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# Coronary computed tomography angiography compared with single photon emission computed tomography myocardial perfusion imaging as a guide to optimal medical therapy in patients presenting with stable angina: The RESCUE trial

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ORIGINAL RESEARCH

# Coronary Computed Tomography Angiography Compared With Single Photon Emission Computed Tomography Myocardial Perfusion Imaging as a Guide to Optimal Medical Therapy in Patients Presenting With Stable Angina: The RESCUE Trial

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**BACKGROUND:** The RESCUE (Randomized Evaluation of Patients with Stable Angina Comparing Utilization of Noninvasive Examinations) trial was a randomized, controlled, multicenter, comparative efficacy outcomes trial designed to assess whether initial testing with coronary computed tomographic angiography (CCTA) is noninferior to single photon emission computed tomography (SPECT) myocardial perfusion imaging in directing patients with stable angina to optimal medical therapy alone or optimal medical therapy with revascularization.

**METHODS AND RESULTS:** The end point was first major adverse cardiovascular event (MACE) (cardiac death or myocardial infarction), or revascularization. Noninferiority margin for CCTA was set a priori as a hazard ratio (HR) of 1.3 (95% CI=0, 1.605). One thousand fifty participants from 44 sites were randomized to CCTA (n=518) or SPECT (n=532). Mean follow-up time was 16.2 (SD 7.9) months. There were no cardiac-related deaths. In patients with a negative CCTA there was 1 acute myocardial infarction; in patients with a negative SPECT examination there were 2 acute myocardial infarctions; and for positive CCTA and SPECT, 1 acute myocardial infarction each. Participants in the CCTA arm had a similar rate of MACE or revascularization compared with those in the SPECT myocardial perfusion imaging arm, (HR, 1.03; 95% CI=0.61-1.75) (*P*=0.19). CCTA segment involvement by a stenosis of ≥50% diameter was a better predictor of MACE and revascularization at 1 year (*P*=0.02) than the percent reversible defect size by SPECT myocardial perfusion imaging. Four (1.2%) patients with negative CCTA compared with 14 (3.2%) with negative SPECT had MACE or revascularization (*P*=0.03).

**CONCLUSIONS:** There was no difference in outcomes of patients who had stable angina and who underwent CCTA in comparison to SPECT as the first imaging test directing them to optimal medical therapy alone or with revascularization. CCTA was a better predictor of MACE and revascularization.

**REGISTRATION INFORMATION:** URL: https://www.clinicaltrials.gov/. Identifier: NCT01262625.

**Key Words:** angina ■ cardiovascular imaging ■ coronary computed tomography angiography ■ coronary revascularization ■ ischemia ■ nuclear medicine

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For Sources of Funding and Disclosures, see page 8.



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## CLINICAL PERSPECTIVE

### What Is New?

- This randomized, controlled, multicenter, comparative efficacy outcomes trial tested whether initial testing with coronary computed tomographic angiography is noninferior to single photon emission computed tomography myocardial perfusion imaging in directing patients with stable angina to optimal medical therapy alone or optimal medical therapy with revascularization.
- Participants in the coronary computed tomographic angiography arm had similar rate of major adverse cardiovascular events or revascularization compared with those in the single photon emission computed tomography myocardial perfusion imaging arm.

### What Are the Clinical Implications?

- This trial provides further evidence in support of a coronary computed tomographic angiography first strategy for the diagnosis and management of patents presenting with symptoms of stable angina.

### Nonstandard Abbreviations and Acronyms

| | |
|---|---|
| **OMT** | optimal medical therapy |
| **ICA** | invasive coronary angiography |

Ischemic heart disease is the main cause of morbidity and mortality worldwide, and will likely remain so for at least the next decade.[1,2] The goal in treating patients with symptoms suggestive of stable ischemia is to diagnose them in the most efficient way possible in order to reduce their risk of death and myocardial infarction.[2,3] All patients with coronary artery disease (CAD) with or without revascularization should be treated with guideline-driven optimal medical therapy (OMT).[3,4] A number of trials,[5–7] including the most recent ISCHEMIA (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) trial,[8] showed no evidence to suggest that an initial invasive strategy, as compared with an initial conservative strategy, reduced the risk of ischemic cardiovascular events or death. Moreover, elective invasive coronary angiography (ICA) in chronic stable angina has been shown to be of low yield in many patients,[9] and has the potential to directly increase the number of unnecessary invasive catheter-based and surgical revascularization procedures.[10] Myocardial perfusion by single photon emission computed tomography myocardial perfusion imaging (SPECT-MPI) has been the main noninvasive strategy used as a gatekeeper to ICA and percutaneous coronary intervention, but its effectiveness is low as an index of obstructive disease by ICA.[11]

Coronary computed tomographic angiography (CCTA), an anatomic imaging modality, is a potential alternative to SPECT-MPI as the first line of testing in patients with stable chest pain and suspected CAD, and is now the recommended first line of testing in the United Kingdom[12,13] and in developing countries, where the modality of CT is easily accessible and where morbidity and mortality caused by CAD is on the rise.[12–15]

In this trial we assess, in a head-to-head comparison, CCTA- and SPECT-MPI-driven imaging algorithms.

