Utility of exercise electrocardiography testing for the diagnosis of coronary artery disease in a remote Australian setting

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Abstract

Objective: To determine the utility of exercise electrocardiography testing (EET) in evaluating suspected coronary artery disease in a remote Australian setting where a significant proportion of patients are Indigenous Australians.

Design: Retrospective cohort study with grouping based on EET results.

Patients and setting: 268 patients with suspected coronary artery disease who underwent EET at Alice Springs Hospital — a specialist teaching hospital in Central Australia with no resident specialist cardiology service — in the period 1 June 2009 to 31 May 2010.

Main outcome measures: Diagnosis of coronary artery disease, based on coronary angiography and/or admission with acute coronary syndrome, in the 24 months after EET.

Results: Indigenous patients were younger, more likely to be women and were twice as likely as non-Indigenous patients to have a chronic disease. Indigenous patients and those with a chronic disease had a higher proportion of inconclusive results. Completed EET had a positive predictive value of 48.1% (95% CI, 28.7%–68.1%) and a negative predictive value of 96.5% (95% CI, 93.2%–98.5%). Similar results were seen among Indigenous and non-Indigenous patients.

Conclusions: In regional and remote Australian settings, EET remains an important tool for the diagnosis of coronary artery disease. It is useful, and is reassuring to patients and clinicians if the result is negative, particularly in a remote Indigenous Australian population with a significant burden of cardiovascular risk.

Coronary artery disease (CAD) remains the leading cause of death in Australia, both in the general population and also among Aboriginal and Torres Strait Islander peoples (referred to henceforth as Indigenous Australians).[1] Indigenous Australians are three times as likely to suffer a major coronary event than are non-Indigenous Australians,[2] and cardiovascular disease remains the leading cause of Indigenous mortality and the main contributor to the mortality gap between Indigenous and non-Indigenous Australians.[3] Furthermore, the burden and severity of other diseases that predispose to CAD are higher among Indigenous Australians.[4]

Patients with an acute coronary syndrome (ACS), as defined by electrocardiography results and biochemical markers, proceed to coronary angiography, which is considered the gold standard diagnostic tool for CAD; however, its use is limited due to its invasive nature, cost and accessibility.[5] In the absence of a definite ACS, less invasive, and often more accessible, exercise stress testing is used. Stress testing determines the significance of a patient's symptoms by indicating whether functional myocardial ischaemia occurs and therefore whether further investigations, including coronary angiography, are needed.

Alice Springs Hospital (ASH), in the Northern Territory, services a dispersed population of 45 000 people spread over 1 million square kilometres, of whom 44% are Indigenous Australians.[6] ASH is about 1500 kilometres from the nearest angiography facilities and relies on exercise electrocardiography testing (EET) to prioritise patients for further investigation of possible CAD. Patients with a "positive" test are typically referred for coronary angiography, and patients with a "negative" test are usually reassured and assumed to be at low risk of significant CAD.[7] Inconclusive test results typically lead to referral for stress echocardiography — the timing of which is reliant on the frequency of visiting cardiologists. Consequently, the results of EET are heavily relied upon to inform a diagnosis and management plan. In non-Indigenous populations, the usefulness of EET has been reflected in its reported high negative predictive value of 99%.[8-11] We chose to retrospectively audit the performance of EET in our local population, as its diagnostic utility in a setting with a significant proportion of Indigenous Australians has not been studied. In addition, we assessed the significance of inconclusive EET results with regard to subsequent clinical outcomes, as patients with inconclusive results may be at increased risk of CAD-related events while waiting for further diagnostic testing.

Methods

We undertook a retrospective audit of data for patients with suspected CAD who underwent EET between 1 June 2009 and 31 May 2010. We excluded patients with a pre-existing diagnosis of CAD and those not permanently residing in the NT. Data collected included patient demographics, CAD risk factors, results of the EET, and clinical outcomes for the following 2 years as documented in the patients' medical records.

