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Rational investigation of upper abdominal pain

Background

Upper abdominal pain is a common problem with an extraordinary diversity of possible causes. Many patients have no structural disease, and making the correct diagnosis can be a challenge. The roles of endoscopy, testing for *Helicobacter pylori*, and imaging techniques have been debated widely and continue to be a matter for discussion.

Objective

This article details the value of various investigations in the setting of specific presentations of upper abdominal pain.

Discussion

Functional dyspepsia is a common cause of upper abdominal pain but the diagnosis should only be made after consideration of more serious pathology. The various organic causes of upper abdominal pain and the appropriate investigations are discussed. Early endoscopy is advisable in the presence of alarm symptoms and in patients over 55 years of age.

■ **Upper abdominal pain (UAP) is one of the most common presenting symptoms in primary care; the spectrum of possible causes is wide, and its management can be challenging. Differential diagnoses range from acute life threatening illnesses such as aortic dissection and myocardial infarction, to relatively benign conditions such as gastro-oesophageal reflux disease (GORD) or functional dyspepsia. Many of the serious conditions are difficult to exclude without elaborate or invasive tests. Unusual causes need to be considered, especially in the young, the immunocompromised, the pregnant, and the elderly.**

The prevalence of UAP in western countries is approximately 25% when typical reflux symptoms are excluded, or about 40% when included.^{1,2} The clinical presentation of individual causes of UAP can be variable, and a detailed history and a thorough physical examination are still the most useful assessment tools. Particular attention should be given to the timing of the pain, for example its relationship to food intake (peptic ulcer, GORD, mesenteric ischaemia) or exercise (myocardial ischaemia), its duration (hours raises the possibility of gallstones and their complications) and the presence of alarm symptoms such as dysphagia, vomiting, gastrointestinal bleeding and weight loss. Most patients presenting with UAP suffer from recurrent or chronic symptoms.

Chronic or recurrent UAP

In the majority of patients investigated for dyspeptic symptoms no organic cause is found; most probably have functional dyspepsia. The diagnostic criteria for functional dyspepsia and its sub-entities, postprandial distress syndrome (mainly postprandial fullness and early satiety) and epigastric pain syndrome, are shown in *Table 1*.³ The diagnosis of functional dyspepsia is one of exclusion and can



only be safely made when routine blood tests, upper endoscopy and upper abdominal ultrasound have excluded organic causes. If the upper abdominal symptoms are associated with altered bowel motions or relieved by defaecation, irritable bowel syndrome (IBS) should be considered.⁴ However, IBS more commonly causes bilateral lower, rather than upper, abdominal discomfort or pain and should be present for at least 3 days per month for at least 3 months. Symptoms are associated with bloating, a sense of incomplete evacuation and variable stool frequency and consistency.

GORD and peptic ulcers

The most common organic causes of recurrent epigastric pain are GORD and peptic ulcer disease. It has been argued that correlation between symptoms and disease in the upper gastrointestinal tract is poor and that the investigation of patients with predominant

heartburn and predominant epigastric pain should be the same. However, the authors believe that there are signs and symptoms that, if present, point toward a particular diagnosis. Gastro-oesophageal reflux may be associated with epigastric discomfort, but the diagnosis is more readily made when there is typical retrosternal burning with or without regurgitation and the characteristic – some say, pathognomonic – sign of the patient's open hand moving up and down along the line of the oesophagus. There is a well documented association with asthma.⁵ A response to acid suppression supports the diagnosis but does not differentiate it from other causes of dyspepsia. Alarm symptoms such as dysphagia, odynophagia, gastrointestinal bleeding, weight loss, symptoms of aspiration (especially when lying in bed at night) and recurrent respiratory tract infections warrant investigation by endoscopy and/or barium swallow. Manometry and ambulatory oesophageal pH monitoring are not generally required

Table 1. Diagnostic criteria* for functional dyspepsia

- Must include one or more of the following:
 - bothersome postprandial fullness
 - early satiation
 - epigastric pain
 - epigastric burning

And

- No evidence of structural disease (including at upper endoscopy) that is likely to explain the symptoms

* Criteria fulfilled for the past 3 months with symptom onset at least 6 months before diagnosis

Diagnostic criteria* for postprandial distress syndrome

- Must include one or both of the following:
 - bothersome postprandial fullness, occurring after ordinary sized meals, at least several times per week
 - early satiation that prevents finishing a regular meal, at least several times per week

