



POSITION STATEMENT ON THE EVALUATION OF PATIENTS PRESENTING WITH SUSPECTED ACUTE CORONARY SYNDROMES DURING THE COVID-19 PANDEMIC

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A pandemic of Coronavirus-19 disease was declared by the World Health Organisation on March 11th 2020. The pandemic is expected to place unprecedented demand on health service delivery.

This position statement has been developed by the Cardiac Society of Australia to assist clinicians to continue to deliver rapid and safe evaluation of patients presenting with suspected acute cardiac syndrome at this time.

The position statement complements, and should be read in conjunction with, the National Heart Foundation of Australia & Cardiac Society of Australia and New Zealand: Australian Clinical Guidelines for the Management of Acute Coronary Syndromes 2016: Section 2 'Assessment of Possible Cardiac Chest Pain'. [1]

Introduction

Under normal circumstances acute undifferentiated chest pain accounts for ~5-10% of adult emergency department (ED) presentations. In the context of the COVID-19 pandemic this proportion will fall as the denominator increases due to a substantial increase in presentations with influenza like illness (ILI). Anecdotal evidence from multiple sources suggests that in the context of the pandemic the absolute number of all ED presentations, other than ILI, has fallen. This includes chest pain presentations.

Usually 5-20% of patients presenting with chest pain prove to be due to acute coronary syndrome (ACS). This proportion is unlikely to fall and may increase if lower risk patients are disproportionately discouraged from presenting. Missed ACS has a poor prognosis and will ultimately create a substantial cost to health services and the community. [2]

The usual goals of assessment of suspected ACS in the hospital setting are of particular importance in an environment of increased demand on health service.

- Minimise unnecessary hospital admission
- Minimise ED and hospital length of stay
- Rationalise use of diagnostic investigations
- Rapidly identify patients with ACS or other important medical conditions
- Sustain patient safety

The aim of this document is to provide evidence-based guidance to assist clinicians to meet these goals in the context of the unique demands placed on health services during the COVID-19 pandemic. The scope of this advice is limited to patients presenting acutely with symptoms suggestive of a coronary origin and in whom a diagnosis of ACS is considered.

General principles

The general principles of evaluation of patients presenting with possible ACS remain unchanged

1. Is the diagnosis ST elevation myocardial infarction?
2. What other acutely life-threatening conditions need to be considered (e.g. pulmonary embolus, aortic dissection)?
3. Is the diagnosis non-ST-elevation acute coronary syndrome?
4. Is the diagnosis symptomatic coronary artery disease other than the above?
5. Can a short term (e.g. 30 day) risk of a major adverse cardiac event be excluded with a high degree of certainty?
6. Does the patient understand what to do in the event of recurrent symptoms after discharge from hospital?

Risk stratification

High risk patients

Criteria that identify patients ‘high risk’ of ACS or other important cardiac disease should remain unchanged (Box 1). The further investigation and management of this group may need to be modified according to local access and capacity in the context of the COVID-19 pandemic. This discussion is beyond the scope of this paper but has been addressed in a recent associated position statements. [3] Careful evaluation of patients clinical features should guide the subsequent diagnostic pathway to minimise over-investigation and reduce risks of infection among staff.

In a large proportion of patients stratification as ‘high risk’ is based on a finding of troponin values above the reference range; usually the 99th centile of a healthy reference population. Clinicians should be mindful that elevated troponin levels can indicate acute myocardial infarction (AMI) or myocardial injury due to a broad range of potential aetiologies. The true prevalence of acute myocardial injury in patients with COVID-19 illness is not well established and the role of cardiac biomarkers in the routine assessment of patients with COVID-19 is controversial and beyond the scope of this paper.

Intermediate risk patients

Patients at ‘intermediate risk’ of ACS are those who do not exhibit ‘high risk’ features but in whom the short-term risk of AMI or major adverse cardiac events (usually defined as a composite of cardiovascular death, ACS and unplanned revascularisation) is generally considered higher than acceptable for discharge without further investigation. This group pose a diagnostic challenge and consume significant health resources. The 2016 Australian Clinical Guidelines for the Management of Acute Coronary Syndromes provide the basis for risk stratification and management of patients presenting to emergency departments with symptoms of possible ACS. [1] Ideally, patients should continue to be managed according to these guidelines and receive care guided by the evidence-based Suspected ACS Assessment Protocols described therein.

In anticipation of increased demand on ED and hospital services the integrity of established management pathways for the evaluation of patients with chest pain are likely to be challenged and require adaptation. A number of widely applicable, evidence-based approaches have been described since the 2016 guidelines that can safely and rapidly re-stratify a substantial proportion of ‘intermediate risk’ patients as ‘low risk’ to facilitate earlier discharge from hospital. Broadly these diagnostic strategies fall into two groups:

- Early identification of low risk patients who do not require further testing for ischemia, either by
 - Using a single test of troponin on presentation, or
 - Clinical risk stratification and serial testing of ECG and troponin only
- Identification of low risk patients who can safely be discharged from ED with expedited out-patient review and consideration of further testing

Whilst these criteria can be used on an individual patient basis substantial ‘system wide’ gains are possible using a strategic approach to chest pain assessment. [4]

