ORIGINAL REPORTS: CARDIOVASCULAR DISEASE AND RELATED RISK FACTORS

THE IMPACT OF AN ACUTE MYOCARDIAL INFARCTION GUIDELINE AND PATHWAY ON RACIAL OUTCOMES AT A UNIVERSITY HOSPITAL

Marcus Leon Williams, MD; George Hill, PhD; Mary Jackson, RN

Objective: Historically, African Americans who present with acute myocardial infarction were less likely to survive or be revascularized compared to Whites in the United States. Variation in practice has been implicated as a cause. Some researchers have proposed that the explanation for this variation was that coronary artery disease (CAD) was less severe in African Americans than Whites. A university hospital compared the extent of CAD by race for its acute myocardial infarction (AMI) patients and determined the effect of implementing evidenced-based guidelines on racial differences in cardiovascular outcomes.

Methods: From 1991 to 1994, using the National Registry for Myocardial Infarction 1 and the hospital AMI database, 323 of the 521 consecutive patients were catheterized during their initial admission. The extent of CAD was defined as the frequency of CAD stenosis ≥70% seen in the major coronary arteries and/or their major branches. Cardiac function was measured by left ventricular ejection fraction (LVEF). Short-term hospitalized outcomes were determined for death, treatment, and coronary revascularization.

Results: We assessed 82 (25.4%) African Americans and 241 (74.6%) Whites. No significant difference in the frequency of stenosis ≥70% or clinical outcomes existed between races. However, African Americans had a lower LVEF of 49.13% compared to 54.98% for Whites ($P=.04$). African Americans were 2.54 times more likely to have LVEF <45% ($P=0.024$). We saw no racial difference in death, coronary artery bypass graft, percutaneous transluminal coronary angioplasty, or thrombolytic therapy.

Conclusion: In high-risk AMI patients, this study found no difference in the burden of CAD by race. However, for African Americans, left ventricular function was more depressed. The use of an AMI management guideline and pathway-driven protocol resulted in no significant racial difference in cardiac interventions or clinical outcomes. A guideline or protocol-driven approach to the management of AMI may significantly reduce the observed racial variation in quality care. (*Ethn Dis*. 2006; 16:653–658)

Key Words: Acute Myocardial Infarction, Left Ventricular Ejection Fraction, Coronary Artery Disease

From the University of North Carolina at Chapel Hill, North Carolina (MLW, GH, MJ); University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Oakland; VAMC Hospital, East Orange; New Jersey (MLW).

Address correspondence and reprint requests to Marcus L. Williams, MD; Cardiac Associates of North Jersey; 43 Yawpo Avenue; Oakland, NJ 07436; 201-337-0066; 201-337-7414 (fax); mlwson99@verizon.net

INTRODUCTION

While in the United States, the death rate for acute myocardial infarction (AMI) is declining in most ethnic groups, the rate of decline has been slower for African Americans.[1–4] Multiple studies have reported that African Americans die at a younger age of heart disease compared to Whites and are more likely to die of sudden death.[5–10] The National Hospital Discharge Survey found that African Americans had between 10% and 70% higher in-hospital, age-adjusted death rates for AMI.[4] The NHANES follow-up report found that the odds ratio for the relative age-adjusted combined risk for coronary heart disease (CHD), acute myocardial infarction (AMI), and coronary death in African Americans between the ages of 25–54 years was 1.76 times that of Whites.[6]

A lower coronary revascularization rate has been linked as one of the causes of the increased cardiovascular morbidity and mortality found in African Americans in the United States.[11]

While the cause for this difference in outcomes may be multifactorial, less aggressive therapy to reduce major cardiovascular events is a major contributor to the difference in outcomes by race. A lower coronary revascularization rate has been linked as one of the causes of the increased cardiovascular morbidity and mortality found in African Americans in the United States.[11] A nationwide study of patients with renal disease found that Whites were three times more likely to receive a cardiac procedure than African Americans.[12] Whites were twice as likely to undergo a cardiac catheterization and three times more likely to undergo coronary artery bypass grafting or angioplasty. A review of the national Veterans Affairs (VA) database found that Whites were more likely to undergo cardiac catheterization, angioplasty, and coronary artery bypass surgery at significant odds ratios

of 1.38, 1.50, and 2.22, respectively.[13] Some have suggested that this disparity for African Americans who presented with CHD may be linked to studies that suggest that African Americans have less epicardial coronary artery disease.[14] If this finding is true, it could help explain the lower rate of therapeutic interventional procedures in African Americans.