* Criteria fulfilled for the past 3 months with symptom onset at least 6 months before diagnosis

Supportive criteria

- Upper abdominal bloating or postprandial nausea or excessive belching can be present
- Epigastric pain syndrome may coexist

Diagnostic criteria* for epigastric pain syndrome

- Must include all of the following:
 - pain or burning localised to the epigastrium of at least moderate severity at least once per week
 - pain is intermittent
 - not generalised or localised to other abdominal or chest regions
 - not relieved by defaecation or passage of flatus
 - not fulfilling criteria for gallbladder and sphincter of Oddi disorders

* Criteria fulfilled for the past 3 months with symptom onset at least 6 months before diagnosis

Supportive criteria

- Pain may be of a burning quality but without a retrosternal component
- Pain is commonly induced or relieved by ingestion of a meal but may occur while fasting
- Postprandial distress syndrome may coexist

Source: Tack J, Talley NJ, Camilleri M, et al. Functional gastroduodenal disorders. *Gastroenterology* 2006;130:1466–79



except when surgical therapy for reflux is being considered or to exclude rare conditions such as achalasia.

Persisting symptoms of volume reflux – regurgitation of gastric contents which no longer burn – implies that there is maximal acid suppression and may necessitate referral for consideration of surgery (fundoplication). There are no good data that prokinetic agents are useful in volume reflux but they may be trialled in patients with delayed gastric emptying. Patients often re-present when their symptoms recur after acid suppressive medication is stopped: they should be advised that the problem (‘leaking valve’) is not cured by acid suppressive medication. Repeat investigations are not necessary unless there has been a change in the symptom pattern. Proton pump inhibitors are preferable to H₂ antagonists as they are more potent, well tolerated and have minimal risks of side effects with long term use. There may be a pH dependent decrease in absorption of iron from the diet, and there have been reports of increased risks of enteric infection (eg. with *Clostridium difficile*) while on potent acid suppression.⁶ There is a common misconception that gastric acid is necessary to digest food and an explanation of the role of the pancreatic and biliary secretions in this regard can be helpful.

What are the indications for gastroscopy?

It is still unclear whether early endoscopy is necessary in cases of undiagnosed dyspepsia. When confronted with chronic intermittent epigastric pain or burning, one seeks ‘alarm’ features (Table 2). If any of these features are present, and in patients over 55 years of age, referral for upper endoscopy is advisable. The age limit has been a matter of debate, and groups at higher risk of gastric malignancy (eg. Asian background) who present with new dyspeptic symptoms should probably be offered endoscopy at a younger age. Ingestion of aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs) would also lower the threshold for referral. Gastroscopy is generally safe, but a small risk is associated with factors such as extreme age, obesity, and advanced respiratory or cardiac disease. A barium meal may be an alternative if endoscopy is unavailable, but this has inferior specificity and sensitivity for the detection of structural causes of epigastric pain⁷ and does not yield any tissue samples for further examination.

Table 2. Indications for upper gastrointestinal endoscopy in UAP

- Signs of gastrointestinal bleeding or anaemia
- Weight loss
- Vomiting
- Progression of symptoms
- Dysphagia
- Previous gastric surgery
- Family history of gastrointestinal carcinoma
- Over 55 years of age

Noninvasive testing for *Helicobacter pylori* followed by eradication and appropriate follow up (test and treat), may be cost effective in patients without alarm symptoms. A meta-analysis comparing early endoscopy to a test and treat strategy in patients without alarm symptoms showed a small advantage in symptom control at 1 year in the endoscopy group (RR 0.95, 95% CI: 0.95–0.99), but given the higher cost, early endoscopy was not thought to be cost effective.⁸ Epidemiological studies using serological testing have found *H. pylori* infection rates in the Australian population to be 15–40%.^{9,10} A test and treat strategy may be more efficient in high risk population groups such as the elderly or immigrants from countries with a high *H. pylori* prevalence (see the article by Stenström et al this issue).

Pancreatic causes

Malignancy of the pancreas or the bile ducts may present with the insidious onset of abdominal pain, and is commonly associated with anorexia, weight loss, and jaundice. Abdominal ultrasound may detect biliary dilatation but is insensitive for either tumour. Computerised tomography (CT) may detect a pancreatic mass but often an endoscopic retrograde cholangiopancreatography (ERCP) or magnetic resonance imaging (MRI) is needed to make the diagnosis.

