Establishing Diagnosis of Chronic Abdominal Pain: Gastroenterologist View

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Introduction

Abdominal pain is a common complaint encountered in gastroenterology practices [1]. Most patients with abdominal pain have a functional disorder (e.g., irritable bowel disorder) or a benign and self-limited condition. However, abdominal pain may sometimes indicate a serious or life-threatening illness. The primary role of the gastroenterologist is to differentiate organic from functional disease and to provide directed treatment for the underlying cause of pain. The clinical challenge and expense of evaluating abdominal pain arises from the concern over missing a structural or organic disease.

Many gastrointestinal and systemic disorders may cause abdominal pain (Table 3.1). The gastroenterologist must consider these myriad possibilities and carry out a rationale evaluation based on plausible causes. Functional disorders should be considered once organic pathology has been confidently excluded. This chapter will focus on the diagnostic tools which gastroenterologists and internists utilize in the evaluation of abdominal pain, ranging from a careful history to sophisticated invasive testing.

History

The clinician must initially adopt a broad differential diagnosis that becomes more focused as the investigation progresses. The history should inquire about the characteristics of abdominal pain including the onset, duration, location, nature, radiation, associated features, and relieving and aggravating factors. Establishing the duration of pain is very useful in narrowing the differential diagnosis. Chronic abdominal pain is defined as constant or intermittent pain occurring for greater than 6 months. Acute abdominal pain is when pain has been occurring for up to several days, and sub-acute abdominal pain is from several days to 6 months. After establishing chronicity, the location, nature, and radiation of pain should be determined to help focus attention to certain pathologies. Upper abdominal pain can arise from biliary, pancreatic, gastric, and duodenal pathology. Mid-abdominal pain likely originates from the small bowel (e.g., Crohn's disease, celiac disease, bacterial overgrowth, partial small bowel obstruction, chronic mesenteric ischemia). Lower abdominal pain arises from the colon (e.g., irritable bowel syndrome, colitis), bladder, or reproductive organs. It is important to differentiate between constant and intermittent chronic abdominal pain. While intermittent pain can have many causes, constant abdominal pain results from only a few gastrointestinal etiologies (Table 3.2). The presence of aggravating and relieving factors can be quite informative. Pain that is positional in nature is likely to be of musculoskeletal origin. Worsening of pain with eating is typical in peptic ulcer disease, chronic mesenteric ischemia, and in the presence of biliary and pancreatic pathologies. Relief with bowel movements is expected with constipation and irritable bowel syndrome (IBS). Pain related to menstruation may signify a gynecological cause. The clinician should probe for coexisting symptoms such as nausea, vomiting, diarrhea, blood in stools, and systemic symptoms like fever or rash. The presence of diarrhea suggests IBS, chronic pancreatitis, inflammatory bowel disease, celiac disease, and bacterial overgrowth. "Alarm" symptoms of fever, weight loss, night sweats, appetite, or nocturnal awakening often indicate organic pathology.

Rare medical causes of abdominal pain should be considered when structural etiologies are ruled out. Recurrent attacks of fever, joint pain, and abdominal pain suggest familial Mediterranean fever [2]. Recurrent attacks of abdominal pain, tachycardia, constipation, and dark urine suggest acute intermittent porphyria. The presence of hyponatremia, hyperkalemia, and hyperpigmentation should raise suspicion for

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Table 3.1 Etiology of chronic abdominal pain

