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Coronary CT Angiography versus Standard Evaluation in Acute Chest Pain

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Abstract

Background—It is unclear whether an evaluation incorporating coronary computed tomographic angiography (CCTA) is more effective than standard evaluation in the emergency department in patients with symptoms suggestive of acute coronary syndromes.

Methods—In this multicenter trial, we randomly assigned patients 40 to 74 years of age with symptoms suggestive of acute coronary syndromes but without ischemic electrocardiographic changes or an initial positive troponin test to early CCTA or to standard evaluation in the emergency department on weekdays during daylight hours between April 2010 and January 2012. The primary end point was length of stay in the hospital. Secondary end points included rates of discharge from the emergency department, major adverse cardiovascular events at 28 days, and cumulative costs. Safety end points were undetected acute coronary syndromes.

Results—The rate of acute coronary syndromes among 1000 patients with a mean (\pm SD) age of 54 ± 8 years (47% women) was 8%. After early CCTA, as compared with standard evaluation, the mean length of stay in the hospital was reduced by 7.6 hours ($P<0.001$) and more patients were discharged directly from the emergency department (47% vs. 12%, $P<0.001$). There were no undetected acute coronary syndromes and no significant differences in major adverse cardiovascular events at 28 days. After CCTA, there was more downstream testing and higher radiation exposure. The cumulative mean cost of care was similar in the CCTA group and the standard-evaluation group (\$4,289 and \$4,060, respectively; $P=0.65$).

Conclusions—In patients in the emergency department with symptoms suggestive of acute coronary syndromes, incorporating CCTA into a triage strategy improved the efficiency of clinical decision making, as compared with a standard evaluation in the emergency department, but it resulted in an increase in downstream testing and radiation exposure with no decrease in the overall costs of care. (Funded by the National Heart, Lung, and Blood Institute; ROMICAT-II ClinicalTrials.gov number, NCT01084239.)

Treatment of Patients with Acute chest pain but an inconclusive initial evaluation with the use of biomarkers and electrocardiographic (ECG) testing is often diagnostically challenging

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and inefficient. The majority of patients with acute coronary syndromes have underlying coronary artery disease.¹ Contrast-enhanced coronary computed tomographic angiography (CCTA) has high sensitivity and specificity for the detection of clinically significant coronary artery disease, as compared with invasive coronary angiography, in patients in stable condition with suspected or known coronary artery disease.²⁻⁵

Rule Out Myocardial Infarction/Ischemia Using Computer Assisted Tomography (ROMICAT-I),⁶ a blinded observational study involving patients in the emergency department with suspected acute coronary syndromes, and other studies^{7,8} have shown that normal findings on CCTA have a very high negative predictive value for ruling out acute coronary syndromes during the index hospitalization and the occurrence of major adverse cardiovascular events over the next 2 years.^{7,9} The results of two previous randomized, multicenter trials^{10,11} suggest that CCTA may facilitate safe and earlier triage of low-risk patients and that CCTA can rule out coronary artery disease faster than stress myocardial-perfusion imaging. However, imaging the coronary anatomy with CCTA can involve more procedures and greater costs than functional testing.¹² Thus, equipoise exists regarding the effectiveness of incorporating CCTA into an evaluation strategy in the emergency department.

The objectives of this study were to compare the effectiveness of a CCTA-based evaluation strategy with that of standard evaluation in the emergency department for patients with symptoms suggestive of an acute coronary syndrome and to evaluate the downstream testing, cost, and radiation exposure associated with CCTA.

Methods

Study Design and Oversight

ROMICAT-II was designed as a randomized, controlled, multicenter trial in which an evaluation and management strategy that included CCTA as a first diagnostic test performed as early as possible was compared with a standard emergency department evaluation for patients with acute chest pain suggestive of an acute coronary syndrome. After random assignments had been made to initial CCTA or standard evaluation without CCTA, patient care in both groups was not mandated by the study protocol but instead was at the discretion of local physicians. The design of ROMICAT-II has been described in detail previously,¹³ and the study protocol is available with the full text of this article at NEJM.org.