Chronic pancreatitis is an unusual cause of ongoing UAP and can be difficult to diagnose and manage. Steatorrhoea is seen only in advanced disease. The presence of pancreatic calcification on plain abdominal X-ray, ultrasound or CT scan is suggestive, if not diagnostic, of chronic pancreatitis. The majority of cases are alcohol related. However, in many patients, imaging may be normal and lipase levels may be within the reference range or only slightly elevated. Chronic pancreatitis should be suspected in those with a history of heavy alcohol intake, patients with previous attacks of pancreatitis, or when there is chronic ductal obstruction.

Bowel causes

Coeliac disease is probably a rare cause of epigastric pain. It is still underdiagnosed, and it is reasonable to order screening serological testing, currently with IgG and IgA to tissue transglutaminase (tTG). Coeliac disease may be associated with iron or folate deficiency with or without anaemia. If screening tests for coeliac disease are positive, endoscopy and duodenal biopsy should be performed before dietary modification.

Crohn disease, affecting only the upper gastrointestinal tract, is relatively rare but may cause recurrent epigastric pain or dyspepsia. Approximately 70% of patients who suffer from Crohn disease have disease affecting the terminal ileum and/or right colon. Colicky, periumbilical pain always warrants investigation, small bowel series or an ultrasound directed specifically to the assessment of the small bowel; as does the presence of right iliac fossa pain or a mass. Ulcerative colitis and Crohn disease affecting the left colon and/or rectum most commonly present with diarrhoea and rectal bleeding, although left sided lower abdominal pain may be present. If these conditions are suspected, the appropriate test is a sigmoidoscopy or colonoscopy.



Acute severe UAP

Biliary causes

Pain suggestive of biliary causes is characteristically located in the epigastrium or right upper quadrant. It is often, but not always, severe, and typically lasts for several hours. There is often a history of prior intermittent symptoms. Appropriate initial investigations include a full blood count, liver tests and lipase. Abdominal ultrasound is the initial imaging modality of choice given its sensitivity for detecting cholelithiasis, its noninvasive nature and its accessibility.

Cholelithiasis is common and often asymptomatic, so care should be taken not to attribute dyspeptic symptoms to gallstones. Gallstones causing pain without evidence of complications such as fever or jaundice should lead to a nonurgent referral to a surgeon for consideration of cholecystectomy. The presence of fever, a raised neutrophil count or other inflammatory markers raises the possibility of cholecystitis, and rarely, liver abscess. If there is pain, fever and jaundice or biliary obstruction (cholestatic liver tests and intra- and extra-hepatic duct dilatation on ultrasound), the most likely diagnosis is ascending cholangitis and urgent treatment should be instituted: admission to hospital, blood cultures, intravenous antibiotics and prompt referral for duct drainage and relief of obstruction (ERCP).

The threshold for ordering a full blood count, liver tests and ultrasound should be low in unwell, elderly patients who often present with less specific signs and symptoms. In a review of 168 geriatric patients presenting to a hospital emergency department with cholecystitis confirmed at surgery, 84% had neither right upper quadrant nor epigastric pain, while 5% had no pain at all.¹¹ Similarly, fever may not be present and cholangitis not suspected.

If there is clinical suspicion of bile duct stones or in a patient postcholecystectomy, an ultrasound is still the initial imaging modality of choice even though it has a sensitivity of only about 55% for choledocholithiasis. Biliary dilatation may be used as a surrogate marker to increase the sensitivity,^{12,13} but patients who have had a cholecystectomy may have common bile duct diameters of over 8 mm making interpretation difficult. In this situation either endoscopic ultrasound or magnetic resonance cholangiopancreatography is the best next investigation – but neither is widely available. If strongly suspected, an ERCP may confirm the diagnosis of choledocholithiasis and enable definitive therapy. Standard CT offers little more than ultrasound and carries the risks associated with radiation and contrast injection; CT cholangiography, where available, may improve the accuracy.

Sphincter of Oddi dysfunction (SOD) is rare and typically manifests as biliary pain in the absence of gallstones. The finding of a transient elevation, then prompt normalisation of liver enzymes in association with an episode of pain with or without a common bile duct over 8 mm in diameter, are supportive of the diagnosis. Patients with SOD may present postcholecystectomy. The gold standard for diagnosing SOD is ERCP with manometry, but this is associated with a high risk of postprocedure pancreatitis and has limited availability. Sphincter of Oddi dysfunction is itself a putative cause of chronic pancreatitis.¹⁴

In patients with normal biochemistry and ultrasound findings, ERCP should be delayed or avoided, but patients who have liver enzyme elevation associated with episodes of pain may benefit from endoscopic sphincterotomy. Noninvasive tests for SOD (fatty meal ultrasound and hepatobiliary scintigraphy) are unrewarding: even when used in combination the sensitivity and specificity are poor.

