ORIGINAL ARTICLE

Coronary CT Angiography and 5-Year Risk of Myocardial Infarction

The SCOT-HEART Investigators*

ABSTRACT

BACKGROUND

Although coronary computed tomographic angiography (CTA) improves diagnostic certainty in the assessment of patients with stable chest pain, its effect on 5-year clinical outcomes is unknown.

METHODS

In an open-label, multicenter, parallel-group trial, we randomly assigned 4146 patients with stable chest pain who had been referred to a cardiology clinic for evaluation to standard care plus CTA (2073 patients) or to standard care alone (2073 patients). Investigations, treatments, and clinical outcomes were assessed over 3 to 7 years of follow-up. The primary end point was death from coronary heart disease or nonfatal myocardial infarction at 5 years.

RESULTS

The median duration of follow-up was 4.8 years, which yielded 20,254 patient-years of follow-up. The 5-year rate of the primary end point was lower in the CTA group than in the standard-care group (2.3% [48 patients] vs. 3.9% [81 patients]; hazard ratio, 0.59; 95% confidence interval [CI], 0.41 to 0.84; P=0.004). Although the rates of invasive coronary angiography and coronary revascularization were higher in the CTA group than in the standard-care group in the first few months of follow-up, overall rates were similar at 5 years: invasive coronary angiography was performed in 491 patients in the CTA group and in 502 patients in the standard-care group (hazard ratio, 1.00; 95% CI, 0.88 to 1.13), and coronary revascularization was performed in 279 patients in the CTA group and in 267 in the standard-care group (hazard ratio, 1.07; 95% CI, 0.91 to 1.27). However, more preventive therapies were initiated in patients in the CTA group (odds ratio, 1.40; 95% CI, 1.19 to 1.65), as were more antianginal therapies (odds ratio, 1.27; 95% CI, 1.05 to 1.54). There were no significant between-group differences in the rates of cardiovascular or noncardiovascular deaths or deaths from any cause.

CONCLUSIONS

In this trial, the use of CTA in addition to standard care in patients with stable chest pain resulted in a significantly lower rate of death from coronary heart disease or nonfatal myocardial infarction at 5 years than standard care alone, without resulting in a significantly higher rate of coronary angiography or coronary revascularization. (Funded by the Scottish Government Chief Scientist Office and others; SCOT-HEART ClinicalTrials.gov number, NCT01149590.)

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Patients with stable chest pain suggestive of coronary heart disease can be evaluated with a variety of noninvasive stress tests that incorporate electrocardiography, radionuclide scintigraphy, echocardiography, or magnetic resonance imaging.[1-6] Over the past 50 years or more, these techniques have been shown to be useful in assisting with the diagnosis of coronary heart disease, as well as in providing important prognostic information. As such, they are the focus of current international guidelines for the assessment of patients with stable chest pain.[4-6]

Coronary computed tomographic angiography (CTA) is increasingly being used to assess patients with stable chest pain because it has high sensitivity and specificity for the detection of coronary heart disease.[7,8] In the Scottish Computed Tomography of the Heart (SCOT-HEART) trial,[9] we previously found that among patients who had been referred to a cardiology clinic with stable chest pain, CTA clarified the diagnosis and altered subsequent investigations and treatments.[9] Subsequent post hoc analyses showed that the use of CTA in addition to standard care resulted in better clinical outcomes than standard care alone.[10] The Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) also involved patients with symptoms suggestive of coronary heart disease who underwent further noninvasive testing.[11,12] In a head-to-head comparison of functional testing with CTA, no significant difference in clinical outcomes was observed.

Both the SCOT-HEART and PROMISE trials followed patients for a relatively short time (20 to 22 months), and the longer-term effects on coronary heart disease events are unknown. We now report the 5-year clinical outcomes of the SCOT-HEART trial[13] to determine the effect of CTA on longer-term investigations, treatments, and clinical events.

METHODS

TRIAL DESIGN AND OVERSIGHT

This open-label, randomized, controlled, parallel-group trial was performed at 12 centers across Scotland. The trial, which has been described previously,[9,10,13] was conducted with the approval of the South East Scotland Research Ethics Committee. The protocol, available with the full text of this article at NEJM.org, was designed by the grant applicants with input from the trial steering committee (see the Supplementary Appendix, available at NEJM.org).

The funders had no role in the design or conduct of the trial or in the collection, analysis, or reporting of data. The steering committee vouches for the accuracy and completeness of the data and the analyses and for the fidelity of the trial to the protocol.