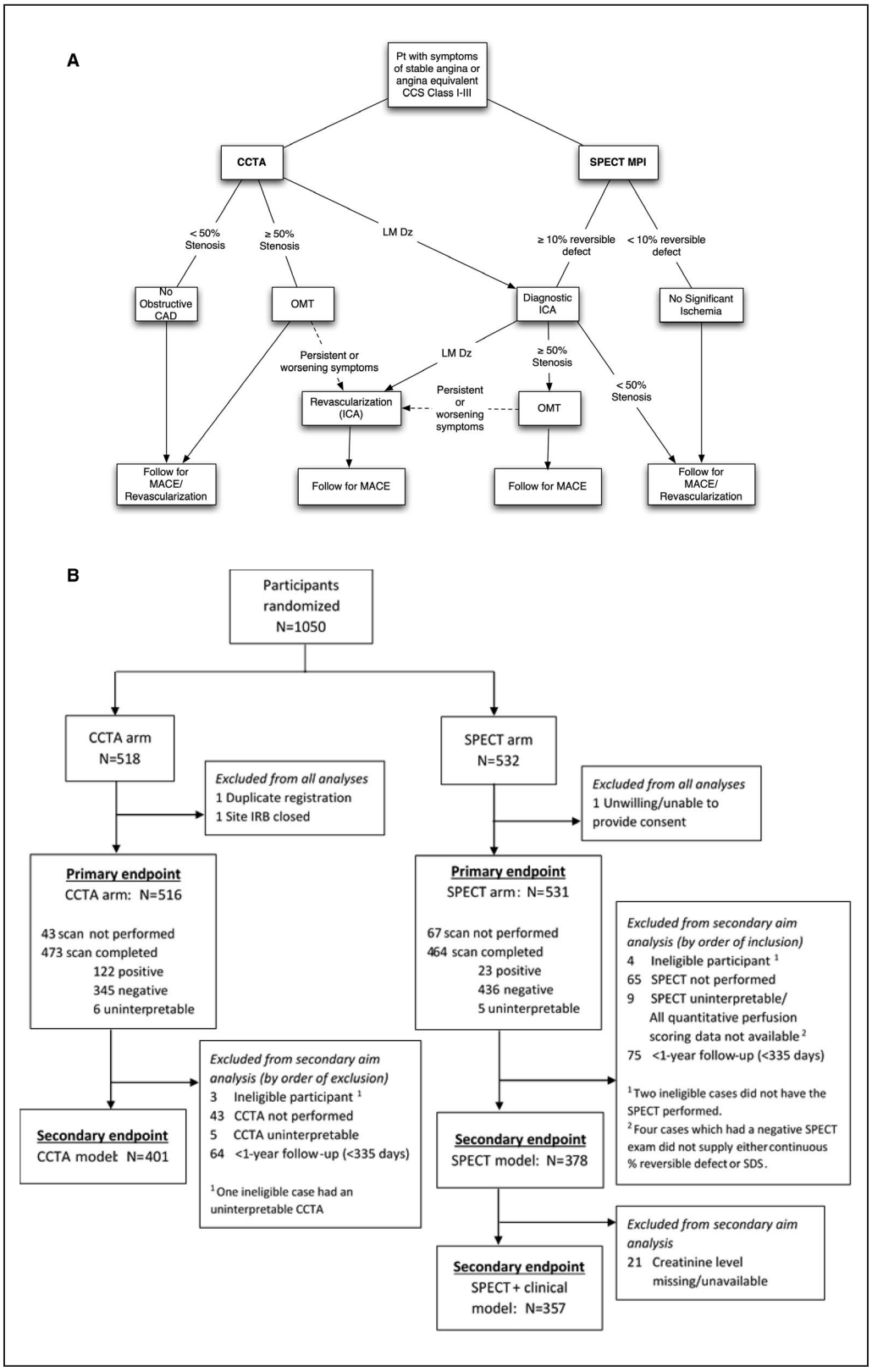
## METHODS

Requests to access the data set may be submitted to the American College of Radiology (ACR) Center for Research and Innovation (CRI) via https://dart.acr.org.

