Acute coronary syndrome

The challenge of identifying low-risk patients

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Reliable identification of patients who have presented with symptoms of ACS and are at low risk for serious clinical events is beneficial to both patients and the healthcare system. Methods to achieve this are needed as clinical gestalt alone cannot reliably define those patients with serious clinical event rates below 1% at 30 days.

Key points

- **Acute coronary syndrome (ACS) comprises both acute myocardial infarction and unstable angina.**
- **Clinical gestalt cannot be reliably used to exclude ACS in patients in whom the diagnosis is considered.**
- **General practitioner assessment of the patient with possible ACS comprises early ECG, rapid clinical assessment and referral to a hospital emergency department.**
- **Definitive risk stratification includes serial troponin testing.**

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Acute coronary syndrome (ACS) comprises acute myocardial infarction (AMI) and unstable angina. Patients with ACS present with a wide range of symptoms including chest pain and discomfort, dyspnoea, dizziness, arm pain and neck or jaw pain. These symptoms are also described in many other conditions (e.g. gastro-oesophageal reflux disease) that are associated with less serious outcomes than ACS. In Australia, more than 55,000 patients are admitted to hospital with confirmed ACS each year, and an estimated five times as many are assessed to exclude this diagnosis.[1,2] Risk stratification tools assist in the assessment of patients with possible ACS.

Although GPs play a crucial role in the management of patients with coronary artery disease (CAD), the diagnosis of ACS cannot usually be excluded in the community setting. Following initial GP assessment and management, all patients with acute cardiac symptoms require referral for assessment of serial biomarkers and ECGs, and often objective testing for coronary ischaemia. Reliable identification of patients who have presented with symptoms of ACS and are at low risk for serious clinical events is beneficial to both patients and the healthcare system.

The evaluation and management of patients with possible ACS in general practice are considered in this article, along with the methods used in hospital to reliably identify low-risk patients who are suitable for early discharge and follow up.

Clinical assessment

Chest pain is a frequent complaint for patients presenting to both emergency departments and general practices, with the most common serious underlying cause being ACS.[3] In the general practice setting, the assessment of patients with chest pain should consist of a focused history, examination and an early ECG. The initial aim of the history and examination should be to identify whether the patient is likely to have an emergent cause for their symptoms such as an ACS, as outlined in Box 1.

A 12-lead ECG should be obtained and reviewed by a doctor within 10 minutes of presentation of a patient with chest pain, in order