Variation in care, regardless of etiology (ie, race, age, sex, access, efficiency, etc) is associated with poorer clinical outcomes. Several studies have demonstrated that programs that focus on reducing the observed variation in clinical practice reduce variability and improve the quality of patient care.[15] Such interventions could also reduce the racial disparity seen in clinical outcomes for AMI.

When appropriately implemented, clinical guidelines and clinical pathways have demonstrated significant reductions in clinical practice variation with substantial improvement in quality of care indicators.[16] The University of North Carolina (UNC) implemented a quality assurance program that uses clinical pathways and guidelines to reduce variation and improve outcomes for its AMI patients.[18] We report on the impact of this project on in-hospital clinical outcomes and therapeutic intervention by race. Specifically, we wanted to determine whether such a program could minimize racial differences in outcome for our AMI patients.

METHODS

Patient Enrollment

All patients admitted to the coronary care unit (CCU) at UNC hospitals with a diagnosis of AMI were enrolled in this study from January 1991 to December 1994. These patients had new ST segment elevation or depression in two or more contiguous leads with new Q waves and/or significant elevation of their cardiac enzymes. A significant elevation of the cardiac enzymes was defined by a creatine phosphokinase total that was at least twice as high as the upper limit of normal for the hospital laboratory or a diagnostic elevation of creatine kinase. Out of 521 patients recruited, 323 (62%) had a cardiac catheterization performed during their initial admission. These patients were included in this study. Only African Americans and Whites were enrolled. Race was based on what the patient reported.

The Quality Assurance Program

This program had three parts: 1) an evidence-based clinical guideline[17]; 2) a clinical pathway based on national benchmarks; and 3) a database using the National Registry of Myocardial Infarction (NRMI) to track outcomes and provide regular feedback to the staff and hospital.[18] The hospital appointed a team of physicians, nurses, and support staff to develop, organize, and implement this Quality Assurance (QA) project. This group met monthly to review progress and oversee the changes necessary for success. Every month part of the team met with new house staff starting in the CCU and in the emergency department. They were oriented and taught the clinical guideline and pathway. The nursing staff in the two departments also had regular orientations and reviews. The CCU nursing staff recorded NRMI data, which were reviewed with them and the house staff on a quarterly basis. All treatments and evaluations were determined by the clinical guideline, and variation from the guideline was documented. A clinical pathway was developed and placed in the CCU. It was used on all AMI patients, and the nursing staff did their charting on the pathway chart. Variations from the pathway and the reason for deviation from the pathway were documented on the clinical pathway chart. These were reviewed at least monthly, and interventions to improve compliance with the guideline and pathway were made after these assessments.

Registry

The National Registry of Myocardial Infarction (NRMI) is a phase IV (post-marketing), observational, collaborative endeavor sponsored by Genentech, Inc, in which the UNC Hospital System was one of 1073 contributing hospitals.[18] The purpose of the registry was to collect uniform, prospective data on the treatment of patients with AMI that: 1) could be used globally to analyze national practice patterns for infarct treatment; 2) could be used locally to compare practice patterns and outcomes; and 3) could be used to monitor the frequency of specific adverse events of the recombinant tissue-type plasminogen activator (r-tPA, Activase).

Endpoints

The primary endpoint was racial differences in in-hospital clinical outcomes. These outcomes refer to in-hospital death and therapeutic interventions (cardiac catheterization, percutaneous transluminal coronary angioplasty [PTCA], coronary artery bypass graft [CABG], and use of thrombolytics).

The secondary endpoint focuses on determining the prevalence of severe coronary epicardial vascular disease by race. This endpoint looked at whether a difference in revascularization (ie, PTCA or CABG) was based on race for the same severity of disease. Critical stenosis was defined as a coronary artery with a $\geq$70% stenosis, the cut off used for determining whether a vessel should be revascularized. This criterion is subject to strong clinician bias, but it was chosen because it represents ''real life'' application and clinical decision-making. The number of major coronary arteries with a critical stenosis was determined per patient. A major coronary artery was defined as the right coronary, the circumflex, the left anterior descending, the left main, and any major side branches to these major arteries. Burden of disease was defined as the total number of critical stenoses

present per patient and also as an aggregate for the group combined. The other secondary endpoint was left ventricular function. Left ventricular function was determined by measuring the left ventricular ejection fractions (LVEF). The left ventricle was drawn from still images of the ventriculogram during systole and diastole, and the ejection fraction was calculated by using a planimeter method.

