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Exercise Electrocardiography and Computed Tomography Coronary Angiography for Patients With Suspected Stable Angina Pectoris
A Post Hoc Analysis of the Randomized SCOT-HEART Trial

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IMPORTANCE Recent European guidance supports a diminished role for exercise electrocardiography (ECG) in the assessment of suspected stable angina.

OBJECTIVE To evaluate the utility of exercise ECG in contemporary practice and assess the value of combined functional and anatomical testing.

DESIGN, SETTING, AND PARTICIPANTS This is a post hoc analysis of the Scottish Computed Tomography of the Heart (SCOT-HEART) open-label randomized clinical trial, conducted in 12 cardiology chest pain clinics across Scotland for patients with suspected angina secondary to coronary heart disease. Between November 18, 2010, and September 24, 2014, 4146 patients aged 18 to 75 years with stable angina underwent clinical evaluation and 1417 of 1651 (86%) underwent exercise ECG prior to randomization. Statistical analysis was conducted from October 10 to November 5, 2019.

INTERVENTIONS Patients were randomized in a 1:1 ratio to receive standard care plus coronary computed tomography (CT) angiography or to receive standard care alone. The present analysis was limited to the 3283 patients who underwent exercise ECG alone or in combination with coronary CT angiography.

MAIN OUTCOMES AND MEASURES The primary clinical end point was death from coronary heart disease or nonfatal myocardial infarction at 5 years.

RESULTS Among the 3283 patients (1889 men; median age, 57.0 years [interquartile range, 50.0-64.0 years]), exercise ECG had a sensitivity of 39% and a specificity of 91% for detecting any obstructive coronary artery disease in those who underwent subsequent invasive angiography. Abnormal results of exercise ECG were associated with a 14.47-fold (95% CI, 10.00-20.41; $P < .001$) increase in coronary revascularization at 1 year and a 2.57-fold (95% CI, 1.38-4.63; $P < .001$) increase in mortality from coronary heart disease death at 5 years or in cases of nonfatal myocardial infarction at 5 years. Compared with exercise ECG alone, results of coronary CT angiography had a stronger association with 5-year coronary heart disease death or nonfatal myocardial infarction (hazard ratio, 10.63; 95% CI, 2.32-48.70; $P = .002$). The greatest numerical difference in outcome with CT angiography compared with exercise ECG alone was observed for those with inconclusive results of exercise ECG (6 of 283 [2%] vs 18 of 283 [6%]), although this was not statistically significant (log-rank $P = .05$).

CONCLUSIONS AND RELEVANCE This study suggests that abnormal results of exercise ECG are associated with coronary revascularization and the future risk of adverse coronary events. However, coronary CT angiography more accurately detects coronary artery disease and is more strongly associated with future risk compared with exercise ECG.

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Editorial
Supplemental content

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Chest pain is one of the most common presenting symptoms for outpatients in contemporary medical practice. Determining whether chest pain is due to coronary artery disease (CAD) is imperative for directing appropriate symptomatic and preventive therapies.[1] Although taking a comprehensive history and performing a clinical assessment can be sufficient for some patients, further testing is often required to clarify the diagnosis.

Exercise electrocardiography (ECG) has historically been the mainstay of investigating chest pain in patients who are suspected to have CAD,[2-5] providing both diagnostic and prognostic information.[4,6-9] It has a specificity of 85% to 90% for detecting obstructive CAD, which is comparable to established stress imaging techniques, such as nuclear myocardial perfusion imaging, echocardiography, or magnetic resonance perfusion.[10-12] The weakness of exercise ECG lies in its low sensitivity. Abnormal results of exercise ECG have a sensitivity of 45% to 50% for obstructive CAD depending on the pretest probability,[10,13] and therefore exercise ECG has limited power to rule out CAD. For this reason, the 2019 European Society of Cardiology and 2016 National Institute for Health and Care Excellence guidelines recommend an imaging test in preference to an exercise ECG to detect or rule out CAD.[14,15] However, the American College of Cardiology and American Heart Association guidelines recommend noninvasive stress testing (exercise ECG) as the initial diagnostic test for patients with intermediate pretest risk who are able to exercise and have interpretable resting ECG results.[16] Exercise ECG is low cost, does not use ionizing radiation, and is widely accessible. As such, patient factors and local resources must be taken into account when choosing a test modality, which is reflected in the differences in these guidelines.[14-16] Finally, the guidelines also recognize the clinical and prognostic information that may be afforded by exercise ECG beyond its diagnostic performance alone.

