

# Diagnosis and Management of Noncardiac Chest Pain

Tian Li, MBBS, MS, Manar Al Jawish, MD, Dilhana Badurdeen, MBBS, MD,  
and Andree H. Koop, MD

Division of Gastroenterology, Mayo Clinic Florida, Jacksonville, Florida

## Corresponding author:

Dr Andree H. Koop  
4500 San Pablo Road  
Jacksonville, FL 32224  
Tel: (904) 953-6970  
Fax: (904) 953-7366  
E-mail: [koop.andree@mayo.edu](mailto:koop.andree@mayo.edu)

**Abstract:** Noncardiac chest pain is a challenging condition often encountered by primary care providers, emergency medicine physicians, and gastroenterologists. It is frequently accompanied by persistent symptoms, diagnostic uncertainty, decreased quality of life, and high health care burden. Gastroesophageal reflux disease is the most common esophageal cause followed by functional chest pain, and at least half of patients with noncardiac chest pain have psychiatric comorbidities such as anxiety or depression. Management is focused on identification of an underlying cause to target treatment and address psychiatric comorbidities. This article discusses the evaluation and management of the common gastrointestinal causes of noncardiac chest pain.

**N**oncardiac chest pain (NCCP) is defined as retrosternal chest pain or discomfort, often indistinguishable from cardiac-type pain, that persists despite a negative cardiac evaluation. This is a challenging condition characterized by diagnostic uncertainty, considerable morbidity, elevated health care costs, work absenteeism, social impairment, and decreased quality of life.<sup>1-3</sup> Patients with NCCP have a similar symptom burden as patients with cardiac chest pain and often undergo multiple investigations in addition to having frequent presentations to the emergency department and hospitalizations.<sup>4-6</sup> NCCP is common, estimated to account for 2% to 5% of all emergency department visits and 6% of primary care visits, and has an estimated community prevalence of 13%.<sup>5,7,8</sup> Up to 60% of patients presenting to the emergency department for chest pain may have a noncardiac etiology.<sup>9</sup> Management of NCCP is challenging owing to heterogenous causes and high rates of psychiatric comorbidity, including anxiety, depression, and panic disorder.<sup>5,8-11</sup> Gastroesophageal reflux disease (GERD) is the most common gastrointestinal cause followed by functional chest pain and esophageal motility disorders. The goal of this article is to discuss the evaluation and management of the common gastrointestinal causes of NCCP, including GERD, esophageal motility disorders, and functional chest pain.

## Keywords

Noncardiac chest pain, gastroesophageal reflux disease, functional chest pain, esophageal motility disorders, hypercontractile esophagus, distal esophageal spasm

**Table 1.** Common Causes of NCCP

Category	Common causes	Comments
Gastrointestinal	GERD	Most common GI etiology; objective findings of GERD portend good treatment response to PPI trial
	Esophageal motility disorders	Hypercontractile esophagus and distal esophageal spasm found in 10% or less of patients
	Functional chest pain	Associated with visceral hypersensitivity
Musculoskeletal	Costochondritis	Reproducible pain on physical examination
	Fibromyalgia	Widespread musculoskeletal pain and other somatic symptoms such as fatigue
Psychiatric	Anxiety and panic disorder	Common cause of patients with NCCP presenting to the emergency department
Respiratory	Pneumonia, pulmonary embolism, pneumothorax, pleurisy	Often accompanied by shortness of breath or infectious symptoms (pneumonia)
Neurologic	Herpes zoster (shingles)	Painful vesicular rash related to herpes zoster virus

GERD, gastroesophageal reflux disease; GI, gastrointestinal; NCCP, noncardiac chest pain; PPI, proton pump inhibitor.