ASH uses the Bruce protocol for conducting EET, aiming to achieve a target age- and sex-based heart rate, exercise duration and workload (based on metabolic equivalents [METS]).[9] A positive result was one or more of: angina during exercise; ST-segment depression that was >1 mm and/or downsloping; reduction in blood pressure of >10 mmHg from baseline and/or multiple ventricular premature complexes or runs of ventricular tachycardia. A negative test result was recorded if the patient was asymptomatic with a normal electrocardiogram and blood pressure response on completion of maximal testing. A patient who failed to complete the test for reasons other than those that would classify the test as being positive was reported as having an inconclusive test result.[10]

1 Descriptive details of 268 patients who underwent exercise electrocardiography testing 1 June 2009 – 31 May 2010

	All patients		Indigenous patients		Non-Indigenous patients		
	No.	Proportion (95% CI)*	No.	Proportion (95% CI)*	No.	Proportion (95% CI)*	P†
Age in years, median (IQR)	–	49.0 (41.6–57.5)	–	45.7 (39.1–55.3)	–	51.0 (44.9–58.6)	0.004‡
Total number	268	100%	108	40.3%	150	56.0%	–
Women	118	44.0% (38.0%–50.2%)	64	59.3% (50.0%–68.7%)	52	34.7% (27.0%–42.4%)	< 0.001
History of smoking	103/245	42.0% (35.8%–48.5%)	48/100	48.0% (37.9%–58.2%)	55/145	37.9% (30.0%–46.4%)	0.12
Family history of CAD	67/155	43.2% (35.3%–51.4%)	24/45	53.3% (37.9%–68.3%)	43/110	39.1% (29.9%–48.9%)	0.10
Any chronic disease	189/262	72.1% (66.3%–77.5%)	88/108	81.5% (72.9%–88.3%)	101/148	68.2% (60.1%–75.6%)	0.02
Diabetes mellitus	80/250	32.0% (26.3%–38.2%)	57/107	53.3% (43.7%–62.9%)	23/143	16.1% (10.0%–22.2%)	< 0.001
Hypertension	132/252	52.4% (46.0%–58.7%)	71/107	66.4% (56.6%–75.2%)	61/145	42.1% (33.9%–50.5%)	< 0.001
Dyslipidaemia	139/237	58.6% (52.1%–65.0%)	71/98	72.4% (62.5%–81.0%)	68/139	48.9% (40.4%–57.5%)	< 0.001
Renal impairment (eGFR < 60 mL/min/1.73 m^2)	18/215	8.4% (5.0%–12.9%)	14/98	14.3% (8.0%–22.8%)	4/111	3.6% (1.0%–9.0%)	0.02
Albuminuria (ACR > 3.4 mg/mmol)	26/48	54.2% (39.2%–68.6%)	25/38	65.8% (48.6%–80.4%)	1/8	12.5% (0.3%–52.7%)	0.02
Renal impairment or albuminuria	35/216	16.2% (11.6%–21.8%)	31/99	31.3% (22.4%–41.4%)	4/111	3.6% (1.0%–9.0%)	< 0.001

* Unless otherwise indicated. † χ^2 unless otherwise indicated. ‡ Wilcoxon rank-sum test. ACR = albumin : creatinine ratio. CAD = coronary artery disease. eGFR = estimated glomerular filtration rate. IQR = interquartile range. ◆

Clinical outcomes were reviewed for 2 years after EET for details of subsequent coronary angiography results consistent with CAD, readmission to ASH for investigation of chest pain and readmission to ASH with a separation diagnosis of an ACS. Our assessment of the overall utility of EET was based on the risk of having a coronary angiogram suggestive of either CAD or an ACS within 24 months of testing.

