Research, Audit and Clinical Practice

Exercise Stress Test Utility in Patients with Chest Pain Presumed to be of Cardiac Origin

P Bennett & P Dyer

Abstract

Introduction: *NICE stated exercise stress tests (EST) should not be used to diagnose obstructive coronary artery disease in patients presenting with chest pain presumed to be of cardiac origin.*

Methods: *A retrospective review of 209 patients with presumed cardiac chest pain was done. EST results, GRACE scores and need for invasive coronary angiogram (ICA) were analysed to predict the need for readmission, intervention and future events.*

Results: *The sensitivity of the EST in identifying obstructive coronary artery disease was 70%. The EST, ICA and the GRACE 6-month mortality had a 77%, 70% and 81% negative predictive value (NPV) for readmission respectively.*

Conclusion: *EST, GRACE scores and ICA are useful in providing prognostic information but are poor predictors of readmission. Follow up and education programmes are needed to reduce this burden.*

Keywords

Exercise stress tests, predictive value, chest pain, acute coronary syndrome.

Key Points

- Exercise stress testing, GRACE score and coronary angiography are good prognostic indicators but all are poor predictors of the likelihood of readmission to hospital with chest pain.
- Readmission with chest pain is a common occurrence irrespective of the discharge diagnosis and investigation pathway; active follow up and education of patients who present acutely with chest pain is needed to reduce this increasing burden.

Introduction

In March 2010, the National Institute for Health and Clinical Excellence (NICE) issued guidance on the assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin.[1] It emphasised calculating the likelihood of coronary artery disease (CAD), based on initial clinical assessment and 12-lead electrocardiogram (ECG) findings, before considering diagnostic investigations.

The guidance also stated that exercise electrocardiography (ECG) or exercise stress test (EST) had no role in diagnosing obstructive coronary disease.This advice represents a significant departure from the traditional assessment of patients who present with chest pain presumed to be of cardiac origin where the EST has, for many years, been the predominant test to assess cardiovascular risk as opposed to diagnosing coronary artery disease. NICE believes that EST poses particular problems of poor sensitivity (high false negatives) and/or difficulties in interpretation in women and patients with conduction disease (such as left bundle branch block) and diabetes.[2] NICE also argued that although the EST can be used to diagnose CAD, other imaging techniques can do the same but more cost effectively. In contrast, a 2012 American guideline for the diagnosis and management of patients with stable ischemic heart disease (SIHD) recommends the standard exercise ECG for risk assessment in patients with SIHD who are able to exercise to an adequate workload and have an interpretable ECG[3] (Figure 1). This approach is supported by a 1989 meta-analysis of 147 published studies.[4]

The purpose of stress testing in the context of the acute evaluation of patients who present to hospital with chest pain is not to definitively rule coronary artery disease in or out. Rather, it is a short-term prognostic tool to aid in the safe disposition of patients. Studies have shown excellent short-term (1-6 month) cardiovascular prognosis for patients discharged from the ED or observation unit after a negative exercise test result.[5] EST has an excellent negative predictive value of around 97%.[6]

Chest pain is a very common symptom, affecting 20-40% of the general population during their lives. In England and Wales, chest pain accounts for up to 1% of visits to GPs, approximately 700,000 visits (5%) to emergency departments and up to 25% of emergency admissions to hospital.[1] Thus, the first presentation of patients with coronary artery disease could be acutely, as an emergency.Obstructive CAD is the cause of the chest pain in a significant proportion of patients.[7]

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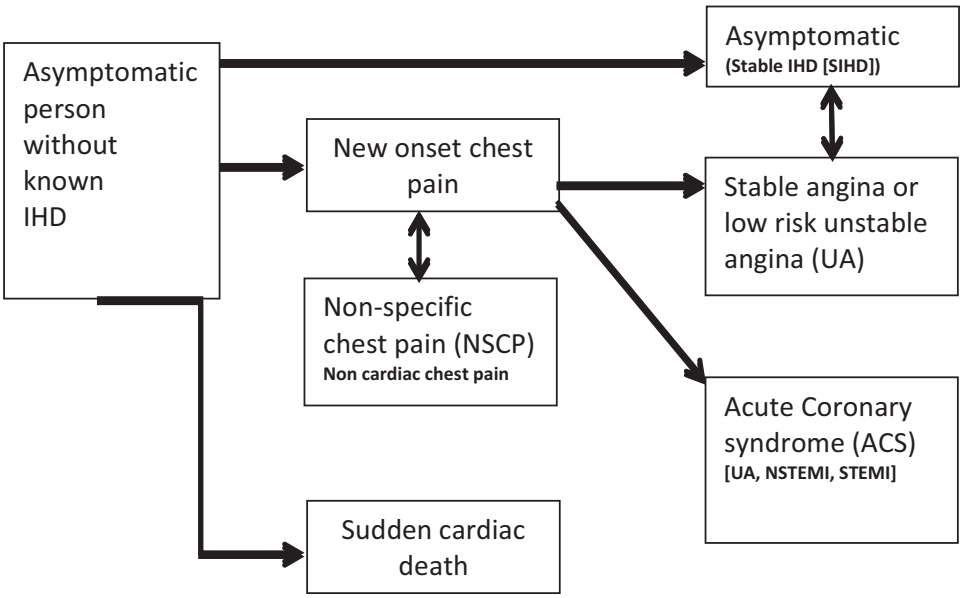

