



A comparison of cardiac computerized tomography and exercise stress electrocardiogram test for the investigation of stable chest pain: the clinical results of the CAPP randomized prospective trial

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Received 3 July 2014; accepted after revision 11 November 2014

Aims

To determine the symptomatic and prognostic differences resulting from a novel diagnostic pathway based on cardiac computerized tomography (CT) compared with the traditional exercise stress electrocardiography test (EST) in stable chest pain patients.

Methods and results

A prospective randomized controlled trial compared selected patient outcomes in EST and cardiac CT coronary angiography groups. Five hundred patients with troponin-negative stable chest pain and without known coronary artery disease were recruited. Patients completed the Seattle Angina Questionnaires (SAQ) at baseline, 3, and 12 months to assess angina symptoms. Patients were also followed for management strategies and clinical events. Over the year 12 patients withdrew, resulting in 245 in the EST cohort and 243 in the CT cohort. There was no significant difference in baseline demographics. The CT arm had a statistical difference in angina stability and quality-of-life domains of the SAQ at 3 and 12 months, suggesting less angina compared with the EST arm. In the CT arm, there was more significant disease identified and more revascularizations. Significantly, more inconclusive results were seen in the EST arm with a higher number of additional investigations ordered. There was also a longer mean time to management. There were no differences in major adverse cardiac events between the cohorts. At 1 year in the EST arm, there were more Accident and Emergency (A&E) attendances and cardiac admission.

Conclusion

Cardiac CT as an index investigation for stable chest pain improved angina symptoms and resulted in fewer investigations and re-hospitalizations compared with EST.

Clinical trial registration

<http://www.controlled-trials.com/ISRCTN52480460>.

Keywords

cardiac computerized tomography • exercise stress electrocardiogram • stable chest pain

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Introduction

Since its development in 1928, the exercise stress electrocardiogram test (EST) has evolved to become the cornerstone of the assessment of patients with suspected stable coronary artery disease (CAD).¹ However, concern persists about its ability to accurately detect CAD. Both the Joint American Cardiology Colleges and the European Society of Cardiology quote sensitivity and specificity of 67–68% and 70–77%, respectively.^{2,3}

NICE Clinical Guideline 95 (CG95)⁴ in the UK proposed a role of more accurate but more expensive imaging techniques in the primary assessment of chest pain. One such technique is cardiac computerized tomography (CT) coronary angiography, with the diagnostic performance of the technique 64 and above detector CT scanners are well established.^{5–7}

Cardiac CT for the Assessment of Pain and Plaque (CAPP) is a prospective randomized trial designed to compare CT with EST in patients with suspected stable CAD presenting to Rapid Access Chest Pain Clinics (RACPC) [ISRCTN52480460]. This article reports the clinical difference between a novel cardiac CT pathway and the traditional EST standard of care in terms of symptoms, diagnosis, and management, and 1-year follow-up.

Methods

The study protocol was approved by the Office for Research Ethics Committee Northern Ireland (ORECNI) and the South Eastern Health and Social Care Trust (SEHSCT) Research and Development Committee. The study was also supported by the Northern Ireland Medical Physics Agency, the Northern Ireland Cardiovascular Research Network, and the Northern Ireland Clinical Trials Unit.

Patients

The CAPP trial prospectively evenly randomized 500 patients who were referred to RACPCs with symptoms of stable chest pain to EST or cardiac CT from September 2010 to November 2011. Stable chest pain was defined as troponin negative without symptoms suggestive of unstable angina. Unstable angina was defined as (i) crescendo angina (more severe, prolonged, or frequent) superimposed on a pre-existing pattern of stable, exertion-related angina pectoris, or (ii) angina pectoris at rest.^{8,9}

Cardiac clinics

All patients were recruited through two National Health Service (NHS) RACPCs within the one health care trust. Patients were referred by primary care physicians or non-cardiologists and were seen within 2 weeks of referral.

All patients had their age, gender, risk factors, and chest pain characteristics documented. Pain type was classified as typical, atypical, or non-anginal according to defined criteria.^{4,10} This was performed by a non-investigator clinician before randomization. The probability of significant CAD was calculated from the Diamond Forrester table in CG95.⁴ In keeping with this, risk factors associated with high cardiovascular risk included diabetes and/or smoking and/or a cholesterol level >6.47 mmol/L. A fasting serum total lipid profile and glucose level were sampled on the day of RACPC attendance. Details of exclusion criteria have been reported previously,¹¹ but in summary, there are standard contraindications to both EST and cardiac CT.