Etiology	Typical diagnostic tests	Treatment
Organic		
Gallstones	US, HIDA scan	Cholecystectomy
Cholangitis	RUQ US, ERCP	ERCP
Appendicitis	CT scan	Appendectomy
Peptic ulcer disease	Upper endoscopy, *H. pylori* testing	Proton pump inhibitor treatment of *H. pylori*
Chronic pancreatitis	EUS, CT scan, MRI,	Life style modifications Pancreatic enzymes Celiac plexus block
Inflammatory bowel disease	CTE, colonoscopy, EGD	5-ASA, Budesonide, prednisone, Imuran, 6-MP, cyclosporine, Anti-TF agents
Mesenteric ischemia	Mesenteric ultrasound, CT angiography	Endovascular or surgical revascularization
Hernias	CT scan	Hernia repair
Intestinal obstruction	CT scan, small bowel series	Surgical repair
Abdominal adhesions	Ct scan, small bowel series	Lysis of adhesions Symptomatic management
Abdominal neoplasms	CT scan, MRI, EUS	Surgical resection Endoscopic resection
Lactulose intolerance	Breath testing Trial of withdrawal	Lactulose avoidance
Small bowel bacterial overgrowth	Breath testing	Antibiotics
Gastroparesis	Gastric emptying study	Promotility agents
Pelvic inflammatory disease	Laboratory testing Gram stain and microscopic examination of vaginal discharge Ultrasound	Antibiotics
Mittelschmertz	History	Symptomatic management
Diabetic neuropathy	History	Symptomatic management
Eosinophilic gastroenteritis	Upper and lower endoscopy	Budesonide Prednisone Oral cromolyn
Familial Mediterranean fever	History Genetic testing	Colchicine
Hereditary angioedema	C4 esterase levels	Avoid triggers C1 esterase inhibitor replacement protein Ecallantide Icatibant
Porphyria	Porphyria screen	Avoid triggers Intravenous hemin
Celiac artery syndrome	Mesenteric ultrasound CT angiogram MR angiogram	Surgery
Superior mesenteric artery syndrome	Mesenteric ultrasound CT angiogram MR angiogram	Surgery
Abdominal migraine	History	Anti-migraine medications
Herpes Zoster	Physical examination PCR Viral culture DFA test	Nucleoside analogues
Lead poisoning	Blood lead level	Reduce lead exposure Chelation therapy
Neuromuscular		

(continued)

Table 3.1 (continued)

Etiology	Typical diagnostic tests	Treatment
Anterior cutaneous nerve entrapment syndrome	History and physical examination	Local anesthetic injection
Myofascial pain syndrome	History and physical examination	Physical therapy Anti-depressants Sedatives
Slipping rib syndrome	History and physical examination	Local anesthetic injection
Thoracic nerve radiculopathy	X-ray MRI	Treatment based on underlying process
Functional gastrointestinal disorders		
Gallbladder dyskinesia	HIDA scan	Cholecystectomy
Sphincter of oddi dysfunction	Timed HIDA scan ERCP with manometry	ERCP with sphincterotomy
Functional abdominal pain syndrome	History and physical examination Exclusion of other etiology	Tricyclic antidepressants
Functional dyspepsia	History and physical examination Upper endoscopy *H. pylori* testing	Acid suppressive drugs Eradication of *H. pylori* Antidepressants
Irritable bowel syndrome	History and physical examination	High-fiber diet
	Exclusion of other etiology	Antispasmodics Lubiprostone SSRI TCA
Levator ani syndrome	History and physical examination	Sitz baths Perineal strengthening exercises

Table 3.2 Etiology of chronic constant abdominal pain

Chronic pancreatitis
Malignancy
Abscess
Psychiatric
Inexplicable

adrenal insufficiency. Hereditary angioedema should be considered in patients with intermittent abdominal pain who have a history of recurrent angioedema without urticaria. History of exposure, metallic taste in mouth, and cognitive impairment should direct attention to heavy metal poisoning. The presence of coexisting medical illnesses may also suggest a cause of abdominal pain. A history of vasculopathy raises suspicion of chronic mesenteric ischemia. A history of physical or sexual abuse is common in patients with functional gastrointestinal disorders [3]. A family history of gastrointestinal malignancy, pancreatic disorders, or inflammatory bowel disease should be elicited.

Physical Examination

A complete abdominal examination includes inspection, auscultation, percussion, and palpation. Surgical scars on inspection should be noted. Identification of a bruit on auscultation may indicate chronic mesenteric ischemia. Light and deep palpation should be performed to check for masses, ascites, hernias, and organomegaly. Observing the patient's response to palpation can be helpful in differentiating functional from organic disease. A closed eye sign and stethoscope sign are seen more in functional gastrointestinal disorders. A closed eye sign is when patients close their eyes during examination [4], in contrast to patients with acute abdominal pain whose eyes open in fearful anticipation. The stethoscope sign is the detection of less tenderness during pressure with a stethoscope than with palpation [5]. Hover sign and Carnett's sign are seen in abdominal wall pain. Hover sign is when lightly touching the area of pain and patient guards the area with his hand or grabs the examining hand [6]. Carnett's sign is increased abdominal tenderness when the patient tenses their abdominal muscles [7]. Patients with chronic abdominal pain may still present with an acute abdomen and care should be taken to look for peritoneal signs of rebounding and guarding.

