Myocardial Infarction in Treated Hypertensive Patients
The Paradox of Lower Incidence but Higher Mortality in Young Blacks Compared With Whites

Michael H. Alderman, MD; Hillel W. Cohen, DrPH; Shantha Madhavan, DrPH

Background—Despite the impressive decline in coronary heart disease death rates, a mortality differential between blacks and whites persists. Our study objective was to determine whether excess mortality among well-controlled hypertensive black men compared with whites is due to differences in disease incidence or in case fatality.

Methods and Results—Of 3382 male subjects (1266 blacks and 2116 whites) enrolled between 1973 and 1996 and followed up through 1997 in a work-site hypertension control program, 2343 were followed up until 60 years of age, and 1884 were followed up until >60 years of age (either continuing after 60 years [n=845] or beginning treatment at ≥60 years [n=1039]), with a mean follow-up of 5.2 and 5.5 years, respectively. During follow-up, 186 myocardial infarction (MI) events (including 31 revascularizations) occurred, with 63 in patients <60 years and 123 in patients ≥60 years of age. Age-adjusted MI incidence was nearly twice as high for whites as blacks in younger (6.3 versus 3.4/1000 person-years) and older (14.1 versus 7.5 person-years) subjects. In contrast, the age-adjusted case fatality rate was 3-fold higher for younger blacks than for whites (37.8% versus 12.2%). In older patients, case fatality did not differ significantly between blacks and whites (37.6% versus 50.3%). In separate Cox regression analyses, among younger blacks but not younger whites, history of diabetes and smoking were significantly associated with both incidence and fatality.

Conclusions—In these treated male hypertensive patients with good blood pressure control (139.6/85.7 mm Hg), young blacks, despite a lower MI incidence, had higher MI mortality than did their white counterparts. Their higher case fatality rate was associated with fewer coronary artery revascularizations and a higher prevalence of diabetes and smoking. (Circulation. 2000;101:1109-1114.)

Key Words: myocardial infarction • mortality • hypertension • race

Despite recent declines, coronary heart disease (CHD) remains the leading cause of death in America. However, declines in CHD mortality have been greater for whites than blacks, thus amplifying the long-standing mortality differential of blacks and whites. The excess in black death rates may be due to differences in either disease incidence or case fatality. Available evidence, while not conclusive, suggests that blacks have a higher case fatality rate from acute CHD events than whites. It is possible, however, that variations in risk factors such as hypertension or its treatment may also contribute to the greater CHD mortality of blacks in America.

To address this issue, we examined the incidence and outcome of acute myocardial infarction (MI) in a working population of treated hypertensive patients in New York City, NY. Here, we report that in a setting of equivalent and satisfactory blood pressure (BP) control, the incidence of MI was markedly lower for blacks than whites, both young and old. However, in those <60 years of age, case fatality was markedly greater for blacks than whites. As a result, total CHD mortality of young blacks, despite fewer events, actually exceeded that of whites.

Methods

Patient Recruitment

The study design and methods of this work site–based treatment cohort have been previously described. Study subjects were mildly to moderately hypertensive, were identified through screening for high BP, and were entered a union-sponsored treatment program in New York City between 1973 and 1996.

Eligibility Criteria

BP eligibility criteria initially included systolic BP ≥160 mm Hg and/or diastolic BP ≥95 mm Hg at screening and 2 consecutive follow up visits or the use of antihypertensive medication at screening. Entry BP criteria were reduced to systolic ≥140 mm Hg and/or diastolic ≥90 mm Hg in 1993 according to the recommendation of the Joint National Committee (JNC V) on Detection, Evaluation, and Treatment of High Blood Pressure.

© 2000 American Heart Association, Inc.

Circulation is available at http://www.circulationaha.org

1109
Patient Evaluation
Baseline information included demographic data, personal medical history, cigarette smoking status, physical examination by a nurse and physician, ECG findings (as recorded by program physicians), routine clinical chemistry, and measurement of urine protein and electrolytes. At each annual reexamination, intervening history was recorded. All clinical data were obtained and treatment decisions were made according to a protocol approved by the institutional review committee.