All patients prior to attendance to clinic were advised to stop any rate-limiting drugs 72 h before attendance in case of randomization to the EST

arm. Patients were randomized at clinic using the permuted block randomization technique.

Exercise stress electrocardiogram test

EST was performed using a standard Bruce protocol treadmill with continuous 12-lead ECG monitoring and registration at 1-min intervals. Manual blood pressure monitoring was performed every 2 min.

Criteria for discontinuation of the test were ST changes of depression >0.3 mV or elevation >0.1 mV; blood pressure changes of systolic >230 mmHg or diastolic >130 mmHg or a >10 mmHg systolic blood pressure drop; arrhythmias such as sustained ventricular tachycardia, increasing frequency of polymorphic ventricular complexes, or altered atrioventricular or intraventricular conduction; and patient symptoms of exhaustion, extreme dyspnoea, or angina. EST results were classified as negative, positive, or inconclusive as defined by previous criteria.³

CT image acquisition

Patients in the CT arm underwent both a calcium score (CS) and subsequent computerised tomography coronary angiogram (CTCA), regardless of initial CS. These were performed on a 64-detector platform (Philips Brilliance 64 Cleveland, Ohio, USA). As per departmental policy, both oral and intravenous beta blockers were used for heart rate control pre-scan. A heart rate of <65 bpm or below was considered optimal for imaging, although CTCA would have been performed below the level of 70 bpm. Patients with heart rates above 70 bpm despite intravenous beta blockers were rescheduled for a later date with larger doses of oral pre-procedure. A non-contrast enhanced, axial prospective triggered CS was performed at 3-mm slice thickness with milliamperes optimized per patient and a standard 120 kV.

CTCA contrast medium enhancement was achieved with a biphasic injection protocol. An aliquot of 80–100 mL of iodinated contrast material (Ioversal, Optiray 350 mgI/mL, Covidien, Hampshire, UK) was administered through an 18-gauge intravenous antecubital fossa cannula at a flow rate of 6 mL/s followed by a saline chaser of 50 mL at 3.5 mL/s. An automated bolus tracking technique prospectively monitored contrast arrival in the descending aorta. A threshold of 110 Hounsfield units (HU) was used to initiate the scan. Image acquisition was in the cranio-caudal direction, and the scan field of view was refined using precise anatomical landmarks cross referenced from the coronary CS. Images from CTCA were reconstructed at 0.8-mm slice thickness with the standard reconstruction filter. Scan parameters (kV, mAs) were optimized by the imaging clinician and were patient specific. The choice of a retrospective gating, or an axial prospective triggering algorithm, was at the discretion of the clinician. For all retrospective examinations, ECG dose modulation was applied (DoseRight Cardiac, Philips Healthcare, Cleveland, Ohio, USA).

The effective radiation dose of each CTCA was estimated by multiplying the dose-length product by a chest-specific conversion coefficient ($\kappa = 0.014 \text{ mSv mGy}^{-1} \text{ cm}^{-1}$).¹²

Analysis of CT images

CS was assessed using a semi-automated analysis package (Heartbeat CS, Philips Cleveland). Areas of calcification within the coronary arteries were identified from a transaxial image stack, and a validated algorithm was used to calculate the total Agatston score.¹³ CTCA images were evaluated for the presence of coronary artery stenosis by an experienced cardiologist and radiologist using the anatomical American Heart Association 15-point score.¹⁴ A coronary diameter stenosis >50% in a major epicardial artery >2 mm was considered significant, which is in keeping with previous work.^{15–17} Such results were deemed positive and could involve either calcified or non-calcified disease. Diameter

stenosis <50% but >0% was considered non-significant and together with the presence of no disease (CAD = 0%) was deemed negative. If any large vessels (>2 mm) in diameter could not be evaluated due to excessive calcifications, motion artefacts, or inadequate contrast filling, the study was deemed inconclusive.

Measurement of disease-specific health status

Health status related to angina was assessed via the use of the SAQ¹⁸ at baseline, 3, and 12 months. The SAQ is a specific quality-of-life measure that uses 19 questions to quantify five clinical domains of health status related to CAD: angina frequency, physical limitations, quality of life, angina stability, and treatment satisfaction. Scores range from 0 to 100, with higher scores indicating fewer symptoms and better health status. All baseline questionnaires were completed via face-to-face interview on the day of enrolment at the clinic, with follow-up questionnaires performed via telephone by the research team. If however patients were unable to be contacted by telephone on three separate occasions, they were given the opportunity to self-complete by postal return.