Modern coronary computed tomography (CT) angiography has excellent accuracy for the detection of obstructive CAD, with a recent individual patient-level data meta-analysis reporting a sensitivity of 97% and a specificity of 86%.[17-19] A previous study has reported on the reproducibility and nondiagnostic rate of coronary CT angiography (5%).[20] Another study has highlighted higher nondiagnostic rates for 64-slice scanners compared with 320-slice scanners.[21] To our knowledge, CT angiography is the only imaging modality that has been associated with a reduction in myocardial infarction in randomized clinical trials.[22-25] Guidelines have increasingly advocated the use of coronary CT angiography for the investigation of chest pain, particularly in those who have possible angina, no previous CAD, and a lower clinical likelihood of obstructive CAD.[14,15,26]

The Scottish Computed Tomography of the Heart (SCOT-HEART) trial is an open-label, multicenter randomized clinical trial comparing standard care and standard care plus coronary CT angiography for patients with suspected angina pectoris due to coronary heart disease.[20,22] Standard care included exercise ECG for 79% of all participants (1632 of 2073). In this post hoc analysis, we reassess the diagnostic, therapeutic, and prognostic benefits associated with exercise ECG in contemporary clinical practice and assess the additional incremental value of combined functional and anatomical testing for patients with suspected angina pectoris due to coronary heart disease.

Key Points

Question What is the benefit of exercise electrocardiography in contemporary clinical practice?

Findings This post hoc analysis of a randomized clinical trial found that abnormal results of exercise electrocardiography were associated with a 14.47-fold increase in coronary revascularization and a 2.57-fold increase in mortality from coronary heart disease at 5 years or in cases of nonfatal myocardial infarction at 5 years. When combined with exercise electrocardiography, coronary computed tomography angiography had a stronger association with 5-year coronary events compared with exercise electrocardiography alone.

Meaning Although abnormal results of exercise electrocardiography are associated with coronary revascularization and future risk of adverse coronary events, coronary computed tomography angiography may identify additional undetected coronary artery disease and add to clinical decision-making and may be more strongly associated with future risk.

Methods

Study Design and Population

This is a post hoc analysis of the SCOT-HEART trial. The primary analysis and 5-year outcomes have been published previously.[20,22] Between November 18, 2010, and September 24, 2014, patients aged 18 to 75 years who had stable chest pain and who had been referred by a primary care physician to an outpatient cardiology clinic were eligible for inclusion. All patients underwent a routine clinical evaluation, including, if deemed appropriate, symptom-limited exercise ECG. The symptoms, provisional diagnosis, further investigations (stress imaging or invasive coronary angiography), and treatment strategy were documented at the end of the clinic visit, before recruitment and randomization. Patients were then randomly assigned in a 1:1 ratio to receive standard care plus coronary CT angiography or to receive standard care alone. The randomization incorporated the use of minimization to balance age, sex, body mass index (calculated as weight in kilograms divided by height in meters squared), diabetes, history of coronary heart disease, and atrial fibrillation. The present analysis was limited to the 3283 patients who underwent exercise ECG alone or in combination with coronary CT angiography. Ethical approval was acquired from the Health Research Authority Research Ethics Committee for the original SCOT-HEART trial, and written consent was obtained from all participants.

Investigations

Exercise ECG was performed using the Bruce protocol.[27] The testing regimen was adjusted to the patient's tolerance, aiming for 6 to 12 minutes of exercise and achieving at least 85%

of their maximum heart rate. Heart rate, blood pressure, and ECG results were obtained at baseline and during each stage of the protocol. Patients were questioned about any symptoms during exercise. Testing was terminated when the patients achieved their target heart rate or developed limiting symptoms, unequivocal ischemia, or an inappropriate blood pressure response. During recovery, patients were closely monitored with repeated observations until full recovery.[27]

Results of exercise ECGs were categorized as abnormal, inconclusive, or normal by the attending clinician. These categories were not independently adjudicated, and specific data regarding the exercise test findings, such as hemodynamic response, ST segment shift, or exercise time, were not recorded in the trial database. Coronary CT angiography was performed as a study procedure, as described previously.[20,22]

Obstructive CAD based on results of coronary CT angiography was defined as stenosis with a luminal cross-sectional area of more than 70% in a major epicardial vessel or more than 50% in the left main stem. Stenoses with a luminal cross-sectional area were classified as normal (<10%), nonobstructive (≥10 and ≤70%), or obstructive (>70%).

Invasive coronary angiograms were reported using the 15-segment model. Stenoses with a luminal cross-sectional area were classified as nonobstructive (≥10% and ≤70%) or obstructive (>70%). Prognostically significant CAD was defined as stenosis of the left main stem of more than 50%, obstructive 3-vessel disease, or 2-vessel disease including stenosis of the proximal left anterior descending coronary artery.

