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Relative diagnostic, prognostic and economic value of stress echocardiography versus exercise electrocardiography as initial investigation for the detection of coronary artery disease in patients with new onset suspected angina

Konstantinos Zacharias ^{a,b}, Shahram Ahmadvazir ^a, Asrar Ahmed ^a, Benoy N. Shah ^a, Dionisio Acosta ^b, Roxy Senior ^{a,c,*}

^a Department of Cardiovascular Medicine and Institute for Medical Research, Northwick Park Hospital, Harrow, UK

^b Centre for Health Informatics and Multi-professional Education, University College London, UK

^c Cardiovascular, Biomedical Research Unit, Department of Cardiology, Royal Brompton Hospital, Imperial College London, London, UK

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ABSTRACT

Objectives: We hypothesised that stress echocardiography (SE), may be superior to exercise ECG (ExECG), for predicting CAD and outcome, and cost-beneficial, when performed as initial investigation in newly suspected angina. *Methods:* All patients seen in 2011, with suspected angina, no history of CAD, pre-test likelihood of CAD of >10% and who underwent SE or ExECG as first line were identified retrospectively. Cost to diagnosis was calculated by adding the cost of all tests, up to and including coronary angiography (CA), on an intention-to-treat basis. Follow-up data on cardiac death and myocardial infarction (MI) were collected, 26 months after the presentation of the last study patient.

Results: A total of 456 patients underwent ExECG (224 (49%) negative, 93 (20%) positive, 139 (31%) inconclusive) and 241 underwent SE (200 (83%) negative, 35 (15%) positive, 6 (2%) inconclusive) as first line. In patients subsequently undergoing CA, CAD was present in 46% (37/80) of patients with positive ExECG vs. 72% (23/32) patients with positive SE (p = 0.01). Mean cost to diagnosis was £456 for the ExECG vs. £360 for the SE group (p = 0.002). Over a mean follow-up period of 31 \pm 5 months, cardiac events were 2% each in negative SE vs. negative ExECG (p = 0.9).

Conclusions: SE is superior to ExECG for prediction of CAD and is cost-beneficial when used as initial test in patients with no history of CAD presenting with suspected angina.

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1. Introduction

Patients presenting with chest pain account for over 500,000 outpatient appointments per year in the UK with an estimated cost to the National Health Service of around £52 million [1]. Most hospitals in the UK offer a form of Rapid Access Chest Pain Clinic (RACPC) service, with the intention to evaluate whether these patients suffer from coronary artery disease (CAD). Diagnostic testing is recommended for the majority of these patients, with the exception of those with the lowest (<10%) pretest probability of CAD [2]. Due to perceived cost implications, Exercise electrocardiogram (ExECG) is still widely used in the UK and Europe as the first test, and is the initial test of choice in the US in patients with normal baseline ECG, who can exercise [3]. Stress echocardiography (SE) is a

E-mail address: roxysenior@cardiac-research.org (R. Senior).

well-established alternative technique, used for the assessment of CAD. The advent of tissue harmonic imaging, digital image acquisition and, lately, trans-pulmonary echo-contrast agents have all led to improved image quality, feasibility, reproducibility and accuracy of SE [4–6].

A previous study has indicated that SE is more cost-effective than ExECG for the risk stratification of patients presenting with suspected acute coronary syndrome [7]. Another large study has also previously shown superior cost-effectiveness of SE compared to ExECG in patients with stable angina who are able to exercise [8]. However this latter study included patients with pre-existing CAD, making up 25% of the study population. There is therefore, so far, no data comparing, in a real world setting, SE, including contemporary techniques, to ExECG, in patients, presenting with new-onset suspected stable angina, irrespective of exercise capacity. This population is of particular clinical and economic interest, as it comprises the majority of patients with newly suspected CAD. We thus hypothesised, that SE by virtue of its superior feasibility and accuracy, may be superior to ExECG, both for

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^{*} Corresponding author at: Imperial College London, Royal Brompton Hospital, Sydney Street, London SW3 6NP, UK. Tel.: +44 2073497740; fax: +44 2073518604.

the prediction of CAD and for the cost to diagnosis when used as the initial test for the evaluation of patients with no previous history of CAD who present with suspected stable angina.

2. Methods

2.1. Study design

A retrospective analysis of all patients seen in the RACPC of our local hospital during 2011 was performed. Information was collected from electronic hospital records with regard to the initial clinic attendance and any subsequent cardiac investigations. The study was approved by our local research department. Patients who presented with new onset chest pain, with no previous history of CAD and with a pre-test probability of CAD of >10%, who underwent SE or ExECG as the initial investigation were identified. We excluded patients with unstable angina, defined as rest chest pain of more than 10 min, onset of angina within two months with crescendo pattern and with significant resting ST-T changes. The decision to undergo either test was made by the attending clinician and was dependent on factors such as the presence of resting ECG changes or medical comorbidities that may have made a patient unsuitable for ExECG (e.g. LBBB, chronic respiratory disease, mobility issues) and on the departmental availability of ExECG or SE slots. Patients would generally undergo a resting ECG but not a resting echocardiogram, as a routine, prior to the functional test. Patients with a known history of ischaemic heart disease based on previous myocardial infarction, previous coronary revascularisation (coronary angioplasty or cardiac surgery), or evidence of flow limiting CAD on previous angiography, were excluded from further analysis. The pre-test probability of CAD was calculated for each individual patient based on the description of the documented symptoms and the presence of risk factors using the algorithm from NICE guidelines [2,9]. For the purposes of the study, the posttest probability of CAD was deemed to be high in cases with a positive functional test, low in cases with a negative functional test and intermediate in cases with an inconclusive functional test.