PATIENT POPULATION AND RANDOMIZATION

Patients 18 to 75 years of age who had stable chest pain and who had been referred by a primary care physician to an outpatient cardiology clinic were eligible for inclusion.[9,10,13] Exclusion criteria are listed in the Supplementary Appendix. All participants provided written informed consent.

All patients underwent a routine clinical evaluation, including, if deemed appropriate, symptom-limited exercise electrocardiography. The symptoms, diagnosis, further investigations (stress imaging or invasive coronary angiography), and treatment strategy were documented at the end of the clinic visit, before recruitment or randomization. Patients were then randomly assigned in a 1:1 ratio to standard care plus CTA or to standard care alone; randomization was performed with the use of a Web-based system to ensure concealment of group assignment. The randomization incorporated the use of minimization to balance age, sex, body-mass index, diabetes mellitus, history of coronary heart disease, and atrial fibrillation.

SUBSEQUENT INVESTIGATIONS AND TREATMENTS

Management of the patient's condition in the light of all available information was at the discretion of the attending clinician. Physicians caring for patients in the CTA group were prompted to consider the results of the CTA in their management decisions, and physicians caring for patients in the standard-care group were prompted to consider a prespecified cardiovascular risk score (the ASSIGN score, which ranges from 1 to 99, with higher scores indicating a higher risk of cardiovascular disease[14]) in their management decisions (additional details are provided in the Supplementary Appendix). Specifically, when there was evidence of nonobstructive (10 to 70% cross-sectional luminal stenosis) or obstructive coronary artery disease on the CTA, or when a patient had an ASSIGN score of 20 or higher, the

attending clinician and primary care physician were prompted by the trial coordinating center to prescribe preventive therapies (e.g., aspirin and a statin).[13]

CLINICAL FOLLOW-UP

There were no trial-specific visits, and all follow-up information was obtained from data collected routinely by the Information and Statistics Division and the electronic Data Research and Innovation Service of the National Health Service (NHS) Scotland, as described previously.[9,10] (Additional information is provided in the Supplementary Appendix.) The inpatient and day-case national data set contains episode-level data from all hospitals in Scotland, for events that occurred in Scotland or that occurred outside Scotland but resulted in a transfer to a hospital in Scotland. These data include diagnostic codes from discharge records, which were classified according to the *International Classification of Diseases, 10th Revision*, and procedural codes from the Classification of Interventions and Procedures of the Office of Population Censuses and Surveys, as described previously.[9,10,15-17]

CLINICAL END POINTS

The clinical end points that were assessed included death (cardiovascular death, noncardiovascular death, death from coronary heart disease, and death from any cause), myocardial infarction, and stroke. The primary end point was death from coronary heart disease or nonfatal myocardial infarction. There was no formal event adjudication, and end points were classified primarily on the basis of diagnostic codes. However, in cases of uncertainty, events and causes of death were categorized by two of the authors, who were unaware of the trial assignments.[9]

PROCESS-OF-CARE END POINTS

Rates of invasive coronary angiography and coronary revascularization (including percutaneous coronary intervention and coronary-artery bypass grafting) were obtained from records of inpatient and day-case episodes and were cross-checked by review of individual coronary angiograms within the national Picture Archiving and Communications Systems.[9,10] Documentation of patients' medications was obtained from the Scottish National Prescribing Information System of the Information and Statistics Division of NHS Scotland (see the Supplementary Appendix).[10]

STATISTICAL ANALYSIS

The original primary end point of the trial was the proportion of patients who received a diagnosis of angina pectoris caused by coronary heart disease at 6 weeks.[9] However, because we acknowledged the potential long-term clinical consequences of a change in diagnosis, our prespecified primary long-term end point was the proportion of patients who died from coronary heart disease or had a nonfatal myocardial infarction at 5 years.[13] On the basis of an estimated 5-year event rate of 13.1%, we hypothesized that the trial would have 80% power to detect a rate of the primary long-term end point that was 2.8 percentage points lower in the CTA group than in the standard-care group. A two-sided P value of less than 0.05 was considered to indicate statistical significance.[13]

All analyses were performed according to the intention-to-treat principle. Missing data were removed from the analyses, except for data on deaths, which were censored at the time the patient was lost from the trial. End points were analyzed with the use of Cox regression models, adjusted for center and minimization variables, and cumulative event curves were constructed. We also performed a post hoc 12-month landmark analysis, since we reasoned that any changes in the use of invasive coronary angiography and the incidence of coronary revascularization that were driven by the results of CTA should have been observed by this time point.