It is important to also perform a complete physical examination looking for systemic disease. Signs of malnutrition, vitamin deficiency, and skin changes can signify organic illness. Skin rashes can be helpful in narrowing the diagnosis. Dermatitis herpetiformis is associated with celiac disease (Fig. 3.1). Erythema nodosum, pyoderma gangernosum, and sweets syndrome may be seen in inflammatory bowel disease (Fig. 3.2). Acanthosis nigricans, Leser–Trélat sign,

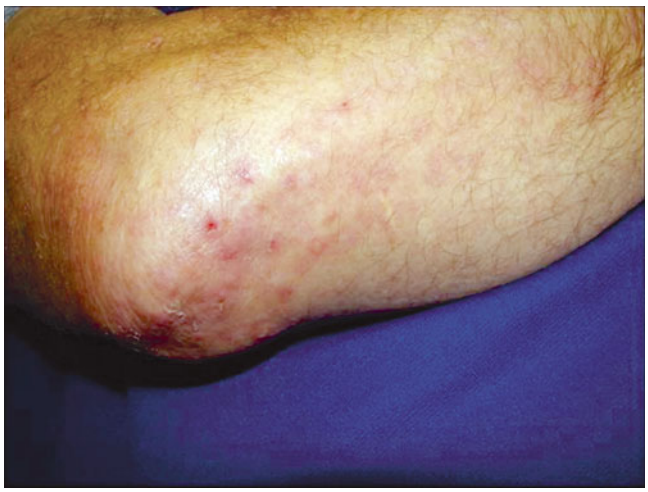

Fig. 3.1 Dermatitis herpetiformis (Thank you to Dr. Pooja Kheera for the picture)

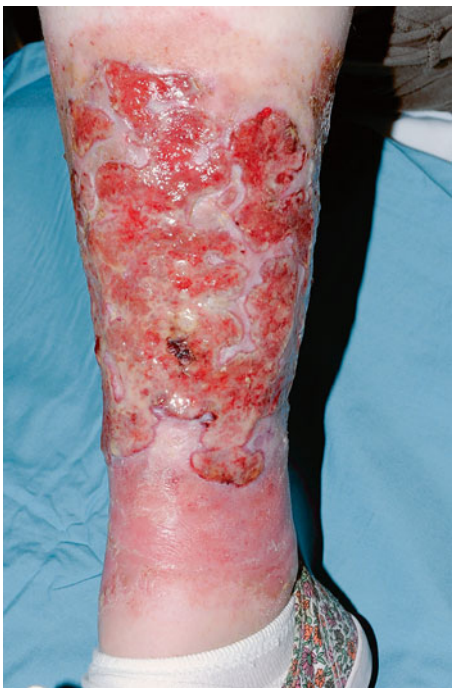

Fig. 3.2 Pyoderma gangernosum (Thank you to Dr. Pooja Kheera for the picture)

hypertrichosis lanuginosa, Tylosis, and Tripe palm can signify underlying malignancy.

Laboratory Testing

Laboratory test abnormalities are common in patients with organic pathology, while normal lab tests are expected in patients with functional bowel disorders. Routine laboratory evaluation includes complete blood cell count (CBC). Anemia can raise suspicion of IBD, celiac disease, or gastrointestinal malignancies. Elevated platelet counts and white blood cell count can be seen in inflammatory diseases. Additional laboratory testing should be based on history and physical examination. Testing for *Helicobacter pylori* antibody should be considered in patients with upper abdominal pain. Celiac serology testing should be considered in those with suspicion of celiac disease. Liver function tests should be checked in those with suspicion of biliary pathology. If recurrent pancreatitis is considered, amylase and lipase should be checked.

Specialized laboratory testing for "rare" medical conditions should be obtained based on clinical suspicion. C4 esterase levels can be checked for hereditary angioedema, cortisol stimulation test for adrenal insufficiency, heavy metal screen for heavy metal poisoning, porphyria screen for acute intermittent porphyria, and genetic testing for familial Mediterranean fever.