Statistical analysis was undertaken using Stata12 (StataCorp). Continuous variables were compared using the Wilcoxon rank-sum test; categorical variables were compared using the χ^2 test. Continuous non-parametric data are presented as medians with interquartile range, and categorical variables are presented as percentages with binomial confidence intervals. Logistic regression models were created using a backwards stepwise approach, including in the first model all variables shown in univariable models to be related to test outcome, as well as variables that differed between Indigenous and non-Indigenous subjects at baseline. All statistical tests were two-sided and P less than 0.05 was taken to indicate statistical significance. Ethics approval for the study was provided by the Central Australian Human Research Ethics Committee.

Results

We reviewed the medical records and EET results of 268 patients who met our inclusion criteria. Descriptive data related to these patients are presented in Box 1. Indigenous identity was not reported for 10/268 patients (3.7%). Indigenous patients were significantly younger than non-Indigenous patients and were more likely to be women. They were also twice as likely to have been diagnosed with one or more chronic diseases (OR, 2.0; 95% CI, 1.1–3.7), particularly diabetes mellitus (OR, 5.9; 95% CI, 3.3–10.7) and chronic kidney disease (OR, 12.2; 95% CI, 4.1–36.1), compared with non-Indigenous patients.

The results of EET and outcomes over the subsequent 24 months are outlined in Box 2. Indigenous patients were less likely to reach a maximum heart rate or adequate workload (> 10 METS) (OR, 10.3; 95% CI, 5.3–20.3). In turn, this translated to a higher proportion of Indigenous patients having inconclusive test results compared with non-Indigenous patients (57/108 v 32/150; $P < 0.001$) and a lower proportion having positive (6/108 v 21/150; $P = 0.03$) and negative (45/108 v 97/150; $P < 0.001$) test results (Box 2). In logistic regression modelling, the major factors independently associated with an inconclusive result were a diagnosis of one or more chronic diseases (OR, 6.0; 95% CI, 2.5–14.1) and identifying as Indigenous (OR, 3.7; 95% CI, 2.1–6.6).

Compared with patients with an inconclusive or negative EET result, patients with a positive result were more likely to proceed to coronary angiography (21/34; $P < 0.001$) and were significantly more likely to present to hospital with chest pain in the following 2 years (11/28; $P = 0.001$). Indigenous patients were less likely than non-Indigenous patients to proceed to coronary angiography (10/34 v 24/34, respectively; $P = 0.114$), and more likely to present with an ACS in the following 2 years (4/108 v 2/139, respectively; $P = 0.25$); however, neither of these differences were statistically significant. Overall, the risk of presenting with an ACS within 24 months significantly increased as the result of EET moved from negative to inconclusive to positive (OR, 4.4; 95% CI, 1.4–14.0). A similar relationship to EET results was seen for re-presentation with chest pain within 12 months (OR, 2.0; 95% CI, 1.3–3.1) and re-presentation with chest pain within 24 months (OR, 2.0; 95% CI, 1.3–2.9).

The sensitivity, specificity and positive and negative predictive values of EET in our sample are summarised in Box 3.

Discussion

EET clearly represents a cheap, non-invasive diagnostic modality for screening patients presenting with suspected CAD. Our findings provide reassurance that, when maximal testing can be completed, EET has performance characteristics that are at least equivalent to those reported in the literature.[8] Even when inconclusive results were included, the lack of a positive EET continued to confer a low risk of a subsequent presentation with an ACS. While the presence of

