Original Report:
Cardiovascular Disease
and Risk Factors

Effect of Race on Outcomes Following Early Coronary Computed Tomographic Angiography or Standard Emergency Department Evaluation for Acute Chest Pain

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Objective: To examine racial differences in outcomes with coronary computed tomographic angiography (CCTA) vs standard emergency department (ED) evaluation for chest pain.

Design: Retrospective analysis of the prospective, randomized, multicenter Rule Out Myocardial Ischemia/Infarction by Computer Assisted Tomography (ROMICAT-II) trial.

Setting: ED at nine hospitals in the United States.

Participants: 940 patients who were Caucasian or African American (AA) presenting to the ED with chest pain.

Interventions: CCTA or standard ED evaluation

Main Outcome Measures: Length of stay, hospital admission, direct ED discharge, downstream testing and repeat ED visit or hospitalization for recurrent chest pain at 28 days. Safety end points: missed acute coronary syndrome (ACS) and cumulative radiation exposure during the index visit and follow-up period.

Results: 659 (66%) patients self-identified as Caucasian and 281 (28%) self-identified as AA. AA were younger and more often female compared with Caucasians, had a higher prevalence of hypertension (64% vs 49%, P<.001) and diabetes (23% vs 14%, P<.001) and a lower prevalence of hyperlipidemia (28% vs 51%, P<.001). ACS was more frequent among Caucasians (10% vs 2%, P<.001). Randomization to CCTA resulted in a reduction in median LOS for Caucasians (7.4 vs 24.7 hours, P<.001) and AA (8.9 vs. 26.3, P<.001; P-interaction=.88). Both AA and Caucasian patients experienced greater radiation exposure and more downstream testing with CCTA compared with standard evaluation.

Conclusions: Early CCTA reduced median LOS for both AA and Caucasian patients presenting to the ED with chest pain by approximately 17 hours compared with standard evaluation. *Ethn Dis*. 2018;28(4):517-524; doi:10.18865/ed.28.4.517.

Key Words: Chest Pain; Acute Coronary Syndromes; Cardiac Computed Tomography; Emergency Department; Ethnicity/Race

Introduction

Despite recent advances, coronary artery disease (CAD) remains the leading cause of mortality in the United States.[1] The burden of cardiovascular disease is strongly related to the number and distribution of modifiable risk factors.[2] The distribution of risk factors is significantly influenced by race: African Americans (AA) have a higher prevalence of hypertension, diabetes and obesity whereas Caucasians have a higher prevalence of hyperlipidemia (although more recent data show a higher incidence of hyperlipidemia among AA).[3,4] Importantly, AA patients with CAD have worse outcomes than Caucasians despite the fact that Caucasians have more extensive atherosclerosis by coronary angiography.[5] Patients presenting to the emergency department (ED) with chest pain suggestive of an acute coronary syndrome (ACS) present a frequent challenge to ED physicians. The most appropriate testing to risk stratify patients is not always clear and the stakes are high, given the potential consequences of missed diagnoses of ACS, both in terms of patient outcomes[6] and malpractice litigation.[7-9] Cardiac computed tomographic angiography (CCTA) is an advanced imaging modality with excellent negative predictive value for the diagnosis of CAD. Multiple large, multicenter, randomized trials have demonstrated that CCTA is a safe and effective alternative to standard evaluation in the ED when implemented early in the evaluation of chest pain and is associated with shorter length of stay (LOS).[10-15] However, informa-

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tion regarding the impact of racial differences on outcomes after CCTA use for evaluation of chest pain in the ED is not available. Using data from the Rule Out Myocardial Ischemia/Infarction by Computer Assisted Tomography (ROMICAT-II) trial, we evaluated the effectiveness and safety, including radiation exposure and downstream testing, of early CCTA in the ED in AA compared with Caucasians presenting with chest pain concerning for ACS.

Methods

De-identified data were obtained from the ROMICAT-II trial through the Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC) of the National Heart, Lung, and Blood Institute under a data use agreement. The Washington University Human Research Protection Office granted this study an exemption from institutional review board oversight.