Figure 1. Spectrum of IHD.
Adapted from 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guidelinefor the Diagnosis and Management of Patients withStable Ischemic Heart Disease (SIHD).

We wanted to assess the use of the EST in predicting future cardiac events, the need for intervention and readmission. We also assessed GRACE (Global Registry of Acute Coronary Evaluation) score and invasive coronary angiogram (ICA) in order to compare their ability to predict these outcomes.

Setting and Background

Heartlands Hospital is part of Heart of England NHS Foundation trust which is a teaching hospital in Birmingham, West Midlands, UK. We use risk assessment strategy for patients who present with chest pain presumed to be cardiac in origin. Briefly this includes history and initial risk stratification with ECG and TIMI score. Those presumed to have cardiac sounding chest pain have serial ECGs and troponin T (TnT) measurements. Those patients who have dynamic ECG changes or significant TnT rise and are deemed suitable for invasive assessment of coronary artery disease had an invasive coronary angiogram (ICA). Those with normal ECG and TnTs were further risk stratified using the GRACE score. Those found to be high risk by the GRACE score proceed to inpatient investigation, usually an EST, while those found to be low risk have an outpatient EST. The EST is only performed if the patient is physically able to do the test.

Methods

We performed a retrospective review of 209 patients who presented with chest pain presumed to be cardiac in origin, without elevated TnT and who went on to have an EST. Patients with a clinical diagnosis of musculoskeletal or non-cardiac chest pain chest pain were excluded.

The GRACE score was calculated in all patients. Results of EST, ICA and details of any readmissions were obtained. We aimed to assess whether the EST or the GRACE score predicted the likelihood of coronary artery disease on angiogram, future events, interventions and readmissions.

Results

209 patients were included in the retrospective review during the study period between November 2008 and September 2011. Of these patients 198 did not have a significant rise in their TnT. Eleven had 'unknown' TnT results. Seventy-four (35.4%) were female and 135 were male (64.5%). The mean age was 57 years (mean age of females was 54 years and males 57 years). The major discharge diagnosis for the patients whose TnT levels were not elevated was "chest pain TnT negative" or "chest pain TnT not elevated", none had the diagnosis of musculoskeletal or non-cardiac chest pain as they were excluded in our search criteria.

Exercise tolerance test results

The exercise tolerance test was attempted in all 209 patients. In 196 patients the result was available for interpretation. In 13 patients the test was not completed or was inconclusive. The majority of exercise tolerance tests were assessed as being negative (69.9%); 17.2% were reported as being positive (Table 1).

Readmissions with chest pain

Forty nine patients (23.4%)were readmitted with chest pain within 12 months of which 12 (5.7%) were admitted within 30 days. Eight were diagnosed as having non-cardiac chest pain and were discharged from the emergency department. Twenty nine patients were diagnosed as having angina, two patients had a significant rise in TnT, 1 of which found to have a pulmonary embolus. Six

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(12.3%) further patients had an angiogram of which 3 patients had stent insertions. Four patients had an EST of which 1 was positive (Table 2).

Initial EST in those patients readmitted

Of the 49 patients readmitted with a further episode of chest pain, 34 had a negative initial EST result (69.4%), 8 had had a positive initial EST result (16.3%), 4 had an equivocal EST result (8%) and in three (6%) no result was obtainable.

Six month mortality calculated by the GRACE Score

Two hundred and nine patients had their GRACE score calculated. One hundred and forty six (69.9%) were calculated as being 'low-risk' (GRACE score<3% mortality at 6 months) and 63 (30.1%) were 'intermediate' or 'high-risk' (GRACE score>3% mortality at 6 months) (Table 3). Those patients who had a normal angiogram (compared to those with an abnormal angiogram) had a higher 6-month calculated mortality by the GRACE score but this did not reach statistical significance (Table 4).

Invasive Angiogram Results

Thirty eight patients had an initial angiogram, 16 (42%) of which were normal and 18 (47%) were abnormal. Of the 38 patients who had an angiogram 16 (42%) of these patients were readmitted. Of those with normal angiograms 7 were readmitted (44%) and of those who had an abnormal angiogram 7(39%) of those patients were readmitted. Ten patients (26%) of those who had an angiogram had stent insertions of which 5 patients were readmitted (50%). In four patients the results of the angiogram were not available.