Data Collection Process

Several staff nurses from the CCU were designated registry coordinators. The registry coordinator recorded data for each patient onto a simple, one-page data form, as described previously.[18] Data were collected on age, race, cardiac risk factors, medication, electrocardiogram (ECG) changes, location of infarct, acute cardiac interventions, and in-hospital clinical outcomes. This form was sent to a central data collection center (ClinTrials Research, Inc, Lexington, Ky, USA) for processing and analysis. In addition, UNC maintained its own database, which included the information on this simple form plus additional information on risk factors and results of cardiac catheterization. Quarterly summaries of the cumulative studywide registry data and confidential, individual parallel tabulations of our local data were sent to us.

Participation in the registry was voluntary. Acute myocardial infarction (AMI) patients were entered consecutively, irrespective of treatment strategy and outcome. Approval of the registry data collection process was reviewed by the UNC Committee on the Protection of Human Rights, and the consent form was waived because it was deemed a noninvasive component of our quality improvement project, which reviewed results of current practice.

Quality Control and Definitions

A quality control process was established to ensure reliable data. Clear definitions were also established for the registry. The reliability and validity of the NRMI protocol has been published elsewhere.[18]

Statistical Analysis

Patient characteristics were tabulated and the relationship between these characteristics was evaluated by the Fisher exact two-tailed *t* test and Wilcoxon chi-square test where appropriate. The confidence interval was set at a minimum of 95%. All statistical analyses were performed with SAS (SAS Institutes, Cary, NC, USA). Continuous variables were reported as mean plus or minus standard deviation (SD). This report was prepared by the biostatistical department of UNC at Chapel Hill.

Table 1. Clinical characteristics of African American and White patients

Variable	*AA**	*White**	*P value*
N	138 (26)	383 (74)	
Age	61 ± 13†	64 ± 12†	.02
Male	79 (58)	238 (63)	NS
Risk factors			
Prior MI	35 (25)	123 (32)	NS
Diabetes	41 (30)	111 (29)	NS
Hypertension	114 (83)	249 (65)	NS

* Results given as number of patients (%).
† Mean ± SD.
AA=African American; SD=standard deviation; NS=not significant; MI=myocardial infarction.

RESULTS

Patient Characteristics

All 521 patients who presented with AMI to the CCU were enrolled from 1991 to 1994 (Table 1). African Americans represented 26% of all AMI. A total of 323 patients were in the subgroup for cardiac catheterization. African Americans made up 25% (*n*=82) of this subgroup (Table 2). African Americans were younger, and slightly more men than women were in both groups. No significant difference in the rate of cardiac catheterization was seen between the two races.

No racial difference was seen in the extent of coronary artery disease (CAD)

Table 2. Demographics of study population

General	AA	Whites	*P* value
n (%)	82 (25%)	241 (75%)	NS
Age	57 ± 13	60 ± 12	.05
Male	46 (56)	164 (68)	NS
Cardiac catheterization results			
CAD ≥70%	61 (74)	178 (74)	NS
1-vessel disease	31 (51)	74 (42)	
≥2-vessel disease	30 (49)	104 (58)	
LVEF <45%	25 (30)	27 (18)	NS
Interventions			
Thrombolytic drug	14 (17)	54 (22)	NS
PTCA	24 (29)	79 (32)	NS
CABG	10 (12)	48 (20)	NS

AA=African American; NS=not significant; CAD=coronary artery disease; LVEF=left ventricular ejection fraction; PTCA=percutaneous transluminal coronary angioplasty; CABG=coronary artery bypass graft.

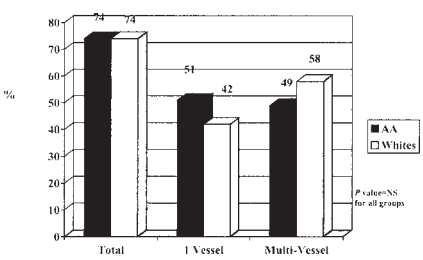

Fig 1. The prevalence of clinically significant stenosis by race. CAD ≥70% stenosis by race. Notes: AA=African American; CAD=cornary artery disease

for the 323 patients who received cardiac catheterization. For both African Americans and Whites the prevalence of a critical stenosis was 74% (Figure 1). Single-vessel disease was found in 51% of African Americans and 42% of Whites. Multiple logistic regression found age to be the only significant predictor of the number of vessels with stenosis ≥70% and not race or sex (Table 3), odds ratio .96 (95% confidence interval .81–.98., *P*=.001). This finding was also true for the total number of vessels with stenosis ≥70% per each racial group at the same odds ratio and *P* value.