Radiologic Imaging

Radiographic tests identify structural abnormalities of the gastrointestinal system. Radiologic evaluation should be tailored based on presenting symptoms, physical examination, and laboratory findings. An abdominal X-ray is a reasonable "screen" for various causes of chronic abdominal pain. It may still detect excessive stool in constipation, calcifications in chronic pancreatitis, appendicolith, partial bowel obstruction from adhesions, and foreign bodies.

Trans-abdominal ultrasound (US) is another safe and noninvasive imaging test, which is fast, portable, and uses no ionizing radiation. The most useful roles of US are in evaluating the hepatobiliary tract and assessing the patency of mesenteric vessels. Right upper quadrant ultrasound evaluates the gallbladder, biliary tree, and adjacent structures. Stones or sludge in the gallbladder may suggest a source of biliary colic or recurrent pancreatitis. Biliary dilation may indicate biliary obstruction arising from a pancreatic mass or bile duct stone. Since US does not easily visualize the distal (periampullary) bile duct, it has relatively poor sensitivity (22–55 %) for detecting common bile duct stones [8, 9]. However, it is able to detect common bile duct dilation that is associated with choledocholithiasis (sensitivity 77–87 %) [9, 10]. In the presence of an intact gallbladder the normal bile duct can range from 3 to 6 mm, while a common bile duct greater than 8 mm is indicative of biliary obstruction [11, 12].

CT scan should be considered based on clinical suspicion of structural pathology and in those with "alarm symptoms." Intravenous contrast (IV) during the CT scan helps establish vascular patency, organ perfusion, and differentiate hypervascular from hypovascular lesions. Oral contrast helps

differentiate collapsed bowel from a collection/mass, identifies leaks and fistulae, detects intestinal obstruction, and assesses wall thickness and enhancement. CT protocols can be modified and tailored based on the clinical suspicion. For example, a CT angiogram is performed by timing image capture when the IV contrast is within the arterial system, allowing detection of aneurysms, artery stenosis, arteriovenous malformation, and thrombosis. A CT enterography uses a neutral oral contrast like Volumen, which provides a more detailed evaluation of inflammation, thickening, and luminal patency of the small bowel [13].

MRI is another cross-sectional imaging modality that is especially useful in the evaluation of biliary and pancreatic disease. MRI imaging uses T1 imaging which highlights fat and T2 imaging which highlights fluid. Although more costly than CT, MRI imparts much less radiation exposure and more detailed imaging in pancreatic and biliary diseases. Magnetic resonance cholangiopancreatography (MRCP) relies on the strong T_2 signal from stationary liquid (bile, pancreatic fluid, etc.) to generate images. The resulting images show fluid-filled structures as bright, producing excellent imaging of the biliary tree and pancreatic duct [14]. MRCP has good sensitivity (85–92 %) and specificity (93–97 %) for detecting choledocholithiasis in two recent systemic reviews [15, 16]. MRCP is able to assess the pancreatic parenchyma, main pancreatic duct, and side branches allowing evaluation of early chronic pancreatitis [17]. Pancreatic duct imaging can be enhanced by the use of secretin. By observing duodenal filling from the pancreatic duct after secretin administration pancreatic exocrine function can be assessed [18]. In one "head to head" study MRCP and EUS were compared to a composite gold standard of endoscopic retrograde cholangiopancreatography (ERCP), pathology, and long-term follow-up. The investigators found EUS was more sensitive than MRCP (93 % vs. 63 %) and equally specific (93 % vs. 90 %) [18]. MR enterography is an alternative to CT enterography in the evaluation of Crohn's disease, especially if there is concern of radiation exposure.

Endoscopy

Endoscopy evaluates the mucosal surfaces of the digestive disease tract. The common diagnostic functions are visual inspection and obtaining mucosal biopsies. Upper endoscopy provides inspection of the esophagus, stomach, and proximal duodenum and detects peptic ulcers, tumors, and inflammation. Colonoscopy examines the rectum, entire colon, and small part of the terminal ileum and detects colitis, tumors, and diverticulae. Upper and lower endoscopies are safe procedures with a low complication rate. Upper endoscopy should be considered in any patient with persistent upper abdominal symptoms with "alarm symptoms," over the age of 55, or persistent symptoms despite an appropriate trial of therapy (e.g., acid-suppressing medications or treatment for *H. pylori*) [19]. Colonoscopy should be considered if there is a suspicion of inflammatory bowel disease, diarrhea, iron deficiency anemia or if the patient is older than 50.