CAD diagnosis and management

All diagnoses at the clinics were made by the clinicians and considered both the clinical picture and the test result. All further investigations ordered were at the discretion of the clinicians and determined by clinical need. Further CAD imaging investigations available included invasive catheter angiography (ICA), radionuclide myocardial perfusion imaging (MPI), and dobutamine stress echocardiogram (DSE) and cardiac CT.

A positive MPI was defined as showing inducible ischaemia (i.e. an inducible perfusion defect that partly or completely normalizes at rest) involving two or more of specified 17 segments.¹⁹ A positive DSE was defined as having inducible ischaemia manifesting as a new or worsening regional wall motion abnormality in at least one segment.²⁰

Disease was classified as non-significant or significant. A diagnosis of significant CAD was reached when there was either a positive functional test (EST, MPI, or DSE) or an anatomical test with visualization of >50% stenosis. A diagnosis of non-significant disease was made when a functional test was negative or an anatomical test had <50% stenosis.

Management options were categorized as no intervention, medical therapy for risk factor or symptom management, percutaneous coronary intervention (PCI), and coronary artery bypass grafting (CABG). All revascularization decisions regarding interventional management were independent from the study protocol and researchers.

Clinical outcomes

All patients were followed up for the number of further investigations required to reach final diagnosis, time to diagnosis, and management. Patients were also followed up for clinical events using electronic patient care records. These were defined as chest pain resulting in A&E Department attendances, hospital admissions, and major adverse cardiovascular events (MACEs). The primary clinical endpoint was major adverse cardiac event MACE, which was defined as all-cause mortality, ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), heart failure admission, and stroke.²¹ Myocardial infarctions (both STEMI and NSTEMI) were defined as troponin T levels >0.1 mmol/L with corresponding electrocardiogram changes in the setting of chest pain.²² Cardiac mortality was defined as death due to heart failure related to CAD, sudden cardiac arrest, fatal myocardial infarction, or end-stage CAD.

Study endpoints

The primary outcome measure of the trial was the difference in the change in scores within the SAQ domains from baseline to 3 months

between the two cohorts. Longer term follow-up was conducted at 1 year. Secondary endpoints included the number of patient hospitalizations, MACEs, further investigations needed, and final CAD diagnoses.

Statistical analysis

The sample size was calculated in relation to the primary outcome, the change of the SAQ score at 3 months from baseline. The SAQ-UK is validated, but there was no definitive measure of longitudinal variation available during the initial phase of the study. This angina-specific instrument was developed in a similar way to the SF-36 generic quality-of-life instrument. Both SF-36 and SAQ domains are scored from 0 to 100, with 0 indicating maximum limitation and 100 no limitation. Because of the similarity between the SAQ-UK and SF-36, SF-36 was used to inform the standard deviation of the sample size calculation. It was therefore assumed that the standard deviation was of the order 20 units and a minimum detectable true difference as 6 units between the arms of the study. A sample size of 175 patients in each arm will have 80% power to detect the above-stated true difference in means using a two-group *t*-test with a 0.05 two-sided significance level. After adjusting for 30% dropout rate in a longitudinal study, 500 patients (250 patients in each arm) were recruited.

Post hoc power calculations showed that there was an 80% power to determine a true differential of 5.5 as statistically significant.

Frequency, percentage mean \pm standard deviation, and range (minimum to maximum) are used to summarize the variables as appropriate. For the analysis of percentage comparison within the groups, a Fishers Exact test was performed. The SAQ scores between the two groups were tested for statistically significant difference at baseline, 3, and 12 months. The difference in the change in SAQ scores from baseline at 3 months and 12 months was tested for statistical significance using independent *t*-test.²³ Fisher's exact test was also used to compare percentages of patients with further hospital appointments within the two cohorts.

Statistical analyses were performed using Stata/IC 12.0 and R 3.0.2 with an intention-to-treat approach. All the observations available at each time point were used in the analysis. All the statistical analyses were two tailed, and a *P*-value of <0.05 was considered as statistically significant.

Results

Demographics

Of the 500 patients with suspected CAD who were randomised, 9 did not receive the allocated test and 3 others withdrew after 3 months. This meant that 245 patients in the EST cohort and 243 in the CT cohort were followed up at the 1-year period, *Figure 1*. Baseline demographics are seen in *Table 1*.