2.2. Exercise ECG

Patients underwent ExECG using the standard Bruce protocol treadmill testing. Endpoints were fatigue, severe ischaemia (severe chest pain, >2 mm ST depression), severe hypertension (systolic BP > 220 mm Hg), hypotension (systolic BP < 90 mm Hg), presyncope or arrhythmia. Patients who achieved a work-load of \geq 9 METS or achieved 85% of target heart rate, without any symptoms, haemodynamic compromise or ECG changes were considered to have a negative test. Patients, who developed significant chest pain, hypotension, arrhythmia, or \geq 1 mm planar or down-sloping ST depression in two or more leads of the same territory, during exercise or in recovery, were considered to have a positive test. All other patients were considered to have aphysiologists and interpreted by the attending clinicians.

2.3. Stress echocardiography

Patients underwent SE using either treadmill or pharmacological testing at the discretion of the cardiologist performing the test as per departmental protocol [7]. A two-dimensional echocardiogram was performed in the lateral decubitus position. Digital images, with tissue harmonic imaging, of the left ventricle (LV) were obtained in the parasternal long-axis, short-axis and apical, four-, two- and three-chamber views using an IE33 echocardiography system with an S5 probe (Philips, Best, Netherlands). Exercise stress echocardiography (ESE) was performed using the standard symptom-limited treadmill exercise protocol, with images acquired immediately (within 90 s) after peak exercise. In patients who were deemed unsuitable for exercise testing, dobutamine was infused peripherally in 3 min dose increments,

starting from 10 µg/kg/min and increased to 20, 30 and 40 µg/kg/min. If no end-point was reached, atropine was added to the continuing dobutamine infusion, up to a maximum of 1.2 mg. Endpoints were the achievement of 85% of age-predicted maximum heart rate; development of ischaemia; achievement of peak dose; or the occurrence of intolerable side-effects. Peak stress or immediate post-exercise images with the best endocardial definition were selected and displayed alongside the corresponding baseline images. In technically difficult patients (when two or more segments were not adequately visualised at rest), intravenous contrast (Sonovue, Bracco, Italy) was used to enhance endocardial bor-

2.4. Image analysis

On-line digital images were interpreted qualitatively for the presence, extent and location of segmental wall motion abnormality (WMA). An experienced operator (RS) analysed the images for systolic wall thickening and endocardial wall motion according to a four-point score (1: Normal; 2: Hypokinetic; 3: Akinetic; 4: Dyskinetic motion) using a 17segment left ventricle (LV) model. The stress echocardiogram was considered negative if all segments were normal at baseline and peak stress. Patients with evidence of WMA at rest or development of regional WMA at peak stress were deemed to have a positive stress echocardiogram. Patients with un-interpretable images or patients that failed to achieve the target heart rate were considered to have an inconclusive test.

der definition. Bolus injections of 0.3-0.5 ml were administered through

a peripheral cannula followed by a flush with 0.9% NaCl solution.

2.5. Coronary angiography

The decision to perform coronary angiography was taken at the discretion of the attending clinician with knowledge of the non-invasive test results. Standard techniques were used for performing the angiogram. Images were analysed using a visual quantitative scoring system, with CAD defined as >50% luminal diameter narrowing in one or more epicardial coronary arteries or their major branches. The cut-off value of 50% was used as it has been previously shown to convey prognostic significance [10].

2.6. Cost analysis

The cost analysis was performed using data from the NHS resource tariff of 2011–2012 [11]. Resource use data was collected for all patients on an intention-to-treat basis. We took into account cases where investigations were performed as well as cases where investigations were requested but were not performed due to patients not attending. Cost to diagnosis was defined as the sum of all investigations performed up to and including the point when diagnosis or presumed absence of CAD was deemed established. These included a diagnostic CA, a negative functional test or a decision not to proceed with any further tests.

2.7. Follow up

Data was collected by means of electronic searches of the hospital databases and the NHS registry. Follow-up time was calculated from the day of the initial test to either the date of the cardiac event or the date the database search was performed. Cardiac death was defined as death associated with known or suspected myocardial infarction (MI), life threatening cardiac arrhythmia (VT or VF) or heart failure based on clinical assessment, serum cardiac markers (Troponin I), ECG or cause of death listed on national registry. Non-fatal MI was defined according to established criteria [12]. Coronary revascularisation was defined as percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). Follow-up assessment was performed by a research technician, who was blinded to the study group.

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