The LVEF was significantly lower in African Americans at 49.13% compared to 54.98% in Whites (*P*=.04) (Figure 2). The odds ratio found that African Americans had a 2.54 (95% confidence interval 1.13–5.72) times greater chance of having LVEF <45% (*P*=.024).

Clinical Outcomes

For the subgroup that received cardiac catheterization, the rates of thrombolytic drug use, PTCA, and CABG were similar for both races (Figure 3). Within the African American group were two deaths, compared with 10 in the White group (*P*≤.737). This number represented a mortality rate of 2.4% for African Americans, compared with 4.1% for Whites.

DISCUSSION

This study found no significant racial difference in clinical outcome or revascularization compared to what has been reported in the literature. The use of thrombolytics, PTCA, or CABG between the two races during their initial hospitalization was similar. Mortality was slightly lower at 2.4% for African Americans compared to 4.1% for Whites, but this result was not significant. The Thrombolysis in Myocardial Infarction (TIMI) phase II trial showed comparable one-year mortality rates for African Americans, Hispanics,

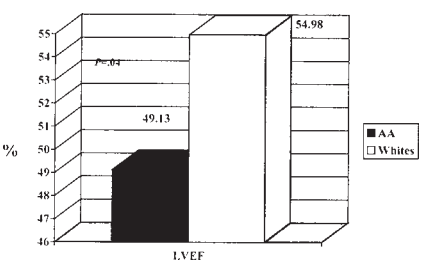

Fig 2. The mean left ventricular ejection fraction by race. Notes: Odds ratio: 2.54 times more likely to have LVEF <45%. *P*=.024. AA=African American; LVEF=left ventricular ejection fraction

and Whites.[25] This study was an AMI trial in which all patients received a thrombolytic and then were randomized to either conservative medical therapy or early invasive therapy. The similar clinical outcomes by race could be explained in part by the use of a protocol-driven and highly structured approach to the implementation of the TIMI study. This approach would minimize certain clinician or patient biases, so that rates of intervention and treatment would be similar. Acute myocardial infarction (AMI) patients at UNC hospital were placed on clinical pathways driven by evidenced-based clinical guidelines.[18] This practice resulted in less variation in care and in-hospital outcomes, similar to what was observed in the TIMI.

This may be the first study to compare the extent of revascularizable

Table 3. The significant predictors of CAD and outcome by multiple logistic regression

Predictor	Odds Ratio	95% CI	*P* value
Number of vessels with stenosis ≥70 %			
Sex (1=f)	1.52	(.92–2.53)	.105
Age	.96	(.94–.98)	<.001
Race(1=AA)	1.08	(.63–1.87)	.770
Total number of vessels with stenosis ≥70 %, per each racial group			
Sex (1=f)	1.34	(.81–2.23)	.259
Age	.96	(.94–.98)	<.001
Race (1=AA)	1.29	(.75–2.23)	.359
Mortality outcome by severity score			
Sex (1=f)	1.34	(.73–2.34)	.308
Age	.95	(.93–.97)	<.001
Race (1=AA)	1.08	(.60–2.09)	.770

CAD=coronary artery disease; CI-confidence interval; f=female; AA=African American.

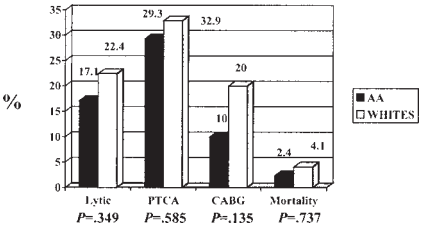

Fig 3. The racial incidence of major clinical outcomes. Notes: AA=African American; PTCA=percutaneaous transluminal coronary angioplasty; Lytic = thrombolytic drug use; CABG= coronary artery bypass graft