Treatments and Outcomes

All patients underwent clinical assessment and had documentation of their diagnosis, investigations, and treatment plan prior to trial randomization. Patient management was at the discretion of the attending clinician and was not protocolized. Additional functional imaging tests could include stress echocardiography, radionuclide myocardial perfusion imaging, or magnetic resonance myocardial perfusion imaging. Treatments included medical therapy, such as antiplatelet, statin, β-blocker, calcium channel blocker, and other antianginal therapies, as well as coronary angiography with a view to percutaneous coronary intervention.

At 6 weeks, clinicians were asked to review their diagnosis, investigations, and treatment plan in view of information from the coronary CT angiogram (exercise ECG plus coronary CT angiogram) or the cardiovascular risk score (exercise ECG alone). Alterations in diagnosis, investigation, and treatment were documented. The primary clinical end point was death from coronary heart disease or nonfatal myocardial infarction at 5 years.[20,22]

Statistical Analysis

Statistical analysis was conducted from October 10 to November 5, 2019. Categorical data are presented as frequencies, and continuous variables are presented as mean (SD) values or median (interquartile range) values. Comparisons between groups were made using a paired *t* test. End points were analyzed with the use of Cox proportional hazards regression models, adjusted for minimization variables (study group, age [>60 years], sex [male], body mass index [>30], diabetes, previous coronary heart disease, and atrial fibrillation). The cumulative event rate for the primary outcome was analyzed with Kaplan-Meier curves and the log-rank test. All analyses were performed with the use of R software, version 3.6.1 (R Foundation for Statistical Computing). All *P* values were from 2-sided tests, and results were deemed statistically significant at $P < .05$.

Results

Of the 4146 trial participants, 3283 (79%) underwent exercise ECG and had results available; these participants comprised the study population (**Table**; **Figure 1**). Half the study population (1651 [50%]) were randomized to undergo coronary CT angiography. Results of most exercise ECGs were normal (2188 [67%]), leaving 529 ECGs (16%) with abnormal results and 566 ECGs (17%) with inconclusive results.

Diagnosis of Coronary Artery Disease

Of the 1651 patients randomized to undergo coronary CT angiography, 1417 (86%) underwent CT. For those with normal results of exercise ECG (925 [65%]), more than half had either obstructive (137 [15%]) or nonobstructive (379 [41%]) CAD detected on CT angiography scans (eFigure 1 and eTable 1 in the Supplement). Conversely, of 349 patients with obstructive CAD, 137 (39%) had a normal exercise ECG.

In total, 768 of 3283 patients underwent invasive coronary angiography (eTable 2 in the Supplement). Obstructive disease was identified more frequently in those with abnormal results of exercise ECG, with a similar prevalence in both study groups. However, those with normal or inconclusive results of exercise ECG were more likely to have obstructive disease identified in the coronary CT angiography group (88 of 112 patients [79%]) compared with those in the standard care group (47 of 197 patients [24%]) (eTable 2 in the Supplement). For those who underwent invasive coronary angiography, abnormal results of exercise ECG had a sensitivity of 39%, a specificity of 91%, a positive predictive value of 58%, and a negative predictive value of 82% for detecting any obstructive CAD and a sensitivity of 77%, a specificity of 86%, a positive predictive value of 38%, and a negative predictive value of 96% for detecting prognostically significant obstructive CAD.

Treatment

Participants with abnormal results of exercise ECG were more likely than those with inconclusive or normal results to be recieving antiplatelet therapy (494 of 529 [93%] vs 386 of 566 [68%] vs 685 of 2188 [31%]) and statin therapy (463 of 529 [88%] vs 342 of 566 [60%] vs 599 of 2188 [27%]) at baseline, regardless of study allocation (Table). Participants with normal or inconclusive results of exercise ECG were more likely to start antiplatelet therapy than those with an abnormal result (170 of 2188 [8%] vs 26 of 566 [5%] vs 2 of 529 [0.4%]; $P < .001$) and statin therapy (190 of 2188 [9%] vs 33 of 568 [6%] vs 5 of 529 [1%]; $P < .001$). Rates of initiation and discontinuation of preventive therapy and referral for invasive coronary angiogra-