## Quality of Life and Health Care Burden

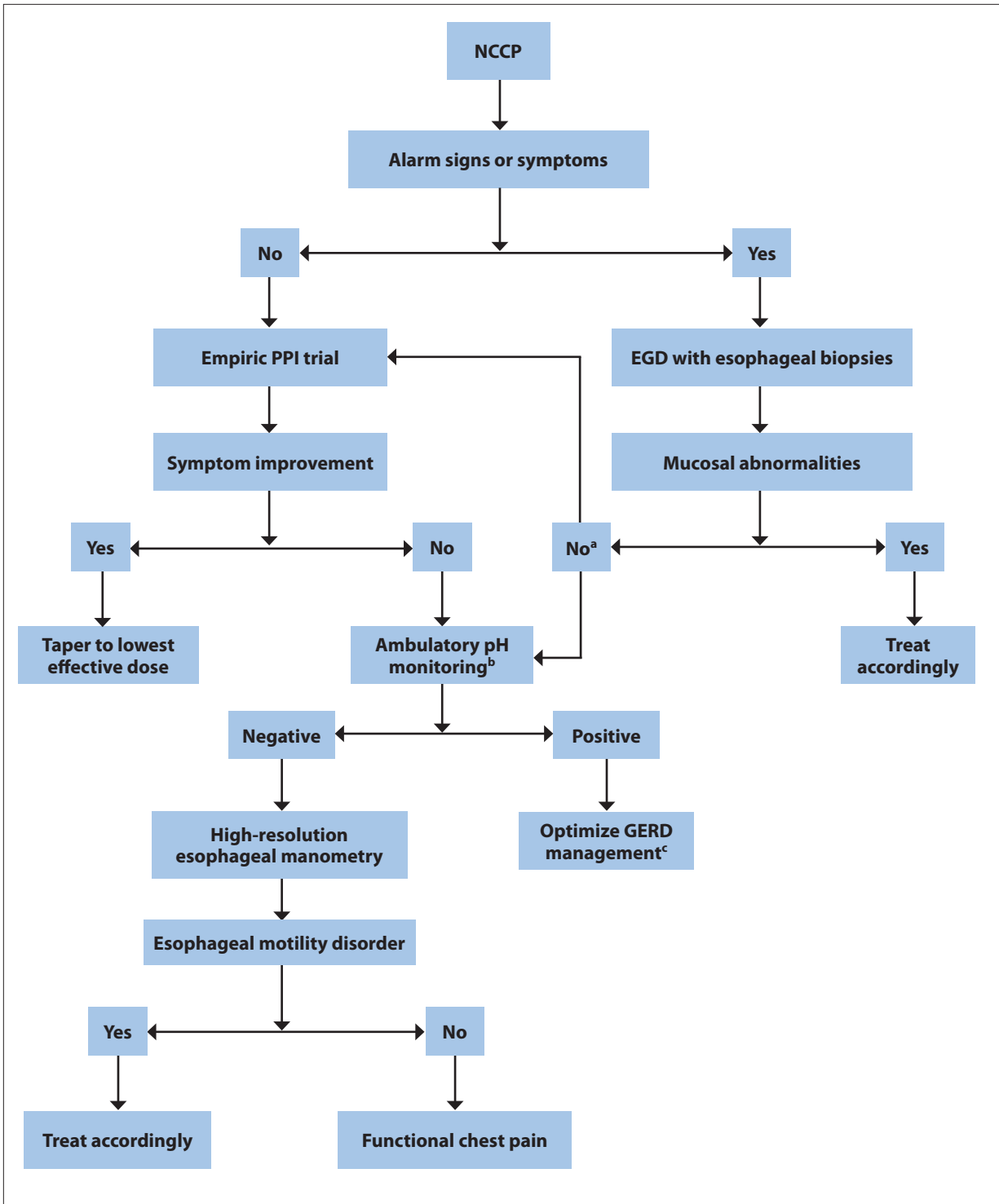
NCCP is associated with a decreased quality of life and an increased burden on the health care system.<sup>12</sup> Of patients evaluated in the emergency department and later diagnosed with NCCP, as many as 90% continued to have chest pain 2 years later.<sup>13</sup> Patients with multiple comorbidities and a high Charlson Comorbidity Index may be more likely to present for evaluation.<sup>14</sup> Compared with patients who have cardiac chest pain, patients with NCCP have reported similar or greater chest pain severity, higher symptom burden, and lower quality of life, although they have demonstrated lower 1-year all-cause mortality.<sup>5,15</sup> Owing to persistent symptoms, patients with NCCP often undergo repeat investigations, especially when hospitalized.<sup>4</sup> There is a high incidence of comorbid anxiety and depression with NCCP, and these patients demonstrate worse chest pain and quality of life.<sup>16-18</sup> Despite having a negative evaluation for ischemic heart disease, cardiac anxiety in patients with NCCP may lead to decreased physical activity.<sup>19</sup> Patients with NCCP commonly report work absenteeism and, when physically at work, an inability to perform their duties.<sup>2</sup>

