Nice guidance on the investigation of chest pain

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The NICE guidance on chest pain provides a structured and evidence-based approach to the diagnosis and triage of patients with chest pain and provides a series of improvements on the status quo. However, the challenge is the high prevalence of occult vascular disease in our community, especially in older people and at younger ages in men than in women. There is also a high prevalence of chest pain (20%-40% of the population) but this is frequently non-cardiac in origin. Among those presenting to their primary care doctor with chest pain, the final diagnosis was not ischaemic heart disease in 83%. Nevertheless, because of the high prevalence of asymptomatic coronary disease there may be an unintended consequence: detection of incidental non-obstructive coronary disease. This non-obstructive coronary disease may not have been responsible for the symptoms and may “convert” an individual into a cardiac patient. Further, do we have good evidence that defining the anatomy with CT and angiography in those with non-obstructive disease will change the secondary prevention treatments that should be provided based on the patient’s risk factors? From a professional and economic viewpoint we must also consider the implications for changes in clinical practice and the increased demands on finite human and economic resources.

Strengths of the guidance include the emphasis on establishing an early and accurate diagnosis based on clinical, electrocardiographic and biomarker assessments among those presenting with suspected cardiac chest pain (see page 974). Appropriately, there is emphasis on very early identification of ST elevation infarction and on the remainder of acute coronary syndromes (in one diagnostic pathway) and on managing those with stable angina (second diagnostic pathway). The subsequent management of these conditions is dealt with in separate NICE guidance. The NICE guidance on chest pain also emphasises the importance of providing clear and accurate information to the patients and explanation of the diagnostic pathway.

WHAT IS THE PROBLEM WITH CURRENT MANAGEMENT OF CHEST PAIN?

As approximately a quarter of all emergency hospital admissions are for chest pain, robust triage pathways and accurate diagnostic tools are of major importance. International publications show that the diagnosis of acute myocardial infarction (MI) is missed and a patient discharged in approximately 2% of cases, and many patients are left with diagnostic uncertainty about whether the pain is of cardiac origin, even when infarction is “ruled out”. Although ST elevation infarction can be identified with high diagnostic accuracy based on the ECG and clinical findings, non-ST elevation MI has less specific ECG changes and the threshold for differentiation from unstable angina is dependent on the sensitivity of the biomarker (troponin) assay. Further, troponin elevation does not equal infarction: several non-coronary causes of myocyte necrosis may precipitate troponin elevation (for example, arrhythmias, heart failure, myocarditis, pulmonary embolism). Hence, improved triage and diagnosis pathways are needed.

Without a systematic and evidence-based approach to differentiating chest pain and establishing a diagnosis, the patient and the patients’ carers may be left in limbo. For example, a discharge statement, “chest pain MI excluded”, is unhelpful as it does not establish a positive diagnosis and does not exclude prognostically important or other symptomatic coronary heart disease. Furthermore, inadvertent discharge of patients with acute coronary syndrome (ACS) or with MI is well documented. For example, in a study of patients presenting to emergency departments in 10 US hospitals (10,689 patients), 2.1% of those with acute infarction were mistakenly discharged home and 2.3% of those with unstable angina were mistakenly discharged. The advent of more accurate and specific biomarkers of necrosis has improved diagnostic accuracy but currently requires a prolonged period of about 12 h of observation. However, even in the absence of biomarkers of necrosis the patient may have obstructive coronary disease with stress-induced ischaemia, and a further proportion have incidental non-obstructive coronary disease unrelated to the presenting symptoms.

The guideline emphasises clinical assessment and a resting 12-lead ECG in the initial investigation of any patient with suspected ACS. The ECG can be performed in the pre-hospital setting, facilitating early triage, provided that this does not significantly delay transfer to hospital. It is critically important to detect evolving ST elevation myocardial infarction and although the patient may not have diagnostic ST elevation at initial presentation, these signs can evolve over minutes or hours. The retrospective finding of evolved MI the following morning is a serious error and a missed opportunity to salvage myocardium.

DELAYS IN ESTABLISHING THE DIAGNOSIS

Once a patient arrives in hospital the NICE guideline recommends measuring troponin immediately in all patients with a recent episode of cardiac sounding chest pain, but it recognises that repeat sampling 10–12 h after the onset of symptoms is required to exclude MI. Newer very high-sensitivity troponin assays can identify patients earlier (within about 2 h) but need testing in large unselected cohorts of patients with suspected cardiac pain. Importantly, the NICE guidance emphasises that troponin should not be interpreted in isolation, but in the context of the clinical history in ECG changes.