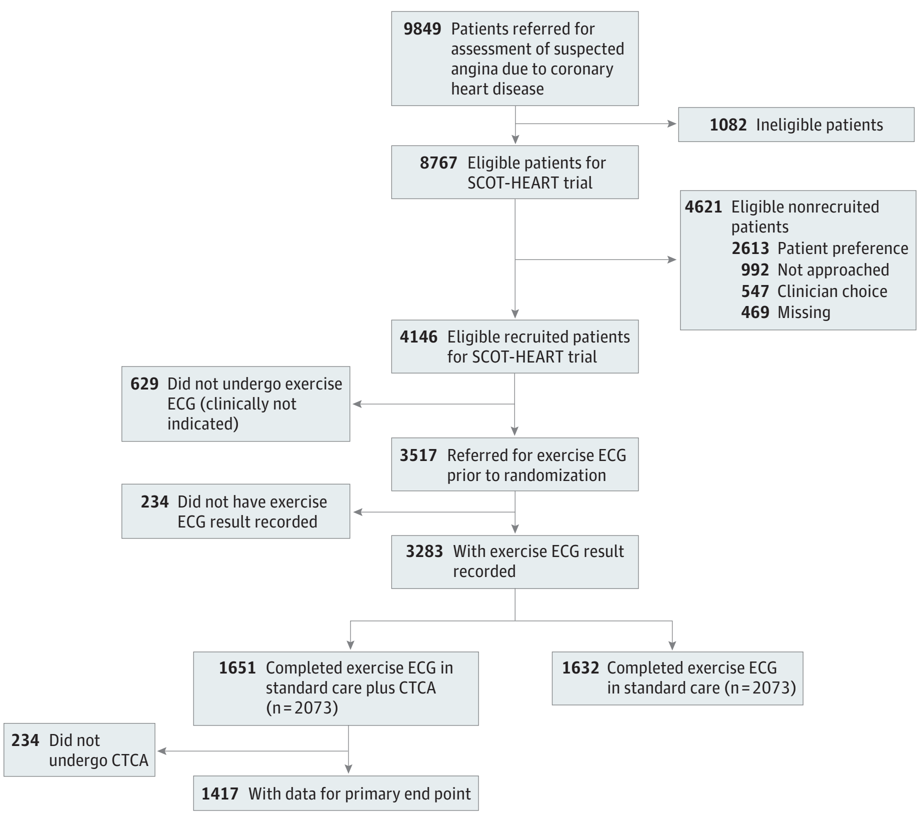
Table. Baseline Characteristics of Patients Stratified by Exercise ECG Outcome

Characteristic	Patients, No. (%) Exercise ECG outcome Abnormal (n = 529)	Inconclusive (n = 566)	Normal (n = 2188)	Overall (N = 3283)	*P* value
Male sex	367 (69)	299 (53)	1223 (56)	1889 (58)	<.001
Age, median (IQR), y	62.0 (56.0-67.0)	60.0 (53.0-66.0)	55.0 (48.0-62.0)	57.0 (50.0-64.0)	
Hypertension	197 (37)	229 (40)	698 (32)	1024 (31)	<.001
Hyperlipidemia	487 (92)	400 (71)	1028 (47)	1915 (58)	<.001
Diabetes	67 (13)	72 (13)	1988 (91)	327 (10)	.001
Previous CHD	70 (13)	63 (11)	148 (7)	281 (9)	<.001
Family CHD	195 (37)	265 (47)	895 (41)	1355 (41)	.004
Smoking status[a]	248 (47)	358 (63)	1105 (51)	1711 (52)	<.001
Previous CVD	18 (3)	28 (5)	59 (3)	105 (3)	.03
Previous PVD	2 (0.4)	14 (2)	15 (1)	31 (1)	<.001
Chest pain diagnosis					
Nonanginal	29 (5)	109 (9)	1206 (55)	1344 (41)	<.001
Atypical angina	78 (15)	197 (35)	506 (23)	781 (24)	
Typical angina	422 (80)	260 (46)	476 (22)	1158 (35)	
Baseline antiplatelet therapy	494 (93)	386 (68)	685 (31)	1565 (48)	<.001
Baseline statin therapy	463 (88)	342 (60)	599 (27)	1404 (43)	<.001

Abbreviations: CHD, coronary heart disease; CVD, cerebrovascular disease; ECG, electrocardiography; IQR, interquartile range; PVD, peripheral vascular disease.

[a] Current smoker and ex-smokers.