Angina symptoms

The median scores of each SAQ domains at baseline, 3, and 12 months are shown in *Figure 2*. The change from baseline to the other time points can be seen in *Table 2*, highlighting patients' change in angina over time in both arms. The change in the score was significantly improved in the CT arm compared with the EST arm in the angina stability and quality-of-life domains at 3 and 12 months. This suggests that more patients in the CT arm compared with EST had an overall greater improvement in symptoms.

Results of clinical investigations

There were no complications after any investigation in this study.

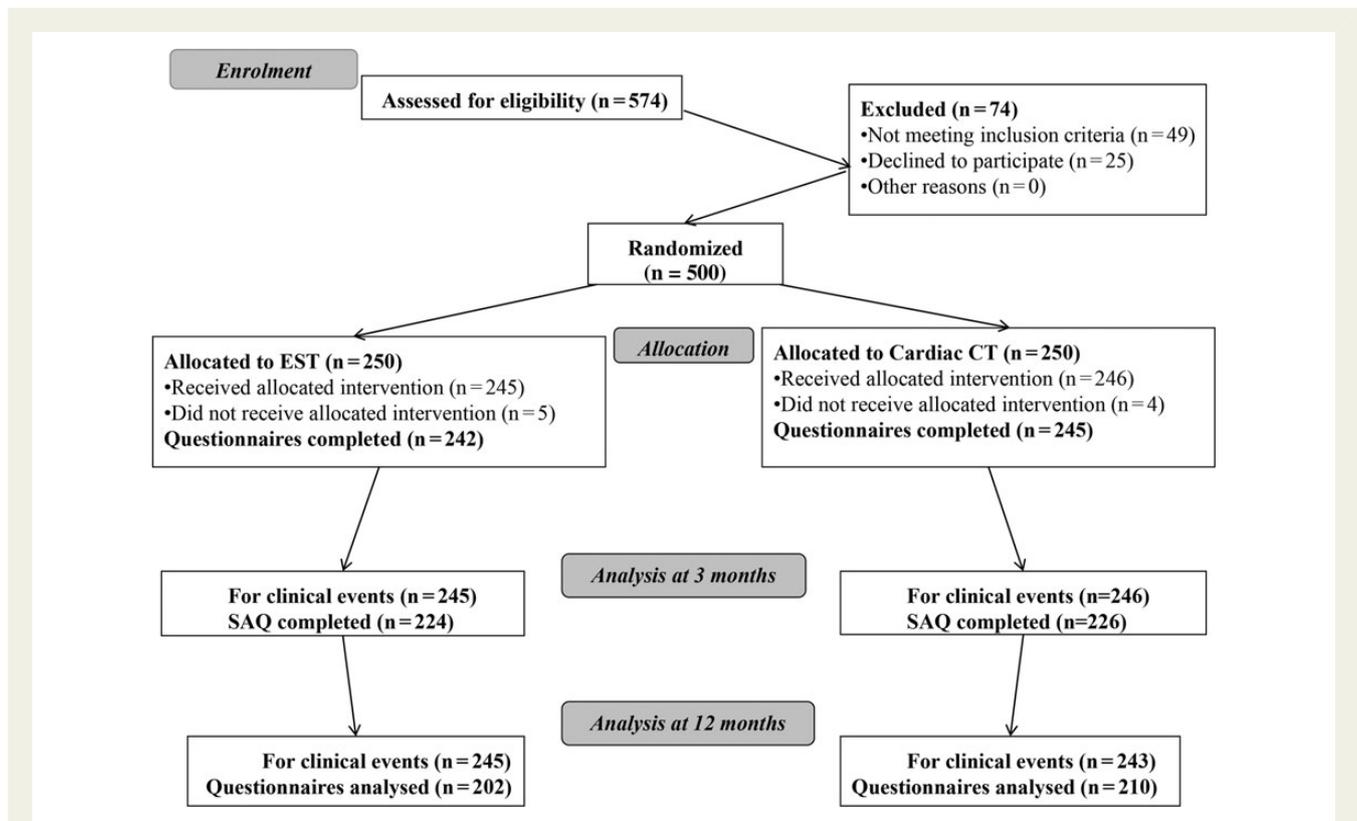


Figure 1 CONSORT flow diagram of trial.