Study Population

Patient enrollment began on April 23, 2010, and ended on January 30, 2012, at nine hospitals in the United States. All patients provided written informed consent to participate in the study. Eligibility criteria were chosen according to the ROMICAT-I study,⁶ with the goal of enrolling a population with a similar prevalence of acute coronary syndromes (approximately 8%). Eligible patients were 40 to 74 years of age, presented to the emergency department with chest pain (or the anginal equivalent) of at least 5 minutes' duration within 24 hours before presentation in the emergency department, were in sinus rhythm, and warranted further risk stratification to rule out acute coronary syndromes, as determined by an attending physician in the emergency department. Major exclusion criteria were a history of known coronary artery disease, new diagnostic ischemic changes on the initial ECG, an initial troponin level in excess of the 99th percentile of the local assay, impaired renal function (creatinine level, >1.5 mg per deciliter [132.6 μ mol per liter]), hemodynamic or clinical instability, known allergy to an iodinated contrast agent, a body-mass index (the weight in kilograms divided by the square of the height in meters) greater than 40, or currently symptomatic asthma.

Study Protocol

Eligible patients were identified, provided written informed consent, and were randomly assigned at their initial evaluation in the emergency department during weekday daytime hours. Patients were randomly assigned in a 1:1 ratio to either CCTA as part of the initial evaluation in the emergency department or the standard evaluation strategy in the emergency department at that site. All test results were provided to emergency department physicians in real time. Additional care was not mandated by the study protocol in either randomization group.

The discharge diagnosis was based on the local physicians' assessment. The discharge diagnoses were adjudicated separately by a clinical end-points committee in a predefined sample of 242 patients, which included all patients with acute coronary syndromes, the first 8 patients enrolled at each site, 4% of patients discharged with cardiac symptoms, and a randomly selected subgroup of 10% of all patients. The definitions of acute coronary syndromes are provided in the Supplementary Appendix, available at NEJM.org.

To ascertain potentially undetected acute coronary syndromes and as a safety measure, patients discharged within 24 hours after presentation in the emergency department were contacted by telephone within 72 hours to assess their clinical status. A follow-up telephone call to all patients was also conducted 28 days after discharge. During telephone calls, information on repeat visits to the emergency department or rehospitalizations for recurrent chest pain (including diagnostic testing, interventions, and clinical events during follow-up) was obtained and verified by the collection of medical records.

CCTA

Before the start of the study, participating sites were not routinely performing CCTA in patients in the emergency department to detect acute coronary syndromes, but they were required to use at least 64-slice CT technology for patient assessment. Protocols involving both retrospectively ECG-gated and prospectively ECG-triggered CCTA were permitted, with use according to published guidelines.¹⁴ The use of tube modulation to lower radiation exposure was strongly encouraged. CCTA images were interpreted on-site in real time, and the results were communicated to the responsible clinician.

End Points

The prespecified primary end point was the length of the hospital stay, defined as the time from presentation in the emergency department to the time of the discharge order. This end point was chosen because it reflects the summary of actions taken in response to clinical information and test results, as well as logistical, cost, and medical and legal considerations in participating centers.

Secondary effectiveness end points included the time to diagnosis, defined as the time from presentation in the emergency department until the first diagnostic test that led to the diagnosis of an acute coronary syndrome, or as the time from presentation in the emergency department to the final test that was used to rule out an acute coronary syndrome. The rate of direct discharge from the emergency department was defined as the proportion of patients discharged from the emergency department without admission to an observation unit or the hospital. Resource utilization was defined as any diagnostic testing (CCTA, exercise treadmill testing, nuclear imaging, stress echocardiography, or cardiac catheterization) or interventions from the index assessment in the emergency department to follow-up at 28 days, and it included resources used during repeat visits to the emergency department or hospitalization for recurrent chest pain. Cumulative radiation exposure was defined as radiation exposure from testing, including CCTA, nuclear perfusion imaging, and invasive

coronary angiography, measured in millisieverts and calculated with the use of standard methods¹⁵ during the index care episode (the visit to the emergency department and hospitalization) and follow-up. Health care costs during the index care episode were assessed from reports from hospital cost-accounting systems and physician billing records and were adjusted to 2011 dollars. Mean costs for patient care, diagnostic testing, and interventions during the index care episode were used to estimate the costs during follow-up.

Safety variables prespecified as secondary end points included an undetected acute coronary syndrome (defined as an unexpected cardiovascular event within 72 hours after hospital discharge in patients with a hospital stay of <24 hours), to ensure that potentially earlier discharge in the CCTA group was not associated with increased adverse events, major adverse cardiovascular events (defined as death, myocardial infarction, unstable angina, or urgent coronary revascularization within 28 days), and periprocedural complications (stroke, bleeding, anaphylaxis, or renal failure). These predefined safety variables were adjudicated by an external, independent clinical-events committee.

