

Exercise treadmill tests in patients with low cardiovascular risk: are we wasting our time?

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ABSTRACT

INTRODUCTION: The efficacy and cost-effectiveness of exercise treadmill testing for patients with low cardiovascular risk is unclear. This is due to the low incidence of coronary artery disease in this population and the potential for false-positive results leading to additional invasive and expensive investigation.

AIM: To investigate the value of exercise treadmill testing (ETT) as a predictor of coronary artery disease in patients with different levels of cardiovascular risk.

METHODS: An observational study was completed on an outpatient population from a chest pain clinic ($n = 529$). Cross-tabulations and binary logistic regressions were used to examine relationships between variables.

RESULTS: A negative ETT result was recorded for 72.5% of patients with low cardiovascular risk compared to 54.3% of those with moderate or high risk. Within the low cardiovascular risk group, patients with symptoms atypical for cardiac ischaemia were 11.1-fold more likely to have a negative ETT result. Of the patients with positive or equivocal ETT results, coronary artery disease was subsequently confirmed in only 23.1% of the low cardiovascular risk group compared to 77.2% of those with moderate or high cardiovascular risk.

DISCUSSION: Results show low cardiovascular risk patients are significantly more likely to return negative ETT results, particularly when associated with atypical symptoms. Similarly, positive or equivocal ETTs in this group are significantly more likely to be false positives. This suggests the ETT is not efficacious in predicting coronary artery disease in patients with low cardiovascular risk. Is it therefore appropriate to offer exercise testing to this cohort or should alternative management strategies be considered?

KEYWORDS: Exercise treadmill test; risk assessment; chest pain; coronary artery disease; retrospective studies

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Introduction

Chest pain is a common symptom associated with a variety of diagnoses from the serious to the benign. It often leads to consideration of underlying ischaemic heart disease and it is imperative the possibility of this is effectively assessed.

If a resting electrocardiogram (ECG) fails to demonstrate evidence of ischaemia, the exercise

treadmill test (ETT) may be used to look for signs of myocardial ischaemia during exertion. There are many other test modalities that can be used (their availability depends on local resources and expertise), but the ETT is perhaps the most cost-efficient, least invasive and readily available method.¹ However, the ETT is not a perfect tool and it is known to give false-positive results, particularly in women and low-risk patients, and

false-negative results in higher-risk patients.² This makes interpretation challenging, often leading to more invasive and costly tests such as coronary angiography or potentially missing a diagnosis in high-risk patients, as stated in the seminal study by Detry *et al.*³

To minimise this risk, it is important to consider both the probability of the disease existing in the individual before the test has been performed and the sensitivity and specificity of the ETT; 67% and 72%, respectively, as reported by Gibbons *et al.*¹ This will help determine the accuracy of the results. This assessment of pre-test probability assists with decisions to proceed with particular diagnostic tests and helps avoid unnecessary testing. Pre-test probability is based on clinician experience, patients' presenting symptoms, physical examination and presence of cardiovascular risk factors.¹ In patients presenting with typical symptoms of angina, their pre-test probability will most likely be calculated as moderate or high, depending on gender and age and, as a result, the predictive value of the test is increased.

Cardiovascular disease (CVD) is the primary cause of mortality in New Zealand and represents 40% of all deaths.⁴ The costs related to CVD are of national concern. In the 2011/12 financial year, CVD-related hospitalisations cost the health service NZ\$501 million.⁵ Coronary artery disease accounted for 57% of these admissions. In the latest review from the National Health Committee, the estimated cost to the health system from coronary artery disease alone was NZ\$287 million per annum.⁶ Of interest is the recommendation by Fihn *et al.* who found that diagnostic testing in patients with a >90% or <10% pre-test probability of disease should be discontinued as it adds little to subsequent patient management.⁷ Due to increasing fiscal pressures in health care, it is timely to assess these issues.

Methods

An observational study of data from patients attending a chest pain clinic over an 18-month period was conducted. All patients aged 35–80 years who completed an ETT using the Bruce protocol for the assessment of stable coronary

WHAT GAP THIS FILLS

What is already known: The incidence of coronary artery disease is lower in patients with lower cardiovascular risk than in those with moderate or high cardiovascular risk. Exercise treadmill testing (ETT) is a useful tool to rule out obstructive coronary artery disease due to its high negative predictive value.

