Utility of Routine Exercise Stress Testing among Intermediate Risk Chest Pain Patients Attending an Emergency Department

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Background	To assess the utility of routine exercise stress testing (EST) in patients at intermediate risk of acute coronary syndrome (ACS) according to the Heart Foundation of Australia/Cardiac Society of Australia and New Zealand (HFA/CSANZ) guidelines.
Method	Prospective observational study of patients presenting to the Emergency Department (ED) with chest pain suggestive of ACS between November 2008 and July 2014. Participants included 1205 patients who presented to the ED with chest pain suggestive of ACS and who met the HFA/CSANZ intermediate risk criteria. The outcome was diagnosis of ACS occurring on presentation or within 30 days of presentation to the ED. ACS included acute myocardial infarction and unstable angina pectoris.
Results	Twenty (1.66%) of the intermediate risk patients were diagnosed with ACS. Of the 777 patients who underwent EST, eight had ACS. EST identified all ACS cases except for one patient with a negative test, who was ultimately diagnosed with ACS following angiography. 164 patients deemed inappropriate to undergo EST underwent an alternative form of objective testing, of which 12 were positive for ACS. 264 patients underwent no objective testing.
Conclusion	EST stratifies intermediate risk patients to a near zero short-term risk of ACS. However, the overall yield of EST within this group of patients is extremely low. Intermediate risk patients with normal zero and six hour biomarkers have a very low probability of ACS, and over half of these patients ultimately diagnosed with ACS in this group were deemed unsuitable for EST anyway. Future research should focus on the identification of patients who do not require EST and the inclusion of routine EST within the HFA/CSANZ guidelines should be reconsidered.
Keywords	Exercise stress test • Acute coronary syndrome • Objective testing

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Background

Up to 10% of all adult patients presenting to the Emergency Department (ED) require assessment for acute coronary syndrome (ACS) [1]. In the absence of a test that is both sensitive and specific for ACS, ED physicians utilise a range of clinical information to assess the risk of ACS in this substantial cohort. Recommendations of the National Heart Foundation and Cardiac Society of Australia and New Zealand (HFA/CSANZ) from 2006 [2] require physicians to risk stratify patients using detailed assessment incorporating electrocardiography (ECG), historical features, risk factors and serial troponin testing over 6-12 hours with sensitive assays. This process stratifies less than 5% of patients as low risk, approximately 65% as intermediate risk and one third as high risk [3].

The HFA/CSANZ guidelines then recommend that intermediate risk patients undergo provocative testing for myocardial ischaemia as an inpatient, or at the earliest opportunity optimally within 72 hours, to rule out unstable angina pectoris (UAP) [2]. Exercise stress testing is the most commonly used modality of provocative testing for a patient with a normal ECG who is not taking digoxin and who is without physical limitations [4]. Numerous studies from the United States have found that a negative exercise stress test (EST) is accurate, safe and cost-effective in excluding ACS in low risk patients [5–7]. However, such studies also report low positive predictive values [7] and high rates of indeterminate tests (around 25%) [3,8]. Therefore, the lengthy assessment process may yield equivocal results or place the patient at unnecessary risk, by necessitating further invasive investigations such as coronary angiography. A number of studies also have found that EST adds limited diagnostic information beyond clinical data and biomarkers [5], particularly for younger individuals [9].

There is currently an absence of Australian data on the diagnostic accuracy of provocative testing in ED patients, who require objective testing for coronary artery disease (CAD) within the HFA/CSANZ guidelines. Such data will help to clarify the relevance of provocative testing within this HFA/CSANZ intermediate risk group. This study will quantify the number of individuals with positive or indeterminate exercise stress tests who were subsequently diagnosed with ACS. The study also will report the number of patients who were unable to perform an EST and the reasons for such inability.

Methods

Study Design

This study is an analysis of data from two studies on ED patients with potential ACS. The first study was a prospective observational study including adult patients presenting to the ED of a tertiary hospital with an annual census of approximately 70,000 ED patients. The second was an interventional study using the same criteria for enrolment. The study protocols were approved by the institution's Human Research and Ethics Committee.

Participants

Patients were recruited for both studies during working hours (0800 to 1700) and included if they were aged $\geq$18 years, presented to the ED with at least five minutes of chest pain suggestive of ACS and were being investigated for ACS. In accordance with American Heart Association case definitions [10], pain suggestive of ACS includes acute chest, epigastric, neck, jaw, or arm pain; or discomfort or pressure without an apparent non-cardiac source. Research staff recruited all patients in collaboration with the senior treating clinician. All participants provided informed consent allowing their data to be used in cardiac research. The local Human Research Ethics Committee provided a waiver of consent for this analysis in accordance with National Health and Medical Research Council guidelines.

Patients were excluded for the following reasons: there was a clear non-ACS cause for their symptoms; they were unwilling or unable to provide informed consent (e.g. language barrier); staff considered that recruitment was inappropriate (e.g. terminal illness); they were transferred from another hospital; were pregnant; were recruited to the study within the previous 45 days; or were unable or unwilling to be contacted after discharge. Consecutive eligible cases at each site were included. Recruitment for the observational study occurred between November 2008 and January 2011. Recruitment for the interventional study occurred between February 2011 and July 2013. All patients in the observational study were managed according to standard care, which included ECG and troponin testing on presentation and $\geq$ 6 hours after presentation to the ED. Patients in the interventional study underwent an accelerated assessment process where zero and two hour biomarkers were utilised rather than zero and six hour biomarkers. In this cohort, stress testing occurred in those patients who were over 40 years of age and those less than 40 with diabetes and/or an estimated glomerular filtration rate (eGFR) less than 60 mL/min.

Index Test

All ESTs were either conducted by a cardiac scientist in conjunction with a supervising medical officer or were performed as non-physician led EST, which were reported by a medical officer. A standard Bruce protocol was employed where patients completed an incremental protocol unless peak effort, volitional fatigue or clinical signs or symptoms necessitated premature test termination [4]. A positive test was defined as ST segment elevation $\geq$1 mm in leads without diagnostic Q waves (other than V1 or aVR); >2 mm of horizontal or down sloping ST segment depression or marked axis shift; >10 mmHg decrease in systolic blood pressure from baseline; sustained ventricular arrhythmias; or, significant symptoms [4]. An equivocal test was defined where abnormalities occurred that did not reach these diagnostic thresholds.