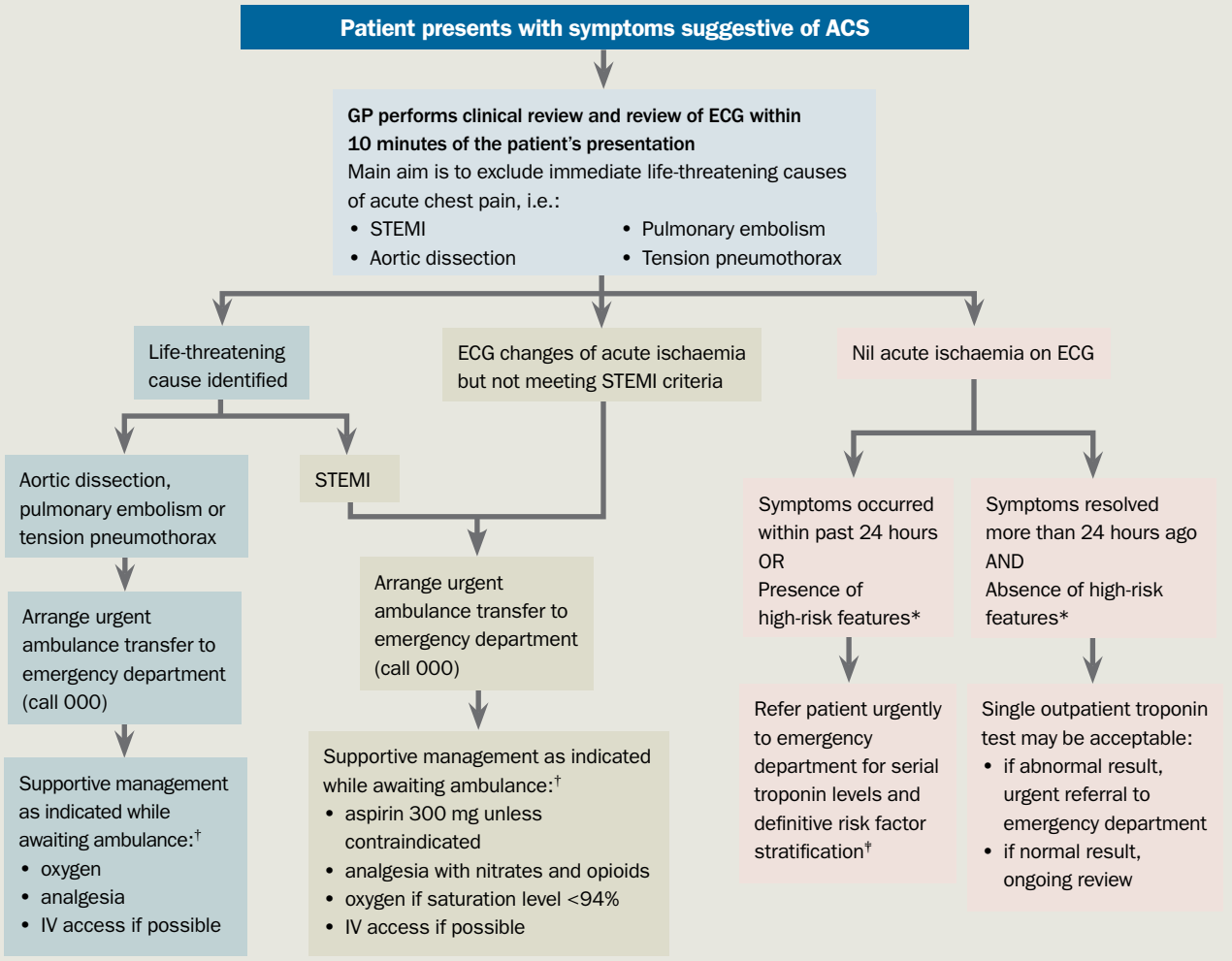
to exclude ST-segment elevation myocardial infarction (STEMI) and assess for other ECG changes suggestive of ACS.[1] It is recommended that all general practices have a system in place to ensure that this rapid clinical review occurs. Training of nonclinical staff through the National Heart Foundation BeAWARE program has been shown to improve recognition by practice reception staff of patients with ACS, and is a useful adjunct to facilitating rapid clinical review.[4] The BeAWARE program comprises an online learning module and in-practice resources to improve awareness of symptoms consistent with ACS and stroke; details can be found at http://www.heartfoundation.org.au/for-professionals/online-learning.

ACS cannot be excluded solely based on patient history and absence of cardiac risk factors.[5,6,7] The wide variety of presenting symptoms contributes to poor clinician reliability in excluding the diagnosis and limits the role of clinician gestalt.[8] Patients with ACS often present with 'atypical' symptoms such as epigastric pain or sharp chest pain with reproducible chest wall tenderness, rather than 'typical' retrosternal chest pain radiating to the left arm or jaw. Subsequently, reliance on typical features results in underdiagnosis of the condition.[9] Several features of pain considered to be atypical (e.g. pain that radiates to the right arm rather than the left arm) are actually associated more often with ACS than are features considered to be typical.[8,10]

1. Life-threatening causes of acute chest pain

- Acute coronary syndrome
  - acute myocardial infarction
  - unstable angina
- Aortic dissection
- Pulmonary embolism
- Tension pneumothorax

Recommended GP management of patients presenting with possible ACS



Abbreviations: ACS = acute coronary syndromes; ECG = electrocardiogram; IV = intravenous; STEMI = ST-segment elevation myocardial infarction.
* High-risk features associated with non-ST-segment elevation ACS are outlined in Box 2 in the article.
† These interventions must not delay transfer to hospital.
‡ Transport as clinically indicated and should be with ambulance if high-risk-features present. In other cases, patients should not drive themselves.

As the diagnosis cannot be reliably excluded clinically, all patients with possible ACS should undergo further investigation irrespective of level of perceived risk.

A summary of the GP evaluation and management pathway for patients with possible ACS is provided in the flowchart. Patients identified as having a STEMI, those at high risk (as outlined in Box 2, taken from the National Heart Foundation of Australia/Cardiac Society of Australia and New Zealand [NHF/CSANZ] 'Guidelines for the management of acute coronary syndromes 2006') and those who appear unwell should undergo emergency transfer to hospital via ambulance. In all other scenarios, patients should be advised not to drive themselves. While awaiting transfer, meaningful interventions should occur, as indicated in the flowchart, provided they do not delay transport to hospital.[11]

Cardiac biomarkers

Cardiac troponin is the biomarker for the identification of myocardial necrosis seen in AMI.[12] Troponin values are used in conjunction with clinical findings and ECG findings to exclude or confirm this diagnosis.[13] Troponin level is a criterion included in most ACS risk stratification tools. It is important to note that a single normal cardiac biomarker result is not sufficient to exclude AMI. The universal definition of AMI requires serial biomarker testing, in order to identify rising or falling levels.[12] Isolated single troponin tests are therefore not recommended in international guidelines.[14,15]