## Exclusion of Cardiac Chest Pain

Patients with acute chest pain are recommended to seek immediate medical care to exclude life-threatening causes, although many patients will not have a cardiac etiology. Recommended evaluation includes a focused history and

cardiovascular examination for life-threatening causes, including acute coronary syndrome, aortic dissection, and pulmonary embolism. In the emergency department, patients should undergo an electrocardiogram and testing with high-sensitivity troponin. Cardiac stress testing may be considered based on the estimated risk for acute coronary syndrome.<sup>20</sup> In the emergency department, patients are often diagnosed with NCCP after a negative cardiac evaluation by an emergency medicine physician or cardiologist. In the outpatient setting, patients are often diagnosed by primary care providers and similarly evaluated with an electrocardiogram and cardiac stress testing.<sup>20</sup> Once a cardiac etiology has been ruled out, other nongastrointestinal etiologies include chest wall pain such as costochondritis, which is characterized by reproducible pain during physical examination.<sup>21</sup> Table 1 lists common gastrointestinal and nongastrointestinal causes of NCCP.

There is some concern that patients diagnosed with NCCP may indeed have a cardiac etiology or develop ischemic heart disease over time, leading to cardiac anxiety in a number of patients.<sup>19</sup> In patients with a normal angiogram or mild nonobstructive coronary artery disease and exertional anginal symptoms, coronary spasm was elicited with acetylcholine in 62%, suggesting that vasospasm may play a pathogenic role.<sup>22</sup> As many as 3% of patients initially diagnosed with NCCP may have an adverse cardiac event within 30 days of diagnosis, with risk factors being older age, male sex, hypercholesterolemia, diabetes, known coronary artery disease, and history of congestive heart failure.<sup>23,24</sup> Thus, providers should



**Figure.** Flow algorithm depicting the evaluation of patients with NCCP.<sup>37,86</sup>

<sup>a</sup>In patients undergoing EGD without diagnostic findings of GERD (ie, erosive esophagitis or Barrett esophagus), ambulatory pH monitoring with wireless telemetry capsule can be considered at the time of EGD. <sup>b</sup>Ambulatory pH monitoring is generally performed after stopping PPI therapy for at least 1 to 2 weeks to evaluate for GERD. <sup>c</sup>In patients with GERD, management may include lifestyle changes, increasing the dose and/or frequency of PPI therapy, or switching to a more potent PPI. Select patients may be considered for referral for antireflux surgery.

EGD, esophagogastroduodenoscopy; GERD, gastroesophageal reflux disease; NCCP, noncardiac chest pain; PPI, proton pump inhibitor.

maintain a high clinical suspicion for a cardiac etiology and consider further diagnostic testing, particularly in patients with multiple cardiac risk factors, before making a diagnosis of NCCP.<sup>24</sup>

### Pathophysiology of Noncardiac Chest Pain

The pathophysiology of NCCP remains poorly understood and includes decreased mucosal integrity related to GERD, increased mucosal inflammatory cells, spastic esophageal motility disorders, and visceral hypersensitivity, among other etiologies. Esophageal hypersensitivity might relate to acid-induced mucosal changes.<sup>25</sup> Mucosal integrity measured by baseline impedance was previously shown to be decreased in the distal esophagus in patients with GERD-related NCCP, and was lower in the proximal esophagus in GERD-negative patients.<sup>26</sup> Patients with NCCP were previously demonstrated to have more esophageal mucosal mast cells compared with healthy controls, hypothesized to lead to NCCP through mast cell activation, impaired mucosal integrity, and altered symptom perception.<sup>27</sup> In a study of 171 patients with NCCP, 24 (14%) had esophageal eosinophilia defined as greater than 20 eosinophils per high-power field; of these, 8 patients had a normal endoscopic evaluation.<sup>28</sup> In patients with chest pain and nutcracker esophagus, an older term now more commonly referred to as hypercontractile or jackhammer esophagus, balloon distension with impedance planimetry demonstrated a lower threshold for chest pain compared with controls, which may suggest visceral hypersensitivity.<sup>29,30</sup> A study of conventional manometry demonstrated higher mean distal pressure amplitude and percentage of simultaneous contractions in patients with NCCP compared with controls.<sup>31</sup>