Table 1 Baseline demographics

| Category | EST arm, Mean ± SD (n = 245) | CT arm, Mean ± SD (n = 243) | P-value |
|-------------------------------|------------------------------|-----------------------------|---------|
| Mean age | 58.9 ± 10.2 | 57.8 ± 10.0 | 0.22 |
| Mean BMI (kg/m ²) | 28.0 ± 3.6 | 27.8 ± 3.6 | 0.53 |
| Sex | 131 males | 138 males | 0.44 |
| Smoker | 47 | 46 | 0.93 |
| Diabetic | 12 | 14 | 0.68 |
| Known hypertensive | 73 | 77 | 0.53 |
| Mean cholesterol (mmol/L) | 5.4 ± 1.1 | 5.3 ± 1.1 | 0.49 |
| Diamond Forrester | | | |
| Overall % | 44.9 ± 30.2 | 47.8 ± 31.7 | 0.34 |
| No. of low risk (<30%) | 107 | 101 | 0.64 |
| No. of medium risk (30–60%) | 62 | 53 | 0.37 |
| No. of high risk (>60%) | 76 | 89 | 0.19 |
| Character of pain | | | |
| Non-angina | 156 (63.7%) | 143 (58.8%) | 0.28 |
| Atypical | 20 (8.2%) | 16 (6.6%) | 0.47 |
| Typical | 68 (27.8%) | 84 (34.6%) | 0.13 |
| Result of index investigation | | | |
| Positive | 47 | 73 | 0.0054 |
| Negative | 132 | 164 | 0.0021 |
| Inconclusive | 66 | 6 | <0.0001 |

EST, exercise stress electrocardiogram test; CT, computerized tomography.

In the EST arm, the mean exercise duration was 7 min 35 s (ranging from 1 min 33 s to 16 min 20 s). Overall, 47 were positive, 132 negative, and 66 inconclusive. In the CT arm, the mean CS was 172.2 ± 490.1 (ranging from 0 to 3901) with a median of 0. One hundred and twenty-six patients had a CS of zero; 92 had a score of 1–400, and 25 had a CS >400. CTCA demonstrated that 73 had significant disease, 58 had non-obstructive disease, 106 had no disease, and 6 were inconclusive due to either heart rate or breathing artefact. The mean effective radiation dose of the CT cohort was 5.37 mSv, with the EST arm receiving no radiation from their index test. Results of the index investigations are seen in Table 1.

Further investigations were carried out at the discretion of the managing physician. Overall in the EST arm, there were 128 further investigations performed and 72 in the CT (*P*-value ≤ 0.0001). The number of secondary tests in both arms is shown in relation to their initial test result in Table 3. In keeping with national guidelines,⁴ all 25 patients with a CS >400 were considered high risk and referred for ICA. Within in both arms, coronary revascularization may have occurred at the same time as ICA. Of note, only one of the scans with a CS >400 did not have significant disease at ICA.

Final CAD diagnosis and management strategy

Final CAD diagnosis and management strategies are shown in Table 3. In the CT arm, there were 29 PCI and 8 CABGs, meaning that there were 37 revascularizations in total, which was 15.2% of the cohort.