2 Exercise electrocardiography testing results and patient outcomes

	All patients		Indigenous patients		Non-Indigenous patients		
	No.	Proportion (95% CI)*	No.	Proportion (95% CI)*	No.	Proportion (95% CI)*	*P*
Exercise electrocardiography test result							
Positive	31/268	11.6% (8.0%–16.0%)	6/108	5.6% (2.1%–11.7%)	21/150	14.0% (8.9%–20.6%)	0.03
Inconclusive	90/268	33.6% (28.0%–39.6%)	57/108	52.8% (42.9%–62.5%)	32/150	21.3% (15.1%–28.8%)	< 0.001
Negative	147/268	54.9% (48.7%–60.9%)	45/108	41.7% (32.3%–51.5%)	97/150	64.7% (56.5%–72.3%)	< 0.001
Coronary angiography performed	34/268	12.7% (8.9%–17.3%)	10/108	9.3% (4.5%–16.4%)	24/150	16.0% (10.5%–22.9%)	0.11
Proportion of coronary angiograms that were positive	18/34	52.9% (35.1%–70.2%)	5/10	50.0% (18.7%–81.3%)	13/24	54.2% (32.8%–74.4%)	0.82
Acute coronary syndrome							
Within 1 year	4/263	1.5% (0.4%–3.8%)	3/108	2.8% (0.6%–7.9%)	1/145	0.7% (0–3.8%)	0.12
Within 2 years	6/255	2.4% (0.9%–5.1%)	4/108	3.7% (1.0%–9.2%)	2/139	1.4% (0.2%–5.1%)	0.25
Acute coronary syndrome and/or positive angiogram							
Within 1 year	20/263	7.6% (4.7%–11.5%)	7/108	6.5% (2.6%–12.9%)	13/145	9.0% (4.9%–14.8%)	0.47
Within 2 years	21/255	8.2% (5.2%–12.3%)	8/108	7.4% (3.3%–14.1%)	13/139	9.4% (5.1%–15.5%)	0.59
Readmission with chest pain							
Within 1 year	55/264	20.8% (16.1%–26.2%)	28/108	25.9% (18.0%–35.2%)	25/146	17.1% (11.4%–24.2%)	0.09
Within 2 years	67/256	26.2% (20.9%–32.0%)	35/108	32.4% (23.7%–42.1%)	30/140	21.4% (14.9%–29.2%)	0.05

* Unless otherwise indicated. ◆

3 Diagnostic utility of exercise electrocardiography testing*

	Prevalence of outcome†	Sensitivity	Specificity	Positive predictive value	Negative predictive value
All patients					
All test results (*n* = 268)	8.5% (5.2%–12.3%)	61.9% (38.4%–81.9%)	94.0% (90.2%–96.7%)	48.1% (28.7%–68.1%)	96.5% (93.2%–98.5%)
Inconclusive results excluded (*n* = 178)	9.0% (5.1%–14.4%)	86.7% (59.5%–98.3%)	90.8% (85.0%–94.9%)	48.1% (28.7%–68.1%)	98.6% (94.9%–99.8%)
Indigenous patients					
All test results (*n* = 108)	7.4% (3.3%–14.1%)	37.5% (8.5%–75.5%)	97.0% (91.5%–99.4%)	50.0% (11.8%–88.2%)	95.1% (88.9%–98.4%)
Inconclusive results excluded (*n* = 51)	9.8% (3.3%–21.4%)	60.0% (14.7%–94.7%)	93.5% (82.1%–98.6%)	50.0% (11.8%–88.2%)	95.6% (84.9%–99.5%)
Non-Indigenous patients					
All test results (*n* = 150)	9.4% (5.1%–15.5%)	76.9% (46.2%–95%)	93.7% (87.9%–97.2%)	55.6% (30.8%–78.5%)	97.5% (92.9%–99.5%)
Inconclusive results excluded (*n* = 118)	9.2% (4.5%–16.2%)	100% (69.2%–100%)	91.9% (84.7%–96.4%)	55.6% (30.8%–78.5%)	100% (96.0%–100%)

* All values are % (95% CI). † Defined as coronary angiogram suggestive of coronary heart disease or an acute coronary syndrome within 24 months of testing. ◆

chronic disease was the main predictor of an inconclusive EET there was also an independently elevated risk associated with being Indigenous. This may be related to physical and social factors, including familiarity with treadmill exercise, and fitness.