Study Subjects
Of 7978 subjects who entered treatment between 1973 and 1996 and were followed up through 1997, 2433 were black and 3212 white. For the study, 2096 Hispanics and 237 others were excluded. The remaining 5645 patients (3382 men and 2263 women), including 191 with a self-reported history of heart attack, were classified into 2 age groups according to follow-up: 3927 (2343 men) with in-treatment follow-up to 60 years of age and 3253 (1884 men) who either continued treatment (n=845) until ≥60 years of age or who entered treatment at ≥60 years (n=1039). Because the average age at entry to therapy was 54 years and there were few patients ≥65 years of age, the age cut for young and old was arbitrarily set at 60 years.

Antihypertensive Drug Therapy
Before 1988, treatment generally began with either hydrochlorothiazide or propranolol or, less commonly, a- and/or other β-adrenergic blockers. After the 1988 report of JNC IV,19 calcium channel blockers and ACE inhibitors were available as first-line drug choices. In 1993, after JNC V, preference for first drug was again given to diuretics or β-blockers.18 All patients were prescribed medication uniformly according to a standardized protocol.

Morbidity and Mortality
Illnesses and deaths were classified according to the International Classification of Disease, ninth revision, clinical modification. The cardiovascular disease event of interest in this study was MI (code 410), including angioplasty or coronary bypass surgery (code 36). The occurrence of a morbid or mortal event was first ascertained by a nurse who systematically monitored reports by patients, family members, or friends regarding hospitalizations or deaths. For patients with >1 event during follow-up, the first incident MI event was the end point in this study. Of all first MI events, deaths that occurred within 28 days from the onset of symptoms were considered fatal cases. Confirmation by hospital records and/or death certificate was possible for 82.2% of the total events. The remaining events were validated by private physician, family, friend, or union records. During follow-up, there were 239 MI events (151 morbid and 88 mortal). The 151 morbid events included 41 revascularizations. Of the 239 Mls, 186 (including 31 revascularizations) occurred in men (63 in patients <60 and 123 in those ≥60 years of age during a mean follow-up of 5.2 and 5.5 years, respectively).

Statistical Analysis
The present analysis has been restricted to 3382 men (1266 black and 2116 white) because more than three fourths of Mls (186 of 239) occurred in men and only 13 Mls occurred in women <60 years. Baseline characteristics of male patients were assessed for comparison according to race and age. Differences between groups were tested for statistical significance by use of the Mantel-Haenszel test controlling for age. Cox proportional hazards regression models20 were constructed for patients with incident MI to determine the association of race with MI mortality while controlling for age at entry, history of cardiovascular disease, history of diabetes, prior treatment, smoking status, left ventricular hypertrophy by ECG, blood sugar, cholesterol, body mass index, and initial systolic BP. Similar models were constructed with MI mortal events as dependent variables. All clinical chemistry measures are reported in SI (Système International) units with conversion factors. All statistical analyses were performed with SPSS (Statistical Package for Social Sciences) software.

Results
Patient Characteristics
There were 954 blacks and 1389 whites among 2343 subjects <60 years of age. Male patients ≥60 years (n=1884) included 631 blacks and 1253 whites (Table 1). Older subjects had higher systolic BP and blood sugar and more frequent history of heart attack and diabetes but were less likely to smoke. The 2 racial groups differed significantly in most characteristics in both age categories. Whites had a higher mean age and cholesterol and were less likely to have left ventricular hypertrophy. Older blacks were more likely to have had a prior heart attack. Current smoking was most common among young blacks. Initial and final BPs of patients <60 years were significantly higher for blacks than whites.

Diuretics use was similar for blacks and whites in both younger (46.0% versus 47.7%, respectively) and older (48.2% versus 52.1%) subjects. This similarity between races was also observed for β-blocker medication among the young (15.8% versus 17.6%) and old (14.7% versus 16.0%).