There are different classifications of assays used for the detection of troponin, including point-of-care (POC) assays and sensitive and highly sensitive laboratory-based assays. They differ in their ability to detect very low concentrations of circulating troponin and therefore have different utility in the assessment of patients with possible ACS. The improved sensitivity of assays has enabled serial troponin testing intervals to be reduced when a highly sensitive troponin assay is used.[16] Currently no POC assay available in Australia has the analytical ability to safely reduce serial testing intervals to less than six to 12 hours.[17]

Single troponin testing may be appropriate in patients who have been free of ACS symptoms for longer than 24 hours, have a normal ECG and do not have any of the high-risk features of ACS outlined in Box 2. In these patients, the troponin test may occur in the community, provided it is performed urgently and with a system in place to ensure an abnormal result triggers medical notification and emergency department referral, regardless of the time of day.[18] All other patients should undergo serial troponin and ECG testing, along with ongoing evaluation and observation, which is not practical in the general practice environment. Subsequently, patients with ACS symptoms occurring within 24 hours of presentation and those exhibiting any high-risk features of ACS should be referred to the emergency department for definitive risk stratification.

2. Features associated with high-risk, intermediate-risk and low-risk non-ST-segment-elevation acute coronary syndromes (from the 2006 Australian ACS management guidelines)[11]*

High-risk features

Presentation with clinical features consistent with ACS and any of the following high-risk features:

- Repetitive or prolonged (>10 minutes) ongoing chest pain or discomfort
- Elevated level of at least one cardiac biomarker (troponin or creatine kinase-MB isoenzyme)
- Persistent or dynamic electrocardiographic changes of ST-segment depression ≥0.5 mm or new T-wave inversion ≥2 mm
- Transient ST-segment elevation (≥0.5 mm) in more than two contiguous leads
- Haemodynamic compromise – systolic BP <90 mmHg, cool peripheries, diaphoresis, Killip Class >I, and/or new-onset mitral regurgitation
- Sustained ventricular tachycardia
- Syncope
- Left ventricular systolic dysfunction (LVEF <0.40)
- Prior percutaneous coronary intervention within 6 months or prior coronary artery bypass surgery
- Presence of known diabetes (with typical symptoms of ACS)
- Chronic kidney disease (eGFR <60 mL/min) (with typical symptoms of ACS)

Intermediate-risk features

Presentation with clinical features consistent with ACS and any of the following intermediate risk features AND NOT meeting the criteria for high-risk ACS:

- Chest pain or discomfort within the past 48 hours that occurred at rest, or was repetitive or prolonged (but currently resolved)
- Age >65 years
- Known coronary heart disease – prior MI with LVEF ≥0.40, or known coronary lesion more than 50% stenosed
- No high-risk changes on electrocardiography (see above)
- Two or more of the following risk factors: known hypertension, family history, active smoking, hyperlipidaemia
- Presence of known diabetes (with atypical symptoms of ACS)
- Chronic kidney disease (eGFR <60 mL/min) (with atypical symptoms of ACS)
- Prior aspirin use

Low-risk features

Presentation with clinical features consistent with an acute coronary syndrome *without* intermediate-risk or high-risk features. This includes onset of anginal symptoms within the last month, or worsening in severity or frequency of angina, or lowering of angina threshold

Abbreviations: ACS = acute coronary syndrome; BP = blood pressure; eGFR = estimated glomerular filtration rate; LVEF = left ventricular ejection fraction; MI = myocardial infarction.

* Reproduced with permission from: Aroney CN, Aylward P, Kelly A-M, et al; Acute Coronary Syndrome Guidelines Working Group. Guidelines for the management of acute coronary syndromes 2006. Med J Aust 2006; 184(8): S1-S30.