A focus should be to reduce the proportion of inconclusive tests. In general, an image-based myocardial stress study, typically echocardiography with dobutamine, is performed when the EET result is inconclusive. These tests are conducted by visiting cardiologists, but waiting periods are variable and may extend to months. In the interim, a person with possible CAD may go without treatment and be at risk of a preventable adverse outcome — demonstrated in our study by the high rates of loss to follow-up and re-presentation with an ACS. Possible solutions include enhanced orientation and education of patients before they undergo EET, and greater use of Indigenous language translators.

Our study was limited by its reliance on retrospective collection of data that were non-standardised. The information gathered was limited to data documented at the time of the EET. Similarly, follow-up of patients re-presenting with ACS or chest pain was restricted to those who presented to ASH. Nonetheless, as the only referral hospital servicing the Central Australian region, most clinically significant events in remote clinics would have been captured. This limitation could be overcome by repeating the audit prospectively.

In summary, EET is likely to remain a useful and important tool in determining the risk of CAD among patients in regional and remote Australian locations where onsite specialist cardiology services are limited. Further attention should be given to how inconclusive test results could be reduced. Positive initiatives may include greater involvement of Indigenous people in the health care workforce associated with EET, exploring patients' understanding of the concepts of CAD and exercise, and educating patients and health care providers. Greater use of myocardial stress testing modalities that do not require specialist cardiologists, such

as cardiac computed tomography angiography, or training local staff to perform stress echocardiography could also be considered as means of enhancing the care of patients with inconclusive results.

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1 Australian Bureau of Statistics. Causes of death, Australia, 2010. Canberra: ABS, 2010. (ABS Cat. No. 3303.0.) http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/3303.02010?OpenDocument (accessed Feb 2013).

2 Mathur S, Moon L, Leigh S. Aboriginal and Torres Strait Islander people with coronary heart disease: further perspectives on health status and treatment. Canberra: Australian Institute of Health and Welfare, 2006. (AIHW Cat. No. CVD 33; Cardiovascular Disease Series No. 25.) http://www.aihw.gov.au/publication-detail/?id=6442467898 (accessed Feb 2013).

3 Penm E. Cardiovascular disease and its associated risk factors in Aboriginal and Torres Strait Islander peoples 2004–05. Canberra: Australian Institute of Health and Welfare, 2008. (AIHW Cat. No. CVD 41.) http://www.aihw.gov.au/publication-detail/?id=6442468095 (accessed Feb 2013).

4 Zhao Y, Dempsey K. Causes of inequality in life expectancy between Indigenous and non-Indigenous people in the Northern Territory, 1981–2000: a decomposition analysis. *Med J Aust* 2006; 184: 490-494.

5 Garber AM, Solomon NA. Cost-effectiveness of alternative test strategies for the diagnosis of coronary artery disease. *Ann Intern Med* 1999; 130: 719-728.

6 Australian Bureau of Statistics. Population distribution, Aboriginal and Torres Strait Islander Australians, 2006. Canberra: ABS, 2007. (ABS Cat. No. 4705.0.) http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/4705.02006?OpenDocument (accessed Feb 2013).

7 Banerjee A, Newman DR, Van den Bruel A, Heneghan C. Diagnostic accuracy of exercise stress testing for coronary artery disease: a systematic review and meta-analysis of prospective studies. *Int J Clin Pract* 2012; 66: 477-492.

8 Gibbons RJ, Balady GJ, Bricker JT, et al. ACC/AHA 2002 guideline update for exercise testing: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). *Circulation* 2002; 106: 1883-1892.

9 Peterson PN, Magid DJ, Ross C, et al. Association of exercise capacity on treadmill with future cardiac events in patients referred for exercise testing. *Arch Intern Med* 2008; 168: 174-179.

10 Hill J, Timmis A. Exercise tolerance testing. *BMJ* 2002; 324: 1084-1087.

11 Newman RJ, Darrow M, Cummings DM, et al. Predictive value of exercise stress testing in a family medicine population. *J Am Board Fam Med* 2008; 21: 531-538. ❑