DOES THE PATIENT NEED RISK STRATIFICATION?

The NICE guidance on management of non-ST elevation ACS emphasises the spectrum of risk across the ACS syndrome. In the 12.5% of patients in the lowest eighth of risk the 6-month mortality is <2% (GRACE score <70), whereas in the half of patients with higher risk scores (GRACE score >112) the 6-month mortality is more than fivefold higher (>9.5%). This information will aid clinical decision making. In contrast, patients are currently transferred for...
Table 1  Percentage of people estimated to have coronary artery disease according to typicality of symptoms, age, sex and risk factors

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Non-anginal chest pain</th>
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<th>Atypical angina</th>
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<td>71</td>
<td>86</td>
<td>20</td>
<td>51</td>
<td>93</td>
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</table>

For men older than 70 with atypical or typical symptoms, assume an estimate >90%. For women older than 70, assume an estimate of 61–90% except women at high risk and with typical symptoms, where a risk of >90% should be assumed. Values are the percentage of people at each mid-decade age with significant coronary artery disease (CAD). Hi = High risk = diabetes, smoking and hyperlipidaemia (total cholesterol >6.47 mmol/L). Lo = Low risk = none of these three. The shaded area represents people with symptoms of non-anginal chest pain, who would not be investigated for stable angina routinely. Note: these results are likely to overestimate CAD in primary care populations. If there are resting ECG ST changes or Q waves, the likelihood of CAD is higher in each cell of the table.

Reproduced from NICE guideline: http://www.nice.org.uk/guidance/CG95. Adapted from Pryor DB, et al.14

DEFINING OTHER CAUSES OF CHEST PAIN

A strength of the NICE guideline is the recommendation that simply excluding acute MI is not sufficient. Other causes of the chest pain need to be considered and managed and a pathway provided for investigation of patients with stable chest pain.

DIAGNOSIS OF ‘STABLE’ CHEST PAIN

The guideline has chosen a diagnostic probability, based on clinical assessment, of >90% likelihood of coronary artery disease (CAD) for diagnostic “rule in” and <10% likelihood of CAD for diagnostic “rule out”. These thresholds are arbitrary, but useful. The guideline has adopted the 1979 Diamond and Forrester criteria3 to stratify patients with chest pain into those with typical angina, atypical angina and non-anginal pain. This stratification then combines the clinical features of the symptoms with other factors including age, gender, cigarette smoking, diabetes mellitus, hyperlipidaemia and the presence of ECG changes.5 The guideline should be commended for re-emphasising the importance and positive predictive value of the clinical history, and for stating explicitly that the diagnosis of angina pectoris can be made on the basis of the clinical history alone.

TESTS FOR CARDIAC PAIN

Two forms of testing are advocated for investigating patients with stable angina thought to be due to CAD: anatomical testing to diagnose coronary arterial narrowing, and non-invasive functional testing for myocardial ischaemia. The guideline has examined the sensitivity and specificity of tests against a ‘gold standard’ of angiographically demonstrated CAD, but this poses a number of problems because of the high prevalence of non-obstructive and functionally unimportant CAD.

Following clinical assessment the guideline recommends invasive angiography as the most cost-effective first test if the likelihood of CAD is 61–90%, and non-invasive functional testing with either myocardial perfusion scintigraphy with SPECT, stress echocardiography, first-pass contrast enhanced magnetic resonance (MR) perfusion or MR imaging for stress-induced wall motion abnormalities if the likelihood of CAD is 30–60%.1 If the likelihood of CAD is 10–29% CT scanning is recommended (with 64 slices or above). The guidance suggests that patients with a low likelihood of CAD will not need further testing (<10% likelihood).

IMPLICATIONS OF THESE INVESTIGATION STRATEGIES

There are major implications associated with these recommendations. As can be seen from table 1 of the full guideline a man >65 years with atypical chest pain and no risk factors or a man >45 years with atypical chest pain and risk factors would exceed the 60% probability threshold for angiography. No women with atypical or non-anginal type pain would exceed this threshold. However, all men and women >65 years with atypical angina would exceed the 30% probability threshold for stress imaging if they have risk factors (table 1).1 The NICE table is based on 1030 patients referred for non invasive testing in an observational study conducted from 1983 to 1985, and only 168 underwent angiography.14 Those authors acknowledge that severe disease and left main disease were less reliably predicted than any coronary disease.14 The extent to which the findings are applicable to CT detection of coronary disease, or current higher-resolution radiological imaging is uncertain. Robust information is required as this formulaic approach to stress imaging and angiography has huge resource implications and may not be in the best interests of patients with atypical chest pain that is likely to be non-cardiac in origin.