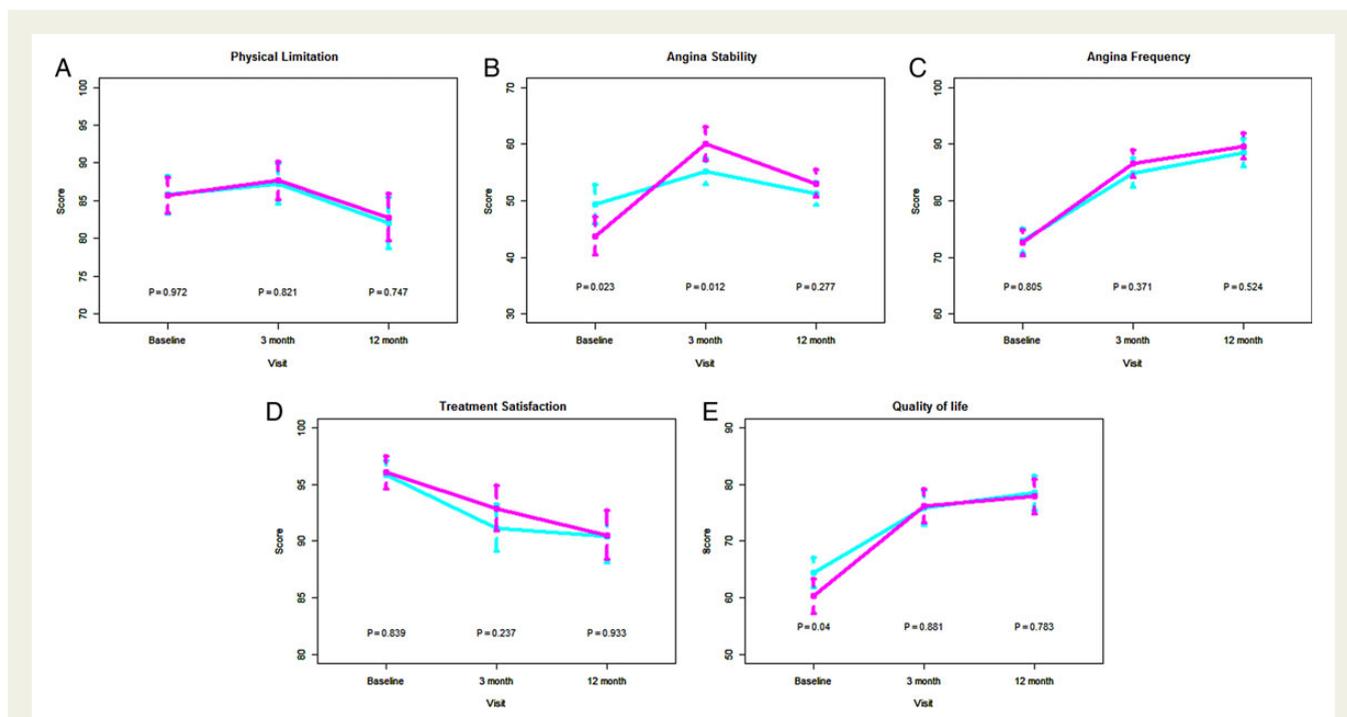


Figure 2 Summary statistics for the SAQ scores at baseline, 90 days, and 1 year.

Table 2 A comparison of the change in SAQ domain scores from baseline to 3 and 12 months

| SAQ subscales | Difference between CT and EST | | | |
|------------------------|--------------------------------------|---------|---------------------------------------|---------|
| | Difference from baseline to 3 months | | Difference from baseline to 12 months | |
| | Mean (95% CL) | P-value | Mean (95% CL) | P-value |
| Physical limitation | -0.54 (-4.3 to 3.3) | 0.779 | 0.33 (-4.3 to 5.0) | 0.889 |
| Angina stability | -11.1 (-17.4 to -4.8) | 0.001 | -6.8 (-12.8 to -0.7) | 0.028 |
| Angina frequency | -2.7 (-6.8 to 1.3) | 0.184 | -1.9 (-6.0 to 2.2) | 0.365 |
| Treatment satisfaction | -2.1 (-5.3 to 1.2) | 0.213 | -1.4 (-5.2 to 2.3) | 0.446 |
| Quality of life | -5.7 (-10.3 to -1.2) | 0.014 | -4.9 (-9.6 to -0.19) | 0.041 |

SAQ, Seattle Angina Questionnaire; CL, confidence limits.

In the EST arm, there were 12 PCI and 7 CABG, giving 19 revascularizations, which was 7.7% of the cohort. The average duration between enrolment and final management for all patients was 46.6 days. For those in the EST, the average duration was 67.0 days compared with 26.3 days in the CT (P -value < 0.0001). For those receiving intervention (PCI or CABG), the average wait in the EST arm was 167.7 days compared with 100.0 days in CT (P -value = 0.03818).

Clinical events and re-hospitalization

At 1 year, there was a single, non-cardiac death in both arms.

In the EST arm, there were 32 A&E chest pain attendances over the 1 year, 17 of which resulted in cardiac admission, with a total of 56 days in hospital. Of these 17, there were 2 with NSTEMI, 3 with unstable angina, and 12 with troponin-negative chest pain. The remaining

15 patients were discharged from the A&E with a diagnosis of troponin-negative chest pain.

In the CT arm, there were eight A&E chest pain attendances, two resulting in cardiac admission, with a total of 7 days in hospital. Of the two admitted, one was due to a NSTEMI and the other unstable angina. The other six patients were discharged from the A&E with a diagnosis of troponin-negative chest pain. There were also more cardiology outpatient attendances in the course of the year in the EST arm compared with CT arm, *Tables 3 and 4*.