Statistical Analyses

All statistical analyses were performed by an independent data coordinating center on the basis of an intention-to-treat analysis. Continuous data are presented as means \pm SD and medians with interquartile ranges. Comparisons between groups were performed with the use of an independent-sample t-test for continuous variables, Fisher's exact test for categorical variables, and the Wilcoxon rank-sum test for ordinal variables. A two-sided P value of less than 0.05 was considered to indicate statistical significance. Concordance between the discharge diagnosis made at the study site and the independently adjudicated diagnosis in a selected subpopulation was assessed with the use of the kappa statistic.

The study was designed to have greater than 83% power with the use of a t-test at a two-sided 5% significance level if the true between-group difference in the length of stay in the hospital was at least 8.3 hours. Details of the simulation are described elsewhere.¹³

The study did not have predefined stopping rules or boundaries with respect to the primary end point or safety end points. Rather, the data and safety monitoring board was responsible for assessing every case in which an acute coronary syndrome might have been undetected.

Results

Study Population

Of 1000 enrolled patients, 501 were randomly assigned to CCTA and 499 were randomly assigned to a standard evaluation in the emergency department. All patients were included in the intention-to-treat analysis (Fig. 1). CCTA was not performed in 28 patients (6%) because of the patient's decision to decline CCTA (9 patients), safety concerns (5 patients), unavailability of CCTA (5 patients), or technical difficulties (9 patients). Overall, 987 of 1000 randomly assigned patients (99%) had complete follow-up at 28 days. The original medical records for repeat visits to the emergency department or hospitalizations were available in all cases.

Baseline characteristics of the study population are shown in Table 1. After a complete evaluation, 75 patients (8%) had a final diagnosis of an acute coronary syndrome. Agreement between the site and independent adjudication for the discharge diagnosis was very high (concordance, 98% [236 of 242 patients]; kappa, 0.94).

Primary and Secondary Effectiveness End Points

The effectiveness end points are shown in Table 2. The primary end point met the prespecified criterion for significance, since the average length of the hospital stay in the group of patients randomly assigned to CCTA was decreased by 7.6 hours, as compared with the group randomly assigned to a standard emergency department evaluation ($P<0.001$). Figure 2 shows the cumulative distribution of discharged patients with length-of-stay data in the two groups. Notably, 50% of the patients in the CCTA group were discharged within 8.6 hours after presentation, as compared with 10% of the patients randomly assigned to a standard evaluation in the emergency department. In the subgroup of patients with a final diagnosis of an acute coronary syndrome, the length of stay in the hospital was similar after CCTA and after standard evaluation in the emergency department.

In the overall cohort and also in the subgroups with or without a final diagnosis of an acute coronary syndrome, the mean time to diagnosis was significantly decreased with CCTA as compared with a standard evaluation. Patients in the CCTA group were more often directly discharged from the emergency department (47%, vs. 12% of patients in the standard-evaluation group; $P<0.001$), with fewer admissions to an observation unit.

Safety End Points

Prespecified clinical adverse events were infrequent in this trial (Table 2). No cases of undetected acute coronary syndromes were identified in either study group. Overall, there were eight major adverse cardiovascular events during the 28-day follow-up: six after standard evaluation in the emergency department (four myocardial infarctions and two cases of unstable angina pectoris for which percutaneous coronary intervention was required) and two after CCTA (one myocardial infarction and one case of unstable angina pectoris for which percutaneous coronary intervention was required) ($P = 0.18$). In both of the latter patients, CCTA established clinically significant coronary artery disease during the index hospitalization, but both patients had negative stress tests and were initially treated medically. Two periprocedural complications occurred in the CCTA group (perioperative bleeding after cardiothoracic surgery for an identified anomalous coronary artery and a transient increase in the creatinine level after CCTA without the need for dialysis in a patient with a urethral stone and hydronephrosis), and no periprocedural complications occurred in the standard-evaluation group.

Resource Utilization and Radiation Exposure

Table 3 shows resource utilization. Overall, more diagnostic testing was performed in the CCTA group than in the standard-evaluation group ($P<0.001$). Both the cumulative rate of invasive coronary angiography during the index hospitalization and follow-up and the rate of coronary revascularization were higher among patients in the CCTA group than among patients in the standard-evaluation group, but the differences were not significant ($P=0.06$ and $P=0.16$, respectively) (Table 3).