ROMICAT-II was a randomized, controlled, multicenter trial consisting of 1000 patients enrolled at nine hospitals in the United States between April 23, 2010 and January 30, 2012. The trial was designed to evaluate use of CCTA as a first diagnostic test as early as possible compared with standard ED evaluation of acute chest pain suggestive of ACS. The study design, inclusion and exclusion criteria, and primary results were reported previously.[13,16] The study was approved by the institutional review board at each participating site and all participants provided informed consent. Eligible patients were between the ages of 40 and 74 years and presented to the ED during weekday, daytime hours with symptoms suggestive of ACS but without ischemic electrocardiographic (ECG) changes or an initial positive troponin. Race was defined by self-report.

All patients were randomized to CCTA or to the standard ED evaluation strategy, as dictated by local attending physicians in the ED. CCTA was performed with at least 64-slice CT technology; both retrospectively ECG-gated and prospectively ECG-triggered CCTA protocols were permitted. The standard ED evaluation strategy could include no diagnostic testing, functional testing (exercise treadmill test, exercise or pharmacological nuclear imaging, stress echocardiography) or invasive coronary angiography. Patients were contacted by phone within 72 hours if discharged within 24 hours of ED presentation to evaluate for possible missed ACS. Patients were followed up for 28 days after discharge from the ED or hospital by phone interview and questioned regarding repeat ED visits or hospitalizations for recurrent chest pain and diagnostic testing/interventions; reported events were verified with medical records.

We evaluated the effectiveness and safety, including radiation exposure and downstream testing, of early cardiac computed tomographic angiography in the emergency department in African Americans compared with Caucasians presenting with chest pain concerning for acute coronary symptoms.

The primary end point was length of stay (LOS) defined as the time from ED presentation to the time of the discharge order. Secondary effectiveness end points included rates of direct ED discharge (defined as the proportion of patients discharged from the ED without being admitted to an observation unit or hospital), hospital admission and diagnostic testing (defined as any of the following: CCTA, transthoracic echocardiography, exercise treadmill test, nuclear stress test, stress echocardiography or invasive coronary angiography). Additional secondary end points included rates of invasive coronary angiography, percutaneous coronary intervention (PCI) or coronary artery bypass surgery (CABG) and repeat ED visit or hospitalization for recurrent chest pain at 28 days. Safety end points included missed ACS (unexpected cardiovascular event within 72 hours after hospital discharge in patients with a hospital stay of <24 hours) and cumulative radiation exposure during the index visit and follow-up period. Radiation exposure from testing was calculated

in mSv for CCTA, nuclear perfusion imaging and invasive coronary angiography using standard methods;[17] a conversion coefficient of .014 for the chest was used for CCTA scans.

Comparisons between racial groups were conducted using Student's two sample t-test and Fisher's exact test for continuous and categorical variables, respectively. Ordinal variables and variables with non-normal distributions were summarized by the median (1st quartile, 3rd quartile) and compared using the Mann-Whitney U-test. To determine if the association between length of stay and treatment varied with respect to race, quantile regression models were built to evaluate the interaction between race and treatment. Both unadjusted and adjusted models were