ERCP

During an ERCP, a side-viewing endoscope is passed into the duodenum to identify the major papilla. The bile and/or pancreatic ducts are cannulated and injected with contrast to provide detailed fluoroscopic imaging of the ducts. ERCP is not a benign procedure and carries risks of pancreatitis, cholangitis, bleeding, and perforation. Due to the risks careful patient selection is needed when considering ERCP. With the advent of MRCP imaging, the use of ERCP as a purely diagnostic procedure has waned. However, ERCP is a vital part of the therapeutic armamentarium for patients with pancreaticobiliary diseases. A number of tools (catheters, balloons, stents, etc.) can be passed into the duct to allow therapeutic interventions such as removing stones, dilating strictures, and placing stents for drainage. In the setting of chronic abdominal pain, ERCP aids in the evaluation and management of sphincter of Oddi dysfunction and chronic pancreatitis.

The sphincter of Oddi is a smooth muscle sphincter which surrounds the opening of the bile and pancreatic ducts at their entry into the duodenum. It consists of three components (biliary, pancreatic, and common). Impaired drainage through the sphincter due to spasm or stenosis is termed sphincter of Oddi dysfunction (SOD). Clinically this can present as either recurrent biliary type pain or recurrent pancreatitis. Patients with biliary sphincter of Oddi dysfunction typically present with episodic epigastric or right upper quadrant pain that may radiate to the right shoulder blade following cholecystectomy. The reason biliary SOD is mostly recognized in patients who have undergone cholecystectomy may be related to the removal of the gallbladder that was functioning as a reservoir to accommodate increased pressure in the biliary tree. The gold standard for diagnosing SOD is ERCP with manometry. Manometry involves placing a thin catheter in the biliary or pancreatic sphincter and directly measuring the pressure. The first report of ERCP in the management of SOD was published in 1989 [20]. In a double-blinded study 47 patients with suspected SOD were randomized to endoscopic sphincterotomy or sham sphincterotomy. Manometry identified 23 patients with increased sphincter pressure who were eligible for randomization. Sphincterotomy improved pain scores in 10 of 11 patients with elevated sphincter pressure. In patients who received the sham procedure only 3 of the 12 patients showed

Table 3.3 Modified Milwaukee classification

SOD Type	Typical biliary pain	Abnormal liver enzymes[a]	Dilated bile duct greater than 8 mm	Response rate[b] to sphincterotomy (%)
1	+	+	+	65–95
2	+	Either abnormal liver enzymes or dilated bile duct		50–63
3	+	–	–	12–28

[a] Abnormal liver enzymes—AST, ALT, or AP > 2 times normal values documented on two or more occasions
[b] Reviewed in Corazziari E. Sphincter of Oddi Dysfunction. Dig Liver Dis 2003;35 Supple 3:S26–9
SOD Sphincter of Oddi Dysfunction

improvement in pain scores. Patients with suspected biliary SOD are classified according to the revised Milwaukee classification as this helps predict outcomes after biliary sphincterotomy [21, 22] (Table 3.3).

In SOD patients, ERCP has a high rate of pancreatitis occurring up to 25 % of time [23–25]. Several noninvasive tests have been studied in SOD, but they have not gained widespread use due to poor sensitivity and specificity. The mainstay of treatment is endoscopic sphincterotomy. Prior to referring a patient for ERCP and sphincter of Oddi manometry for SOD, it is important to adequately exclude other causes of pain. A careful history and review of lab and imaging tests helps to verify that the pain is truly biliary or pancreatic in nature, and that the clinical features support the diagnosis (e.g., elevated liver function tests, dilated ducts). Finally patients must be carefully counseled as to their chances of benefit based on the Milwaukee classification, and the significant risk of pancreatitis which may rarely be life-threatening.