Multiple studies have implicated visceral hypersensitivity as an underlying pathogenic mechanism.<sup>29,32,33</sup> Specifically, patients with NCCP have demonstrated lower resting esophageal pain thresholds compared with healthy controls in response to esophageal acid perfusion.<sup>32,34,35</sup> Among 181 patients with NCCP who underwent an esophageal balloon distension test, chest pain was reproducible in 75% and there was evidence of esophageal hypersensitivity in 37%.<sup>33</sup>

### Psychiatric Comorbidities

Psychiatric comorbidities, including depression, anxiety, and panic disorder, are present in at least half of patients with NCCP and are associated with decreased quality of life.<sup>18</sup> NCCP may be the presenting symptom of panic disorder, which accounts for as much as 40% of emergency department visits for NCCP.<sup>10,11</sup> In patients presenting to the emergency department with NCCP,

11% developed panic disorder over 2 years of follow-up.<sup>36</sup> Treatment of psychiatric comorbidities can lead to significant improvement in overall well-being and quality of life.<sup>37</sup> All patients with NCCP, particularly patients with functional chest pain, should be evaluated for psychiatric comorbidities, preferably by a psychiatrist or psychologist with expertise in disorders of gut-brain interaction (DGBIs). Treatments focused on psychiatric comorbidities may lead to improved symptoms of depression and anxiety as well as chest pain.

### Gastroesophageal Reflux Disease Diagnosis and Management

GERD is the most common cause of NCCP, occurring in 30% to 60% of patients and predictive of response to a proton pump inhibitor (PPI).<sup>38,39</sup> Given the high prevalence of GERD, this should be the first condition considered in patients with NCCP.<sup>39</sup> GERD is defined as the presence of troublesome symptoms such as heartburn, regurgitation, or chest pain in combination with reflux-related pathology. Chest pain related to GERD can be indistinguishable from ischemic cardiac-type pain, highlighting the importance of a negative cardiac workup before gastrointestinal evaluation.<sup>40,41</sup> The presence of heartburn and regurgitation with NCCP may further suggest that GERD is the underlying cause. Higher scores on the GerdQ (Gastroesophageal Reflux Disease Questionnaire) were shown to predict response to PPI therapy, including in patients with coronary artery disease.<sup>42</sup>

If alarm signs or symptoms are present, such as unintentional weight loss, dysphagia, unexplained iron deficiency anemia, family history of gastrointestinal malignancy, or gastrointestinal bleeding, initial evaluation of NCCP should include upper endoscopy (Figure). However, in the absence of these signs/symptoms, an appropriate first step is to initiate a PPI trial. PPIs are the most commonly prescribed medications for GERD and have demonstrated superior symptom relief and healing of erosive esophagitis compared with histamine H<sub>2</sub>-receptor antagonists.<sup>40</sup> Multiple studies have demonstrated significant improvement in NCCP in patients with GERD, with sensitivity and specificity rates for PPI trial approaching 80%.<sup>43-47</sup> Although the dose and duration of PPI trial have not been standardized, patients are typically treated with a daily or twice-daily PPI for 4 to 8 weeks.<sup>40</sup> For patients started on a daily PPI, the dose can be increased to twice daily after 1 to 2 weeks if symptom improvement is suboptimal. Symptom improvement is typically defined as at least 50% symptom reduction during treatment.<sup>38-40</sup> One study found that patients with GERD-related NCCP will have significant symptom improvement as early as a few days after starting a PPI.<sup>45</sup> A PPI trial was demonstrated