Sensitivity, Specificity, Negative Predictive and Positive Predictive Values

The EST had a 77% negative predictive value for readmission within 12 months and 67% for an abnormal angiogram. An angiogram had a 70% negative predictive value and 28% positive predictive value for readmission. The calculated GRACE 6-month mortality score had an 81% negative predictive value for readmission within 12 months (Table 5). The EST did, however, have a 97% negative predictive value for readmission within 30 days.

Discussion

Patients who present acutely to hospital with cardiac sounding chest pain may or may not have coronary artery disease. The initial assessment is to identify those patients with acute coronary syndrome (ACS) i.e. unstable angina or acute myocardial infarction. The term non-specific chest pain (NSCP) is often applied to hospitalised patients that neither have an ACS nor display evidence of coronary ischaemia. NSCP represents a heterogeneous group of patients; indeed nearly 40% of such patients have co-existing CAD meaning prognosis is not necessarily benign.[7] A systematic literature review by Ruddox *et al* has shown the mean one-year total mortality rate among patients with NSCP was 3.2% (inter-study range 1.4% to 8.1%). The mean one-year mortality rate among 'ACS/high-risk' patients was 18.0% (inter-study range 14.0% to 19.9%). The mean one-year readmission rate for patients with NSCP was 17.5% (inter-study range 2.5% to 40%).[7]

The results of our study confirmed previous findings that the sensitivity of the EST in identifying obstructive coronary artery disease was around 70%. The EST is, however, a good prognostic indicator.

Table 1. Exercise Tolerance Test Result.

Negative	146 (69.9%)
Positive	36 (17.2%)
Equivocal	14 (6.7%)
Inconclusive/Failed	11 (5.3%)
Unknown	2 (0.96%)
Total	**209**

Table 2. Readmissions with Chest Pain.

Readmission final diagnosis	Number
Angina	29
NSTEMI	1
Pulmonary Embolus	1
Non-cardiac Chest Pain	8
Self-Discharged	1
Unknown	9
Total	**49**

Table 3. Six Month Mortality Calculated by the GRACE Score.

GRACE score 6-month mortality (%)	Number of patients	Percentage	Number Readmitted	% of those patients
0.4	9	4.3	2	22
0.6	9	4.3	3	33
0.8	18	8.6	1	6
1	87	41.6	16	18
2	22	10.5	5	23
3	18	8.6	3	17
4	14	6.7	2	14
5	7	3.3	4	57
6	7	3.3	4	57
7	4	1.9	2	50
8	2	0.95	1	50
9	2	0.95	2	100
10	2	0.95	0	0
11	2	0.95	1	50
12	2	0.95	2	100
15	1	0.48	1	100
Total	**206**	**98.33**	**49**	**24**

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Table 4. Calculated GRACE Score 6-Month Mortality (%) of Initial Angiogram Results.

	Mean GRACE Score 6-Month Calculated Mortality (%)	Median GRACE Score 6-Month Calculated Mortality (%)
Normal Angiogram (n=17)	2.9	3.0
Abnormal Angiogram (n=16)	1.8	1.0

T-Test: Two-Sample Assuming Equal Variances p= 0.06.

Only 1 patient (2%) who had a negative EST of the 49 readmitted with chest pain actually had a NSTEMI. Readmission with chest pain is a common occurrence; our dataset showed that it occurred in almost one quarter of patients. We also showed that the EST had poor sensitivity for identifying patients who are likely to be readmitted with chest pain. A negative EST,however, was, a good predictor of the reduced likelihood of readmission within the next 30 days (NPV 97%) i.e. a good short term prognostic indicator. Comparative trust wide data shows the readmission rate for patients who present with chest pain to be between 10-12%. The invasive angiogram and the 6-month mortality as calculated by the GRACE score did not fare any better in identifying those patients who are likely to be readmitted with chest pain. Therefore none of the current tests or assessments are good predictors of readmission in the medium to longerterm.

Readmission with chest pain is not a hard end point and thus should not be considered when assessing cardiovascular outcomes. However, it must be considered when evaluating the cost of care. Readmission with chest pain has been shown to be a common occurrence even after percutaneous coronary intervention (PCI). DeFilippi *et al*[8] found that 30% of patients who had an EST returned to the ED with chest pain of which 16% were readmitted compared to only 10% and 3% respectively for those who had an invasive coronary angiogram.However, Mallidi *et al*[9] showed that an inpatient EST was associated with reduced ED attendance. Within 1 year, 314 (10.7%) patients returned to the ED with chest pain, and 148 (47%) of these were readmitted. Patients who had a stress test at index admission were less likely than those who did not have a stress test to return to the ED (9.2% vs. 14.4%; p<0.001).

