Clinical focus

Cardiology series — 2

The approach to patients with possible cardiac chest pain

Chest pain is a confronting symptom for patients and clinicians alike. Some patients presenting with chest pain will have serious acute illness with a high short-term risk of mortality, but this will be excluded in most patients. Chest pain is one of the most common causes of attendance at hospital emergency departments (EDs) and a frequent cause of presentations to general practice. Missed diagnosis, with associated adverse outcomes, can occur when chest pain assessment is based on clinical features alone.

Regardless of the clinical setting, a stepwise approach should be applied to patients with chest pain (Box 1). In the absence of trauma, the primary focus should be exclusion of four potentially fatal conditions: acute coronary syndrome (ACS; encompassing acute myocardial infarction and unstable angina), pulmonary embolism, aortic dissection and spontaneous pneumothorax. ACS is by far the most common of these. All these conditions may present without immediately obvious physical signs, but the latter three may be accurately excluded by rapid diagnostic testing (predominantly medical imaging). However, ACS is more challenging as it cannot be readily excluded with an acceptable level of accuracy on initial clinical evaluation or with a single investigation. After excluding these conditions, attention should be turned to chronic but serious conditions that may require additional evaluation, such as stable coronary artery disease or aortic stenosis. Next, non-life threatening conditions that may benefit from specific therapy (eg, herpes zoster, gastro-oesophageal reflux) should be considered. If the clinician is confident that all these causes have been excluded, the patient can be reassured that the chest pain is due to an insignificant cause.

Here, we focus on several evolving areas relating to the assessment of patients with possible cardiac chest pain, including risk stratification, cardiac biomarkers and the role of non-invasive testing for myocardial ischaemia and coronary artery disease. This article is aimed at all clinicians who assess patients with acute, undifferentiated chest pain. It is not a systematic review, but we have directed the reader towards these where appropriate.

The aim of chest pain assessment

There is a dichotomy in the assessment of patients with possible ACS. First, early and accurate identification of patients with ST-segment-elevation myocardial infarction (STEMI) enables provision of emergency reperfusion therapy, which has a major impact on outcome, while accurate identification of patients with other types of ACS (non-ST-segment elevation myocardial infarction [NSTEMI] or unstable angina) allows for early initiation of targeted treatment known to improve outcomes in these groups. Second, accurate exclusion of myocardial ischaemia in patients with chest pain is essential to minimise the morbidity and mortality associated with missed diagnoses, while avoiding unnecessary overinvestigation in those without the disease. However, assessment is complex because of the diversity of clinical presentations of ACS and the lack of a single diagnostic test for the entire spectrum of disease.

Despite recognition that clinical systems are imperfect, a high degree of safety in chest pain assessment processes is demanded. A recent large survey of emergency physicians suggests that the target rate of unexpected adverse outcomes in patients with a negative chest pain assessment should be <1% at 30 days; this target is likely to be equally stringent in primary care. Achieving this level of safety in a timely and cost-effective fashion in an era of increasing demand on acute services presents challenges. This must be considered when the potential value and safety of new developments are assessed.

Clinical approach and risk stratification

Most current diagnostic strategies for acute chest pain focus on the identification of ACS and are based on the premise...
that other obvious diagnoses have been excluded with accurate clinical assessment.

Systematic reviews of the diagnostic value of clinical features in the assessment of chest pain have largely been carried out in hospital settings, where the prevalence of serious disease is higher than in general practice. It is widely understood that no single clinical feature or combination of features can be used to exclude ACS with sufficient sensitivity to obviate the need for further investigation. Thus, a strategic approach based on clinical risk stratification, a period of observation, electrocardiography and serial biomarker evaluation has emerged. In all settings, a 12-lead electrocardiogram (ECG) should be performed immediately in patients presenting acutely with chest pain to exclude ST-segment-elevation.

In general practice, the aim should be to differentiate patients who require urgent hospital-based assessment for possible ACS from those with more stable symptoms who may be investigated on an outpatient basis. Limited access to investigations encourages the use of clinical judgement or clinically based decision rules to triage patients who can continue to be managed safely in primary care. Several such decision rules exist, but with limited validation for use in primary care. Despite the lower prevalence of coronary disease in patients presenting with chest pain in primary care, the same limitations found in hospital-based cohorts apply to the value of clinical assessment. A recent well conducted Swedish study concluded that the accuracy of clinical assessment of chest pain by general practitioners was high, but insufficient to safely rule out coronary artery disease. Clinicians in general practice should refer patients promptly to hospital for assessment when features suggesting a diagnosis of ACS are present (Box 2).