### Study Design

The RESCUE (Randomized Evaluation of Patients with Stable Angina Comparing Utilization of Noninvasive Examinations) Trial is a phase III, randomized, controlled, multicenter, comparative efficacy study, designed to compare 2 diagnostic imaging/treatment paradigms that use CCTA or SPECT-MPI for assisting in the diagnosis of ischemic heart disease in patients with stable angina symptoms, and guiding subsequent treatment (Figure 1A). Stable angina was defined as having Class I or II angina by the Canadian Cardiovascular Society.[16] The study design was previously reported, to include the Consolidated

**Figure 1. RESCUE (Randomized Evaluation of Patients with Stable Angina Comparing Utilization of Noninvasive Examinations) Schema and Consolidated Standards of Reporting Trials (CONSORT) diagram.**
**A**, Patients with symptoms of stable angina were randomized to receive either CCTA or SPECT-MPI. Diagnostic ICA was performed in select patients according to the schema. All were followed for MACE/revascularization. **B,** CONSORT diagram. There were 1050 patients who were randomized (518 CCTA, 532 SPECT-MPI). CCTA was performed in 473 and SPECT-MPI was performed in 464. There were 401 patients for CCTA and 378 patients for SPECT-MPI for evaluation of the secondary end point. CAD indicates coronary artery disease; CCS, Canadian Cardiovascular Society; CCTA, coronary computed tomographic angiography; ICA, invasive coronary angiography; LMD, Left main disease; MACE, major cardiovascular events; OMT, optimal medical therapy; and SPECT-MPI, single photon emission computed tomography myocardial perfusion imaging.




Standards of Reporting Trials flow diagram, which we re-present in Figure 1B.[17,18] The study protocol was approved by the Institutional Review Boards at each study site, or through a commercial Institutional Review Board (Advarra Schulman). All patients provided written, informed consent. In the CCTA arm, patients without left main disease were treated with OMT. In the SPECT-MPI arm, patients with ≥10%

reversible defect were directed to ICA, and patients without left main disease by ICA were treated with OMT. The Data Coordinating Center generated the random allocation sequence and assigned participants to the 2 study arms in equal proportions. Blocked randomization was used, stratified by sex and participating institution. Randomization was done at the time of study enrollment. All investigators and site coordinators involved in the trial were blinded to randomization until after patient recruitment and assignment to the study arm (initial imaging test). The site coordinators enrolled the participants.

The RESCUE (Randomized Evaluation of Patients with Stable Angina Comparing Utilization of Noninvasive Examinations) trial, funded by the Agency for Healthcare Research and Quality and the American College of Radiology Imaging Network Fund for Imaging Innovation, began in 2011, and was completed in 2014. Adherence to OMT was determined by patient follow-up. Participants with positive cardiac-related findings on their CCTA or SPECT/MPI were contacted at a minimum of 4 time points (at 2 weeks and 2, 6, and 12 months). Participants with negative findings on CCTA or SPECT MPI were contacted at a minimum of 2 time points (6 and 12 months). Participants were then contacted every 6 months until the conclusion of the trial.[18] The main funding mechanism was through the American Recovery and Reinvestment Act. Unfortunately, this limited the time possible for patient recruitment and follow-up. As a result, the recruitment goal was not achieved which limits the statistical power for data analysis.

## Statistical Analysis

The primary aim of the study was to compare the time-dependent rates of the composite primary end point (major adverse cardiovascular event [MACE], comprising cardiac-related death or acute myocardial infarctions [AMI], and revascularization) across the 2 arms of the trial. Time to the primary end point was measured from randomization to CCTA or SPECT-MPI to the first occurrence of any of the component events. The primary analysis was conducted from an intent-to-treat perspective, with time to event compared between the CCTA and SPECT-MPI arms using Kaplan-Meier curves with log-rank test. Cox regression models were used to estimate the hazard ratio to compare against the predefined noninferiority margin. The study was designed to achieve sufficient power with 4300 subjects in order to test the noninferiority of CCTA compared with SPECT-MPI to guide medical therapy, where the noninferiority margin was defined as a hazard ratio of 1.3 (95% CI=0, 1.605). The hazard ratio 1.3 margin was chosen in that, given the projected sample size, it would provide 85% power.[18]

Secondary aims of the trial were (1) to evaluate the ability of available prognostic indices to predict the composite outcome status (MACE and revascularization) at 1 year, and (2) to develop a new predictive index of composite outcome status at 1 year using RESCUE data. For these secondary analyses, patients with <1-year follow-up (defined as <335 days) were excluded from analysis, as were ineligible patients and patients without the respective randomized scan or with an uninterpretable scan. The ability of the Modified Duke Score from CCTA,[19] and percent reversible defect size on SPECT to predict 1-year composite outcome status were assessed by receiver operating characteristic analysis, with comparison by arm performed using the method of DeLong.[20]

In developing a new predictive index, the Modified Duke Score was replaced with a predictive model based upon the raw CCTA stenosis data. The American Heart Association (AHA) 16-segments were graded as being normal (0%), very mild (1%–29%), mild (30%–49%), moderate (50%–69%), or severe (≥70%) stenosis. Because of the relatively few MACE events, these were grouped to < 30%, 30%–49%, and ≥50% for subsequent analysis. A new index was derived using the individual AHA 16-segment stenosis scores. The association between each coronary artery segment and composite outcome status at 1 year was assessed using the exact $\chi^2$ test (for categorical predictors), the nonparametric Wilcoxon rank sum test (for continuous predictors), and by the C-statistic from univariate logistic regression. Segment selection was performed using the grouped least absolute selection and shrinkage operator method[21] with tuning parameter identified using 5-fold cross-validation in order to limit overfitting. Selected segments were then combined into an ordinary multivariate logistic regression model, with predictive ability of the new index final model summarized using the C-statistic.