Earlier identification of low risk patients who do not require further testing for ischaemia: Single troponin testing on presentation

Several individual studies and a number of large meta-analyses have shown that in patients without high-risk features a single test of cardiac troponin using a highly sensitive troponin assay can identify patients at a very low risk of death AMI, or other major adverse cardiac events, at 30 days with very high sensitivity and negative predictive value (Table 1). [5-8] A number of caveats are required in the interpretation and implementation of these studies:

- To date studies reporting an excellent outcome based on a single very low level of troponin using a high sensitivity assay have been retrospective analyses of studies where in practice patients have followed serial troponin pathways and in many cases have been admitted to hospital for observation. Initial prospective data do, however, suggest that discharge based on a single troponin is both effective and safe. [Personal communication Prof N Mills, Edinburgh]
- All of these studies utilise decision thresholds close to the limits of analytical precision which differ between troponin assays. Consequently it is imperative that clinicians are familiar with the troponin assay in use at their institution and that only data derived with that specific assay is used to formulate a diagnostic strategy. Fortunately, this approach has been tested for the majority of assays commonly in use in Australia and New Zealand.
- Most studies have shown a modest reduction in the sensitivity for rule-out of end points in patients presenting early after the onset of symptoms. In cases where patients have presented early, a second test should be performed two hours after the onset of symptoms.
- It is important to recognise that these diagnostic strategies have been designed to aid risk stratification for short term (30 day) adverse cardiac outcomes and *not* to definitively exclude a diagnosis of coronary artery disease (*see general considerations below*)

Earlier identification of low risk patients who do not require further testing for ischaemia: Clinical risk stratification

A proportion of patients presenting to ED with chest pain are at a very low risk of coronary artery disease and once AMI and other possible serious differential diagnoses have been excluded may be suitable for early discharge from hospital without further investigation for coronary artery disease. In a large (n=1366) Australian, single centre, prospective intervention study no further investigation was performed in patients meeting the criteria defined in Box 2. Two hundred and forty-four (18%) of the cohort met these criteria and there were no diagnoses of acute coronary syndrome at 30 days of follow up. [9]

Intermediate risk patients not meeting above criteria for re-stratification to low risk

Intermediate risk patients who cannot be re-stratified as low risk by the criteria above should continue to be managed according to the existing 2016 Australian Clinical Guidelines for the Management of Acute Coronary Syndromes.

Given the challenges that may be encountered in access to further testing for ischaemia or coronary artery disease either during the initial admission or early following discharge a conservative approach to exclusion of AMI is justified. If a highly sensitive troponin assay is utilised then serial testing of troponin at 0 and 3 hours can be used to exclude AMI with a high degree of sensitivity to allow discharge from hospital. [1]

Subsequent clinical follow-up and judicious use of further investigation for ischaemia or coronary artery disease within 30 days should be organised according to local availability and capacity. Decisions regarding the need for further testing should be reviewed by the most senior clinician available. This may take the form of early chest pain ‘hot clinics’ utilising telehealth follow-up or closer collaboration with primary care, or private providers, in order to facilitate further investigation in an ambulatory setting.

General considerations

Ideally, all centres will continue to utilise already established, guideline-based strategies of chest pain assessment in the context of the COVID-19 pandemic. However, it is apparent in contingency planning that modification of existing processes may be required to accommodate unprecedented demand on health services. The modifications to chest pain assessment described in this paper are evidence based but have not to date been widely used in Australia and New Zealand. The safety of these approaches can be underpinned through a number of additional measures, including

- Patients identified as being at low risk and discharged directly from ED should be fully informed of, and understand, the steps to be taken in case of recurrent symptoms
- The level of risk of an individual patient, and requirement for additional investigation should be clearly communicated to the patient and their general practitioner. The fact that risk stratification for ACS *does not exclude* a diagnosis of underlying coronary artery disease should be made clear.
- In patients where decisions regarding further investigation are deferred until after discharge, consideration may be given to establishing a process of early telehealth/telephone follow up within 30 days with emphasis on screening for recurrent symptoms.

Conclusions

This paper describes adaptations to existing guidelines for the evaluation of patients presenting acutely to hospital with symptoms of chest pain or other symptoms of possible ACS. Figure 1 shows the basic framework of an integrated pathway of chest pain assessment, incorporating the suggested amendments, that could be adapted for local use.

The evidence supporting these adaptations to existing guidelines indicates that in patients discharged from hospital the sensitivity to exclude AMI during admission is >98% with a negative predictive >99% with similar parameters for the risk of ACS at 30 days of follow up.

