Investigation and management of noncardiac chest pain

In this series, we present authoritative advice on the investigation of a common clinical problem, specially commissioned for family doctors by the Board of Continuing Medical Education of the Royal Australasian College of Physicians.

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Recurrent acute or chronic pain in the anterior chest is common, with up to 25% of the Australian adult population reporting chest pain symptoms over the previous year. Clearly not all these people seek medical attention, but for the majority of patients who do, the chest pain will be due to benign, noncardiac causes. These patients may be relieved that they have been given the 'all clear' for cardiac disease, but they will still be in pain. In a significant proportion, quality of life can be reduced, leading to increased work absenteeism and disruption of daily activities. These patients may also have a new set of concerns, having now received a different diagnosis for their pain.

Causes of noncardiac chest pain (NCCP)

There is a wide variety of possible contributors to NCCP. A focused history and examination are useful in narrowing the differential diagnoses.

Oesophageal causes

Conditions of the oesophagus, such as gastro-oesophageal reflux disease (GORD), spastic disorders, and the increasingly recognised syndrome of oesophageal hypersensitivity, are often implicated as causes of NCCP (Table 1). The oesophagus has very similar innervation to the heart and oesophageal pain can mimic cardiac pain. Indeed, the relation between the heart and oesophagus may be more complex than previously suspected in light of recent evidence that oesophageal acidification causes changes in cardiac blood flow in patients with syndrome X. The mechanisms behind oesophageal pain may include mucosal irritation, hypermotility and hypersensitivity, or any combination of these. The pain is mediated by nerves in the oesophageal mucosa and muscularis propria.

The most common oesophageal cause of NCCP is GORD. Symptoms of GORD are associated with NCCP, and up to 50% of patients with NCCP will have an abnormal oesophageal acid exposure on ambulatory pH testing.

The pain mechanism behind oesophageal hypermotility has not been identified but it may involve local muscle ischaemia. There are several conditions associated with oesophageal hypermotility, and some may be difficult to detect. For example, one form of oesophageal spasm may involve only the outer (longitudinal) muscle layer of the oesophagus, which can currently be detected only using intraluminal ultrasound.

Some patients with NCCP have been shown to have oesophageal hypersensitivity to balloon distension or electrical stimulation of the mucosa and

IN SUMMARY

- **Noncardiac chest pain (NCCP) is common and diagnosis can be difficult; however, in most cases the natural history is benign.**
- **The most common underlying cause of NCCP is gastro-oesophageal reflux disease. Resolution of symptoms following treatment with a proton pump inhibitor (PPI) may obviate the need for further investigations.**
- **If treatment with a PPI is not effective, other causes should be sought and treated.**

Table 1. Causes of NCCP

Oesophageal causes

- Gastro-oesophageal reflux disease
- Oesophageal spasm/achalasia
- Oesophageal hypersensitivity (functional chest pain)
- Controversial: nutcracker oesophagus/high pressure lower oesophageal sphincter

Other causes

- Musculoskeletal
- Anxiety and chronic pain syndromes
- Pulmonary pathology
  - Pulmonary embolism
  - Lung tumours
- Upper abdominal organs
  - Biliary colic
- Occult cardiac disease

Table 2. Investigations to consider for NCCP

- Trial of high dose acid suppression
- Upper gastrointestinal endoscopy (especially if red flag symptoms present)
- Injection of sites of local tenderness (e.g. xiphisternal joint)
- Upper abdominal ultrasound
- CT scan of the chest
- Bone scan
- Oesophageal manometry and/or ambulatory pH study

demonstrate increased secondary allodynia (sensitisation away from the area of stimulation). Whether oesophageal hypersensitivity represents one disorder or many has not been established, nor has the nature of the underlying pathophysiology (in particular, whether it is due to peripheral sensitisation, a central effect, or both). Nevertheless, oesophageal visceral hypersensitivity is likely to be a contributing factor in a substantial proportion of patients with NCCP.

Other causes

There are various non-oesophageal causes of NCCP (Table 1), some of which have specific treatments. Such pain develops in thoracic structures other than the oesophagus and in upper abdominal organs, including the chest wall, lung, great vessels and biliary tree.