Nearly all patients in the CCTA group (484 of 501 patients; 97%), but only 167 of 499 patients randomly assigned to standard evaluation (33%) received radiation exposure from an imaging test or procedure. Hence, cumulative radiation exposure was significantly higher in the CCTA group (Table 3). The mean radiation exposure from CCTA was 11.3 ± 5.3 mSv and was lower than that from single-photon-emission CT (14.1 ± 4.8 mSv, $P<0.001$). The 78 patients who underwent CCTA with the use of an advanced 128-slice, dual-source CT scanner had lower radiation exposure (6.2 ± 3.8 mSv) than did the remaining patients (12.3 ± 5 mSv).

Detailed cost data were available in a subgroup of all 649 patients from five centers (Table 3). The mean costs of care from the initial visit in the emergency department through the 28-day follow-up were similar in the CCTA group and the group that received standard evaluation in the emergency department ($P = 0.65$).

Discussion

This prospective, multicenter, randomized, strategy-controlled trial was designed primarily to assess whether CCTA, incorporated early into an evaluation strategy for patients presenting to an emergency department with chest pain suggestive of an acute coronary syndrome, safely improves the efficiency of clinical decision making, as compared with a standard evaluation in the emergency department. The cumulative costs of diagnostic tests, interventions, and radiation exposure were also evaluated. The average length of stay in the hospital, the primary end point of the trial, was significantly reduced in the CCTA group, as was the time to diagnosis. Furthermore, rates of direct discharge from the emergency department were higher with CCTA than with a standard evaluation in the emergency department. These results were achieved without putting patients at greater risk for undetected acute coronary syndromes and without an increase in the cost of care. However, we observed increased diagnostic testing in the CCTA group and increased radiation exposure.

An important consideration when results show more efficient triage is whether that gain is achieved at the risk of undetected acute coronary syndromes. There were no undetected cases of acute coronary syndromes in either study group, suggesting that the earlier and greater number of discharges in the CCTA group did not result in any missed diagnoses. More major adverse cardiovascular events were observed in the standard-evaluation group than in the CCTA group, though the study did not have the statistical power to support the conclusion that major adverse cardiovascular events may be reduced after a CCTA-based evaluation.

The prevalence of acute coronary syndromes in a patient population is an important determinant of the risk–benefit ratio, given that CCTA is an advanced diagnostic imaging test that entails the administration of iodinated contrast material, radiation exposure, and costs. In our study population of patients who were at intermediate risk for acute coronary syndromes (observed rate of acute coronary syndromes, 7.5%, vs. 2 and 4% in previous studies^{10,11}), a greater number of invasive coronary procedures were performed after CCTA than after a standard evaluation. Information on the presence of anatomical coronary artery disease may influence clinical decision making toward invasive angiography. This concept is consistent with recent data suggesting that in a Medicare population, imaging of the coronary anatomy with CCTA in a nonemergency setting led to greater use of downstream testing and procedures, as compared with functional stress testing.¹²

In this trial, no decrease in total costs for the index visit and during 28-day follow-up was observed in a subgroup of 649 patients from five of nine sites in which complete billing data were available. Long-term outcome data are not available; such data might have allowed a determination of whether CCTA results in fewer repeat visits to the emergency department and hospitalizations over a longer time course.

Cumulative radiation exposure was higher in the group randomly assigned to CCTA than in the standard-evaluation group. Recent data show that diagnostic-quality CCTA imaging can be performed with exposure of less than 5 mSv in selected patients; this suggests that future studies could use lower doses of radiation.^{16,17} Lower-dose radiation should be considered in efforts to apply this strategy more widely, as well as in particular groups of patients.

There are several limitations of the present study and analysis. Enrollment occurred only during weekday hours when all imaging testing was available with technologists and readers on site. However, the results of triage decision making and particularly the timing of decisions to discharge or hospitalize patients would probably be different if the imaging studies were carried out during the night, when testing and interpretation are not as accessible. Similarly, the results cannot be generalized to clinical sites that perform a dedicated accelerated diagnostic protocol¹⁸ in the standard evaluation.