Incidence of MI
In younger and older subjects, MI events numbered 63 (18 blacks and 45 whites) and 123 (25 blacks and 98 whites), respectively. Overall age-adjusted MI incidence (the Figure) among both younger and older subjects was roughly twice as high for whites as blacks. Younger whites had an RR of 1.91 and 95% CI of 1.09 to 3.35; for older whites, the RR was 1.91 (95% CI, 1.23 to 2.97) compared with blacks. Cox multivariate analysis (Table 2) revealed that in younger black patients only, current smoking (RR=3.44) and history of diabetes (RR=4.95) were strongly associated with MI. For younger whites, age, cholesterol, and prior treatment were independently and significantly associated factors. None of these had the same magnitude of effect as diabetes and smoking for young blacks. In the older subjects, left ventricular hypertrophy was the only factor associated with MI for blacks, and cholesterol and history of diabetes were the only factors for whites.

Because our classification included revascularization with MI, it is of note that the percent of revascularization was slightly higher for older than younger subjects and more than twice as common (though not significantly so) in both age groups for whites (17.8% and 20.4%, respectively) than blacks (5.6% and 8.0%).
Overall MI Mortality and Case Fatality

Despite a sharply lower incidence, age-adjusted MI mortality rate (Table 3) for younger blacks tended ($P=0.136$) to exceed that of whites. This is explained by a significant 3-fold-higher case fatality rate for blacks compared with whites. In patients ≥60 years of age, the reverse was true for overall MI mortality, with the rate for blacks significantly ($P=0.013$) lower than that for whites.

Case fatality was similar for both ages for blacks. As a result, compared with the younger group, older blacks enjoyed a modestly lower (not significant) age-adjusted case fatality rate than did whites (37.6% versus 50.3%). Older white patients actually had a case fatality 4-fold higher than that for younger patients (50.3% versus 12.2%).

To determine whether the higher mortality rate of young blacks was associated with race after other risk factors were accounted for, a Cox regression model including an interaction term of age and race was performed separately for both age groups. After a significant ($P=0.026$) interaction of age and race was accounted for, race as an independent variable remained significantly ($P=0.0285$) associated with fatal MI, with blacks having the substantially higher risk. Other factors strongly related to MI death were cholesterol, systolic BP, and age at entry. Similar analyses for the older men showed a significant ($P=0.014$) association of race with MI fatality after other covariates were accounted for in the best-fit model. However, this association was reversed in older patients, and black MI mortality was <50% of that for their white counterparts. Other significantly associated risk factors were cholesterol, systolic BP, history of diabetes, and prior treatment.

In further analysis, Cox models for each race within the 2 age categories were performed to identify the risk factors associated with MI mortality (Table 4). In younger blacks, history of diabetes, smoking, cholesterol, and systolic BP were significantly associated with MI deaths. In younger whites, age at entry and systolic BP were the only 2 significantly related factors. In older patients, initial systolic BP was related to fatality for both blacks and whites, as was prior treatment for blacks. Cholesterol and history of diabetes were the other independently associated risk factors for whites.

### In-Treatment Course of Risk Factors

Because history of diabetes and smoking at entry were independently associated with MI incidence and mortality in young blacks, changes in these factors during treatment were examined. Initially, 33% of blacks and 28% of whites smoked, and their blood sugar levels were 5.84 and 5.89 mmol/L, respectively. At their final visit, 26.4% of both blacks and whites smoked, and their mean in-treatment blood sugars were 5.94 and 5.96 mmol/L. Among the older patients, similar observations were made for blacks and whites for smoking at the final visit (18.1% versus 14.0%, respectively) and mean in-treatment blood sugar (6.20 versus 6.26 mmol/L).

Because initial systolic BP was significantly associated with MI mortality in both age groups in each race, the impact of in-treatment systolic BP was assessed in a multivariate analysis and was found not to be associated with mortality in
the 4 race-age strata. Thus, the in-treatment course of risk factor status did not distinguish the experience of the 2 racial groups.

Discussion

In this prospective study of treated hypertensive male patients, we have found differences in the incidence of and fatality from MI by age and race. Whites at any age were twice as likely to sustain an MI as were blacks. In contrast, MI mortality was greater for young blacks than whites. This was not the case for older subjects. The seemingly paradoxical mortality difference among young patients is explained by a sharp variation in case fatality rates. Young black men were 3 times as likely to succumb to an acute MI as were whites. In contrast, there was no racial difference in case fatality in older subjects. Thus, the age-related reversal in MI mortality, previously described in the general population, also occurred in these hypertensive subjects. However, the excess mortality of young blacks cannot be ascribed to frequently cited differences in BP control, access to health care, socioeconomic status, risk factor management,21–23 or a higher incidence of events.