A *P*-value threshold of 0.05 was used to declare statistical significance. Statistical analyses were performed using SAS 9.4 (SAS Institute) or R software (version 3.3.1; R project, http://www.r-project.org).

# RESULTS

Our study was designed to enroll and randomize 4300 participants to the 2 study arms, but given the difficulties of recruiting enough patients to fulfill the stringent entry criteria, as well as time constraints for funding (American Recovery and Reinvestment Act award, 3-year cap), we recruited one quarter of the planned sample size.

Between May 2011 and April 2013, 1050 participants from 44 sites were enrolled and randomized in a 1:1 ratio to either CCTA or SPECT-MPI. Of the 1050 participants, 3 were placed off-study, because of a duplicate registration (n=1), site Institutional Review Boards closure (n=1), and lack of informed consent (n=1). Demographics and CAD risk factors of the remaining 1047 participants are shown in Table S1. Details of the participant flow through the trial are illustrated in the Consolidated Standards of Reporting Trials diagram shown in Figure 1B.

Among the 1047 eligible participants, 110 (10.5%) participants did not have the randomized scan for reasons shown in Table S2. We continued to follow these 110 participants according to the study protocol. Since an intention-to-treat analysis was performed, these 110 participants were included in the analysis of the primary aim. Mean follow-up time for all patients in the trial was 16.2 (SD 7.9) months. Imaging status with types of events is shown in Table S3. There were no cardiac-related deaths observed in the study. There was 1 AMI for patients with negative CCTA, and 2 AMI for patients with a negative SPECT examination. There was 1 AMI each for patients with positive CCTA and SPECT examinations. Among patients with negative CCTA examinations, 4/345 (1.2%) had MACE or revascularization, whereas 14/436 (3.2%) patients with negative SPECT examinations had MACE or revascularization (log-rank $P$=0.03). A total of 25/122 (20.5%) patients with positive CCTA had MACE or revascularization, whereas 8/23 (34.8%) patients with positive SPECT had MACE or revascularization (log rank $P$=0.24). There were 169 (32.8%) patients in the CCTA arm who had incidental findings, 59 of whom required follow-up imaging. In the SPECT MPI arm there were only 9 (1.7%) patients who had incidental findings, 2 of whom required follow-up imaging.

Participants in the CCTA arm had a similar rate of experiencing the primary end point compared with those in the SPECT-MPI arm, with a hazard ratio estimate of 1.03 (95% CI, 0.61–1.75). ($P$=0.19).

Imaging-associated adverse events were uncommon in the trial (Table S4), with only 1 adverse event with an attribution of probable or definite in the CCTA arm that was judged to be moderate or greater in severity. There were no reported adverse events with attribution of probable or definite in the SPECT arm. In the trial overall, there were 10 reported deaths, of which none were determined to be cardiac (7 malignancy, 1 stroke, 1 cocaine drug overdose, and 1 pulmonary end-stage chronic obstructive pulmonary disease).

Of the 145 patients with positive cardiac-related findings on their CCTA or SPECT/MPI, 128 patients could be contacted at 6 months, 118 at 12 months, 88 at 18 months, and 47 at 24 months. Of the 781 patients with negative findings on CCTA or SPECT MPI, 654 could be contacted at 6 months, 618 at 12 months, 391 at 18 months, and 253 at 24 months. Adherence to OMT in patients with a positive examination, including adherence to medical therapy (antihypertensives, medication for diabetes mellitus, and blood thinners) and nonsmoking was described by 44 (34.4%) of the 128 patients who could be contacted at 6 months. Information regarding adherence to OMT is provided in Table S5.

A total of 401 patients were analyzed for CCTA and a total of 378 patients were analyzed for SPECT for purposes of the secondary end points. Relevant exclusions are shown in Figure 1B. The derived Modified Duke Scores are shown in Table S6. The ability of the Modified Duke Score and percent reversible defect size on SPECT-MPI to predict composite outcome status (MACE and revascularization) at 1 year was assessed by receiver operating characteristic analysis (Figure 2). While the Modified Duke Score had a higher area under the curve (area under the curve=0.87, 95% CI, 0.81–0.94) than the percent reversible defect size (area under the curve=0.73, 95% CI, 0.59–0.88), this difference did not achieve statistical significance ($P$=0.08), likely because of the relatively few MACE and revascularization events.

In addition to assessing the prognostic ability of the Modified Duke Score on CCTA and percent reversible defect size on SPECT-MPI, a secondary aim for the trial was to develop a new index from the RESCUE data for prediction of composite outcome status at 1 year. The results from univariate logistic regression models assessing the predictive ability of each of the individual AHA 16-arterial segments are shown in Table S7. The C-statistic corresponds to the receiver operating characteristic area under the curve using the predicted values from the univariate regression model and gives a measure of strength of each predictor. The proximal and mid-left anterior descending artery segments exhibited the largest C-statistics and were the only arterial segments selected by the least absolute selection and shrinkage operator. The new CCTA model using only these 2 segments resulted in significantly better discriminatory ability for the composite outcome than the SPECT percent reversible defect size ($P$=0.02, Figure 3).