**Table 2.** Treatments for Noncardiac Chest Pain by Etiology

Etiology	Treatments
<b>Gastroesophageal reflux disease</b>	<p><b>Lifestyle measures</b></p> <ul style="list-style-type: none"> <li>• Avoid provoking foods (eg, fatty or spicy foods, tomato-based products, caffeine)</li> <li>• Eat smaller, more frequent meals</li> <li>• Remain upright 30 minutes after eating</li> </ul> <p><b>Medications</b></p> <ul style="list-style-type: none"> <li>• Over-the-counter antacids (calcium carbonate)</li> <li>• Antihistamine H2-receptor blockers</li> <li>• Proton pump inhibitors</li> </ul> <p><b>Procedural/surgical management</b></p> <ul style="list-style-type: none"> <li>• Endoscopic transoral incisionless fundoplication</li> <li>• Surgical fundoplication</li> </ul>
<b>Spastic esophageal motility disorders</b>	<p><b>Supplements/medications</b></p> <ul style="list-style-type: none"> <li>• Peppermint oil</li> <li>• Anticholinergics (hyoscyamine)</li> <li>• Calcium channel blockers (nifedipine, diltiazem)</li> <li>• Nitrates</li> <li>• Phosphodiesterase inhibitors (sildenafil)</li> </ul> <p><b>Endoscopic therapies</b></p> <ul style="list-style-type: none"> <li>• Botulinum toxin injection</li> <li>• Peroral endoscopic myotomy (in carefully selected patients)</li> </ul>
<b>Functional chest pain</b>	<p><b>Medications</b></p> <ul style="list-style-type: none"> <li>• Tricyclic antidepressants (nortriptyline, imipramine, amitriptyline)</li> <li>• Serotonin and norepinephrine reuptake inhibitors (duloxetine, venlafaxine)</li> <li>• Selective serotonin reuptake inhibitors (sertraline, fluoxetine, citalopram)</li> <li>• Serotonin-2 antagonist-reuptake inhibitors (trazodone)</li> <li>• Others (theophylline, gabapentin, pregabalin)</li> </ul> <p><b>Psychiatric treatments</b></p> <ul style="list-style-type: none"> <li>• Cognitive behavioral therapy</li> <li>• Hypnotherapy</li> <li>• Relaxation training</li> <li>• Diaphragmatic breathing</li> </ul>

to be cost-effective and reduced the number of diagnostic procedures in patients with NCCP.<sup>46</sup>

For patients who do not respond to a therapeutic trial of a PPI, further evaluation of the upper gastrointestinal tract is typically recommended with upper endoscopy and/or ambulatory pH monitoring. To maximize the yield of upper endoscopy for the diagnosis of GERD and

assessment of erosive esophagitis, patients should stop their PPI therapy at least 1 to 2 weeks beforehand.<sup>40</sup> Up to 18% of patients with NCCP were previously demonstrated to have erosive esophagitis.<sup>33,48</sup> Endoscopic evaluation is helpful to rule out other causes of NCCP such as eosinophilic esophagitis or a paraesophageal hernia.<sup>28</sup> In patients with normal endoscopic findings, ambulatory pH monitoring is recommended to establish the presence or absence of GERD by assessing esophageal acid exposure and symptom association. Ambulatory pH monitoring can be performed with transnasal catheter-based testing or a wireless pH telemetry capsule placed during upper endoscopy. Testing with a transnasal catheter is performed for 24 hours, whereas wireless pH telemetry is performed for up to 96 hours and thus is more sensitive for the detection of GERD. In addition to the benefits of placement at the time of endoscopy, wireless pH telemetry avoids the discomfort of a catheter and generally allows patients to better carry on with normal activities.<sup>40</sup> Patients with NCCP and abnormal esophageal acid exposure assessed by ambulatory pH monitoring often have a superior response to PPI therapy.<sup>43,45-47,49</sup> Furthermore, patients with NCCP and positive symptom association on ambulatory pH monitoring were more likely to respond to PPI therapy, with patients having both increased acid exposure and positive symptom association demonstrating the best response.<sup>50,51</sup>

Given the high sensitivity and specificity of a PPI trial for GERD-related NCCP and that most patients are initially seen by primary care physicians, a PPI trial is the recommended first step in patients without alarm symptoms, with further testing reserved for nonresponders.<sup>7,52</sup> The overall number needed to treat with an empiric short-term PPI trial was previously shown to be 3.<sup>53</sup> However, given the association between objective findings of GERD (erosive esophagitis and increased acid exposure on ambulatory pH monitoring) and symptom response to a PPI trial, upfront diagnostic testing with upper endoscopy and/or ambulatory pH monitoring is reasonable in patients with a low pretest probability of GERD who are less likely to respond to a PPI trial. This tailored evaluation may lead to an earlier diagnosis of esophageal hypersensitivity or functional chest pain and targeted treatment.<sup>54-56</sup> In PPI responders, the medication is typically titrated to the lowest effective dose. Treatments for GERD and other causes of NCCP are listed in Table 2.