References

1. Chew DP, Scott IA, Cullen L, et al. National Heart Foundation of Australia & Cardiac Society of Australia and New Zealand: Australian Clinical Guidelines for the Management of Acute Coronary Syndromes 2016. *Heart Lung Circ.* 2016;25(9):895-951.
2. Pope JH, Aufderheide TP, Ruthazer R, et al. Missed diagnoses of acute cardiac ischemia in the emergency department. *N Engl J Med.* 2000;342(16):1163-70.
3. Cardiac Society Of Australia and New Zealand. Consensus Guidelines for Interventional Cardiology Services Delivery During COVID-19 Pandemic in Australia and New Zealand. Sydney: 2020 [Available from: https://www.csanz.edu.au/wp-content/uploads/2020/03/CSANZ_CONSENSUS_GUIDELINES_FOR_INVASIVE_CARDIOLOGY_SERVICES_DELIVERY_DURING_COVID_PANDEMIC_29-March_2020.pdf. Accessed on April 6th 2020]
4. Parsonage WA, Milburn T, Ashover S, et al. Implementing change: evaluating the Accelerated Chest pain Risk Evaluation (ACRE) project. *Med J Aust.* 2017;207(5):201-5.
5. Greenslade J, Cho E, Van Hise C, et al. Evaluating Rapid Rule-out of Acute Myocardial Infarction Using a High-Sensitivity Cardiac Troponin I Assay at Presentation. *Clin Chem.* 2018;64(5):820-9.
6. Pickering JW, Than MP, Cullen L, et al. Rapid Rule-out of Acute Myocardial Infarction With a Single High-Sensitivity Cardiac Troponin T Measurement Below the Limit of Detection: A Collaborative Meta-analysis. *Ann Intern Med.* 2017;166(10):715-24.
7. Chapman AR, Lee KK, McAllister DA, et al. Association of High-Sensitivity Cardiac Troponin I Concentration With Cardiac Outcomes in Patients With Suspected Acute Coronary Syndrome. *JAMA.* 2017;318(19):1913-24.
8. Sandoval Y, Nowak R, deFilippi CR, et al. Myocardial Infarction Risk Stratification With a Single Measurement of High-Sensitivity Troponin I. *J Am Coll Cardiol.* 2019;74(3):271-82.
9. Cullen L, Greenslade JH, Hawkins T, et al. Improved Assessment of Chest pain Trial (IMPACT): assessing patients with possible acute coronary syndromes. *Med J Aust.* 2017;207(5):195-200.

Box 1: High risk criteria for a cardiac cause of chest pain (including ACS and other cardiac diagnoses)

- Ongoing or repetitive chest pain despite initial ED treatment
- Elevated level of cardiac troponin
- Persistent or dynamic ST-segment depression ≥ 0.5 mm, or new T-wave inversion ≥ 2 mm in more than two contiguous ECG leads
- Transient ST-segment elevation (≥ 0.5 mm) in more than two contiguous leads
- Haemodynamic compromise: systolic blood pressure < 90 mmHg, cool peripheries, diaphoresis, Killip class > 1 , and/or new onset mitral regurgitation
- Sustained ventricular tachycardia
- Syncope
- Left ventricular systolic dysfunction (LVEF fraction $< 40\%$)
- Prior AMI, percutaneous coronary intervention or CABG surgery within 6 months

Box 2: Characteristics of low risk patients not requiring further investigation and suitable for early discharge

- No high risk features (see Box 1)
- Age < 40 (< 18 for first nation people)
- No history of diabetes
- No evidence of chronic kidney disease (eGFR ≥ 60 ml/min/1.73m²)
- Cardiac troponin below 99th centile reference limit at 0 and 2 hours

Table 1 Studies evaluating cardiac outcomes in patients with suspected acute coronary syndromes using a single high sensitivity troponin concentration on admission

Troponin Assay	n	Cut off	Other criteria	Primary outcome	Prevalence of primary outcome	Sensitivity	NPV	Secondary outcome	Sensitivity	NPV	Ref
Abbott ARCHITECT hs-cTnI	22457	<5ng/l	No myocardial ischaemia on ECG	30 day Type 1 AMI or cardiac death	12.4%	99.0% (97.3-99.6)	99.7% (99.4-99.8)	Type 1 or Type 2 AMI during admission†	NR	99.4% (00.2-00.6)	7
Roche Diagnostics hs-cTnT	9241	<5ng/l	No new ischaemic ECG change	AMI during admission	15.4%	98.7% (96.6-99.5)	99.3% (97.3-99.8)	30 day MACE*	98.0% (94.7-99.3)	99.0% (96.4-99.7)	6
Beckman Coulter Access hs-cTnI	1871	<2ng/l	No ST elevation on ECG	Type 1 AMI during admission	5.2%	99.0% (94.4-100)	99.8% (99.1-100)	30 day MACE	97.5% (92.7-99.5)	99.5% (98.6-99.9)	5
Siemens Atellica IM hs-cTnI	2212	<3ng/l	No ST elevation on ECG	AMI during admission	12.0%	98.8% (97.5-100)	99.6% (99.1-100)	30 day AMI or death	98.6% (97.2-100)	99.5% (98.9-100)	8
Siemens ADVIA Centaur hs-cTnI	2212	<3ng/l	No ST elevation on ECG	AMI during admission	12.0%	99.2% (98.2-100)	99.7% (99.3-100)	30 day AMI or death	98.9% (97.7-100)	99.6% (99.1-100)	8

* Only includes n=8059 participants in 8 of the 11 studies included for the primary outcome

† Only includes n=16357 participants included in the primary analysis

NR Not reported