Discussion

There are several main conclusions of this study. First, there was a significant difference in two SAQ domains within the CT arm compared

Table 3 The number of further tests, unplanned hospital attendances, and final diagnosis in relation to initial test results

| | Non-significant result from initial test | | Significant result from initial test | | Inconclusive result from initial test | |
|---------------------------------|--|---|--------------------------------------|-----------------------------------|---------------------------------------|---------------|
| | Negative EST (n = 132) | No CAD/non-obstructive on CT (n = 164) | Positive EST (n = 47) | Significant CAD on CT (n = 73) | EST (n = 66) | CT (n = 6) |
| Age | 56.8 | 54.8 | 63.7 | 64.6 | 59.8 | 56.2 |
| Number of males | 76 (57.6%) | 84 (51.2%) | 26 (55.3%) | 52 (71.2%) | 29 (43.9%) | 2 (33.3%) |
| Average Diamond Forrester, % | 39.3 | 37.6 | 58.5 | 67.6 | 50.7 | 32.0 |
| Further tests ordered | | | | | | |
| Total | 19 | 0 | 50 | 66 | 59 | 6 |
| MPI | 10 | | 11 | 5 | 39 | 1 |
| ICA | 4 | | 35 | 61 | 12 | 5 |
| CTCA | 5 | | 3 | | 8 | |
| DSE | | | 1 | | | |
| A&E attendances | 7 | 4 | 16 | 4 | 9 | 0 |
| Unplanned days in hospital | 7 | 3 | 43 | 4 | 6 | 0 |
| Final results | | | | | | |
| Non-obstructive CAD | 129 | 164 | 24 | 5 | 57 | 4 |
| Significant CAD | 3 | 0 | 23 | 68 | 9 | 2 |
| Management | | | | | | |
| CABG | 1 | 0 | 5 | 8 | 1 | 0 |
| PCI | 1 | 0 | 9 | 29 | 2 | 0 |
| Medical management | 3 | 58 | 17 | 35 | 15 | 6 |
| No intervention | 127 | 106 | 16 | 1 | 48 | 0 |

EST, exercise stress electrocardiogram test; CT, computerized tomography; MPI, myocardial perfusion imaging; CTCA, computerized tomography coronary angiography; ICA, invasive coronary angiography; A&E, Accident and Emergency Department; DSE, dobutamine stress echocardiography; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.

with the EST arm at 3 and 12 months, suggesting less angina within the CT arm. Secondly, one in four patients who attended the RACPC and received a conventional EST had an inconclusive result. Thirdly, patients in the EST arm needed more secondary tests to determine a diagnosis with physicians showing more confidence in a negative CT than a negative EST. Fourthly, although overall numbers were small, there was an increased rate of unplanned hospitalization and CAD events within the EST arm in comparison to the CT arm.

The SAQ is a well-established cardiovascular tool. It has been used in a number of large cardiovascular trials involving a wide range of cardiovascular interventions.^{24–27} In this study, the use of cardiac CT for stable chest pain statistically improved angina symptoms. Although the full prognostic implication of this study at this point is unknown, other studies suggest that SAQ scores can predict long-term mortality.^{28,29} Differences in SAQ scores have also been able to predict health economic impact, with Arnold et al.³⁰ concluding that patients with severe angina on SAQ scores had at least twice the cost resource utilization compared with those who were angina free. In a similar light, the improvement in SAQ scores in this study was associated with a decreased 1-year hospital re-attendance rate. This improvement in the SAQ scores seen in the CT arm is most likely linked to the greater identification of CAD and subsequent management in

those with CAD. However, it is also worth considering that earlier reassurance and not requiring secondary investigations may have eased health concerns in those patients without significant CAD. Psychosocial factors affect patients' chest pain symptoms³¹ and CAD mortality,³² with awaiting further interventions is itself a source of stress.³³

In the current context of increased health awareness, high referral rates, and financial constraints, it is more important than ever that patients are referred for investigation appropriately. CT is the cheapest CAD imaging test available within the NHS,³⁴ with a high negative predictive value.^{5–7} Previous studies have suggested a cost and clinical benefit for cardiac CT compared with non-invasive stress imaging modalities.^{35,36} Other studies have compared clinical benefits of EST and CT^{37–41} but not in a prospective, randomized controlled trial. In this study, only 6 (2.4%) in the CT arm had an initial inconclusive test compared with 66 (26.9%) in the EST arm, which is similar to other studies.⁴² Other work has suggested an increased risk of CAD event with un-diagnostic ESTs.⁴³ Our study highlighted an increased rate of secondary care referral, and unscheduled care admission in the EST assessment group as well as significantly less patients diagnosed with significant disease despite similar pre-test probabilities. There was also a significant difference in time between the cohorts