THE “OBSOLETE” EXERCISE ECG

Despite its limitations, exercise ECG stress testing is currently widely used in chest pain and general cardiology clinics and although the sensitivity and the specificity are less good than the imaging techniques listed above, a positive test provides a rapid and cost-effective method of demonstrating myocardial ischaemia. Replacing all exercise ECG facilities with sufficient CT and imaging resources (staff and equipment) will be a significant challenge.

THE ROLE OF COMPUTED TOMOGRAPHY

There are important implications for radiation exposure, especially with the older slower 16-slice scanners. For these reasons the guidelines recommends calcium scoring initially, with no further testing if this is zero. The NICE guideline suggests a high degree of diagnostic accuracy with a sensitivity of 99%.1 However, if the calcium score is >400 the guideline recommends proceeding directly to invasive coronary angiography. Unfortunately, the issues are not as straightforward as suggested by the guideline. For example, there is recent evidence from a multicentre trial using 64-slice CT that a zero calcium score was nevertheless associated with a 50% or greater coronary stenosis in 19% of the population and a 70% or greater coronary stenosis in 15% of the population.15 The probable explanation is that disrupted plaque may not contain sufficient calcium to be detected in the 64-slice CT. Unfortunately, there were not reliable multivariable predictors, using baseline characteristics, for the presence of coronary lesions, other than presentation to an emergency department (OR=4.7, CI 1.13 to 19.75, p value 0.03).15 The authors of this publication conclude that a zero calcium score should not be the gatekeeper for coronary angiography. Nevertheless, recent information indicates that among those with a zero calcium score there is a low rate of progression to an elevated calcium score within 4 years.16
WHAT WILL BE THE IMPACT OF THE PROPOSED INVESTIGATIVE STRATEGIES?

The NICE guideline on chest pain, presented personal communications from two of the authors. These suggested that around 29% of patients were in the <10% likelihood of CAD category, 11–17% in the 10–29% likelihood of CAD category, 17–18% in the 30–60% likelihood of CAD category, about 15% in the 60–90% category and 6–9% in the >90% category. However, these figures are not in accord with a published cohort of 504 randomly selected patients from a complete cohort of 7000 consecutive patients presenting to the emergency department with undifferentiated chest pain.17 Only 3% were in the <10% likelihood of CAD category, 12% in 10–29% likelihood group, 51% in 30–60%

Table 2 A cohort of 500 consecutive patient attending the rapid access chest pain clinic of the Royal Infirmary of Edinburgh in 2009

<table>
<thead>
<tr>
<th>Typicality of symptoms</th>
<th>Invasive angiography, n (%)</th>
<th>Non-invasive imaging, n (%)</th>
</tr>
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<tbody>
<tr>
<td>Non-anginal chest pain</td>
<td>112 (22)</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Atypical angina</td>
<td>245 (49)</td>
<td>29 (12)</td>
</tr>
<tr>
<td>Typical angina</td>
<td>143 (29)</td>
<td>88 (61)</td>
</tr>
<tr>
<td>Total</td>
<td>500 (100)</td>
<td>121 (24)</td>
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</tbody>
</table>

Percentage increases in the lower table are absolute rather than relative.

Figure 1 A cohort of 504 randomly selected patients (from 7000) attending the emergency department of the Royal Infirmary Edinburgh with non-traumatic chest pain.17 Distribution according to the GRACE risk score: 36% low risk (0–15% 6-month death/myocardial infarction (MI)), 33% moderate risk (16–30% 6-month death/MI) and 31% high risk (>30% 6-month death/MI). Pre-NICE, frequency of invasive coronary angiography proposed in the NICE guideline.1

Figure 2 A second cohort of 500 consecutive patients attending the rapid access chest pain clinic of the Royal Infirmary Edinburgh in 2008 (see table 2) Pre-NICE, frequency of invasive coronary angiography in clinical practice in 2008; NICE, frequency of invasive coronary angiography proposed in the NICE guideline.1

CONCLUSIONS

The NICE guidance on chest pain provides a series of important advances over the current status of investigation and triage of chest pain and should be welcomed by the profession. The clearer triage pathways and use of more robust investigation tools will lead to improvements in clinical care. However, a serious concern needs to be addressed: the unintended consequence of investigating patients with stress imaging and/or invasive imaging on the basis of their pre-test probability of coronary disease. A high proportion of such disease may be incidental and non-obstructive (even though of prognostic importance) and evidence supports secondary prevention measures on the basis of vascular risk factors, alone. Thus, we must consider the benefits versus potential harm of investigating most men and many women with chest pain and vascular risk factors. We propose that, before widespread adoption, a prospective study is required to test the risk versus benefit of applying this approach.