Figure 1. CONSORT Diagram: Study Population

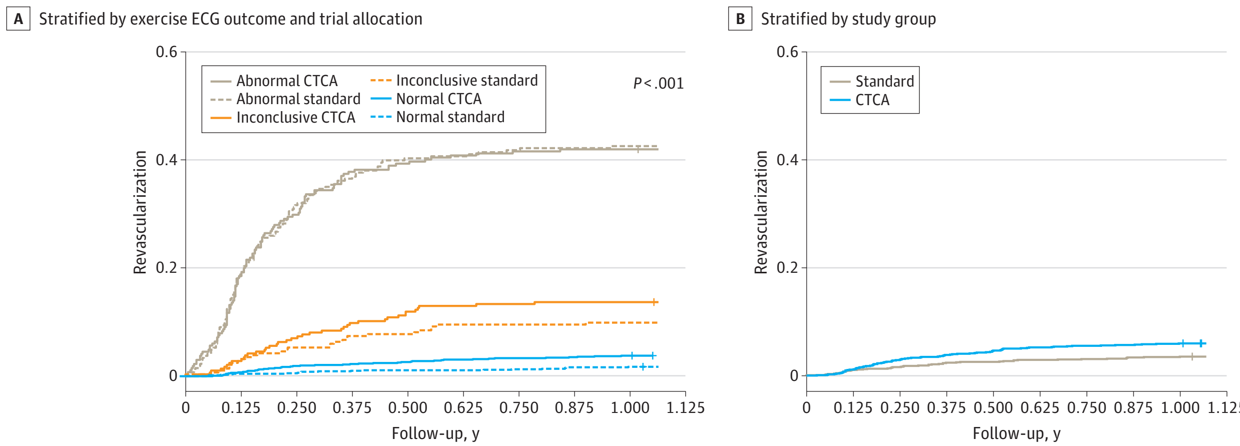


CTCA indicates computed tomography coronary angiography; ECG, electrocardiography; and SCOT-HEART, Scottish Computed Tomography of the Heart.

phy were higher among patients who underwent coronary CT angiography compared with those who received only standard care, particularly among those who had inconclusive or normal results of exercise ECG (eTable 3 in the Supplement).

Compared with normal results of exercise ECG, abnormal results (hazard ratio [HR], 14.47; 95% CI, 10.00-20.41; $P < .001$) or inconclusive results (HR, 3.23; 95% CI, 2.08-5.00; $P < .001$) of exercise ECG were associated with coronary revasculariza-

Figure 2. Cumulative Incidence of Coronary Revascularization



No. at risk					
Abnormal CTCA	264	185	160	154	153
Abnormal standard	265	181	158	154	152
Inconclusive CTCA	284	264	250	246	245
Inconclusive standard	282	267	260	255	254
Normal CTCA	1103	1083	1074	1066	1061
Normal standard	1085	1079	1073	1071	1066

No. at risk					
Standard	1367	1346	1333	1326	1320
CTCA	1387	1347	1324	1312	1306

A, At 1 year stratified by exercise electrocardiography (ECG) outcome (normal, inconclusive, and abnormal) and trial allocation (standard of care and standard of care plus computed tomography coronary angiography (CTCA). B, At 1 year for combined inconclusive and normal exercise electrocardiography stratified by study group (standard of care [standard] and standard of care plus CTCA).

tion at 1 year regardless of study allocation (eFigure 2 and eTable 4 in the Supplement). In a separate multivariable model, obstructive CAD detected on coronary CT angiography scans (HR, 1.70; 95% CI, 1.47-1.97; $P < .001$) and nonobstructive CAD detected on coronary CT angiography scans (HR, 1.17; 95% CI, 1.04-1.33; $P = .01$) were also associated with coronary revascularization at 1 year (eTable 5 in the Supplement).

At 1 year, there was little difference between the 2 study groups in the number of patients with abnormal results of exercise ECG who underwent revascularization (**Figure 2**A). In a combined analysis of those with normal or inconclusive results of exercise ECG, coronary revascularization was more frequently performed for those undergoing coronary CT angiography compared with those undergoing exercise ECG alone (81 of 1387 patients [6%] vs 47 of 1367 patients [3%]; $P = .002$; Figure 2B).