What this study adds: ETT is an ineffective diagnostic test in patients with low cardiovascular risk and atypical symptoms. Any reassurance value of ETT in low cardiovascular risk patients with atypical symptoms is offset by the significant false-positive rate in this group.

artery disease were included.⁸ Data included cardiovascular risk, gender, whether the patient described typical or atypical symptoms for cardiac ischaemia (as determined by location, character, radiation of pain, trigger for pain, dyspnoea, nausea or diaphoresis),¹ coronary artery disease history, results of the ETT (positive, negative or equivocal), and outcomes of further tests such as coronary angiography.⁹ In this clinic, a positive test was based on ST segment depression or elevation of ≥ 1 mm (mm) of horizontal or down-sloping ST segment change for 60–80 ms after the end of the QRS complex and/or provocation of symptoms. A negative ETT meant that no ECG changes or symptoms were provoked with exercise, and in an equivocal result there was some doubt regarding the result due to symptoms or subtle ST changes at high workload. The New Zealand cardiovascular risk assessment was used to risk-stratify all the chest pain clinic patients aged 35–74 years.¹⁰ Patients aged > 74 years were included because they were considered to have a high cardiovascular risk based purely on age.¹⁰ Patients assessed for reasons other than angina, with known coronary artery disease or with an abnormal resting ECG such as left bundle branch block (which makes interpretation of results difficult) were excluded, as were patients unable to perform an ETT; for example, due to difficulties with mobility.

Pearson's Chi-Square test was used to explore the associations between ETT results and gender, cardiovascular risk, and symptom type. For the statistical analysis, cardiovascular risk was

ranked low (< 10%), moderate (10–15%) or high (> 15%). The latter two groups were combined and cross tabulations, odds ratios (OR) and binary logistic regressions were used to explore the following two hypotheses.

Hypothesis 1: low cardiovascular-risk patients are significantly more likely to return a negative ETT result than moderate- or high-risk patients.

Hypothesis 2: low-risk patients who return a positive or equivocal stress test result are significantly less likely to have coronary artery disease confirmed than moderate- or high-risk patients (i.e. they are more likely to return a false-positive ETT result).

Results

Data on cardiovascular risk, symptom types (atypical or typical) and ETT result (negative, positive, equivocal) were available for 529 patients, along with their gender and ethnicity. Results of follow-up testing (angiography or stress echo test) were examined for patients with positive or equivocal ETT results ($n = 179$).

Of the 529 patients, 207 were assessed as low cardiovascular risk, of whom 169 (81.6%) were described as having atypical symptoms; 322 patients were categorised as moderate or high cardiovascular risk, with 219 (68%) describing atypical symptoms. Table 1 shows the number of patients within each cardiovascular risk assessment category. There were 204 females (2 Māori) and 325 males (17 Māori) in the sample. Due to the low representation of Māori, ethnicity was not included in the statistical analyses.

There were 204 patients with a positive or equivocal result for the ETT and of these, 179 went forward for an angiogram or stress echocardiograph. There were 110 positive results from the angiogram or stress echocardiograph confirming coronary artery disease.

Gender was not found to be associated with types of symptoms ($P = 0.631$) or ETT result ($P = 0.328$).

Level of cardiovascular risk was associated with types of symptoms, with 81.6% of low cardiovascular risk patients having atypical symptoms compared to 68.0% of moderate or high cardiovascular risk patients ($P < 0.001$, OR = 2.09, 95% CI: 1.371–3.192). An association between low cardiovascular risk and negative ETT results was observed, with 72.5% of patients with a low cardiovascular risk having a negative ETT result compared with 54.3% of patients with a moderate or high cardiovascular risk ($P < 0.001$, OR = 2.21, 95% CI: 1.518–3.218).

A binary logistic regression, with ETT result (negative or positive/equivocal) as the dependant variable and symptom type and cardiovascular risk as categorical variables, found that the OR of a negative ETT result for type of symptoms (atypical/typical) is 11.09 ($P < 0.001$, 95% CI: 6.936–17.734) and the OR for cardiovascular risk (low/moderate-high) is 1.85 ($P = 0.005$, 95% CI: 1.211–2.838).

Of patients with positive or equivocal ETT results ($n = 179$), 38.5% recorded a negative result in subsequent investigation to confirm the presence of coronary artery disease (either an angiogram or stress ECG); that is, 38.5% of the ETT results were false positives. A Chi-Square test from further investigation results against cardiovascular risk revealed 76.9% of patients with low cardiovascular risk returned a negative test compared with 22.8% of patients with a moderate or high cardiovascular risk ($P < 0.001$, OR = 11.26, 95% CI: 5.233–24.248).

An association also existed between the further investigation result and symptom type, with 53.5% of patients with atypical symptoms returning a negative result compared with 28.7% of

Table 1. Risk percentages, numbers and New Zealand cardiovascular risk (CVR) category

| Risk | N | CVR category* |
|--------------|-----|---------------|
| <2.5% – <10% | 207 | Low |
| 10 – <15% | 164 | Moderate |
| ≥15% | 158 | High |
| Total | 529 | |

* New Zealand Guidelines Group, 2012.¹⁰

patients with typical symptoms ($P = 0.001$, OR = 2.86, 95% CI: 1.530–5.346). Similarly, an association existed between further investigation result and gender, with 54.8% of females returning a negative test compared with 27.4% of males with typical symptoms ($P < 0.001$, OR = 3.22, 95% CI: 1.717–6.033).