## DISCUSSION

In the RESCUE trial, there was no difference in outcomes of patients who had stable angina and who underwent CCTA in comparison to SPECT as the first imaging test directing them to OMT alone or with revascularization. CCTA was a better predictor of MACE

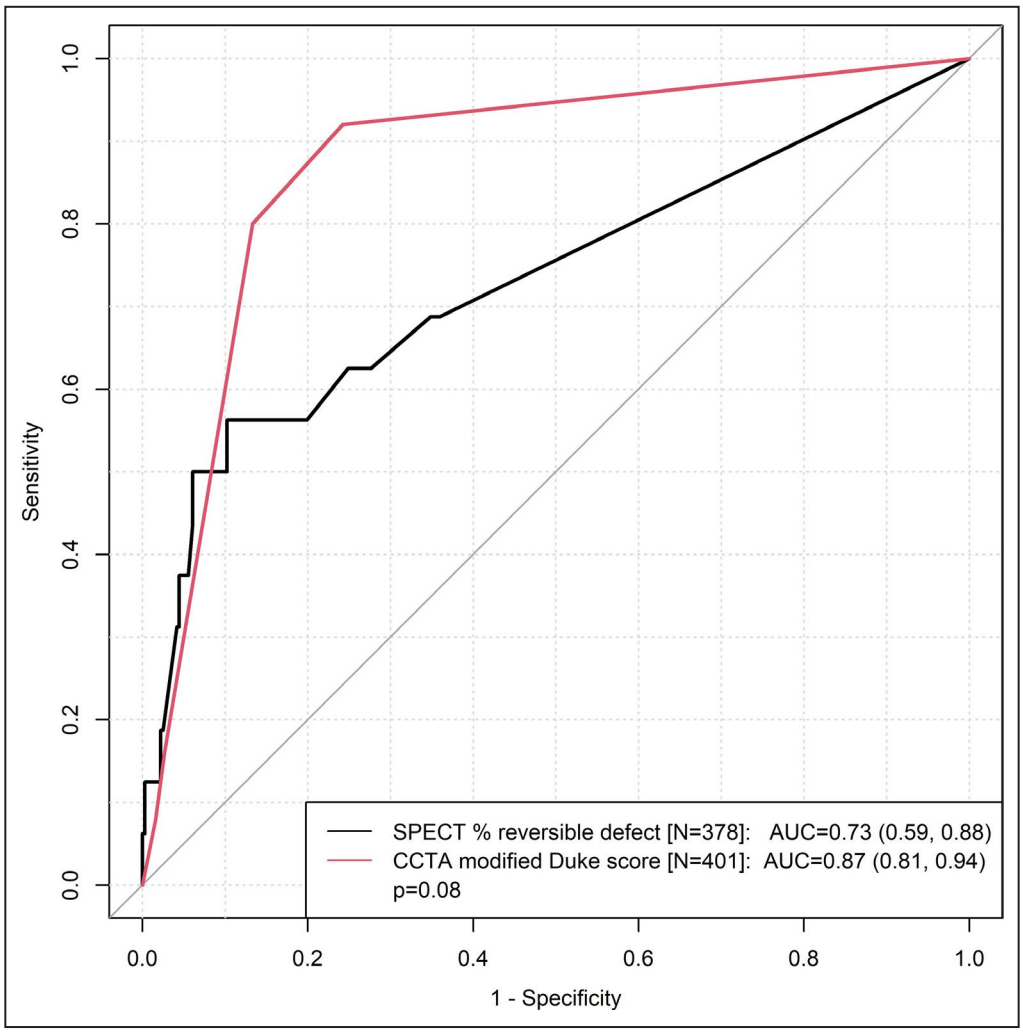



**Figure 2. Receiver operating characteristic curves show a trend towards improved prediction of the composite end point of major cardiovascular events and revascularization at 1 year using the modified Duke score compared with percent reversible defect.**
AUC indicates area under the curve; CCTA, coronary computed tomographic angiography; and SPECT, single photon emission computed tomography.

and revascularization. These findings are consistent with the findings of the recently published ISCHEMIA trial,[8] which showed no evidence that an initial invasive strategy, as compared with an initial conservative strategy, reduced the risk of ischemic cardiovascular events. In the ISCHEMIA trial, patients with an unprotected left main stenosis of at least 50% diameter as determined by CCTA were excluded.[8] RESCUE also excluded patients with left main disease as determined by either CCTA or ICA.