3. The ADAPT accelerated diagnostic protocol[24]*

All parameters have to be negative for the accelerated diagnostic protocol to be considered negative and for the patient to be identified as low-risk

1. Cardiac troponin-I level at 0 and 2 h below institutional cut-off for an elevated troponin concentration using sensitive or highly sensitive assays
2. No new ischaemic changes on the initial ECG
3. TIMI score = 0. Each of the 7 criteria are worth one point:
   a. Age ≥65 years
   b. Three or more risk factors for coronary artery disease (family history of coronary artery disease, hypertension, hypercholesterolaemia, diabetes or being a current smoker)
   c. Use of aspirin in the past 7 days
   d. Significant coronary stenosis (e.g. previous coronary stenosis ≥50%)
   e. Severe angina (e.g. ≥2 angina events in past 24 h or persisting discomfort)
   f. ST-segment deviation of ≥0.05 mV on first ECG
   g. Increased troponin and/or creatine kinase-MB levels (during assessment)

Abbreviations: ADAPT = 2-hour Accelerated Diagnostic Protocol to Assess Patients with Chest Pain Symptoms Using Contemporary Troponins as the Only Biomarker; ECG = electrocardiogram; TIMI = Thrombolysis in Myocardial Infarction.
* Reprinted from: Than M, Cullen L, Aldous S, et al. 2-Hour accelerated diagnostic protocol to assess patients with chest pain symptoms using contemporary troponins as the only biomarker: the ADAPT trial. J Am Coll Cardiol 2012; 59: 2091-2098, with permission from Elsevier.

Defining low-risk patients

Risk stratification tools are a core part of the assessment of patients with possible non-ST-segment elevation ACS. They are used to determine the pre-test probability of ACS and also guide further care. In Australia, the most widely recognised risk stratification tool is that in the NHF/CSANZ 'Guidelines for the management of acute coronary syndromes 2006', and reproduced in Box 2.[11] Often however, the criteria are not strictly applied and clinicians rely on gestalt.[19] Difficulty lies in identifying patients at low risk in whom reassurance and cessation of further investigations for coronary insufficiency is appropriate. Currently there is no internationally recognised definition of 'low-risk' patients, although emergency physicians have identified an acceptable 30-day miss-rate for adverse cardiac events in patients presenting with chest pain as below 1%; this threshold may be appropriate for GPs as well.[20]

When the NHF/CSANZ guidelines are formally applied in the emergency department setting, patients meeting the low-risk criteria are at low risk of harm; however, few patients (<2%) actually meet these criteria.[21] There are many resources available to guide the management of patients with chronic CAD, including guidelines from the Royal Australian College of General Practitioners (RACGP).[22] However, the RACGP does not have specific guidelines for the acute management of patients with possible ACS, and although the Australian College of Rural and Remote Medicine offers management advice for patients with possible ACS, these currently rely upon risk stratification using the NHF/CSANZ guidelines.[11,23]

Newer methods of risk stratification are predominantly used in the emergency department setting, and most incorporate serial cardiac biomarker results, limiting their ability to be useful in general practice. The Thrombolysis in Myocardial Infarction (TIMI) and the Global Registry of Acute Coronary Events (GRACE) scores are used to determine risk of events in patients hospitalised with suspected ACS. Both have been validated in the emergency setting. The HEART (history, ECG, age, risk factors, troponin level) score has been validated for risk-stratifying patients with chest pain in the emergency department and identifying those likely to have a major adverse coronary event within the next six weeks. As yet, the HEART score has not been validated in the general practice setting.

Accelerated diagnostic protocols (ADPs) allow more rapid evaluation of some patients with suspected ACS than do the recommended guidelines. The 2-hour Accelerated Diagnostic Protocol to Assess Patients with Chest Pain Symptoms Using Contemporary Troponins as the Only Biomarker (ADAPT) trial demonstrated that patients presenting with possible ACS to the emergency department could be defined as low risk for ACS and safe for early discharge if they had a normal initial ECG and normal serial troponin levels at presentation and two hours later, with a TIMI risk score of zero (Box 3).[24] Patients in this large Australian and New Zealand study who were defined as low risk had adverse cardiac event rates at 30 days of below 1%. Of note to rural practitioners, the study did not utilise POC testing.

Objective cardiac testing (e.g. exercise stress testing) continues to be recommended for low-risk patients in international guidelines; however, the utility of this approach is questionable. After exclusion of the diagnosis of ACS, ongoing follow-up with the GP is recommended to identify and manage risk factors for CAD, along with investigation and management of alternative causes of patients' symptoms (e.g. gastro-oesophageal reflux disease) as clinically indicated.

Conclusion

The identification of patients presenting with symptoms suggestive of ACS who are at low risk of having this diagnosis is challenging. Newer methods that safely identify those patients with a less than 1% risk of serious conditions utilise serial troponin testing in a monitored environment, and therefore cannot be implemented in most general practice settings. Although patients who have not had symptoms within 24 hours may be suitable for a single outpatient troponin test, most patients with possible ACS presenting to the GP should undergo rapid clinical assessment and referral to an emergency department for definitive risk stratification, which includes serial troponin testing. **CT**

References

A list of references is included in the website version of this article (www.cardiologytoday.com.au).

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Dr Hamilton: None.

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