Clinical Outcomes

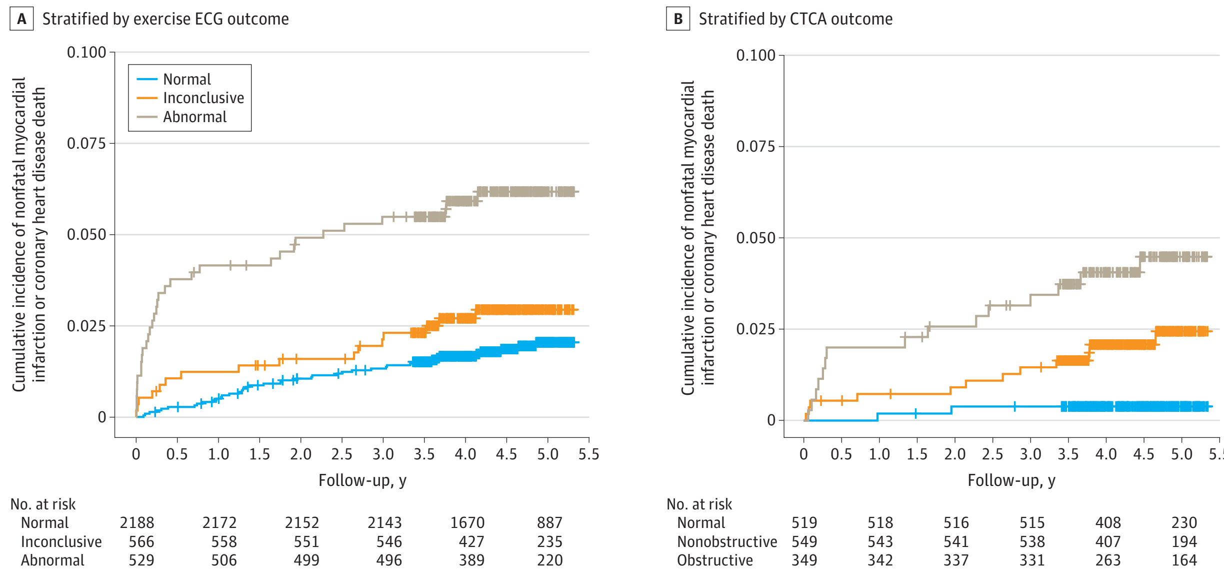
On multivariable Cox proportional hazards regression modeling, patients with abnormal results of exercise ECG had a stronger association with coronary heart disease death or nonfatal myocardial infarction at 5 years compared with those with normal or inconclusive results of exercise ECG, irrespective of study allocation (HR, 2.57; 95% CI, 1.38-4.63; $P < .001$) (**Figure 3**; eTable 6 in the Supplement). However, most events occurred among patients with normal or inconclusive results of exercise ECG (60 of 92 events [65%]) (eTable 7 in the Supplement).

In a separate model examining CT findings, compared with those with normal coronary arteries, the presence of obstructive CAD (HR, 10.63; 95% CI, 2.32-48.70; $P = .002$) or nonobstructive CAD (HR, 5.32; 95% CI, 1.16-24.40; $P = .03$) was strongly associated with death from CAD at 5 years or nonfatal myocardial infarction at 5 years (Figure 3; eTable 8 in the Supplement). There were numerically fewer events with coronary CT angiography compared with exercise ECG alone for those who had abnormal or inconclusive results of exercise ECG (19 of 549 patients [3%] vs 31 of 549 patients [6%]). The difference was most apparent for those with inconclusive results of exercise ECG, although the interaction between groups did not reach statistical significance (inconclusive results: coronary CT angiography, 5 of 285 [2%] vs exercise ECG alone, 13 of 283 [6%]; $P = .05$; abnormal results: coronary CT angiography, 14 of 264 [5%] vs exercise ECG alone, 18 of 266 [7%]; $P = .32$) (**Figure 4**; eTable 7 in the Supplement).

Discussion

In this post hoc analysis of the SCOT-HEART trial, we have demonstrated that abnormal results of exercise ECG remain a specific indicator of obstructive CAD and are associated with future coronary revascularization and risk of myocardial infarction. However, for the large proportion of participants with normal or inconclusive results of exercise ECG, there is a significant amount of unrecognized nonobstructive and obstructive CAD. This finding is consistent with a large body of previous evidence reporting low diagnostic sensitivity for exercise ECG.[2-4] In contrast, coronary CT angiography appears to be associated with greater changes in preventive therapies and improvements in outcomes; this finding is supported by prior SCOT-HEART data that demonstrated improved coronary heart disease outcomes with CT angiography by enabling better targeting of preventive treatments to those with

Figure 3. Cumulative Incidence of Coronary Heart Disease Death or Nonfatal Myocardial Infarction



A, Stratified by exercise electrocardiography (ECG) outcome (normal, inconclusive, and abnormal). B, Stratified by computed tomography coronary angiography (CTCA) outcome (normal, nonobstructive, and obstructive).

CAD, with the potential for cost saving.[28,29] This benefit of CT angiography was most evident among those with inconclusive or normal results of exercise ECG. Overall, an exercise ECG generally serves the clinician well for risk stratification and the selection of patients for coronary revascularization when results are abnormal, but for most patients without abnormal results of exercise ECG, coronary CT angiography provides additional information regarding the presence of CAD, the need for preventive treatments, and the potential for improved long-term clinical outcomes.

The debate continues regarding the relative benefits of functional and anatomical testing in the diagnosis and management of patients presenting with stable chest pain. As we have shown here, both approaches have strengths and limitations, and the selection of the appropriate strategy is critically dependent on the purpose of the test. If the purpose is to establish the reproducibility, severity, and consequences of exercise-induced chest pain symptoms, a functional test may be appropriate. However, the addition of anatomical imaging improves the ability to establish the presence, severity, and prognostic importance of CAD.