Thus, ISCHEMIA showed and RESCUE suggests that CCTA can be effectively used to direct patients to either revascularization (patients with left main disease) and OMT, or OMT alone. Under the ISCHEMIA/RESCUE paradigm, CT fractional flow reserve would be required only in the assessment of left main disease. However, the accuracy of computational fluid dynamics methods to estimate fractional flow reserve by CCTA makes the case for use of CCTA more compelling.[22,23]

Like RESCUE, the PROMISE (Prospective Multicenter Imaging Study for Evaluation of Chest Pain) trial[14] showed more frequent revascularization in patients who underwent CCTA in comparison to SPECT, and there was also a trend towards increased revascularization for CCTA compared with standard care in the SCOT-HEART (Scottish Computed Tomography of the Heart) trial,[24] although it did not reach statistical significance. While one may wonder whether these revascularizations benefited the patient, fewer AMI and coronary heart disease deaths were found in the CCTA arm of SCOT-HEART, suggesting that CCTA was better at identifying patients who ultimately benefitted from revascularization. In RESCUE, CCTA was a better predictor of MACE and revascularization. Previous trials

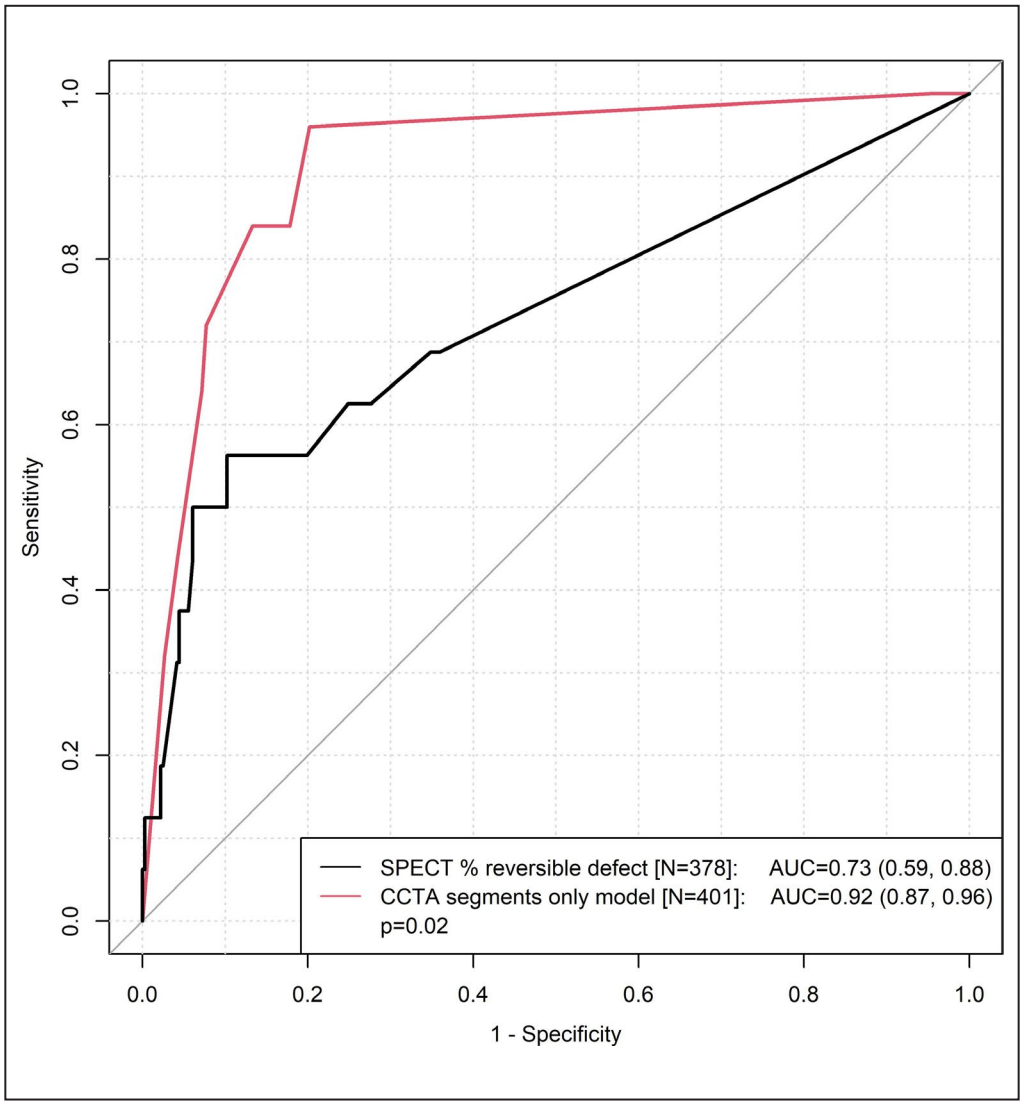



**Figure 3. Proximal and LAD segments for CCTA were significantly better predictors for the composite end point of major adverse cardiovascular event and revascularization than percent reversible defect (Rdefect).**
AUC indicates area under the curve; CCTA, coronary computed tomographic angiography; LAD, left anterior descending artery; and SPECT, single photon emission computed tomography.