The value of further investigation in general practice of patients with an acute onset or ongoing symptoms is limited, given that a normal ECG cannot exclude a significant short-term risk of an adverse outcome, and serial biomarker testing is required to exclude myocardial infarction. Nevertheless, in all settings, the resting ECG has a critical role in identifying patients with ST-segment elevation who require emergency reperfusion therapy. Patients with suspected ACS and ongoing pain, pain within the past 12 hours that has resolved but with an abnormal ECG, or other high-risk features (Box 3) should be referred to hospital as an emergency. Given the release kinetics of troponin, a single troponin test may have value in assessing patients with a normal ECG and no high-risk features who present more than 12 hours after resolution of symptoms suggestive of ACS. In such cases, appropriate mechanisms must be in place for prompt review of results and referral to hospital where necessary. If these facilities are unavailable, patients should be referred to the ED for same-day chest pain assessment.

Demographic and cardiovascular risk factors, such as age and sex, influence population risk of disease but should not unduly influence the assessment of individual patients. In the absence of a clear alternative diagnosis, most patients will require additional investigation to exclude coronary artery disease, and the critical decision is usually not whether, but with what urgency, this should be undertaken. In some countries, rapid-access chest pain assessment clinics offering early assessment of patients (usually within 14 days) have become an integral part of strategies for chest pain assessment as an alternative to ED-based assessment. However, these have not been widely implemented in Australia, and all acute care facilities with an ED should have an evidence-based strategic approach to assessing patients with chest pain.

Patients should be stratified as being at low, intermediate or high risk of short-term adverse outcomes in the context of possible ACS, in line with the joint guidelines of the National Heart Foundation and Cardiac Society of Australia and New Zealand (NHF/CSANZ) stratifying patients with ACS (Box 3). This model has performed well in the ED setting, with 30-day risks of adverse cardiac outcome of 0, 7% and 26% in these risk strata, respectively, when the criteria were strictly applied in one cohort. Risk
stratification models may have greater utility in the ED, where the prevalence of ACS is about 10% (compared with primary care, where rates are lower) and where facilities to further assess patients at increased risk are readily available. The main limitation of this risk stratification model is that few patients qualify as low risk when the criteria are strictly applied. Alternative approaches include the Global Registry of Acute Coronary Events (GRACE) score, which has been shown to identify low-risk patients who do not require further assessment for exclusion of ACS. Consequently, none can be relied on to identify patients who can be safely discharged from the ED without some period of observation and additional investigation. Nevertheless, risk stratification is essential to guide the appropriate use of resources based on pretest probability of ACS.

### Cardiac biomarkers

Cardiac troponin levels have a central role in the diagnosis of acute myocardial infarction. After exclusion of ST-segment elevation and dynamic ST-segment electrocardiographic changes, serial biomarker testing identifies the remaining patients with acute myocardial infarction. Protocols for the use of serial troponin measurements have largely been based on release kinetics in experimental conditions and have tended to require waiting 6–8 hours (or longer) after presentation for the second test. Recent advances in high-sensitivity assays that allow a much shorter interval of 2 hours before the second test and incorporation of serial biomarker levels into overall risk stratification models (Box 4) have demonstrated safe accelerated processes with robust clinical outcome data. These approaches have yet to be incorporated into clinical guidelines, but almost certainly will be in the foreseeable future.

Troponin levels are considered abnormal when they exceed the 99th percentile of a healthy reference population using an assay with sufficient accuracy at this level (<10% coefficient of variation). In practice, few available assays have possessed sufficient accuracy at this level. The recent development of high-sensitivity assays with this level of accuracy and lower levels of detection allows measurable troponin levels to be recorded in most of the healthy population. These assays offer the promise of being able to rule out acute myocardial infarction earlier than was possible with less sensitive assays, as well as further acceleration of risk stratification models, but with the probable cost of diminished specificity. This will require clinicians to have a better understanding of the causes of elevated troponin levels and the kinetics of troponin release at these new lower levels of detection, possibly by incorporating values expressing change or “delta” troponin. The use of delta troponin values has been incorporated into the 2011 addendum to the NHF/CSANZ guidelines, but the evidence for the best approach is still emerging. It is imperative that clinicians have a clear understanding of the characteristics of the local troponin assay used, as reference intervals are not transferable between different troponin assays.