## Esophageal Dysmotility Diagnosis and Management

Esophageal dysmotility is the least common esophageal cause of NCCP and is typically evaluated by high-resolution esophageal manometry (HRM) once other secondary

causes such as GERD have been ruled out.<sup>38</sup> Prior studies of patients with NCCP undergoing esophageal manometry have demonstrated normal findings in 50% to 70% of patients and spastic esophageal disorders in 10% or less.<sup>57-60</sup> The most common abnormalities identified on esophageal manometry are a hypotensive lower esophageal sphincter and impaired (weak) peristalsis, findings associated with GERD.<sup>58,61</sup> Hypercontractile esophagus and distal esophageal spasm, which are spastic disorders of peristalsis, have been implicated in NCCP, although they are rare. These disorders are often accompanied by symptoms of dysphagia.<sup>62</sup> In a study of patients with hypercontractile esophagus, symptoms of NCCP were associated with a greater distal contractile integral (measure of contractile vigor) on esophageal manometry compared with patients with other symptoms such as heartburn.<sup>62</sup> Disorders of esophagogastric junction outflow, including achalasia and esophagogastric junction outflow obstruction, have also been associated with NCCP.

Management of NCCP related to hypercontractile esophagus and distal esophageal spasm is challenging owing in part to the rarity of these findings and the lack of large, randomized, placebo-controlled trials assessing treatment. Of note, the manometric patterns of hypercontractile esophagus and distal esophageal spasm can occasionally be seen in normal, asymptomatic controls and require associated symptoms to be clinically relevant.<sup>30</sup> Esophageal spasm may represent a secondary response to GERD or mechanical obstruction, and exclusion of these causes is important. In a study of patients with what was known as nutcracker esophagus and NCCP, GERD was diagnosed in 65%, and 83% experienced symptom improvement with an antihistamine or PPI.<sup>63</sup> Upper endoscopy is typically performed before HRM to exclude secondary causes such as a stricture, ring, eosinophilic esophagitis, or hiatal hernia. Symptoms of chest pain do not always improve with documented reversal of manometric findings, suggesting that other factors such as visceral hypersensitivity may be contributing.<sup>63</sup> Chronic opioid use is associated with both hypercontractile esophagus and distal esophageal spasm, termed opioid-induced esophageal dysfunction, and clinical improvement may occur with opioid cessation or dose reduction.<sup>64,65</sup>

Multiple medical therapies have demonstrated improvement in patients with spastic esophageal motility disorders. In a study of 8 patients with NCCP, peppermint oil was beneficial with the greatest improvement in patients meeting manometric criteria for distal esophageal spasm and esophagogastric junction outflow obstruction.<sup>66</sup> Smooth muscle relaxants, including anticholinergics, calcium channel blockers (nifedipine and diltiazem), phosphodiesterase inhibitors (sildenafil), and nitrates, have improved symptoms of NCCP but may be limited

by adverse effects such as hypotension or headache. In patients with high amplitude esophageal contractions on conventional manometry, diltiazem led to improvement in chest pain scores and mean distal esophageal peristaltic pressures compared with placebo.<sup>67</sup> In a study of patients with what was known as nutcracker esophagus at that time, nifedipine decreased distal esophageal contraction amplitudes and lower esophageal sphincter pressure, but was no different from placebo in relief of daily chest pain.<sup>68</sup> As chest pain may relate to visceral hypersensitivity rather than manometric findings, some patients may respond better to treatment with neuromodulators. In a study of patients with distal esophageal spasm, omeprazole in combination with diltiazem led to similar clinical improvement compared with omeprazole and fluoxetine.<sup>69</sup>

Small nonrandomized and non-placebo-controlled studies have demonstrated improvement in NCCP in patients with spastic esophageal disorders who have undergone botulinum toxin injection.<sup>70,71</sup> In a study of 29 patients with NCCP and spastic, nonachalasia esophageal motility disorders, 72% had symptom improvement, characterized by a 50% reduction in pain, after undergoing botulinum toxin injection at the gastroesophageal junction. However, in a small double-blind, randomized, sham-controlled study of botulinum toxin for hypercontractile esophageal motility disorders, this treatment was no different from placebo for symptom improvement.<sup>72</sup> Peroral endoscopic myotomy (POEM) has demonstrated benefit in managing chest pain in carefully selected patients with spastic esophageal motility disorders, although this treatment should be considered only once all other therapeutic modalities have failed. In a study of 7 patients with type III achalasia, 6 patients with hypercontractile esophagus, and 1 patient with distal esophageal spasm, all had improvement in chest pain, dysphagia, and manometric characteristics following POEM.<sup>73</sup>