such as the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation),[6] BARI-2D (Bypass Angioplasty Revascularization Investigation 2 Diabetes),[7] and ORBITA (Objective Randomized Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina)[5] trials, while they did not specifically address CCTA, also support the hypothesis that patients with stable angina and CAD other than left main disease could be successfully treated by OMT alone, with mortality outcomes similar to those of patients who had interventions. Regarding the modified Duke score, as with RESCUE, Min et al found that the modified Duke score with CCTA provided prognostic information regarding MACE.[19] Both methods provide a measure of the myocardium at risk.[25]

The results of RESCUE should be interpreted in the context of certain limitations. Limitations of the RESCUE trial include modest adherence rates to OMT. In RESCUE, adherence rates for OMT were comparable in the 2 groups at just below 39% over the follow-up period. This is significantly less than COURAGE,[26] in which adherence to OMT was 80% at 5 years and ISCHEMIA, where adherence to OMT ranged from 73.9% to 81.5%, but comparable to adherence rates in a real-life setting.[27] In COURAGE and ISCHEMIA, higher OMT adherence rates were most likely secondary to not only the regularly scheduled nurse manager visits, but also the provision of medications or some medications at no cost to the patient.[8,26] In RESCUE, power was decreased by reducing the

sample size from 4300 to 1050 patients, event rates were lower than expected suggesting mild-to-moderate ischemic disease, and the period of follow-up was modest, at an average of 16.2 months. The power of the study may have also affected the results of the secondary aims.

The findings in RESCUE do not apply to patients with acute coronary syndromes, low ejection fraction, or heart failure. Patients with left main disease and continued symptomatology despite patient-described adherence to OMT were directed to revascularization.

In conclusion, we compared treatment paradigms with initial imaging with CCTA to initial imaging with SPECT-MPI in directing patients with stable angina to OMT alone or OMT with revascularization and, within the limitations described above, found no difference in patient outcomes. Findings suggest that CCTA is a better predictor of MACE and revascularization.

# APPENDIX

## RESCUE Investigators

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### Disclosures

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### Supplementary Material

**Tables S1–S7**

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# SUPPLEMENTAL MATERIAL

## Table S1. Demographics and CAD Risk factors

| Category | Value | CCTA - Analyzed* (N=516) | SPECT - Analyzed* (N=531) |
|---|---|---|---|
| AGE - YR | MEAN | 57(SD=9) | 58(SD=9) |
| | RANGE | 40-85 | 40-86 |
| | | | |
| BMI** | MEAN | 30 (SD=5) | 29 (SD=5) |
| | RANGE | 16-41 | 17-43 |
| | | | |
| RACE | AMERICAN INDIAN OR ALASKA | 8(2%) | 7(1%) |
| | ASIAN | 11(2%) | 14(3%) |
| | BLACK OR AFRICAN AMERICAN | 73(14%) | 77(15%) |
| | NATIVE HAWAIIAN OR OTHER | 2(<1%) | 1(<1%) |
| | WHITE | 400(78%) | 415(78%) |
| | MULTIPLE RACE ENDORSEMENT | 10(2%) | 5(1%) |
| | UNKNOWN | 12(2%) | 12(2%) |
| | | | |
| ETHNICITY | HISPANIC OR LATINO | 46(9%) | 58(11%) |
| | NOT HISPANIC OR LATINO | 467(91%) | 468(88%) |
| | UNKNOWN | 3(1%) | 5(1%) |
| | | | |
| SEX | FEMALE | 233(45%) | 244(46%) |
| | MALE | 283(55%) | 287(54%) |
| | | | |
| CCSS ANGINA** | CLASS I | 297(58%) | 305(57%) |
| | CLASS II | 183(35%) | 181(34%) |
| | CLASS III | 33(6%) | 35(7%) |
| | | | |
| CARDIAC RISK**+ | CAD, ACS OR AMI FEMALE <65 YEARS AGE | 73(14%) | 74(14%) |
| | DIABETES MELLITUS | 105(20%) | 114(21%) |
| | DIAGNOSIS OF CAD, ACS OR AMI MALE <55 YEARS | 136(26%) | 125(24%) |
| | DYSPNEA | 257(50%) | 258(49%) |
| | HAVE YOU SMOKED CIGARETTES, EVEN A PUFF, IN THE PAST 30 DAYS | 74(14%) | 87(16%) |
| | HYPERCHOLESTEROLEMIA/HYPERLIPIDEMIA | 324(63%) | 313(59%) |
| | HYPERTENSION | 318(62%) | 317(60%) |
| | PRIOR HISTORY OF CAD | 57(11%) | 55(10%) |
| | TRIGLYCERIDEMIA | 114(22%) | 121(23%) |

*** 3 Participants were taken off-study, and are not included in the analysis set**

**** 1034/1047 participants submitted data on the relevant case report form**

**+ Participants may endorse multiple risk factors**

## Table S2. Reasons randomized scan not performed

| | Arm | | |
|---|---|---|---|
| **Reason** | **CCTA** | **SPECT** | **Total** |
| Equipment | 2 | 0 | 2 |
| Ineligible | 0 | 1 | 1 |
| Insurance | 1 | 7 | 8 |
| Medical | 15 | 14 | 29 |
| Participant | 22 | 38 | 60 |
| Scheduling | 2 | 3 | 5 |
| Unknown | 1 | 4 | 5 |
| Total | 43 | 67 | 110 |

