of postprandial early-fullness and slight abdominal discomfort and occasional nausea and vomiting. Thus, due to the nonspecificity of these symptoms, it is quite challenging to correctly diagnose abdominal pain secondary to noncalcific chronic pancreatitis. In contrast, more advanced chronic pancreatitis (or chronic calcific pancreatitis), which is signified by the development of calcifications in the pancreas, is much easier to diagnose.

G&H How commonly does abdominal pain of pancreatic origin occur in the general population?

JC The prevalence of this condition has been reported in anywhere from 12 to 45 patients per 100,000 in the general population, with a male preponderance. However, because this disease is so difficult to diagnose, the true prevalence is likely higher. In fact, patients with noncalcific chronic pancreatitis are often misdiagnosed with irritable bowel syndrome, functional abdominal pain, or other related diseases because most of their diagnostic examinations, blood tests, or endoscopies are normal or only slightly abnormal.

There has been some discussion in the literature that the incidence of noncalcific chronic pancreatitis may have increased over the past several years. It is unclear whether this is due to an actual increase in the disease process or whether physicians are becoming more skilled at diagnosing the disease.

G&H Prior to the use of endoscopic ultrasound (EUS), what were the options for investigating patients with abdominal pain of suspected pancreatic origin?

JC Prior to the use of EUS, there were several options, though there was no gold standard for diagnosing noncalcific chronic pancreatitis and the available tests performed best in advanced pancreatic disease. Physicians usually utilized a combination of tests, one of which was endoscopic retrograde cholangiopancreatography (ERCP). Unfortunately, ERCP examines only the ducts of the pancreas, and ductual change is often not present in early disease. ERCP is unable to obtain information regarding the

parenchyma of the pancreas, where often there are many changes of noncalcific chronic pancreatitis. There is also a very real risk (5–7%) of pancreatitis with ERCP. Thus, ERCP is not very effective in this patient population.

Another type of radiologic examination includes plain abdominal films, which are effective only for patients with chronic calcific pancreatitis. Plain films can detect calcifications in the pancreas, but they cannot detect other subtle changes in the pancreatic parenchyma or ducts. Computed tomography (CT), magnetic resonance imaging, and ultrasound can detect ductal and parenchymal changes but, once again, lack sensitivity for detecting the subtle changes of early disease.

Another option is to conduct direct or indirect functional tests of the pancreas. In direct testing, the pancreas is directly stimulated with either food or hormones such as cholecystokinin or secretin to secrete bicarbonate as well as pancreatic digestive enzymes, both of which can be collected via a tube inserted through the nose and down into the small intestine. The physician can conduct quantitative assays over time on the secreted collections to try to determine whether or not the patient has pancreatic exocrine insufficiency. However, as the pancreas has a tremendous reserve, normally it is not until 90% of the pancreas has been destroyed and replaced with fibrosis that pancreatic exocrine insufficiency is noticeable, which means that this examination is not sensitive enough for detecting early disease. This examination is also quite uncomfortable for patients. Indirect testing of pancreatic exocrine function involves stool testing for spot fecal fat or a 72-hr collection to examine the amount of fat in the stool. If the pancreas is not producing enough digestive enzymes, more fat would be found in the stool than normal.

G&H Could you explain how EUS is used to investigate abdominal pain of possible pancreatic origin?

JC EUS utilizes a specialized endoscope consisting of both a small ultrasound probe and optics at the tip. The scope is guided using a combination of endoscopic and ultrasound landmarks to find and examine structures such as the pancreas. From the patient's perspective, the test is performed in the same way as upper endoscopy: the patient is sedated, and the endoscope is inserted through the mouth down the esophagus into the stomach and then into the duodenum. It is important to note that EUS is very operator-dependent, as the endosonographer must interpret ultrasound images and decide whether the patient has a certain disease process or not. Performing EUS successfully requires an operator who is highly skilled at endoscopy as well as extensively experienced with examining ultrasound images, especially when diagnosing chronic pancreatitis. I believe that EUS is most likely best performed in a specialty high-volume center with an experienced endosonographer.