Abdominal pain is a common and debilitating symptom of chronic pancreatitis. The pathogenesis of pain in CP is multifactorial. However, a major component of the pain may relate to increased intraductal pressure as a result of pancreatic strictures and/or calculi [26]. ERCP has been frequently used to assess and treat ductal pathology arising in chronic pancreatitis. Main pancreatic duct strictures are treated with dilation and placement of stents. Management of obstructing pancreatic ductal calculi may entail extracorpeal shock wave lithotripsy to fragment the stone followed by endoscopic removal of fragmented stones. There is an increased risk of pancreatic cancer in CP and should be excluded in any patient with a ductal stricture.

Endoscopic Ultrasound

Ultrasound imaging has distinct advantages including detailed soft tissue imaging and the ability to provide real-time guidance for tissue sampling. However, US is limited by its inability to image beyond air filled or extremely dense structures (e.g., calcifications). Transabdominal ultrasound does not usually adequately image all of the intra-abdominal structures when there is a large amount of intervening fat or air artifact. Endoscopic ultrasound (EUS) overcomes these limitations by endoscopically placing the ultrasound probe in the stomach and duodenum next to the organs of interest. For example, an ultrasound probe in contact with the duodenal wall will be within 5 mm of the intrapancreatic portion of the common bile duct [27]. EUS is a minimally invasive procedure with a low risk profile similar to upper endoscopy [28]. While EUS has many diagnostic and therapeutic indications, its main role in chronic abdominal pain is evaluation of biliary disorders and chronic pancreatitis.

Chronic pancreatitis (CP) is an inflammatory disease of the pancreas that results in fibrosis and scarring of the pancreas. These changes result in both pancreatic exocrine and endocrine insufficiency. While severe chronic pancreatitis can be seen on radiologic imaging, early CP is harder to detect. This was demonstrated by Walsh in a report titled "Minimal Change Chronic Pancreatitis" [29]. Walsh described 16 patients with typical pancreatic pain but with negative or equivocal imaging work-up. The patients eventually underwent pancreatic resection due to the strong suspicion of CP. Histologic specimens demonstrated subtle, but definite histologic changes of chronic pancreatitis in 15 of the 16 patients. EUS strength lies in being able to detect mild parenchymal and ductal abnormalities not seen on CT scan making it a good test in evaluating patients with typical pancreatic pain, but with non-diagnostic imaging.

The normal endosonographic appearance of the pancreas include homogenous and granular echotexture ("salt and pepper"), smooth gland borders, and a smoothly tapering pancreatic duct. The main pancreatic duct wall and side branches are hard to visualize. The upper limit of normal of the pancreatic duct is 3.6 mm in the head, 3.0 mm in the body, and 2.0 mm in the tail [30]. The EUS changes seen in CP include ductal and parenchymal changes. The parenchymal changes include hyperechoic foci and stranding, lobularity, cysts, and calcifications [31, 32]. The ductal changes include a dilated and irregular main pancreatic duct with hyperechoic walls, ductal calculi, and dilated side branches [31, 32]. Not all features are needed for the diagnosis of CP, and some features may be seen in patients without CP. To help organize the EUS changes of chronic pancreatitis scoring systems have been developed. The traditional EUS scoring system is an unweighted scoring system that has been shown to help diagnose CP [33]. A limitation of this scoring system was that each criterion was weighted equally, though some

criteria have more diagnostic importance. To address these issues the consensus-based Rosemont classification was formed. The Rosemont classification differentiates EUS findings into minor and major categories and established four diagnostic categories (Normal, indeterminate for chronic pancreatitis, suggestive of chronic pancreatitis, consistent with chronic pancreatitis) [34]. The Rosemont criteria look promising but require further validation in multicenter studies. Limitations of EUS include inter- and intra-observer variability, operator dependence, and an incomplete understanding of its true accuracy. Despite these limitations EUS is the best test for evaluating early chronic pancreatitis.

Pancreatic Function Test in Chronic Pancreatitis

Pancreatic function tests (PFT) assess pancreatic exocrine function. Exocrine function may decline in the initial stages of chronic pancreatitis, making PFT a good test for early CP. PFT involves administration of either secretin or CCK which stimulate the exocrine pancreas, followed by collection and analysis of pancreatic secretion.