Inherent in the design of any randomized, comparative-effectiveness trial assessing a testing procedure is the lack of blinding to the intervention. We acknowledge that there may have been a bias in decision making toward earlier discharge in the CCTA group. For both groups of patients, however, the decision making was left to a large number of clinicians at the nine sites who were not directly associated with the study and whose decisions were subject to the same imperatives to provide high-quality clinical care and to take into account medical and legal considerations. Finally, the results of this study may not be applicable to populations that we did not study, including patients younger than 40 years of age and those older than 74 years of age.

In conclusion, in this trial involving patients with suspected acute coronary syndromes, an evaluation strategy incorporating early CCTA, as compared with a standard evaluation strategy, improved the efficiency of clinical decision making for triage in the emergency department, with a shorter length of stay in the hospital and more direct discharges from the emergency department. This improvement appeared to be accomplished safely, without putting patients at greater risk for undetected acute coronary syndromes. There was increased diagnostic testing and higher radiation exposure in the CCTA group, with no overall reduction in the cost of care. These data should allow providers and patients to make informed decisions about the use of this technology as an option for evaluation when symptoms are suggestive of an acute coronary syndrome.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix

Appendix 1:

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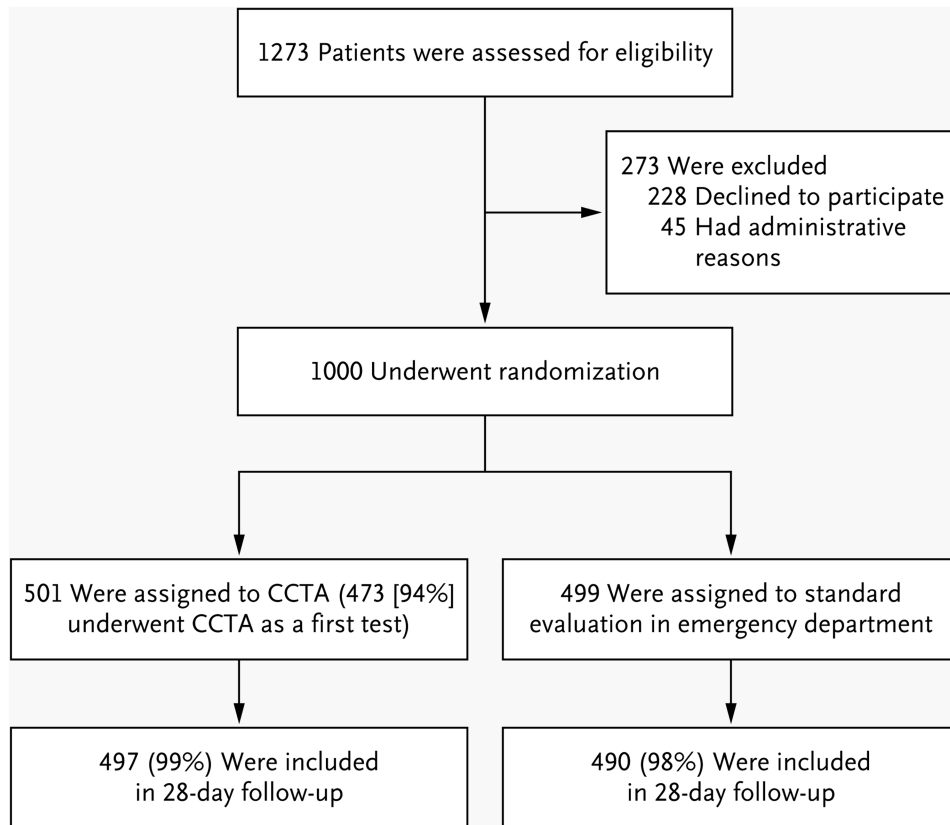
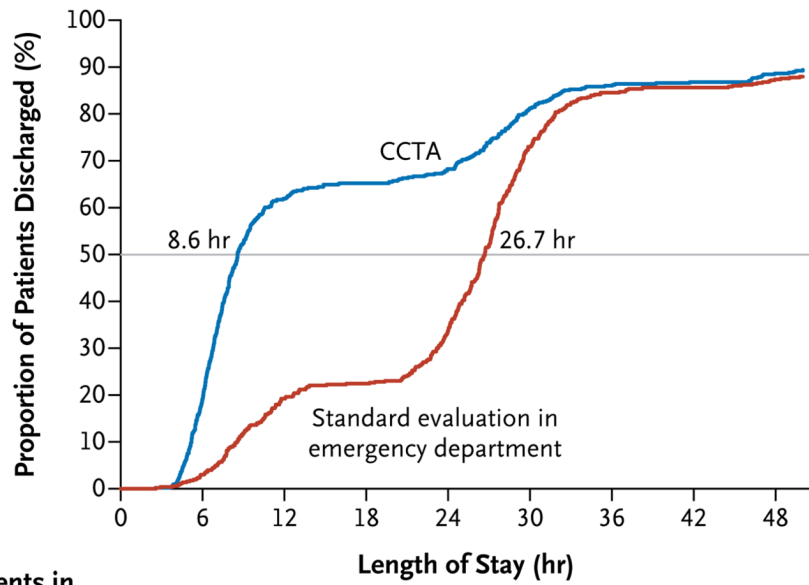