The degree to which cardiac disease has been 'excluded' also needs to be assessed as part of the overall process. One of the causes of 'NCCP' is incompletely investigated or occult cardiac disease.

The prevalence of psychological abnormalities is increased in patients with NCCP, and anxiety and depressive disorders are common. Analogous to other functional disorders such as irritable bowel syndrome, these factors may influence symptom severity and clinic attendance.

Diagnosis

Clinical features that may be helpful in differentiating NCCP include the nature and timing of the pain. An association with other gastrointestinal functions or symptoms, such as heartburn, regurgitation, postprandial pain, relief with antacid, or the presence of odynophagia (pain on swallowing) or dysphagia, suggests an oesophageal origin. Prominent odynophagia implies a mucosal inflammatory cause. A chronic aching pain is rarely cardiac or oesophageal in origin and is more likely to have a musculoskeletal or malignant cause. Changes with position or movement are particularly suggestive of a musculoskeletal problem. Chest pain that has a pleuritic component or is associated with coughing or shortness of breath should prompt pulmonary investigations or cardiac re-evaluation. Chest pain that is part of a constellation of pain symptoms suggests a rheumatological cause or a chronic pain syndrome.

Examination

Examination should focus on the areas where the pain is felt, and sites of local tenderness and trigger points should be carefully sought. Pain relief after injection of these areas with analgesic is diagnostic of a local cause. General examination may reveal other points of tenderness, which suggests a rheumatological cause or chronic pain syndrome. The upper abdomen, lymph node fields, and cardiac and pulmonary systems should be examined for other potential causes of the pain.

Investigations

Investigations to consider for patients with NCCP are listed in Table 2; however, they are often unrewarding unless a specific cause is suspected. Upper gastrointestinal endoscopy is indicated only in the presence of alarm symptoms, as it is an insensitive test for GORD. Acid suppression using proton pump inhibitors can assess the contribution of oesophageal acidification (see management below). Ambulatory pH and stationary or ambulatory manometry studies may be of value for assessing the severity of GORD or the efficacy of acid suppression in those with refractory or unusual symptoms. They should be carried out in specialised units. Stationary oesophageal manometry (Figure) may demonstrate oesophageal spasm or, occasionally, achalasia. Suspect achalasia if the patient has a history of dysphagia and regurgitation. However, the relation between the manometric findings and symptoms may not be clear if patients do not report symptoms experienced at the time of the 'spasm'. Ambulatory studies increase the chance of detecting a relation between abnormalities and symptoms.

Investigation for non-oesophageal causes for NCCP needs to be tailored to the likely conditions based on the history and examination. Biliary disease is an important differential diagnosis with a specific treatment. Patients with intermittent severe chest pain should be investigated with an upper abdominal ultrasound to exclude biliary disease, particularly if liver function tests are abnormal during or shortly after the pain.

Management

Management of NCCP is determined by the hierarchy of probabilities following the history and examination.

As GORD is the most common cause of NCCP, especially when other features of gastro-oesophageal reflux are present, it is reasonable to institute a therapeutic trial of acid suppression. Potent acid suppression should be used, such as a proton pump inhibitor twice daily. This treatment usually needs to be continued for at least a month before the effect can be adequately assessed. A longer assessment period may be required if symptoms are infrequent. If acid suppression is effective, treatment should be reduced to the lowest dose that provides adequate symptom control.

The role of fundoplication in NCCP has not been well examined and no controlled trials have been undertaken yet to address this issue. Fundoplication should probably be reserved for patients who have prominent features of reflux disease and an incomplete response to treatment.

The intermittent use of glyceryl trinitrate spray (Nitrolingual Pumpspray) may relieve pain in patients with oesophageal spasm. If the spasms are frequent, patients may benefit from a calcium antagonist, although the therapeutic response to this medication is often disappointing. Doses that are high enough to have a significant effect on the oesophagus may also induce hypotension. Botulinum toxin (Botox, Dysport) injected into the lower oesophagus has been reported in uncontrolled trials to be effective in up to 70% of subjects with documented oesophageal spasm.