Historically PFTs were performed by using double lumen gastroduodenal collection tubes, which are cumbersome and time-consuming to use limiting their clinical application. Recently, endoscopic PFTs have been shown to be useful with the direct collection of fluid aspirated through endoscopes suction channel.

By performing EUS at the same time of endoscopic PFT both the structure and function of the pancreas can be assessed. A recent retrospective study comparing EUS and endoscopic PFT to histology suggested combined EUS and PFT may increase sensitivity in detecting CP [35].

Conclusion

Chronic abdominal pain may be a challenging diagnosis, as the concern of missing a serious medical condition needs to be balanced with the expense of excessive diagnostic testing in a patient with a functional disorder. Certain testing can also have significant risk of harm as in ERCP for sphincter of Oddi dysfunction and must be considered cautiously. A careful history and physical examination helps guide effective diagnostic testing and limits unnecessary testing. While it is important to confidently exclude organic disease prior to diagnosing a functional disorder, it is also important to prevent the "endless" loop of diagnostic testing many of these patients undergo. Knowing when to stop diagnostic testing is an important and challenging part of managing chronic abdominal pain.

References

1. Mitchell CM, Drossman DA. Survey of the AGA membership relating to patients with functional gastrointestinal disorders. Gastroenterology. 1987;92(5 Pt 1):1282–4.
2. Livneh A, Langevitz P, Zemer D, Zaks N, Kees S, Lidar T, et al. Criteria for the diagnosis of familial Mediterranean fever. Arthritis Rheum. 1997;40(10):1879–85.
3. Drossman DA, Talley NJ, Leserman J, Olden KW, Barreiro MA. Sexual and physical abuse and gastrointestinal illness. Review and recommendations. Ann Intern Med. 1995;123(10):782–94.
4. Gray DW, Dixon JM, Collin J. The closed eyes sign: an aid to diagnosing non-specific abdominal pain. BMJ. 1988;297(6652):837.
5. Drossman DA. Functional abdominal pain syndrome. Clin Gastroenterol Hepatol. 2004;2(5):353–65.
6. Hershfield NB. The abdominal wall. A frequently overlooked source of abdominal pain. J Clin Gastroenterol. 1992;14(3):199–202.
7. Thomson H, Francis DM. Abdominal-wall tenderness: a useful sign in the acute abdomen. Lancet. 1977;2(8047):1053–4.
8. Einstein DM, Lapin SA, Ralls PW, et al. The insensitivity of sonography in the detection of choledocholithiasis. AJR Am J Roentgenol. 1984;142:725–8.
9. Maple JT, Ben-Menachem T, Anderson MA. The role of endoscopy in the evaluation of suspected choledocholithiasis. Gastrointest Endosc. 2010;71(1):1–9.
10. Lapis JL, Orlando RC, Mittelstaedt CA. Ultrasonography in the diagnosis of obstructive jaundice. Ann Intern Med. 1978;89(1):61–3.
11. Parulekar SG. Ultrasound evaluation of common bile duct size. Radiology. 1979;133(3 Pt 1):703–7.
12. Baron RL, Stanley RJ, Lee JK, Koehler RE, Melson GL, Balfe DM, et al. A prospective comparison of the evaluation of biliary obstruction using computed tomography and ultrasonography. Radiology. 1982;145(1):91–8.
13. Paulsen SR, Huprich JE, Fletcher JG, Booya F, Young BM, Fidler JL, et al. CT enterography as a diagnostic tool in evaluating small bowel disorders: review of clinical experience with over 700 cases. Radiographics. 2006;26(3):641–57. Discussion 657–62.
14. Mehta SN, Reinhold C, Barkun AN. Magnetic resonance cholangiopancreatography. Gastrointest Endosc Clin N Am. 1997;7(2):247–70.
15. Romagnuolo J, Bardou M, Rahme E, Joseph L, Reinhold C, Barkun AN. Magnetic resonance cholangiopancreatography: a meta-analysis of test performance in suspected biliary disease. Ann Intern Med. 2003;139(7):547–57.
16. Verma D, Kapadia A, Eisen GM, Adler DG. EUS vs MRCP for detection of choledocholithiasis. Gastrointest Endosc. 2006;64(2):248–54.
17. Czako L, Endes J, Takacs T, Boda K, Lonovics J. Evaluation of pancreatic exocrine function by secretin-enhanced magnetic resonance cholangiopancreatography. Pancreas. 2001;23(3):323–8.
18. Pungpapong S, Wallace MB, Woodward TA, Noh KW, Raimondo M. Accuracy of endoscopic ultrasonography and magnetic resonance cholangiopancreatography for the diagnosis of chronic pancreatitis: a prospective comparison study. J Clin Gastroenterol. 2007;41(1):88–93.
19. Talley NJ, Vakil N, Practice Parameters Committee of the American College of Gastroenterology. Guidelines for the management of dyspepsia. Am J Gastroenterol. 2005;100(10):2324–37.
20. Geenen JE, Hogan WJ, Dodds WJ, Toouli J, Venu RP. The efficacy of endoscopic sphincterotomy after cholecystectomy in patients with sphincter-of-Oddi dysfunction. N Engl J Med. 1989;320(2):82–7.
21. Hogan WJ, Geenen JE. Biliary dyskinesia. Endoscopy. 1988;20 Suppl 1:179–83.