Data are reported as means and standard deviations, medians and interquartile ranges, and hazard ratios or odds ratios with 95% confidence intervals, as appropriate. Because there was no adjustment for multiplicity in the analysis of secondary end points, results are reported as point estimates and 95% confidence intervals. The confidence intervals have not been adjusted for multiplicity, so intervals should not be used to infer definitive treatment effects. All analyses were performed with the use of R software, version 3.4.3 (R Foundation for Statistical Computing). Anonymized data and R code used in the statistical analysis will be made available on request.

RESULTS

TRIAL PARTICIPANTS AND FOLLOW-UP

From November 2010 through September 2014, we recruited 4146 patients with stable chest pain at 12 cardiology centers across Scotland (Fig. S1 in the Supplementary Appendix). Baseline clinical characteristics (Table 1), CTA findings, the influence of each assigned strategy on diagnostic certainty, and subsequent initial management have been reported previously[9,10] (see also Tables S1 through S3 in the Supplementary Appendix). Among patients who remained registered in Scotland throughout the trial (4080 patients [98.4%]), no patient withdrew consent, and we had complete data over a median of 4.8 years (3 to 7 years of follow-up) in both trial groups, comprising 20,254 patient-years of follow-up through January 31, 2018.

SUBSEQUENT MANAGEMENT

During follow-up, patients assigned to CTA were more likely than patients assigned to standard care alone to have commenced preventive therapies (19.4% [402 patients] vs. 14.7% [305 patients]; odds ratio, 1.40; 95% confidence interval [CI], 1.19 to 1.65) and antianginal therapies (13.2% [273 patients] vs. 10.7% [221 patients]; odds ratio, 1.27; 95% CI, 1.05 to 1.54). The overall differences in prescribing persisted over 5 years (Table S4 in the Supplementary Appendix).

At 5 years, there was no difference between the groups in the frequency of invasive coronary angiography; the procedure was performed in 491 patients (23.6%) in the CTA group and in 502 patients (24.2%) in the standard-care group (hazard ratio, 1.00; 95% CI, 0.88 to 1.13) (Fig. 1A). Although we had previously seen a trend toward a higher rate of early coronary revascularization in the group assigned to CTA,[9] there was no difference in the frequency of coronary revascularization between the groups at 5 years; this procedure was performed in 279 patients (13.5%) in the CTA group and in 267 (12.9%) in the standard-care group (hazard ratio, 1.07; 95% CI, 0.91 to 1.27) (Fig. 1B). Beyond the first 12 months, patients assigned to CTA had lower rates of invasive coronary angiography than patients who received standard care alone (hazard ratio, 0.70; 95% CI, 0.52 to 0.95), as well as lower rates of coronary revascularization (hazard ratio, 0.59; 95% CI, 0.38 to 0.90) (Fig. S2 in the Supplementary Appendix).

CLINICAL END POINTS

The rate of the primary long-term end point (death from coronary heart disease or nonfatal myocardial infarction) was lower in the CTA group than in the standard-care group (2.3% [48 patients] in the CTA group vs. 3.9% [81 patients] in the standard-care group; hazard ratio, 0.59; 95% CI, 0.41 to 0.84; P=0.004) (Table 2 and Fig. 2). This difference was driven primarily by a lower rate of nonfatal myocardial infarction in the CTA group than in the standard-care group (hazard ratio, 0.60; 95% CI, 0.41 to 0.87). The results for the components of the primary end point are shown in Table 2.

There was no evidence of heterogeneity of effect on the primary end point across a range of subgroups (Fig. 3) and trial centers (Fig. S3 in the Supplementary Appendix). With the exclusion of the first 50 days of follow-up to account for the delay in the implementation of treatment on the basis of CTA findings,[10] landmark analysis provided a point estimate for the lower rate of the primary end point in the CTA group that was similar to that for the overall 5-year analysis (hazard ratio, 0.53; 95% CI, 0.36 to 0.78). Among the 48 patients assigned to CTA who subsequently met the primary end point, 22 patients had obstructive disease, 17 had nonobstructive disease, 3 had normal coronary arteries on their baseline computed tomographic scan, and 6 did not attend their appointment and therefore did not undergo CTA.