Figure 1. Screening, Randomization, and Follow-up of the Study Patients
CCTA denotes coronary computed tomographic angiography.



No. of Patients in
Emergency
Department
or Hospital

CCTA	501	404	191	174	159	95	70	66	57
Standard evaluation	499	484	403	387	331	135	77	72	63

Figure 2. Length of Stay in the Hospital and Proportion of Patients Discharged

The cumulative frequency of discharge from the index visit according to the length of stay is shown. The horizontal line indicates the median length of stay in the two study groups, which was significantly different (8.6 hours in the CCTA group vs. 26.7 hours in the standard-evaluation group, $P < 0.001$).

Table 1

Baseline Demographic and Clinical Characteristics of the Patients. *

Variable	CCTA (N = 501)	Standard Evaluation (N = 499)	P Value
Mean age — yr	54±8	54±8	0.44
Female sex — %	48	46	0.57
Race or ethnic group — no. (%)			
Black	141 (28)	141 (28)	1.00
White	330 (66)	330 (66)	0.95
Asian	18 (4)	13 (23)	0.47
Other	12 (2)	18 (4)	0.27
Non-Hispanic	435 (87)	422 (85)	0.57
Cardiovascular risk factors — no. (%)			
Hypertension	269 (54)	272 (54)	0.80
Diabetes mellitus	86 (17)	87 (17)	0.93
Dyslipidemia	230 (46)	224 (45)	0.75
Former or current smoker	249 (50)	243 (49)	0.75
Family history of premature coronary artery disease	135 (27)	136 (27)	0.94
No. of cardiovascular risk factors — %			
0 or 1	36	38	
2 or 3	54	52	
4	10	10	
Relevant prior medication — no. (%)			
Aspirin	115 (23)	113 (23)	0.94
Beta-blocker	88 (18)	82 (16)	0.67
Statin	143 (28)	151 (30)	0.58
Initial presentation in emergency department			
Chief symptom — no. (%)			
Radiating or nonradiating chest pain or anginal equivalent	444 (89)	452 (91)	0.47
Arm, jaw, shoulder, or epigastric pain	21 (4)	16 (3)	
Shortness of breath	7 (1)	10 (2)	
Other	29 (6)	21 (4)	
Heart rate — beats/min	78±14	77±14	0.58
Blood pressure — mm Hg			
Systolic	144±23	144±23	0.80
Diastolic	83±13	83±13	0.94
BMI	29.4±5.3	29.1±4.8	0.41
Discharge diagnosis after index emergency department visit or hospitalization — no. (%)			
Noncardiac chest pain	426 (85)	445 (89)	0.16
Noncoronary cardiac pain	7 (1)	8 (2)	

Variable	CCTA (N = 501)	Standard Evaluation (N = 499)	P Value
Coronary chest pain not associated with acute coronary syndrome	25 (5)	14 (3)	
Acute coronary syndrome	43 (9)	32 (6)	
Unstable angina pectoris	35 (7)	17 (3)	
Myocardial infarction	8 (2)	15 (3)	

* Plus-minus values are means \pm SD. BMI denotes body-mass index (the weight in kilograms divided by the square of the height in meters), and CCTA coronary computed tomographic angiography.