### Investigations for myocardial ischaemia and coronary artery disease

In two groups of patients — those who present with symptoms of ACS and in whom myocardial infarction has been excluded, and those with a stable pattern of chest pain symptoms in whom angina cannot be excluded — additional testing is required to identify those who have prognostically important coronary artery disease or unstable angina. This is an area where well established diagnostic tests exist alongside more recent developments, such as computed tomography coronary angiography (CTCA). The anatomical and pathophysiological bases for these tests are not interchangeable, with some depending on the detection of abnormal coronary blood flow (myocardial perfusion scanning) or myocardial ischaemia (stress electrocardiography and stress echocardiography), while invasive angiography and CTCA demonstrate the anatomical basis of coronary artery disease. Each investigation has different limitations depending on patient factors and the need for contrast media and ionising radiation, and the availability of each may depend on access, cost and local expertise (Box 5).

Non-invasive testing for myocardial ischaemia or coronary artery disease is of most value to patients with interme-
4 A proposed algorithm, incorporating an accelerated diagnostic protocol, for assessment of possible cardiac chest pain after exclusion of ST-segment elevation on initial ECG

![Algorithm Diagram]


Diate pretest probability of an ACS. In patients with very low risk of coronary artery disease who have symptoms of non-ischaemic pain, other causes of chest pain should be actively excluded before investigations for myocardial ischaemia or coronary atheroma are considered. Similarly, it may be futile to embark on non-invasive testing (with an attendant risk of a false negative result) in a patient with typical symptoms and a very high risk of coronary artery disease. In such cases, prompt specialist referral for consideration of an early invasive strategy should be the first step.

Investigations may identify the presence or effects of coronary artery stenosis but, where this cannot be achieved, a broader aim is to further refine risk stratification to identify patients at low risk of an adverse outcome after discharge from the hospital or ED. Exercise stress electrocardiography has become largely obsolete as a means of diagnosing reversible myocardial ischaemia, due to insufficient diagnostic accuracy, but it retains a well established role in identifying patients with chest pain who can safely be discharged from the ED. Exercise stress electrocardiography may be limited by patients’ inability to exercise at an adequate level, non-specific electrocardiographic changes (particularly in the setting of an abnormal resting ECG), and false positive results, but it remains attractive by virtue of its low cost and widespread availability.

The combination of cardiac imaging with exercise or pharmacological stress testing can increase accuracy beyond electrocardiography alone (Box 6). In the United States and Europe, cardiac magnetic resonance imaging has emerged as a safe, non-ionising and more accurate alternative to nuclear perfusion scanning, but it remains predominantly a research tool in Australia.

CTCA is the most rapidly evolving test for assessing patients with chest pain and is the most sensitive non-invasive test for identifying coronary artery disease. Recent studies have shown that this technique allows patients to be safely discharged from the ED. A CTCA-based strategy may also be faster than other strategies, particularly when these rely on hospital admission for myocardial perfusion scanning. However, this finding is of limited value in Australia, where myocardial perfusion scanning has not been the principal investigation for chest pain assessment.

It is important to recognise some limitations of CTCA. Elevated heart rate, coronary calcium and obesity all impair image quality. The use of iodinated contrast media is risky in patients with renal impairment or in those taking metformin. In the widely cited Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment (CT-STAT) trial, only 11% of the patients screened met the study’s inclusion criteria. Early studies suggested that CTCA should not be performed until after a second troponin measurement, as myocardial infarctions caused by moderate, rather than severe, coronary stenoses could potentially be missed. This emphasises that the strength of CTCA lies in excluding coronary atheroma. Furthermore, in the presence of known coronary artery disease, functional testing for ischaemia may be a more appropriate choice of investigation.

Some centres perform CTCA with a total radiation dose of <1 mSv, but in most centres, using general CT scanners
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6 Representative performance characteristics of non-invasive tests to identify myocardial ischaemia or obstructive coronary artery disease in patients with chest pain

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise stress electrocardiography</td>
<td>68%</td>
<td>77%</td>
</tr>
<tr>
<td>Stress echocardiography</td>
<td>83%</td>
<td>77%</td>
</tr>
<tr>
<td>Exercise stress myocardial perfusion scan</td>
<td>85%–90%</td>
<td>70%–75%</td>
</tr>
<tr>
<td>Computed tomography coronary angiography</td>
<td>99%</td>
<td>89%</td>
</tr>
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Conclusion

Chest pain is a common presenting symptom with many diagnostic challenges and pitfalls. Medico-legal imperatives such as the National Emergency Access Target render the situation more complicated still. Both technology and the evidence base guiding the approach to the problem have developed considerably since the NHF/CSANZ first commissioned guidelines in this area in 2000. Clinicians can now benefit from a better understanding of risk stratification and enhanced diagnostic tools that make excluding avoidable short-term adverse events with a high degree of accuracy a realistic proposition. The challenge remains to implement these advances as widely as possible in an environment of constrained resources and increasing demand. This will be best achieved by an approach that integrates the technology and evidence into a comprehensive but straightforward and accessible strategy.

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References