Clinical outcomes did not differ between patients who had possible angina and those who had nonanginal chest pain, as defined in the National Institute for Health and Care Excellence (NICE) guidelines (see the Supplementary Methods section and Table S5 in the Supplementary Appendix).[18-20] Although the overall 5-year event rates were higher among patients with possible angina (3.1%) than among those with nonanginal chest pain (1.8%), the absolute difference in the primary end point at 5 years between the CTA group and the standard-care group was similar in these two patient populations (difference of 1.5 percentage points in patients with possible angina and 1.3 percentage points in patients with nonanginal chest pain) (Fig. 3, and

Table 1. Baseline Characteristics of the Participants before Randomization.*

Characteristic	All Participants (N=4146)	Standard Care (N=2073)	Standard Care plus CTA (N=2073)
Male sex — no. (%)	2325 (56)	1163 (56)	1162 (56)
Age — yr	57.1±9.7	57.0±9.7	57.1±9.7
Body-mass index†	29.7±5.9	29.8±6.0	29.7±5.8
Cardiovascular risk factor — no./total no. (%)			
Current or former smoker	2185/4139 (53)	1090/2068 (53)	1095/2071 (53)
Hypertension	1395/4105 (34)	683/2053 (33)	712/2052 (35)
Diabetes mellitus	444/4146 (11)	221/2073 (11)	223/2073 (11)
Hypercholesterolemia	2176/4142 (53)	1077/2070 (52)	1099/2072 (53)
Family history of CHD	1716/4103 (42)	829/2052 (40)	887/2051 (43)
History of CHD — no./total no. (%)	372/4142 (9)	186/2070 (9)	186/2072 (9)
Atrial fibrillation — no./total no. (%)	84/4142 (2)	42/2070 (2)	42/2072 (2)
Relevant medications — no./total no. (%)			
Antiplatelet agent	1993/4142 (48)	984/2070 (48)	1009/2072 (49)
Statin	1786/4142 (43)	884/2070 (43)	902/2072 (44)
Beta-blocker	1357/4142 (33)	672/2070 (32)	685/2072 (33)
ACE inhibitor or ARB	685/4142 (17)	344/2070 (17)	341/2072 (16)
Calcium-channel blocker	377/4142 (9)	194/2070 (9)	183/2072 (9)
Nitrates	1160/4142 (28)	590/2070 (29)	570/2072 (28)
Other antianginal agent	191/4142 (5)	96/2070 (5)	95/2072 (5)
Anginal symptoms — no./total no. (%)‡			
Typical angina	1462/4142 (35)	725/2070 (35)	737/2072 (36)
Atypical angina	988/4142 (24)	486/2070 (23)	502/2072 (24)
Nonanginal chest pain	1692/4142 (41)	859/2070 (41)	833/2072 (40)
Resting ECG results — no./total no. (%)			
Normal	3492/4100 (85)	1735/2051 (85)	1757/2049 (86)
Abnormal	608/4100 (15)	316/2051 (15)	292/2049 (14)
Stress ECG performed — no./total no. (%)	3517/4128 (85)	1764/2063 (86)	1753/2065 (85)
Normal results	2188/3283 (67)	1103/1651 (67)	1085/1632 (66)
Inconclusive results	566/3283 (17)	284/1651 (17)	282/1632 (17)
Abnormal results§	529/3283 (16)	264/1651 (16)	265/1632 (16)
Further investigations — no./total no. (%)	1315/4140 (32)	633/2069 (31)	682/2071 (33)
Stress imaging			
Radionuclide scintigraphy	389/4142 (9)	176/2070 (9)	213/2072 (10)
Other imaging	30/4142 (<1)	16/2070 (<1)	14/2072 (<1)
Invasive coronary angiography	515/4142 (12)	255/2070 (12)	260/2072 (13)
Diagnosis at baseline — no./total no. (%)			
CHD	1938/4142 (47)	982/2070 (47)	956/2072 (46)
Angina due to CHD	1485/4142 (36)	742/2070 (36)	743/2072 (36)

* Plus–minus values are means ±SD. ACE denotes angiotensin-converting enzyme, ARB angiotensin-receptor blocker, CHD coronary heart disease, CTA computed tomographic angiography, and ECG electrocardiography.
† Body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ Anginal symptoms were classified according to the National Institute for Health and Care Excellence (NICE) criteria.[18-20]
§ The results were categorized as abnormal if they showed evidence of myocardial ischemia.

Table S5 and Fig. S4 in the Supplementary Appendix).