Visceral analgesics such as the tricyclic antidepressants (e.g. amitriptyline [Endep, Tryptanol] 20 to 50 mg at night) can be a useful treatment adjunct for patients with troublesome NCCP. How these analgesics work in NCCP is unclear but the therapeutic effect can be prolonged. Treatment is commenced at a low dose and gradually increased until a therapeutic response is obtained, which often occurs in the low 'therapeutic range'. There is little information on the effect of selective serotonin reuptake inhibitors for NCCP.

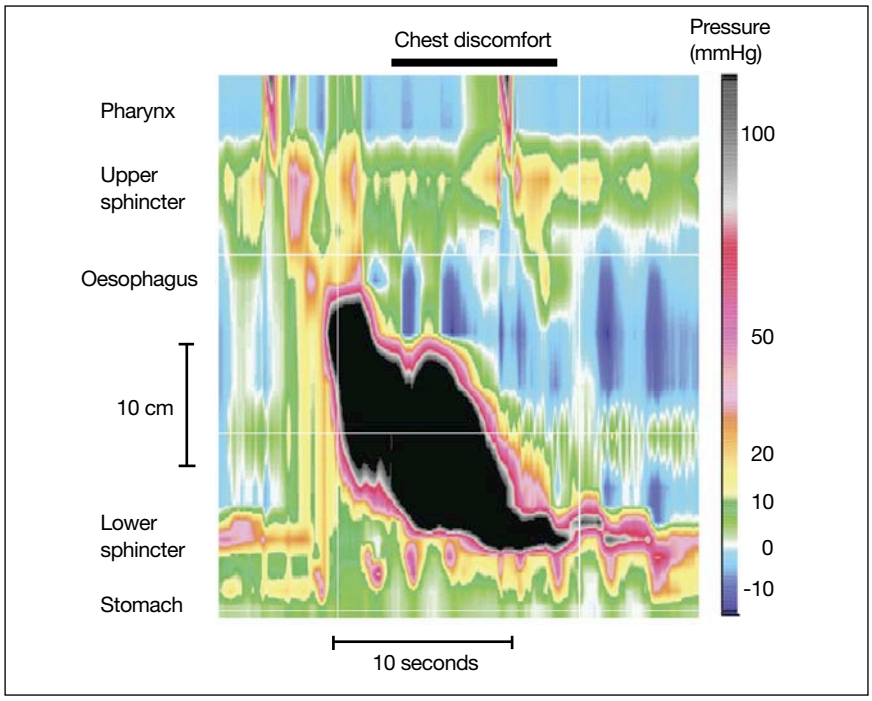

Figure. Spatiotemporal plot of oesophageal motility in a patient with chest pain. Pressure is represented as a colour (see scale on the right) and plotted against time (x-axis) and position (y-axis). The central black area is a synchronous, high amplitude (>300 mmHg), prolonged oesophageal contraction.

In patients with longstanding pain and multiple somatic symptoms, the contribution of psychological factors such as depression, anxiety or panic disorder may be significant. These disorders should be actively sought and treated, possibly in association with a psychologist or psychiatrist. Some patients may need to be managed for a chronic pain syndrome, which often requires specialist assistance.

Possible musculoskeletal causes for the pain should be investigated and managed appropriately. Trigger points (e.g. xiphisternal joint) can be injected with a combination of local anaesthetic and a corticosteroid. This combination has diagnostic as well as therapeutic value.

Patients should be reassured that, in most cases, the prognosis of their condition is benign. In a follow up study, only 4.3% of patients with NCCP died from a cardiovascular related event over an 11-year period, although 75% continued to report chest pain. Providing patients with an acceptable explanation for their chest pain is associated with reduced future use of medical resources. MT

Further reading

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DECLARATION OF INTEREST: Associate Professor Hebbard has been a member of advisory boards for, and received travel support from, AstraZeneca and Pfizer Australia. He has also received research support from AstraZeneca. Dr Gruebel has received research support from Altana Pharma AG, AstraZeneca AG, Roche Pharma AG and the Cancer Foundation, St Gallen-Appenzell, Switzerland.