Table 1. Patient characteristics by race and treatment group

Variable	Caucasian			African American			
	CCTA, (n=330)	Standard evaluation (n=329)	P, diff within race	CCTA, (n=141)	Standard evaluation (n=140)	P, diff within race	P, diff between races
Age, mean, years (SD)	54.83 (8.20)	54.29 (8.40)	.41	51.92 (7.70)	54.61 (7.56)	.003	.026
Female	143 (43%)	144 (44%)	.94	77 (55%)	73 (52%)	.72	.007
Hypertension	162 (49%)	163 (50%)	.94	87 (62%)	94 (67%)	.38	<.001
Diabetes	43 (13%)	47 (14%)	.65	30 (21%)	34 (24%)	.57	<.001
Hyperlipidemia	170 (52%)	169 (51%)	>.99	41 (29%)	37 (26%)	.69	<.001
Former or current smoking	166 (50%)	161 (49%)	.76	74 (52%)	70 (50%)	.72	.67
First degree relative with CAD/ACS/MI	97 (29%)	99 (30%)	.86	33 (23%)	31 (22%)	.89	.032
Risk Factors			.39			.62	.30
0-1	114 (35%)	123 (37%)		59 (42%)	56 (40%)		
2-3	188 (57%)	171 (52%)		66 (47%)	72 (51%)		
≥4	28 (8%)	35 (11%)		16 (11%)	12 (9%)		
Medications							
Aspirin	80 (24%)	74 (22%)	.65	26 (18%)	30 (21%)	.55	.27
Beta-blockers	55 (17%)	54 (16%)	>.99	28 (20%)	27 (19%)	>.99	.26
Statins	98 (30%)	111 (34%)	.28	29 (21%)	25 (18%)	.65	<.001
Chief complaint			.30			.74	.15
Anginal chest pain	293 (89%)	297 (90%)		125 (89%)	127 (91%)		
Epigastric pain	3 (1%)	3 (1%)		3 (2%)	2 (1%)		
Arm/jaw/shoulder pain	9 (3%)	5 (2%)		3 (2%)	5 (4%)		
Shortness of breath	2 (1%)	7 (2%)		5 (4%)	2 (1%)		
Other	23 (7%)	17 (5%)		5 (4%)	4 (3%)		
Medical history							
CHF	4 (1%)	1 (0%)	.37	4 (3%)	4 (3%)	>.99	.027
PVD	5 (2%)	6 (2%)	.77	1 (1%)	1 (1%)	>.99	.36
Chronic lung disease or COPD	13 (4%)	4 (1%)	.046	2 (1%)	4 (3%)	.45	.82
Resting heart rate, mean (SD)	76.89 (15.17)	77.03 (14.46)	.91	79.26 (12.66)	78.04 (15.00)	.46	.10
Systolic blood pressure, mm Hg, mean (SD)	142.72 (22.37)	143.39 (22.64)	.70	146.36 (23.08)	146.34 (23.23)	.99	.042
Diastolic blood pressure, mm Hg, mean (SD)	81.80 (13.35)	81.82 (12.90)	.98	87.09 (12.68)	86.20 (14.60)	.59	<.001
BMI, kg/m^2, mean (SD)	28.88 (5.13)	29.16 (4.79)	.46	30.59 (5.32)	29.40 (4.89)	.05	.006
Primary discharge diagnosis			.31			.77	
Non-cardiac chest pain	277 (84%)	289 (88%)		123 (87%)	128 (91%)		
Non-coronary cardiac chest pain	3 (1%)	5 (2%)		4 (3%)	3 (2%)		
Cardiac chest pain not meeting ACS criteria	13 (4%)	8 (2%)		10 (7%)	6 (4%)		
Acute coronary syndrome	37 (11%)	27 (8%)	.24	4 (3%)	3 (2%)	>.99	
MI	5 (14%)	12 (44%)	.009	1 (25%)	1 (33%)	>.99	
Unstable angina	32 (86%)	15 (56%)		3 (75%)	2 (67%)		

CCTA, coronary computed tomographic angiography; SD, standard deviation; CAD, coronary artery disease; ACS, acute coronary syndrome; MI, myocardial infarction; CHF, congestive heart failure; PVD, peripheral vascular disease; COPD, chronic obstructive pulmonary disease; BMI, body mass index.