DISCUSSION

In our previous report from the SCOT-HEART trial, we found that the use of CTA had a significant effect on the diagnosis and treatment of patients who had been referred for evaluation of stable chest pain, in that it influenced both the certainty and the frequency of the diagnosis of coronary heart disease and led to alterations in management.[9] Here, we report the 5-year clinical outcomes.[13] We found that the use of CTA, with consequent changes in treatment, resulted in a significantly lower rate of death from coronary heart disease or nonfatal myocardial infarction than standard care alone. Although the rates of invasive coronary angiography and coronary revascularization were higher in the CTA group than in the standard-care group in the first few months of follow-up, we did not find any differences in the overall use of invasive coronary angiography and coronary revascularization at 5 years. Our findings suggest that the use of CTA resulted in more correct diagnoses of coronary heart disease than standard care alone, which, in turn, led to the use of appropriate therapies, and this change in management resulted in fewer clinical events in the CTA group than in the standard-care group.

In the SCOT-HEART[9] and PROMISE[11] trials, the use of CTA resulted in a higher rate of detection of obstructive coronary heart disease, as confirmed by invasive coronary angiography, than standard care alone (SCOT-HEART trial) or functional testing (PROMISE trial). Invasive coronary angiography and coronary revascularization are more likely to be used appropriately in patients who receive a correct diagnosis of coronary heart disease[9,11]; patients who receive a correct diagnosis are also more likely to receive appropriate preventive therapies[10] and may have greater motivation to implement healthy lifestyle modifications. In addition, the SCOT-HEART trial encouraged initiation of secondary prevention strategies in patients with nonobstructive coronary artery disease. Among patients in the CTA group, approximately half the subsequent myocardial infarctions occurred among patients who had nonobstructive disease at baseline. This proportion was probably higher among patients who received standard care alone, since nonobstructive disease may have been unrecognized and untreated in some of the patients in that group. In the PROMISE trial, in which preventive therapies were not mandated, two thirds of subsequent cardiac events occurred in patients with nonobstructive disease.[21] Finally, event rates in the two groups in the current trial were similar until diagnoses

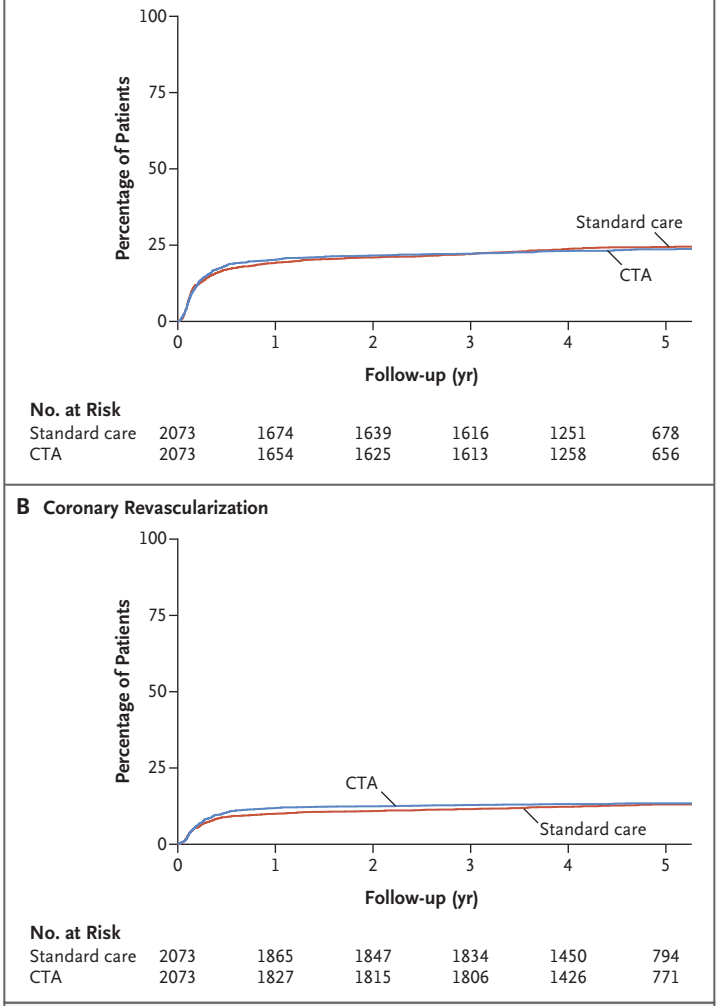

Figure 1. Percentage of Patients Who Underwent Invasive Coronary Angiography and Coronary Revascularization, According to Year of Follow-up.