A binary logistic regression, with the follow-up test (angiography or stress echo test) result (negative or positive) as the dependant variable and symptom type and risk as categorical variables, found that the OR of a negative follow-up test for type of symptoms (atypical/typical) was 2.26 ($P = 0.025$, 95% CI: 1.108–4.619) and the OR for cardiovascular risk (low/moderate-high) was 10.18 ($P < 0.001$, 95% CI: 4.673–22.160).

Discussion

This study showed that patients with low cardiovascular risk were more likely to have a negative ETT than patients with medium or high cardiovascular risk, supporting hypothesis one. Hypothesis two is also accepted, as patients who did return a positive or equivocal test were less likely to have demonstrable coronary artery disease on subsequent investigation. In other words, there was a significant false-positive rate from ETT in the low-risk group.

Negative results: are we wasting our time?

In our study, a high number of negative ETT results were found in patients with low cardiovascular risk (72.5%) compared to those with moderate or high cardiovascular risk (54.3%), a result not uncommon in other literature.^{11–16} For patients proceeding to coronary angiography or stress echo tests, a negative result was seen in 76.9% of patients with a low cardiovascular risk compared to 22.8% of patients with moderate to high cardiovascular risk, which raises the question as to the value of ETT in this low cardiovascular risk group. Negative test results are reliable in ruling out significant coronary artery disease in patients who complete an adequate ETT (patients with normal resting ECGs and achieving at least 6 min of the Bruce Protocol), and this can be helpful for patients and doctors as it

provides reassurance that coronary artery disease is unlikely and allows other causes of symptoms to be pursued.

The rate of false positives in our study was 38.5%, a figure comparable to that found for others in acute and stable low-risk patients.^{13–15} While considering the risk of a false-positive result, ETTs in this group may lead to more anxiety than they allay. Furthermore, a large number of referrals for low-risk patients with atypical symptoms has contributed to increased waiting time for patients triaged with a greater need.

Our study suggests that due to the large numbers of negative- and false-positives test results in the low cardiovascular risk group, ETTs can add little additional information to that attained from thorough clinical assessment.

Effectively ruling out cardiac ischaemia in patients with chest pain is a concern for health care providers, particularly those at the first point of contact (primary care or emergency departments), and being able to gain information that patients' pain is unlikely to be cardiac related is helpful. Although reassurance is valuable, any testing must be considered in the context of a health care system with increasing demand for health resources but limited ability to meet those demands within reasonable timeframes.⁵ Performing ETT for reassurance alone has fiscal implications and puts strain on service provision. Furthermore, ETTs may negatively affect patients by creating unnecessary anxiety and undue stress due to the potential downstream effects of false-positive results leading to invasive procedures that carry an element of risk.^{11,13,17}

Atypical symptom presentation

In addition to the high negative ETT results in this study, chest pain with features not typical for cardiac ischaemia was more often described in the low cardiovascular risk group compared to patients in the moderate to high cardiovascular risk group (81.6% vs 68%, respectively), a finding consistent with other similar research.¹⁵ Atypical symptoms are frequently described by patients presenting to acute care settings, but ETT is often performed before discharge to exclude

acute coronary syndromes. Negative stress tests also predominate in this group, and results from prognostic testing are similar in patients who describe atypical symptoms whether they present acutely or are referred to an outpatient clinic.^{11,14,18,19} This supports the questionable value of ETT in patients with atypical symptoms, particularly if combined with low cardiovascular risk. Recent research suggests it is safe to discharge such patients without ETT.²⁰

In our study, stable patients were referred primarily from general practice with the benefit of pre-referral assessment to determine patients' symptom history, cardiovascular risk and consequent probability of disease.²¹ Access thresholds are now an accepted part of many medical services to ensure effective use of public money and protecting services from becoming overburdened. This research suggests a threshold could be reasonably considered to restrict access to ETT to moderate and high cardiovascular risk groups, and low cardiovascular risk patients with symptoms suspicious for ischaemia only.

Study limitations

This study has inherent weaknesses because randomisation and blinding of diagnostic results was not possible, and the selection of patients may therefore have been biased. Also, there is potential for variations in the classification of symptoms and interpretation of ETT results between different clinicians because two specialist nurses and four cardiologists were involved in the process. However, to standardise data, all clinicians followed the same guidelines and protocols for assessment and interpretation of symptoms and ECG changes. Further, while the study region has a relatively low percentage of Māori (9%), the number of Māori in the data suggests either significant issues of equity of access or problems with the recording of ethnicity in the hospital. Finally, this study was performed in a single location in a regional city of New Zealand and generalisability is difficult to achieve. While reliability and validity enhance the possibility to generalise information from one population to another, it is not possible in this study due to its retrospective design and single-centre location.²²

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