22. Behar J, Corazziari E, Guelrud M, Hogan W, Sherman S, Toouli J. Functional gallbladder and sphincter of oddi disorders. Gastroenterology. 2006;130(5):1498–509.
23. Freeman ML. Role of pancreatic stents in prevention of post-ERCP pancreatitis. JOP. 2004;5(5):322–7.
24. Singh P, Gurudu SR, Davidoff S, et al. Sphincter of Oddi manometry does not predispose to post-ERCP acute pancreatitis. Gastrointest Endosc. 2004;59:499–505.
25. Guda NM, Freeman ML. True culprit or guilt by association? Is sphincter of Oddi manometry the cause of post-ERCP pancreatitis in patients with suspected sphincter of Oddi dysfunction, or is it the patients' susceptibility? Rev Gastroenterol Disord. 2004;4(4): 211–3.
26. Di Sebastiano P, di Mola FF, Buchler MW, Friess H. Pathogenesis of pain in chronic pancreatitis. Dig Dis. 2004;22(3):267–72.
27. Shami VM, Kahaleh M. Clinical gastroenterology: endoscopic ultrasound. Springer Science LLC: New York; 2010.
28. Rathod V, Maydeo A. How safe in endoscope ultrasound? A retrospective analysis of complications encountered during diagnosis and interventional Endosonography in large individual series of 3006 patients from India [abstract]. Gastrointest Endosc. 2002;56(Suppl):S144.
29. Walsh TN, Rode J, Theis BA, Russell RC. Minimal change chronic pancreatitis. Gut. 1992;33(11):1566–71.
30. Wiersema MJ, Hawes RH, Lehman GA, Kochman ML, Sherman S, Kopecky KK. Prospective evaluation of endoscopic ultrasonography and endoscopic retrograde cholangiopancreatography in patients with chronic abdominal pain of suspected pancreatic origin. Endoscopy. 1993;25(9):555–64.
31. Dancygier H, Classen M. Endosonographic diagnosis of benign pancreatic and biliary lesions. Scand J Gastroenterol Suppl. 1986;123:119–22.
32. Lees WR. Endoscopic ultrasonography of chronic pancreatitis and pancreatic pseudocysts. Scand J Gastroenterol Suppl. 1986;123: 123–9.
33. Sahai AV, Zimmerman M, Aabakken L, Tarnasky PR, Cunningham JT, van Velse A, et al. Prospective assessment of the ability of endoscopic ultrasound to diagnose, exclude, or establish the severity of chronic pancreatitis found by endoscopic retrograde cholangiopancreatography. Gastrointest Endosc. 1998;48(1):18–25.
34. Catalano MF, Sahai A, Levy M, Romagnuolo J, Wiersema M, Brugge W, et al. EUS-based criteria for the diagnosis of chronic pancreatitis: the Rosemont classification. Gastrointest Endosc. 2009;69(7):1251–61.
35. Albashir S, Bronner MP, Parsi MA, Walsh RM, Stevens T. Endoscopic ultrasound, secretin endoscopic pancreatic function test, and histology: correlation in chronic pancreatitis. Am J Gastroenterol. 2010;105(11):2498–503.