Patients with stable chest pain were randomly assigned to undergo coronary computed tomographic angiography (CTA) in addition to receiving standard care or to receive standard care alone. Shown are cumulative event curves for the percentage of patients who underwent invasive coronary angiography (Panel A) and coronary revascularization (Panel B) over the course of the 5-year follow-up.

Table 2. Primary and Secondary End Points after a Median Follow-up of 4.8 Years.*

End Point	All Participants (N=4146)	Standard Care (N=2073)	Standard Care plus CTA (N=2073)	Hazard Ratio (95% CI)†
	number of patients (percent)			
Primary end point: death from CHD or nonfatal myocardial infarction‡	129 (3.1)	81 (3.9)	48 (2.3)	0.59 (0.41–0.84)§
Secondary end points				
Death from CHD, nonfatal myocardial infarction, or nonfatal stroke‡	160 (3.9)	97 (4.7)	63 (3.0)	0.65 (0.47–0.89)
Nonfatal myocardial infarction	117 (2.8)	73 (3.5)	44 (2.1)	0.60 (0.41–0.87)
Nonfatal stroke	35 (0.8)	20 (1.0)	15 (0.7)	0.74 (0.38–1.44)
Death				
From CHD‡	13 (0.3)	9 (0.4)	4 (0.2)	0.46 (0.14–1.48)
From any cause	86 (2.1)	43 (2.1)	43 (2.1)	1.02 (0.67–1.55)
Cardiovascular	17 (0.4)	12 (0.6)	5 (0.2)	0.43 (0.15–1.22)
Noncardiovascular	69 (1.7)	31 (1.5)	38 (1.8)	1.24 (0.77–2.00)
Procedures				
Invasive coronary angiography	993 (24.0)	502 (24.2)	491 (23.7)	1.00 (0.88–1.13)
Revascularization¶	546 (13.2)	267 (12.9)	279 (13.5)	1.07 (0.91–1.27)
Percutaneous coronary intervention	431 (10.4)	212 (10.2)	219 (10.6)	1.06 (0.88–1.28)
Coronary-artery bypass grafting	131 (3.2)	62 (3.0)	69 (3.3)	1.12 (0.80–1.58)

* For the composite end points, data are for the first event only.
† The hazard ratios were determined with the use of adjusted Cox regression models. The confidence intervals have not been adjusted for multiplicity, so intervals should not be used to infer definitive treatment effects.
‡ In all cases of death from CHD, the cause of death was myocardial infarction.
§ P=0.004 for the comparison between CTA plus standard care and standard care alone.
¶ A total of 12 patients had percutaneous coronary intervention followed by coronary-artery bypass grafting, and 4 patients had coronary-artery bypass grafting followed by percutaneous coronary intervention.

were confirmed and alterations in treatment were made after approximately 7 weeks,[10] which suggests that the groups were similar at baseline and changes in outcomes occurred only once treatment interventions directed by CTA findings were initiated. We hypothesize that the immediate reductions in events were mediated through the use of aspirin[22,23] and coronary revascularization procedures,[24,25] and that longer-term benefits are attributable to lifestyle modification[26] and statin therapy.[27]

Previous studies have suggested that the use of CTA is associated with higher early rates of both invasive coronary angiography and coronary revascularization.[9,11,28] Over the 5-year follow-up, we found that these higher procedure rates were no longer apparent. We performed landmark analyses at 12 months to distinguish the immediate effects of CTA from the longer-term consequences. We found that beyond 12 months, rates of invasive coronary angiography and coronary revascularization were higher in the standard-care group than in the CTA group. This would be consistent with both the emergence of unrecognized disease and nonfatal myocardial infarction in the standard-care group and the reduction in disease progression in the CTA group owing to the implementation of lifestyle modifications and preventive therapies.[27]

Some observers have highlighted the low cardiovascular event rates in trials of CTA involving patients with stable chest pain, which has prompted others to suggest that such patients should not undergo cardiovascular testing at all. In the SCOT-HEART trial, we enrolled patients with a broad range of cardiovascular risks. Overall, we observed event rates of approximately 4% over 5 years, which equates to 8% over 10 years. However, half the trial population had normal or near-normal coronary arteries, which implies

that patients with nonobstructive or obstructive coronary heart disease would have 10-year event rates of approximately 16%. This highlights the importance of promptly and accurately identifying the presence of coronary heart disease.