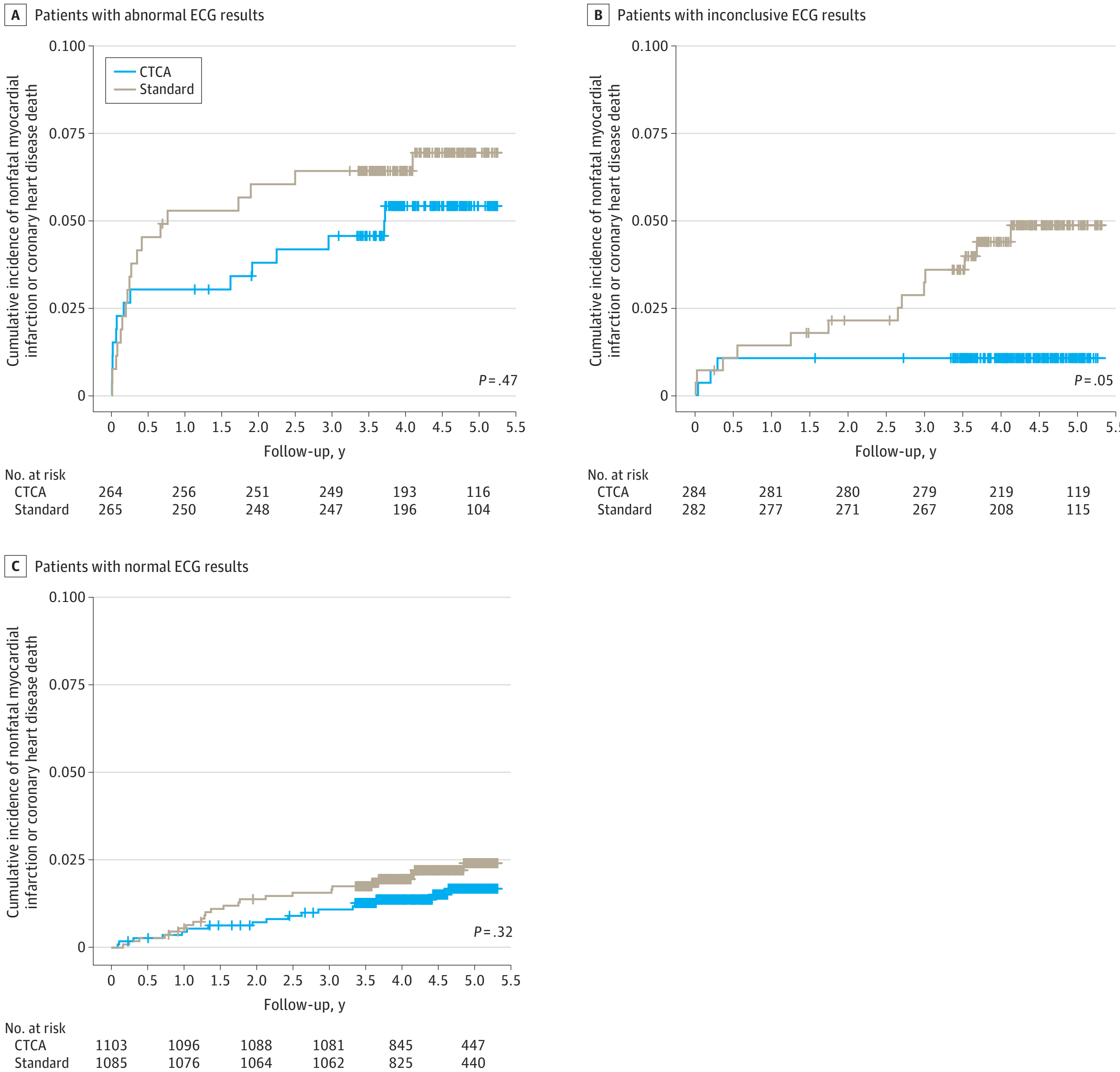
The added benefit of coronary CT angiography after exercise ECG is most apparent for patients with inconclusive results of exercise ECG, for whom coronary CT angiography provides clarity in detecting CAD and thereby in improving therapeutic decisions. More important, the 2019 European Society of Cardiology guidelines[14] and the 2012 American Heart Association guidelines[16] encourage the use of coronary CT angiography if noninvasive testing is contraindicated or if results are inconclusive. Our data support this recommendation, in keeping with prior reports that coronary CT angiography increases the certainty of the diagnosis of CAD for patients with chest pain despite prior exercise ECG.[20,22,28-32]