Once the pancreas is located via EUS, the endosonographer looks for signs of inflammation within the pancreas. There are 9 basic features of inflammation: a dilated pancreatic duct, an irregular pancreatic duct, hyperechoic duct walls, and prominent side branches (the ductual features) as well as hyperechoic strands, hyperechoic foci, lobularity, cysts, and calcifications (the parenchymal features). When at least 4 of these features are present, there is a high probability that the patient has chronic pancreatitis. Having said that, it is unclear which features (other than calcifications), if any, are more important than the others, and which more strongly suggest the presence of chronic pancreatitis. Age should also be taken into account when looking for chronic pancreatitis. The above inflammatory changes in the pancreas may become more common in patients as they age. Thus, the older the patient, the higher the threshold should be to make the diagnosis of chronic pancreatitis.

G&H How does the sensitivity and specificity of EUS in the investigation of abdominal pain of suspected pancreatic origin compare with that of other options?

JC The main benefit of EUS over other radiologic studies is that because the ultrasound probe is placed so close to the pancreas (only a few millimeters away), it is possible to scan the pancreas at a relatively high frequency and generate very high-resolution images. The spatial resolution of EUS images is much greater than that of any other radiologic examination. In contrast to ERCP, EUS has the capability of examining not only the ducts of the pancreas but the pancreatic parenchyma at a very high resolution. This is important because, as mentioned above, patients with noncalcific chronic pancreatitis may have limited ductal changes.

A good study showing how EUS performs in diagnosing chronic pancreatitis is a recent study performed by Varadarajulu and colleagues, which looked at patients undergoing surgery for partial or complete pancreatectomy, usually due to cancer. Prior to surgery, the patients underwent EUS and imaging of pancreatic parenchyma far from the tumor. The researchers compared their EUS findings to the histology correlates of the surgical resection specimen. Histology correlates have been shown to be the most accurate method of diagnosing noncalcific chronic pancreatitis. The study demonstrated that EUS had a sensitivity of 90.5% and a specificity of 85.7% in detecting noncalcific chronic pancreatitis based on histology correlates. Also of note, CT missed the diagnosis

in all of the cases of noncalcific chronic pancreatitis. This study offers great evidence of the excellent performance characteristics of EUS in patients with noncalcific chronic pancreatitis.

G&H What is the usual method for pain management in this patient population? Does EUS have a therapeutic role?

JC The standard medical treatment for patients with chronic pancreatitis is primarily avoidance of the agent that caused it (usually alcohol). Occasionally, pancreatic enzymes may help not only with the digestion and absorption of food but may also help with the pain. Nevertheless, these patients usually require chronic narcotic pain therapy. The primary therapeutic role of EUS is celiac plexus block, in which the echoendoscope locates the celiac plexus, the collection of nerves through which pain sensation from the pancreas is transmitted to the brain, and a combination of the anesthetic bupivacaine and the steroid triamcinolone is injected. This reduces the inflammation and decreases the number of pain signals sent to the brain, causing patients to feel less pain. Unfortunately, celiac plexus block is only moderately effective. It may improve pain scores and decrease narcotic usage in only approximately 50% of patients; it is rare for a celiac plexus block to eliminate all of the pain. Nevertheless, celiac plexus block is a very safe procedure and one that we commonly offer to patients with chronic pancreatitis. If it is effective, patients are usually brought back to reinject the area around their celiac plexus every 2–6 months for pain management.

As noncalcific chronic pancreatitis is challenging to diagnose, many patients with the condition may go undiagnosed. They may require narcotics to manage their pain, causing them to be labeled as narcotic-dependent or drug seekers and stigmatizing them in the eyes of their family and community. That is why EUS is so important; I believe that it is currently the best tool that we have available for diagnosing and treating noncalcific chronic pancreatitis and one that should be utilized more frequently in the appropriate patient population.

G&H Are there any disadvantages or risks associated with using EUS in this patient population?

JC EUS is a very safe examination. The risks associated with EUS are the same ones associated with upper endoscopy: primarily risks related to sedation or perforation. At our institution, we minimize sedation risks by utilizing nurse anesthetist–administered propofol to assist in the sedation of our patients.

G&H What do you foresee as the next steps for future research?

JC Larger studies with histologic correlates, similar to the study conducted by Varadarajulu and colleagues, are needed to continue to evaluate the performance characteristics or the sensitivity and specificity of EUS in this disease process. In addition, we need longitudinal studies in which patients are diagnosed with noncalcific chronic pancreatitis via EUS and then followed over time to determine whose disease advances to the chronic calcific stage. Also needed are more data in larger populations on the role of celiac plexus block or neurolysis (which refers to injecting alcohol around the nerves, thereby destroying them). These patients should be followed over a long time period, with study outcomes primarily involving the use of narcotics and patient function.

Suggested Reading

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