Strategies to stratify patients before testing have been proposed and are included in current guidelines.[4-6] However, these strategies still lead to overtesting, owing to the poor predictive accuracy of the current scoring systems.[20,29] Recently, NICE has recommended a simple symptom-based approach that would classify patients into one of two categories: those with nonanginal chest pain and those with possible angina.[19] We found that patients with possible angina were at higher risk than those with nonanginal chest pain, especially in the first 3 to 6 months after the onset of symptoms, which perhaps reflects the fact that patients with recent onset of angina pectoris constitute a particularly high-risk group.[30,31] However, overall, all patients appeared to derive similar benefits from CTA, which raises the question of whether more widespread testing may be helpful, irrespective of symptoms. Our data suggest that 63 patients with stable chest pain would need to be referred for CTA to prevent 1 fatal or nonfatal myocardial infarction over the course of 5 years.

We acknowledge that there are some limitations of the trial. First, this was an open-label trial, and ascertainment bias is inherent to the trial design. Because event adjudication was not blinded and clinical diagnoses were coded with knowledge of the assigned trial group, the risk of ascertainment bias is probably higher. This risk may have been mitigated, however, by the fact that the primary long-term end point was composed of hard clinical events. Second, we do not have data on lifestyle alterations during follow-up and can only speculate that these may have been greater in the CTA group than in the standard-care group. Third, cardiovascular-risk thresholds for the initiation of preventive therapies have fallen since the trial was completed, and it is unclear whether the benefits of CTA will be maintained with these lower thresholds. Finally, the benefit of CTA with respect to the rate of death from coronary heart disease and nonfatal myocardial infarction (1.6 percentage points lower than the rate with standard therapy) may be considered modest, but this absolute benefit is similar to, if not greater than, the benefits achieved in recent pharmaceutical interventional trials involving patients with established coronary heart disease.[32-34]

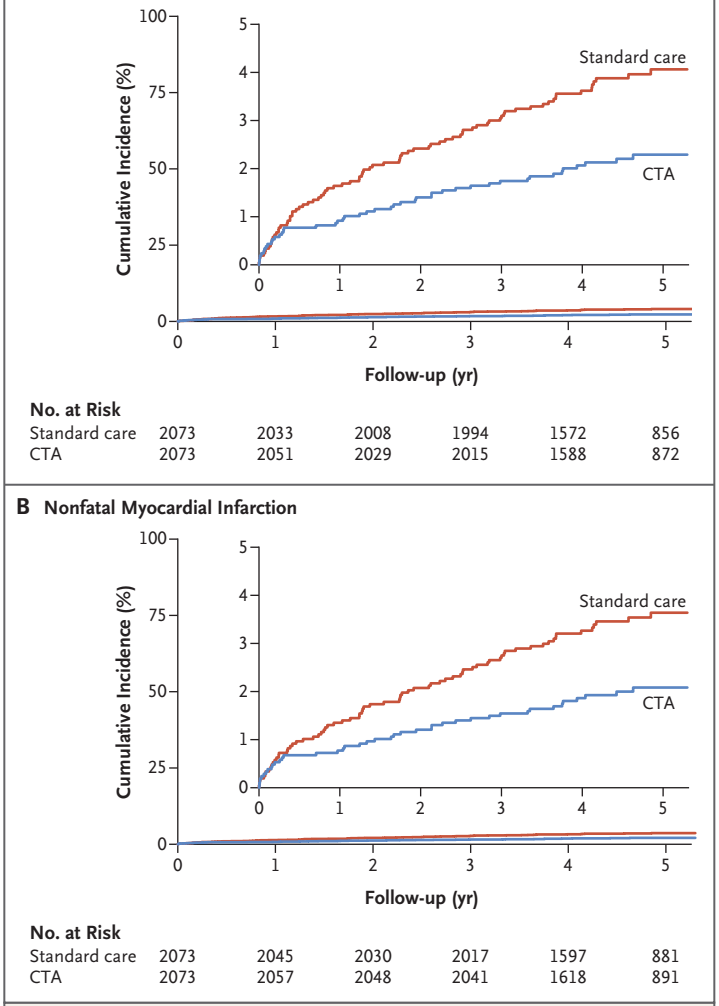

Figure 2. Cumulative Incidence of Death from Coronary Heart Disease or Nonfatal Myocardial Infarction.

Panel A shows cumulative event curves for the primary end point of death from coronary heart disease or nonfatal myocardial infarction among patients assigned to CTA in addition to standard care and those assigned to standard care alone. Panel B shows the cumulative risk of nonfatal myocardial infarction in each group. The inset in each panel shows the same data on an enlarged y axis.