CAD by race in the patients at highest risk for ischemic heart disease, those presenting with AMI. While African Americans were younger and more were women, no difference was seen in the extent of revascularizable coronary disease. This was true whether one looked at number of vessels per patient or as an aggregate total for the whole group. Multiple logistic regression found that age, not race or sex, predicted the severity of CAD. Our finding stands in contrast to the those of the Coronary Artery Surgery Study (CASS) trial, which reported that African Americans had significantly less multivessel coronary disease compared to Whites.[19] Multiple other studies have reported that both African American men and women have a higher rate of normal coronary arteries at cardiac catheterization than Whites.[19–24] Carryon reported a rate of 68% compared to 21% in Whites.[23] An autopsy study in the 1960s found that African Americans had fewer raised coronary lesions than Whites.[21] This difference in the present study may be explained in part by patient selection. The UNC patients were post-AMI, a group of patients with an increased prevalence of advanced critical epicardial disease. The other reports, including those from the CASS trial, may select a broader, more dilute group with a lower prevalence of advanced epicaridial disease. Based on the similar pattern of CAD for the UNC patient, one would expect similar rates of revascularization, which was confirmed in this population of AMI patients at UNC.

The only observed difference was in left ventricular function, which was significantly lower in African Americans. African Americans had LVEF 49% compared to 55% for Whites. African Americans were 2.54 times more likely to have LVEF <45%. Logistic regression found that race was a significant predictor of LVEF. The Thrombolysis in Myocardial Infarction (TIMI) trial also found no racial difference in mortality between African Americans and Whites.[23] They reported a significantly lower LVEF for African American males at 43.3% compared to 47.6% for White males. They found that more African American and Hispanic patients than White patients had LVEF <35%. The cause for this observation is unknown but may be related to co-morbid disease. While the prevalence of hypertension in our study was similar between the two groups, African Americans appeared to show a higher trend at 83% vs 65%. Hypertension may be problematic for African Americans, who experience a three-fold higher likelihood of left ventricular hypertrophy, and even when blood pressure is equally controlled, the degree of subsequent left ventricular hypertrophy is higher.[26] Yancy has reported on several genetic polymorphisms in African Americans that could predispose to worse left ventricular dysfunction. Most recently, a polymorphism in the expression of nitrous oxide synthetase has been linked to worse left ventricular function in African Americans. The African American Heart Failure Trial published a dramatic 43% decrease in mortality for African Americans who received a combined nitric oxide donor and antioxidant.[27] This study underscored a possible mechanism for explaining some of the disparities seen in left ventricular function by race. However, further investigation is needed in this area.

Multiple logistic regression found that age, not race or sex, predicted the severity of CAD.

Potential Limitations

This study has several limitations. First, it was an observational study at a tertiary center. This was not an interventional study, but the results suggest an interventional study looking at guideline implementation on racial variation in outcomes should be done. In addition, our results were only derived from this center, so this information may not be generalizable. Since many AMI patients may not be referred to a tertiary center, our results may not reflect the true pattern of practice and outcome by race for the state of North Carolina. UNC had successfully implemented a practice guideline, which may have significantly reduced practice variation within the center. Second, the number of patients in this study was small. With a larger sample size, some racial trends in differences might have become significant. These results should encourage further research into defining the relationship between guideline implementation and racial variation in outcomes. Third, because these data were taken from a registry, the data forms were not independently validated. The limited baseline data collection in this simple registry also renders interpretation of some of the findings less certain. Finally, this study focused on a very narrow time frame for outcomes. Some reports have reported poorer out-of-hospital outcomes for African Americans compared to Whites, which would not have been captured by this study. This higher rate could bias the selection process for African Americans in favor of the lower risk group being admitted to the hospital.

The results of our study were consistent with the large TIMI phase II trial for AMI, which lends credibility to our findings. It supports the concept that protocol- or guideline-driven clinical medicine improves outcomes and narrows variation for all races.

CONCLUSION

The successful implementation of evidence-based practice guidelines and a clinical pathway for AMI at UNC led

to no difference in the rate of cardiac interventions or mortality by race. By establishing a standardized approach to the AMI patient and by streamlining their care, deviation from guideline driven recommendations can be minimized. This pilot project provides a potential solution for reducing the racial variation in care and clinical outcomes for AMI described in the United States.

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AUTHOR CONTRIBUTIONS

Design concept of study: Williams, Hill
Acquisition of data: Williams, Jackson
Data analysis interpretation: Williams, Hill
Manuscript draft: Williams, Hill
Statistical expertise: Williams
Administrative, technical, or material assistance: Williams, Jackson
Supervision: Williams