Table 2. Length of stay by race and treatment group, adjusted[a]

	Standard evaluation		CCTA			
	Median estimate	95% CI	Median estimate	95% CI	P for difference	P for interaction
Caucasian	24.7	(18.6, 30.9)	7.4	(1.4, 13.4)	<.001	.93
African American	26.3	(20.0, 32.6)	8.9	(2.6, 15.2)	<.001	

a. The following adjustment variables were included: age; sex; hypertension; diabetes; hypercholesterolemia/hyperlipidemia; first degree relative with coronary artery disease/acute coronary syndrome/acute myocardial infarction; statin treatment; resting heart rate; systolic blood pressure; diastolic blood pressure; body mass index and primary discharge diagnosis.
Median estimates calculated using the overall observed marginal frequencies and means.
CCTA, coronary computed tomographic angiography.

created. Adjusted models included the following additional independent variables: age, sex, hypertension, diabetes, hyperlipidemia, first degree relative with CAD/ACS/myocardial infarction (MI), statin use, resting heart rate, systolic blood pressure, diastolic blood pressure, body mass index (BMI) and primary discharge diagnosis. Overall observed marginal frequencies and means were used to obtain model-derived LOS estimates. Unadjusted analyses were conducted for all secondary outcomes. For radiation dose, quantile regression was used and for dichotomous outcomes, logistic regression models were created to evaluate the interaction between race and treatment. For the interaction between race and treatment for number of diagnostic tests, the cumulative logit partial proportional odds model was used. P's <.05 were considered statistically significant. All analyses were conducted in SAS (version 9.4; SAS Institute Inc., Cary, NC).

Results

Of the 1000 patients in ROMICAT-II, 940 patients were included in this analysis, of whom 659 (70%) were Caucasian and 281 (30%) were AA. The remaining 60 patients (6%), identified as Asian or other, were excluded from analysis. Patients who were protocol eligible but not enrolled (n=228), were of similar age (53.7±8.7, P=.44), but more likely female (47% vs 60%, P=.0005), and AA (28% vs 39%, P=.002; data not shown). Table 1 presents the baseline characteristics of the ROMICAT-II patients stratified by race and randomized evaluation arm. Of the 471 patients in the CCTA arm, 330 (70%) were Caucasian and 141 (30%) were AA. Of the 469 patients in the standard evaluation arm, 329 (70%) were Caucasian and 140 (30%) were AA. Overall, AA patients were younger (average age 53.26 years vs 54.56 years; P=.0226) and more often female (53% vs 44%; P=.007), hypertensive and diabetic. They also had higher systolic blood pressure, diastolic blood pressure and BMI. Caucasian patients were more likely to have hyperlipidemia requiring a statin and to have a first-degree relative with CAD. The total number of cardiac risk factors did not differ by race. The presenting symptom was anginal chest pain in 90% of both AA and Caucasians. The primary discharge diagnosis differed between AA and Caucasians. Caucasians had a five-fold increase in the diagnosis of ACS (10% vs 2%).

Among both Caucasian and AA patients, the adjusted median LOS was significantly reduced for CCTA compared with standard evaluation (Table 2). The association between CCTA vs standard evaluation and median LOS did not differ between races (P-interaction=.93).

There were more direct ED discharges for both Caucasian and AA patients evaluated with CCTA compared with standard ED evaluation (Table 3). The CCTA group had significantly more diagnostic testing at both the index visit and the total study period in both races (Table 3). The referral for cardiac catheterization, PCI or CABG did not differ by chest pain evaluation strategy for either race. The rate of return to the ED within 28 days for recurrent chest pain differed by race. Among Caucasians, the rate of return was reduced in the CCTA group compared with the standard evaluation group but did not reach significance (2.4% vs 4.9%, P=.10), while for AA, the rate of ED return was higher in the CCTA group (4.3% vs 1.4%, P=.17; P-interaction=.049).

There were no cases of missed ACS in either race or evaluation arm. The median radiation exposure dur-