## Table S3. Imaging status by MACE and revascularization outcome

| | Scan Not Performed | | | Missing Endpoint | Un-interpretable Scan | | Negative Scan | | | Positive Scan | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | AMI | Revasc. | No Event | No Event | AMI | No Event | AMI | Revasc. | No Event | AMI | Revasc. | No Event | N |
| **CCTA** | 0 | 0 | 43 | 0 | 0 | 6 | 1 | 3 | 341 | 1 | 24 | 97 | 516 |
| **SPECT** | 3 | 1 | 63 | 1 | 1 | 3 | 2 | 12 | 422 | 1 | 7 | 15 | 531 |
| **Total** | 3 | 1 | 106 | 1 | 1 | 9 | 3 | 15 | 763 | 2 | 31 | 112 | 1047 |

## Table S4. Imaging-associated Adverse Events

| Grade | ARM | | | | | | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | CCTA | | | | | | SPECT | | | | | | |
| | Relation to Study Procedure | | | | | Total | Relation to Study Procedure | | | | | Total | |
| | Unrelated | Unlikely | Possible | Probable | Definite | | Unrelated | Unlikely | Possible | Probable | Definite | | N |
| **Mild** | 0 | 1 | 3 | 0 | 0 | 4 | 1 | 0 | 0 | 0 | 0 | 1 | 5 |
| **Moderate** | 2 | 0 | 0 | 0 | 1 | 3 | 0 | 2 | 0 | 0 | 0 | 2 | 5 |
| **Severe** | 3 | 0 | 0 | 0 | 0 | 3 | 2 | 0 | 0 | 0 | 0 | 2 | 5 |
| **Life threatening** | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 1 |
| **Fatal** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Total** | 5 | 1 | 3 | 0 | 1 | 10 | 4 | 2 | 0 | 0 | 0 | 6 | 16 |

## Table S5. Patient adherence to OMT

| Group | Follow-up | Compliant | N | Percent |
|---|---|---|---|---|
| All Cases | 6m | 44 | 128 | 34.4 |
| All Cases | 12m | 45 | 118 | 38.1 |
| All Cases | 18m | 39 | 88 | 44.3 |
| All Cases | 24m | 19 | 47 | 40.4 |
| All Cases | Total | 147 | 381 | 38.6 |
| | | | | |
| CCTA Cases | 6m | 39 | 108 | 36.1 |
| CCTA Cases | 12m | 37 | 97 | 38.1 |
| CCTA Cases | 18m | 31 | 74 | 41.9 |
| CCTA Cases | 24m | 16 | 40 | 40.0 |
| CCTA Cases | Total | 123 | 319 | 38.6 |
| | | | | |
| SPECT Cases | 6m | 5 | 20 | 25.0 |
| SPECT Cases | 12m | 8 | 21 | 38.1 |
| SPECT Cases | 18m | 8 | 14 | 57.1 |
| SPECT Cases | 24m | 3 | 7 | 42.9 |
| SPECT Cases | Total | 24 | 62 | 38.7 |

## Table S6. CCTA Modified Duke Score

| **Modified Duke prognostic score** | **N** | **%** |
|---|---|---|
| (1) <50% stenosis | 287 | 71.6% |
| (2) >=2 stenoses 30-49% (including 1 artery w/ proximal disease) or 1 vessel w/ 50-69% stenosis | 44 | 11.0% |
| (3) 2 stenoses 50-69% or 1 vessel w/ >=70% stenosis | 28 | 7.0% |
| (4) 3 stenoses 50-69% or 2 vessels w/ >=70% stenosis or proximal left anterior descending stenosis >=70% | 28 | 7.0% |
| (5) 3 vessels >=70% stenoses or 2 vessels >=70% stenosis w/ proximal left anterior descending | 6 | 1.5% |
| (6) Left main stenosis >=50% | 8 | 2.0% |
| **Total** | **401** | **100.0%** |

**Table S7. Results of univariate logistic regression models, summarizing the ability of individual AHA 16-arterial segments to predict composite outcome status (MACE and revascularization) at 1 year.**

| Predictor | C-statistic |
|---|---|
| LAD mid | 0.86 |
| LAD proximal | 0.76 |
| RCA mid | 0.71 |
| LAD distal | 0.69 |
| LAD diagonal 1 | 0.68 |
| LCX proximal | 0.68 |
| RCA distal | 0.63 |
| LAD diagonal 2 | 0.62 |
| RPDA | 0.61 |
| RCA proximal | 0.59 |
| LCX obtuse marginal 2 | 0.59 |
| LCX distal | 0.59 |
| Left main | 0.57 |
| Ramus | 0.57 |
| LCX obtuse marginal 1 | 0.57 |
| LPDA | 0.50 |