Pancreatic causes

Acute pancreatitis presents with severe epigastric pain lasting for hours, or rarely, days. Careful history taking may reveal predisposing factors for pancreatitis – gallstones, alcohol and ‘the rest’, including medications. If there is any suspicion of pancreatitis, the patient should have blood tests including lipase, liver tests, full blood count, C-reactive protein, creatinine and electrolytes, calcium and glucose. If pancreatitis is confirmed by a lipase of >5 times the upper limit of normal, hospital admission is recommended. Treatment mainstays are aggressive fluid resuscitation and analgesia. Measuring amylase levels confers no benefit over lipase alone as it is much less specific and does not increase the sensitivity for detecting pancreatitis. Abdominal ultrasound may demonstrate cholelithiasis or choledocholithiasis but cannot exclude bile duct stones as a cause of pancreatitis given its low sensitivity. A CT scan of the abdomen is not necessary unless the patient has evidence of severe pancreatitis; the presence of pancreatic necrosis increases the risk of abscess formation and indicates a poorer prognosis. Patients who have severe gallstone pancreatitis may benefit from early ERCP and removal of residual common bile duct stones; there is a decreased length of hospitalisation but no demonstrated improvement in mortality.

Other causes

Acute severe pain can be caused by diseases of the aorta – dissection or ruptured aneurysm – which need to be excluded in patients with vascular disease or if signs of shock are present, especially if the pain radiates to or originates from the back. Other causes of severe pain include perforated duodenum, mesenteric ischaemia and acute intestinal obstruction; suspicion of any of these requires prompt hospitalisation. Heart and lung diseases, including acute myocardial ischaemia, pericarditis, lower lobe pneumonia and pleurisy, should always be considered, and depending on the individual’s risk profile, an electrocardiogram (ECG), cardiac enzymes and chest X-ray, also looking for free subdiaphragmatic air, should be obtained. Plain abdominal X-ray is often unhelpful in the investigation of UAP but may be used to look for faecal overload, perforated viscus, or intestinal obstruction, for which the sensitivity lies in the order of 50–60%.

Left upper quadrant pain may be due to splenic pathology such as enlargement, abscesses or infarction, as seen in myeloproliferative disease, sickle cell anaemia, or acute infection (eg. Epstein-Barr virus or malaria).

Acute hepatitis is an infrequent cause of UAP and other symptoms will be present. In chronic viral hepatitis or cirrhosis, hepatocellular



carcinoma and/or portal vein thrombosis should be considered with alpha-fetoprotein assay, ultrasound with or without Doppler studies, and/or triple phase CT of the liver. Thrombosis of the hepatic veins or the inferior vena cava – Budd-Chiari syndrome, often associated with a myeloproliferative syndrome, a hypercoagulable state or malignancy – causes right upper quadrant pain, ascites and abnormal liver tests. Ultrasound with Doppler studies of the hepatic veins may help make the diagnosis.

Appendicitis, especially in pregnant women or if the appendix is retrocaecal, is a rare cause of UAP. Fitz-Hugh-Curtis syndrome, or perihepatitis, is right upper quadrant pain due to liver capsule infection in pelvic inflammatory disease. Most are caused by urogenital *Chlamydia trachomatis* infection, which is most commonly found in young women. It may be confused with cholecystitis and the diagnosis may only be made at laparoscopy. Urinary polymerase chain reaction (PCR) testing for chlamydia may prevent unnecessary surgery and should be considered in the appropriate setting.

Musculoskeletal causes of UAP are not infrequently encountered but largely remain a diagnosis of exclusion. Other rare causes of acute UAP include *Herpes zoster*, haematologic causes such as Henoch-Schönlein purpura or acute leukaemia, or manifestations of systemic diseases such as porphyria, diabetes mellitus, familial Mediterranean fever or typhoid.

Summary

The causes of UAP are legion: initial investigations could include tests such as full blood count, liver enzymes, and lipase; ultrasound is the imaging modality of choice, but there is no substitute for an adequate history and physical examination. The presence of alarm features should prompt consideration of upper gastrointestinal endoscopy, but its role in their absence is still a matter for debate.

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