Table 2

Primary and Secondary Effectiveness and Safety End Points.*

End Point	CCTA (N = 501)	Standard Evaluation (N = 499)	P Value
Length of hospital stay — hr			
All patients in intention-to-treat analysis			<0.001
Mean	23.2±37.0	30.8±28.0	
Median	8.6	26.7	
Interquartile range	6.4–27.6	21.4–30.6	
Patients with final diagnosis other than acute coronary syndrome			<0.001
Mean	17.2±24.6	27.2±19.5	
Median	8.1	26.3	
Interquartile range	6.2–24.6	20.6–29.5	
Patients with final diagnosis of acute coronary syndrome			0.87
Mean	86.3±72.3	83.8±61.3	
Median	56.9	71.8	
Interquartile range	46.2–95.9	45.2–96.7	
Time to diagnosis — hr			
All patients in intention-to-treat analysis			<0.001
Mean	10.4±12.6	18.7±11.8	
Median	5.8	21.0	
Interquartile range	4.0–9.0	8.5–23.8	
Patients with final diagnosis other than acute coronary syndrome			<0.001
Mean	10.6±12.3	18.8±12.0	
Median	6.1	21.1	
Interquartile range	4.0–9.6	8.7–23.8	
Patients with final diagnosis of acute coronary syndrome			0.002
Mean	8.0±15.1	17.1±9.5	
Median	4.4	14.9	
Interquartile range	3.3–5.6	7.4–25.1	
Discharge status — no. (%)			
Direct discharge from emergency department	233 (47)	62 (12)	
Admission to observation unit	153 (30)	301 (60)	
Admission to hospital	107 (21)	125 (25)	
Left against medical advice	8 (2)	11 (2)	
Follow-up for recurrent chest pain within 28 days — no.			
Repeat visit to emergency department	14	19	0.38
Repeat hospitalization	7	7	
Safety — no.			
Undetected acute coronary syndrome	0	0	
Periprocedural complications	2	0	0.50

End Point	CCTA (N = 501)	Standard Evaluation (N = 499)	P Value
Length of hospital stay — hr			
Major adverse cardiovascular events at 28 days — no.	2	6	0.18

* Plus-minus values are means \pm SD.

Table 3

Resource Utilization, Radiation Exposure, and Costs of Care.*

Variable	Index Visit		Index Plus Follow-up Visit		P Value
	CCTA (N = 501)	Standard Evaluation (N = 499)	CCTA (N = 501)	Standard Evaluation (N = 499)	P Value
Diagnostic testing — no. of patients (%) [†]					<0.001
No testing [‡]	9 (2)	109 (22)	9 (2)	89 (18)	
1 test	376 (75)	337 (68)	359 (72)	350 (70)	
2 tests	116 (23)	53 (11)	133 (27)	60 (12)	
Functional testing — no. (%) [§]					<0.001
SPECT	50 (10)	124 (25)	58 (12)	133 (27)	
Stress echocardiography	20 (4)	102 (20)	20 (4)	102 (20)	
ETT	12 (2)	147 (29)	22 (4)	162 (32)	
Invasive coronary angiography — no. (%)	54 (11)	36 (7)	59 (12)	40 (8)	0.06
Intervention — no. (%)					
PCI	24 (5)	14 (3)	27 (5)	17 (3)	0.16
CABG	5 (1)	4 (1)	5 (1)	4 (1)	0.99
Cumulative radiation exposure — mSv/patient	13.9±10.4	4.7±8.4	14.3±10.9	5.3±9.6	<0.001
Costs of care — U.S. dollars					<0.001
Emergency department					
Mean	2,101±1,070	2,566±1,323			
Median	1,770	2,293			
Interquartile range	1,435–2,161	1,592–3,583			
Hospital					0.19
Mean	1,925±6,697	1,308±5,333			
Total					0.75
Mean	4,026±6,792	3,874±5,298	4,289±7,110	4,060±5,452	
Median	1,937	2,742	1,946	2,809	
Interquartile range	1,504–4,057	1,755–3,832	1,514–4,164	1,822–4,060	

* Plus-minus values are means \pm SD. Percentages may not sum to 100 because of rounding. CABG denotes coronary-artery bypass grafting, ETT exercise treadmill testing, PCI percutaneous coronary intervention, and SPECT single-photon-emission computed tomography.

[†] Diagnostic testing included CCTA, ETT, SPECT, stress echocardiography, and invasive coronary angiography.

[‡] Serial measurement of biomarkers and electrocardiographic testing were not considered as diagnostic tests in this table.

[§] At the index visit, functional testing was the second test in the CCTA group and the first test in the standard-evaluation group.

[¶] Radiation exposure included exposure from CCTA, SPECT, and invasive coronary angiography.

^{//} Costs included those for patients discharged directly from the emergency department and those discharged from an observation unit.