## Functional Chest Pain

Functional gastrointestinal disorders, now referred to as DGBIs, are defined as a group of disorders characterized by gastrointestinal symptoms in the absence of obvious structural abnormalities. DGBIs may be related to any combination of motility disturbances, visceral hypersensitivity, altered mucosal function, immune function, gut microbiota, and/or central nervous system symptom processing.<sup>74</sup> Functional chest pain is categorized as 1 of the 5 functional esophageal disorders according to Rome IV criteria and is a known diagnostic classification of NCCP. This diagnosis requires symptoms of retrosternal chest pain or discomfort and the absence of associated esophageal symptoms such as dysphagia and heartburn. Exclusion



of other sources of chest pain is required, including cardiac causes, GERD, eosinophilic esophagitis, and major esophageal motility disorders. To exclude these disorders, evaluation with upper endoscopy and esophageal biopsies, ambulatory reflux monitoring, and HRM is performed.<sup>75</sup> These criteria must be fulfilled for the prior 3 months with symptom onset at least 6 months prior to diagnosis and frequency of symptoms at least once per week.<sup>75</sup>

Functional chest pain accounts for approximately one-third of patients diagnosed with esophageal-related NCCP and is the second most common cause of NCCP after GERD.<sup>75-77</sup> Although the pathophysiology is not completely understood, altered pain perception and visceral hypersensitivity are considered to be the hallmark of functional chest pain.<sup>78-80</sup> Secondary visceral hypersensitivity may develop following acid exposure to the distal esophagus and remain after the original insult has resolved. Increased mucosal mast cell infiltration was previously shown to influence esophageal hypersensitivity.<sup>81,82</sup>

### Treatment of Functional Chest Pain

As visceral hypersensitivity is proposed as the underlying mechanism of functional chest pain, neuromodulators targeting pain processing are the mainstay of treatment, including serotonin and norepinephrine reuptake inhibitors, tricyclic antidepressants, selective serotonin reuptake inhibitors, theophylline, gabapentin, pregabalin, and trazodone.<sup>83-86</sup> In a study using impedance planimetry to assess esophageal hypersensitivity, theophylline led to an increase in the esophageal cross-sectional area and distensibility of the esophageal wall with a decrease in the frequency and severity of chest pain.<sup>87</sup> Intravenous citalopram was shown to increase the threshold for discomfort during esophageal balloon distention, and prolonged the acid perfusion time to induce the perception of heartburn and discomfort.<sup>88</sup> In a systematic review of randomized placebo-controlled trials, chest pain improved independent of depression scores with venlafaxine, imipramine, and sertraline, and clinical global improvement occurred with venlafaxine, sertraline, paroxetine, and trazodone.<sup>85,89,90</sup> These medications are typically administered at lower doses for chest pain than for psychiatric indications and can take 4 to 8 weeks to start having analgesic effects. These treatments are helpful given the high incidence of comorbid psychiatric disease, including anxiety, depression, and panic disorder, in more than 50% of patients.<sup>5,8-11</sup> As such, other psychiatric treatments, including cognitive behavioral therapy and hypnotherapy, have demonstrated effectiveness in improving the frequency and intensity of chest pain as well as improving quality of life.<sup>91-97</sup> A Cochrane review of 17 randomized controlled trials investigating psychological interventions,

including cognitive behavioral therapy, relaxation therapy, and hypnotherapy, showed modest benefit particularly with a cognitive behavioral framework, although the beneficial effects appeared restricted to the first 3 months after intervention.<sup>98</sup>

### Conclusion

NCCP is a common disorder that greatly impacts quality of life and is associated with a high health care burden and comorbid psychiatric disease. After exclusion of a cardiac cause, management is focused on identifying an underlying etiology to target treatment by using upper endoscopy, ambulatory pH monitoring, and HRM. The most common esophageal cause of NCCP is GERD followed by functional chest pain, and a PPI trial is the most common initial step in management. In patients with functional chest pain, treatment with neuromodulators and psychiatric interventions such as cognitive behavioral therapy may improve chest pain severity and also treat comorbid psychiatric disease. Despite known triggers such as GERD, the mechanism of NCCP remains poorly understood, and further research is needed to better understand the pathophysiology to target treatment in all patients, including those with comorbid psychiatric disease and visceral hypersensitivity.

### Disclosures

*The authors have no relevant conflicts of interest to disclose.*

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