Table 5. Sensitivity, Specificity, Negative Predictive and Positive Predictive Values.

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
EST and Abnormal angiogram	78	67	67	67
EST and 30 Day Readmission	38	88	13	97
EST and 12 Month Readmission	19	80	22	77
Angiogram and Readmission	50	47	28	70
Calculated GRACE 6-Month Mortality Percentage and Readmission	44	75	36	81

Readmission in patients following PCI is also a common occurrence. Schwart *et al* performed a retrospective analysis of the 30-day outcomes of the first 150 patients undergoing PCI in their centre.[10] Within 30 days of discharge, 14.7% (22) of patients sought medical help. In the majority, this was due to chest pain. Of the patients who presented with chest pain (n=14) only 1 patient had a STEMI: the most common diagnosis was atypical chest pain (n=9). The aetiology of the atypical chest pain is unclear. A form of post-PCI syndrome has been previously described.[11] This can range from pain presumed to result from vessel stretch and traumatic wall injury to a true, perhaps autoimmune mediated post-cardiac injury syndrome.[11] Although post-PCI pain is not associated with adverse early outcomes,[12] there is some suggestion that those patients experiencing post-PCI pain are a cohort at higher risk of restenosis.[12]

Analysis of Hospital Episode Statistics (HES) database show that total readmissions to hospital within 30 days is costing the NHS £1.6 billion.[12] It also reveals a wide variation between hospitals with readmissions accounting for up to 15.0% of average turnover in some hospitals to less than 1.0% in others. The average figure per Trust is just over £11 million. Nearly 50% of readmitted patients return to hospital within 7 days of their initial discharge (including 15% of readmissions within 1 day of discharge), potentially costing acute trusts £300 million in lost annual income or 1.5% of PbR tariff.[13] Non-cardiac chest pain is the 4th most common reason for readmission, accounting for 4% of all readmissions.[14] Department of Health data show the 30-day readmission rate for chest pain was between 8-12.5%.[14] Mechanisms to reduce chest pain readmission are important to decrease the cost of this common condition. Readmission with chest pain should therefore be considered when evaluating the cost of the service.

The management of patients with NSCP to prevent further readmission has not been the primary goal of acute care. The primary aim of acute assessment when patients present with cardiac chest pain is to diagnose or excludeACS, with little emphasis on the follow up those in whom ACS has been excluded. Spalding *et al* followed up for one year 108 patients with atypical chest pain(after excluding 142 patients with cardiac pain). Forty of these patients did not have a discharge diagnosis. Of the remaining 68 patients the pain was thought to be musculoskeletal in 25, cardiac in 21, gastrointestinal in 12 and respiratory in 10. At follow up data were available for 103 (96%) patients. Persisting symptoms were recorded by 61% of patients and the

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mortality rate was 2.9% (3 patients) compared with 18.3% in those with the cardiac pain diagnosis. Half of the patients with atypical pain had undergone further investigations and 14% had been readmitted. The yield of investigative procedures was generally low (20%), gastroscopy providing the greatest yield;at the end of the year 27 patients remained undiagnosed.[15]

Kisely *et al* followed up 113 patients admitted with chest pain for three years. Fifty five represented their first admission and the remaining 47 had been admitted previously. Eighty patients had ischaemic heart disease, 17 had non-specific pain and 13 were excluded because of other organic causes for their pain. There was no difference in psychiatric morbidity. Patients with recurrent admissions for non-specific chest pain were younger, predominantly male and they also had a history of greater alcohol and cigarette use than patients with ischaemic heart disease. Patients with non-specific pain who did not have an organic cause showed similar rates of re-admission to those with ischaemic heart disease before and after the study.[16] Like this study other studies among inpatients have shown a strong association with heavy alcohol and cigarette use. This may be an important contributing factor, possibly through changes in oesophageal motility.[17,18, 19]

Non-specific chest pain (NSCP) or atypical chest pain is a common diagnosis in the acute medical setting. Exclusion of coronary artery disease is only the first step in management, and many patients in spite of the absence of an organic cause for their symptoms, show continued morbidity which might respond to identification and treatment. Follow up clinics for such patients should be introduced with the aim of finding a diagnosis but also to provide reassurance to the patient that the associated mortality is low which may impact of the number of readmissions.

Readmission rates among advanced angina sufferers have been shown to be reduced by applying patient-centred principles. This involves patient empowerment i.e. providing patients with the knowledge and understanding of what they want and need and encouraging shared decision-making. Education is critical if patients (and carers) are to share in decisions. Enrolment of patients into an education programme has been shown to reduce readmission rates.[20] The key to the programme is the demystification of angina and teaching patients how to manage the condition better.

Conflict of Interest

This study was funded entirely by the authors and they have no conflict of interest with any third party.

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