It is important to discriminate between nonobstructive CAD, obstructive CAD, and angina pectoris secondary to CAD.[33,34] Although functional testing can only assist in the diagnosis of the latter 2 conditions,[35-40] a strength of functional testing is the objective assessment of the reproducibility and severity of symptoms.[9,41,42] This strength underlies our finding that abnormal results of exercise ECG were associated with a 14.47-fold increase in coronary revascularization, which was not associated with coronary CT angiography. However, coronary CT angiography was associated with increased rates of coronary revascularization for those with normal or inconclusive results of exercise ECG, associated with its greater sensitivity for detecting CAD.[2,11,20,23,26,43]

Our data also show that exercise ECG is valuable in the risk stratification of patients with chest pain, in keeping with a large body of both historic and contemporary data.[4,12,44] Compared with patients with normal results of exercise ECG, those with abnormal results of exercise ECG had a 2.57-fold increased risk of death from coronary heart disease or nonfatal myocardial infarction. Similarly, in the Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) trial, severely abnormal results of functional testing were associated with a 2.13-fold increase in the risk of cardiovascular death or myocardial infarction.[9,25,26,45] However, we found that coronary CT angiography was associated with improved prognostic discrimination because patients with obstructive CAD had an 10.63-fold increased risk of death from coronary heart disease or of nonfatal myocardial infarction compared with those with normal coronary arteries. This finding is also consistent with the finding from the PROMISE trial.[9,25,45,46]

Unlike other trials,[25,47] the SCOT-HEART trial did not undertake a head-to-head comparison of functional and

Figure 4. Cumulative Incidence of Coronary Heart Disease Death or Nonfatal Myocardial Infarction



A, Patients with abnormal electrocardiography (ECG) results by treatment allocation (standard of care [standard] and standard of care plus computed tomography coronary angiography [CTCA]. B, Patients with inconclusive ECG results by treatment allocation. C, Patients with normal ECG results by treatment allocation.

anatomical testing. Instead, it assessed the additional benefit of coronary CT angiography to the contemporaneous standard of care, which included exercise ECG testing for most patients.

Limitations

We acknowledge a number of limitations of our analysis. First, this was a post hoc analysis of the SCOT-HEART trial, and our present findings are thus hypothesis generating. Second, as a pragmatic trial, exercise ECGs were classified by the attending clinician, and there was no core laboratory or independent review of the test findings. We therefore recognize that there is the potential for misclassification, although the proportion of inconclusive test results is compatible with prior studies,[48] and the classification of the exercise ECG was performed prior to study randomization, minimizing the risk of bias. Furthermore, we believe that this represents real-life clinical practice in which clinicians diagnose and care for patients based on their interpretation of clinical history, examination, and test results. Third, exercise ECG was not performed for all patients and was not randomized, which creates potential for selection bias; consequently, these data cannot directly compare the effectiveness of functional vs anatomical testing. Nevertheless, our trial design does allow us to explore the extent of CAD in those who underwent exercise ECG but did not undergo invasive coronary angiography, something that other trials have been unable to provide. Fourth, patients who underwent coronary CT angiography had their treatments changed and had higher levels of secondary preventive therapy. Therefore, our risk estimates for coronary CT angiography are conservative and may have been even greater if patients had not had preventive therapies initiated. Fifth, the size of some subgroups was small and limited our ability to make firm conclusions regarding the identification of those who might benefit most from coronary CT angiography after exercise ECG.

Conclusions

Exercise ECG remains a useful functional assessment for the identification of symptomatic obstructive CAD. An abnormal test result is strongly associated with coronary revascularization and adverse outcomes. However, for a large proportion of patients who undergo exercise ECG, coronary CT angiography detects unrecognized CAD, better informs allocation of therapies, and is strongly associated with risk of myocardial infarction, particularly for those with normal or inconclusive results of exercise ECG.

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Concept and design: Bing, Dweck, Mills, Williams, Villines, Newby, Adamson.
Acquisition, analysis, or interpretation of data: Singh, Bing, van Beek, Mills, Williams, Villines, Newby, Adamson.
Drafting of the manuscript: Singh, Bing.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Singh, Bing, Villines, Adamson.
Obtained funding: Newby.
Administrative, technical, or material support: van Beek, Newby.
Supervision: Dweck, van Beek, Mills, Newby, Adamson.

Conflict of Interest Disclosures: Dr van Beek reported receiving grants from the Chief Scientist Office, Scotland, during the conduct of the study; personal fees from Aidence and Mentholatum; nonfinancial support from Imbio and Siemens Healthineers; and being the founder of Quantitative Clinical Trials Imaging Services, Inc, outside the submitted work. Dr Mills reported that The University of Edinburgh has received research grants from Abbott Diagnostics and Siemens Healthineers; in addition, Dr Mills reported receiving honoraria from Abbott Diagnostics, Siemens Healthineers, and Roche Diagnostics. No other disclosures were reported.

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