Competing interests None.

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Diastolic stress testing: a new trick to evaluate the ageing heart

Zoran B Popović, Brian Griffin

Exertional shortness of breath in the absence of an obvious cardiac abnormality is a perplexing and relatively common clinical scenario especially in older patients. These patients often undergo multiple evaluations by different specialists and end up without a definitive diagnosis and, more importantly, without any specific therapeutic target to improve their symptoms. In some of these patients, exercise intolerance is attributed to respiratory disease, in others to deconditioning or obesity and in many diastolic abnormalities are claimed as the underlying problem without substantiating data. In their article in this edition of Heart, Tan et al describe a study of diastolic function on exercise in a group of patients with treated hypertension without significant diastolic dysfunction at rest whose functional capacity is significantly reduced (see page 948).1 Their findings that these patients exhibit significant abnormalities of diastolic function on limited exercise and that these induced diastolic abnormalities relate to the degree of functional limitation are an important contribution to our understanding of the pathophysiology of functional impairment in older hypertensive patients. This paper also highlights the potential utility of diastolic stress testing as a diagnostic modality in this patient population.

It is not surprising that exercise stress will provoke diastolic abnormalities that are not apparent at rest. Indeed, diastolic abnormalities, as a rule, accompany systolic abnormalities during stress, and demand ischaemia leads first to diastolic, and then to systolic abnormalities. One can roughly divide diastolic function parameters into ‘traditional’ or ‘hard’, and ‘contemporary’ or ‘soft’ indices. Traditional diastolic function indices are usually considered as measures of relaxation, diastolic stiffness and filling pressure (which results from the interaction of relaxation, stiffness and preload). Relaxation occurs first with mitral valve closure, followed by left ventricular (LV) filling along the pressure–volume curve that is defined by LV stiffness, and finally, results in LV end-diastolic pressure. By default, measuring traditional indices means measuring LV filling pressures invasively, which is impractical in routine clinical diagnostic assessment and is particularly difficult on exercise.

In clinical practice, we most often use ‘contemporary’ indices, almost exclusively obtained by echocardiography. These indices can be considered ‘soft’ as they often reflect factors other than ‘traditional’ indices.2 However, ‘contemporary’ indices give us a slightly different description. Here, the diastolic process starts with LV untwisting. This represents the early relaxation of epicardial fibres, which in turn releases the elastic elements within the ventricle and leads to clockwise motion of the apex. This process starts in the second part of the systole, and reaches its maximum at the time of aortic valve opening, preceding the beginning of isovolumic relaxation as defined by ‘traditional’ indices. Next, the mitral valve opens owing to development of LV suction. Suction can be quantified by early diastolic intraventricular pressure gradient, or by its surrogate, colour-M mode flow propagation velocity. This is followed by downward motion of the mitral annulus and outward motion of the LV wall, which results in the early filling flow through the mitral valve. Of note, all of the previous phenomena occur in this definite order both in sickness and disease, and show some correlation with ‘traditional’ parameters of relaxation. In contrast, the shape of the second half of the early mitral filling wave depends on LV stiffness: the greater the stiffness, the shorter the LV filling.

The biggest drawback of ‘contemporary’ indices is that their values are a result of mixed influences of relaxation, stiffness and filling pressures or even some other parameters, such as LV geometry. A potential strength is that in contrast to ‘traditional’ pressure-based parameters, echocardiography can provide regional estimates of both relaxation and stiffness indices obtained by measurement of regional deformation (strain and strain rate) and velocity. However, the comprehensive non-invasive assessment of diastolic dysfunction is complex and time consuming at rest and becomes more difficult with the effect of increased heart rate with exercise. Fusion of the early diastolic flow velocity and the atrial contraction velocity occurs at higher heart rates and makes their differentiation impossible. Furthermore, obtaining a technically adequate assessment is difficult in a patient who is fighting for breath while exercising.

Despite these difficulties, Tan and colleagues have shown that diastolic stress testing by Doppler echocardiography is both feasible and useful.3 They compared patients with heart failure and normal ejection fraction (HFNEF) due to hypertension with healthy volunteers. Patients had a much lower exercise tolerance than healthy volunteers, despite being of similar age, gender, blood pressure and ejection fraction. Both groups underwent a challenging exercise protocol of supine symptom limited exercise testing, with the target heart rate of 100 bpm during which two-dimensional, pulsed and colour-M mode Doppler data were collected. The