Table 3. Clinical outcomes by race and treatment group

	Caucasian			African American			
	CCTA (N=330)	Standard evaluation (n=329)	P for diff	CCTA (N=141)	Standard evaluation (n=140)	P for diff	P for interaction
Clinical outcomes							
Direct ED discharge	153 (46%)	35 (11%)	<.001	61 (43%)	19 (14%)	<.001	.27
Hospital admission	75 (23%)	82 (25%)	.51	25 (18%)	36 (26%)	.11	.31
Downstream testing							
During index visit	80 (24%)	42 (13%)	<.001	31 (22%)	9 (6%)	<.001	.16
At any point	95 (29%)	48 (15%)	<.001	32 (23%)	9 (6%)	<.001	.18
Diagnostic testing at index			<.001			<.001	.93
0	3 (1%)	70 (21%)		4 (3%)	30 (21%)		
1	247 (75%)	217 (66%)		105 (74%)	101 (72%)		
2	57 (17%)	38 (12%)		22 (16%)	9 (6%)		
≥3	23 (7%)	4 (1%)		10 (7%)	0 (0%)		
Diagnostic testing at index or follow-up			<.001			<.001	.78
0	3 (1%)	55 (17%)		4 (3%)	28 (20%)		
1	232 (70%)	226 (69%)		106 (75%)	103 (74%)		
2	70 (21%)	41 (12%)		22 (16%)	9 (6%)		
≥3	25 (8%)	7 (2%)		9 (6%)	0 (0%)		
Exercise treadmill test during index visit	9 (3%)	109 (33%)	<.001	3 (2%)	24 (17 %)	<.001	.39
One or more SPECT during index visit	31 (9%)	90 (27%)	<.001	17 (12%)	29 (21%)	.05	.11
One or more stress echo during index visit	5 (2%)	45 (14%)	<.001	15 (11%)	57 (41%)	<.001	.32
Invasive coronary angiography							
During index visit	44 (13%)	30 (9%)	.11	7 (5%)	4 (3%)	.54	.83
During index or follow up	48 (15%)	34 (10 %)	.12	8 (6%)	4 (3%)	.38	.63
PCI							NA
During index hospitalization	20 (6%)	13 (4%)	.28	2 (1%)	0 (0%)	.50	
During follow up but not during index visit	2 (1%)	3 (1%)	.69	1 (1%)	0 (0%)	1.0	
During index or follow up	22 (7%)	16 (5%)	.40	3 (2%)	0 (0%)	.25	
CABG							NA
During index hospitalization	4 (1%)	4 (1%)	1.0	1 (1%)	0 (0%)	1.0	
During follow-up but not during index visit	0 (0%)	0 (0%)	1.0	0 (0%)	0 (0%)	1.0	
Return ED visits for chest pain within 28 days	8 (2%)	16 (5%)	.10	6 (4%)	2 (1%)	.28	.049

All values are N (%) unless otherwise indicated.

CCTA, coronary computed tomographic angiography; ED, emergency department; Diagnostic testing defined as any of CCTA, ETT, SPECT, stress echo, of invasive coronary angiography; SPECT, single-photon emission computed tomography myocardial perfusion imaging; PCI, percutaneous coronary intervention; NA, Not applicable (no event for one or more outcomes): CABG, coronary artery bypass graft.

ing the index visit was higher in the CCTA arm compared with standard evaluation for both Caucasian and AA patients, respectively (Table 4). At follow-up, radiation exposure remained significantly higher among patients evaluated with CCTA compared with standard evaluation: 12.0 vs 0.0 mSv among Caucasians and 11.7 vs. 0.0 mSv among AA (P<.001 for both). There was no significant difference between races in radiation exposure at the index evaluation or in the follow-up period.

Discussion

In this retrospective analysis of the prospective, randomized ROMICAT-II trial, both Caucasian and AA patients had a reduction in median LOS when CCTA was implemented early in the ED course for evaluation of chest pain. This reduction in median LOS persisted when adjusting for demographic and cardiac risk factors. Both Caucasians and AA patients had at least 3-fold higher rates of direct discharge from the ED in the CCTA

Table 4. Safety outcomes by race and treatment group

	Caucasian			African American			
	CCTA (n=330)	Standard evaluation (n=329)	P for diff	CCTA (n=141)	Standard evaluation (n=140)	P for diff	P for interaction
Missed ACS with 72 hours	0 (0%)	0 (0%)		0 (0%)	0 (0%)		
Median radiation dose (IQR), index visit	11.7 (7.8, 116.8)	.0 (.0, 12.1)	<.001	11.6 (8.6, 15.9)	.0 (.0, .0)	<.001	.79
Median cumulative radiation dose (IQR)	12.0 (7.9, 17.2)	.0 (.0, 12.4)	<.001	11.7 (8.6, 16)	.0 (.0, .0)	<.001	.60