Table 4 The numbers of patients with further hospital re-attendances

| Number of visit | Number of patients | | P-value |
|--------------------------------|--------------------|-------------|---------|
| | EST | CT | |
| A&E visit leading to admission | | | 0.009 |
| 0 | 232 (94.7%) | 241 (99.2%) | |
| 1 | 10 (4%) | 2 (0.8%) | |
| 2 | 3 (1.2%) | 0 (0%) | |
| Total number of A&E visit | | | 0.025 |
| 0 | 223 (91.0%) | 235 (96.7%) | |
| 1 | 16 (6.4%) | 8 (3.2%) | |
| 2 | 3 (1.2%) | 0 (0%) | |
| 3 | 2 (0.8%) | 0 (0%) | |
| 4 | 1 (0.4%) | 0 (0%) | |
| Cardiology outpatient visit | | | 0.036 |
| 0 | 199 (81.2%) | 217 (89.3%) | |
| 1 | 38 (15.2%) | 24 (9.6%) | |
| 2 | 6 (2.4%) | 2 (0.8%) | |
| 3 | 2 (0.8%) | 0 (0%) | |

EST, exercise stress electrocardiogram test; CT, computerized tomography; A&E, Accident and Emergency Department.

management, which is obviously reflective of the waiting lists within the healthcare system. This time difference may potentially relate to more waiting for second investigations due to inconclusive EST and prompting to early ICA due to visualization of significant coronary lesions on the CT.

There are limitations in this study. First it was a single-centre study. Secondly, due to exclusion criteria of BMI and renal function, there were low numbers of diabetics in this study. Thirdly, this study was conducted in a high-volume CT centre and may not be reproducible in other centres. Fourthly, there is difficulty in contrasting the results of anatomical and functional tests. Those patients with normal EST, MPI, or DSE were classified as having no CAD, but this may not be the case, as there could be the presence of non-significant disease. However, in this study, and indeed in most clinical practice, those without functionally significant disease were treated as having no disease. Conversely, some CT patients with severe anatomical disease may have had intervention without definitive evidence of ischaemia proved through stress imaging or Fractional Flow Reserve (FFR). It could be argued that the cause of the patient's chest pain has not been definitively confirmed. However, this study reflects real-life clinical practice where despite the emergence of FFR, *quantitative coronary angiography* continues to drive revascularization, with all management decisions outside this trial. In everyday clinical practice, both anatomical and functional tests are used in chest pain assessment, with the choice depending on local policy, availability, and clinician expertise. In an ideal academic world, proved ischaemia would drive all elective revascularization, but this trial was a real-world study. Consequently, this study also highlights the danger of using CT. Fifthly, the study was powered to evaluate the difference in SAQ domains, not for prognosis or adverse CAD events. Subsequently, any difference in adverse events may be too small to be

statistically significant. Sixthly, all tests will have false-negative results, meaning patients with significant disease may have been under-diagnosed. However, this is true of all real-life studies and practice. Furthermore, in this study cardiac CT was used for all patients, regardless of pre-test probability. Guidelines suggest that it should be only used for low-risk patients.⁴ In addition, there were relatively high rates of high-risk patients, as defined by the same guidelines.⁴ However, our work is similar to others.^{44,45} Finally, due to the anatomical nature of the test, CT identified more patients with CAD, leading to increased revascularization and medical management. It must be stressed however that the clinical benefit or harm to these patients as well as economic benefit is unknown at this point. The long-term, cost-effectiveness benefit of cardiac CT as a primary imaging tool for stable chest pain patients compared with EST is also unknown. The CAPP study includes a cost utilization analysis, and a longer term follow-up will address this issue.

In conclusion, this study has shown that the use of CT in stable chest pain patients improves patients' symptoms through SAQ scores. The use of CT also reduces the number of 1-year hospital re-attendances. A longer term follow-up is needed to assess any potential economical and prognostic implications.

Conflict of interest: None declared.

Funding

This work was funded by the South Eastern Health and Social Care Trust (SET/10/52). This is a NHS Trust in Northern Ireland. It was also supported by the Northern Ireland Cardiovascular network.

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