In conclusion, in the SCOT-HEART trial, we found that the use of CTA in patients who had been referred to a cardiology clinic for assessment of stable chest pain resulted in a lower subsequent risk of death from coronary heart disease or nonfatal myocardial infarction than standard care alone. This benefit was achieved

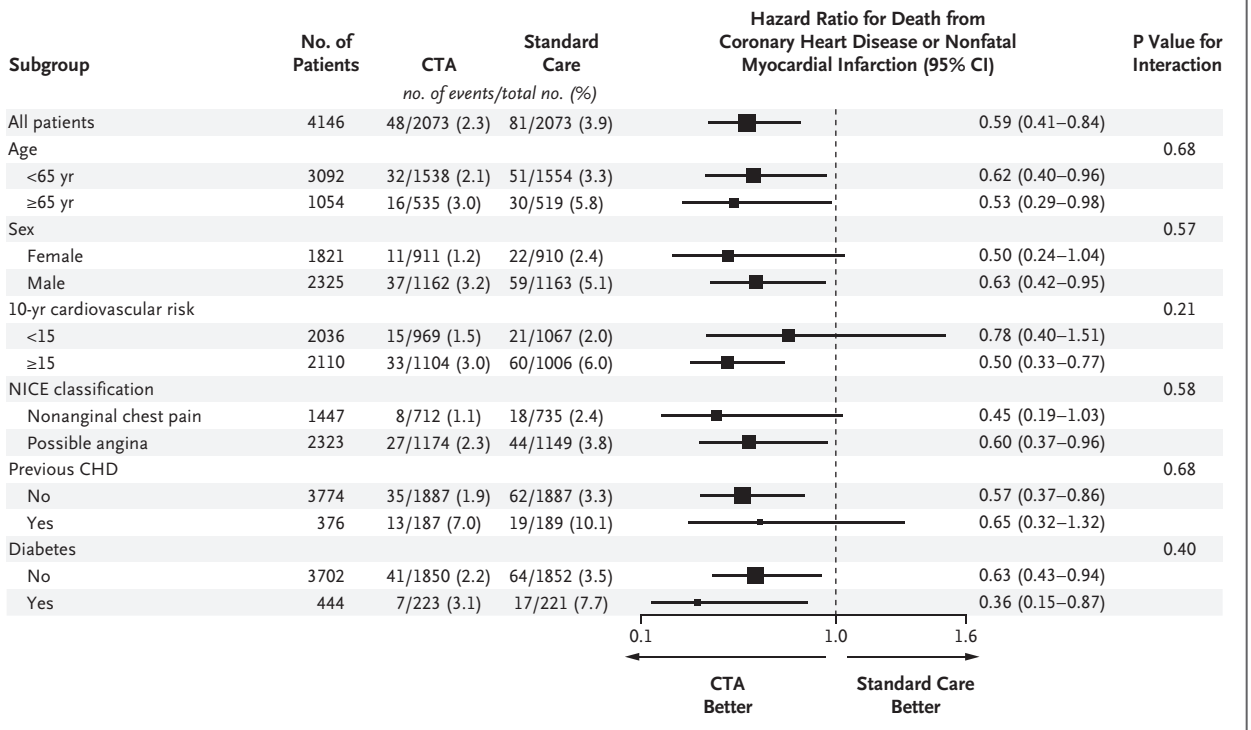

Figure 3. Subgroup Analyses for the Primary End Point of Death from Coronary Heart Disease or Nonfatal Myocardial Infarction at 5 Years.

P values are for the interaction between the randomized groups and the potential risk factor of interest and were calculated in a Cox proportional-hazards analysis that was adjusted for center and minimization variables. P values are reported without adjustment for multiplicity of testing. The sizes of the squares are proportional to the sizes of the subgroups. Ten-year cardiovascular risk was assessed according to the ASSIGN score, which ranges from 1 to 99, with higher scores indicating a higher risk of cardiovascular disease[14]; shown are the number of patients with scores above and below the median score of 15. The National Institute for Health and Care Excellence (NICE) classification is a symptom-based approach that classifies patients with recent onset of chest pain into one of two categories: those with nonanginal chest pain and those with possible angina. CHD denotes coronary heart disease.

without greater long-term use of invasive coronary angiography or coronary revascularization in the CTA group.

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APPENDIX

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