CCTA, coronary computed tomographic angiography; ACS, acute coronary syndrome; IQR, interquartile range.

arm, demonstrating CCTA as an effective tool for early discharge for low-risk patients. AA and Caucasian patients randomized to CCTA were discharged approximately 17 hours earlier than patients evaluated by standard care. Reduced LOS came at the cost of increased radiation exposure and downstream testing.

Our results are consistent with previously established racial differences in modifiable cardiovascular risk factors among the US population. Hypertension, diabetes and obesity are more common among AA patients, whereas hyperlipidemia is more prevalent among Caucasian patients.[18] Current epidemiologic data suggest that AAs have higher mortality associated with CAD than Caucasians. Generally, this difference has been attributed to more underlying comorbidities, reduced access to care and a higher prevalence of traditional cardiac risk factors among AA.[19] Prior studies have also shown that AA patients have a lower prevalence and extent of obstructive CAD on catheterization when compared with Caucasians.[20-22] Studies involving CCTA and electron beam tomography (EBT) have also demonstrated less coronary calcification in AA patients, both before and after adjusting for traditional risk factors.[5,23] Given this apparent uncoupling between risk factor burden, the extent of obstructive CAD and outcome, it seems that gaps still remain in our understanding of racial differences in disease mechanisms.

Considering disparities in risk factors, the extent of CAD and mortality between racial groups, it cannot be assumed that the same approaches of risk stratification apply to patients of different races presenting to the ED with acute chest pain. Our study showed that assessment with CCTA in both races resulted in a 3-fold increase in the likelihood of being discharged directly from the ED, with no missed ACS diagnoses in either racial group. This finding demonstrates the usefulness of CCTA in triaging patients with suspected ACS. Of note, the AA group was significantly more likely to return to the ED within 28 days with recurrent chest pain, suggesting that either other ischemic mechanisms, including microvascular disease, or coronary vasospasm may play a greater role in AA presenting with chest pain. Alternatively, race-related differences in physician-to-patient communication, the ability to promptly schedule outpatient follow-up or health literacy may have been operative. Our findings suggest that in the ED setting, CCTA can be used as an effective triage tool in low-risk AA patients with chest pain. However, further studies of CCTA use in African Americans are required to definitively establish its clinical efficacy in this population.

…both Caucasian and AA patients had a reduction in median length of stay when CCTA was implemented early in the ED course for evaluation of chest pain.

Our study has several limitations. First, the small number of minorities limited the analysis to only AA and Caucasian patients and did not allow for evaluation for differences in other racial or ethnic groups, such as Asians or Hispanics. Second, high-sensitivity troponin testing was not performed

in ROMICAT II. Thus, it cannot be assumed these results would apply to chest pain evaluation with the use of high sensitivity troponin assays. Third, the relatively short follow up of only 28 days does not allow for the assessment of outcome over a longer time. Fourth, the patients who were eligible but not enrolled in the study were more likely to be AA than those enrolled, which may be a source of bias. Finally, the results only apply to patients evaluated during weekday, daytime hours and may not apply to patients who present at other times.

Conclusion

When compared with standard ED evaluation of patients presenting with chest pain suggestive of ACS, early CCTA reduces median LOS in both AA and Caucasian patients while increasing cumulative radiation dose and downstream testing in both races with no improvement in outcomes.

Acknowledgments

Clinical Trial Registration www.clinicaltrials.gov NCT01084239

Conflict of Interest

No conflicts of interest to report.

Author Contributions

Research concept and design: Brown; Acquisition of data: Brown; Data analysis and interpretation: Reinhardt, Babatunde, Novak, Brown; Manuscript draft: Reinhardt, Babatunde, Novak, Brown; Statistical expertise: Novak; Administrative: Brown; Supervision: Brown

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