High prevalence of hypertension and a belief that the consequences of high BP may be more severe for blacks than whites12 have been postulated to contribute to the persisting higher CHD mortality of young black men. Although this study of treated hypertensive patients does not address the issue of hypertensive prevalence, it provides a unique opportunity to compare the impact of therapy for black and white subjects in the context of an identical socioeconomic and healthcare environment.

The goal of antihypertensive therapy is to prevent coronary events. It would appear that this objective was at least as well realized by blacks as whites. Nevertheless, even in this generally favorable setting, young black men were still more likely to die from CHD than whites. Although attained BPs differed slightly, to the disadvantage of blacks, the incidence of first events was still nearly twice as great for whites as blacks. In fact, the in-treatment BP difference was modest and was not significantly associated with mortality in multivariate analysis.

It is possible that differences in other cardiovascular risk factors24–26 or their change during treatment may have accounted for the difference in mortality. In fact, smoking and blood sugar were relatively similar by race during treatment, suggesting that treatment of these other risk factors did not influence our findings. However, both smoking and diabetes were more common among younger black than white men and were significantly associated with both the occurrence of events and the likelihood of their being fatal.21,27 Thus, it is possible that these factors had a greater effect on the severity than the incidence of events.

Work-site treatment does not extend to the management of acute events. Although all patients had similar antihypertensive therapy, health insurance, and access to care, they could be and were actually hospitalized in a wide range of very

### Table 2. Hazard Ratios From Cox Regression Models for MI Incidence

<table>
<thead>
<tr>
<th>Variable</th>
<th>RR for MI Incidence (95% CI)</th>
<th>Age &lt;60 y</th>
<th>Age ≥60 y</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Blacks</td>
<td>Whites</td>
<td>Blacks</td>
</tr>
<tr>
<td>Age</td>
<td>1.01 (0.94–1.09)</td>
<td>1.10† (1.03–1.17)</td>
<td>1.00 (0.94–1.07)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>1.02 (0.90–1.16)</td>
<td>0.97 (0.90–1.05)</td>
<td>0.91 (0.80–1.03)</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>1.01‡ (1.00–1.02)</td>
<td>1.01† (1.00–1.01)</td>
<td>1.01 (1.00–1.02)</td>
</tr>
<tr>
<td>LVH</td>
<td>1.13 (0.35–3.63)</td>
<td>0.74 (0.17–3.09)</td>
<td>2.52* (1.08–5.84)</td>
</tr>
<tr>
<td>Smoker</td>
<td>3.44* (1.25–9.51)</td>
<td>1.59 (0.84–2.99)</td>
<td>0.86 (0.35–2.14)</td>
</tr>
<tr>
<td>History of CVD</td>
<td>1.62 (0.44–5.96)</td>
<td>1.29 (0.61–2.72)</td>
<td>1.93 (0.75–4.92)</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>1.02 (1.00–1.05)</td>
<td>0.99 (0.98–1.01)</td>
<td>1.01 (0.99–1.03)</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>4.95† (1.31–18.66)</td>
<td>1.79 (0.62–5.15)</td>
<td>2.40 (0.68–8.44)</td>
</tr>
<tr>
<td>Prior treatment</td>
<td>0.56 (0.19–1.58)</td>
<td>2.07* (1.05–4.07)</td>
<td>1.82 (0.79–4.20)</td>
</tr>
</tbody>
</table>

LVH indicates left ventricular hypertrophy; CVD, cardiovascular disease.

*P<0.05, †P<0.01, ‡P<0.10.

### Table 3. Age-Adjusted Mortality Rate and Case Fatality of MI in Hypertensive Male Patients by Race and Age

<table>
<thead>
<tr>
<th>Race</th>
<th>Mortality Rate/1000 person-y</th>
<th>Case Fatality, %</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age &lt;60 y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blacks</td>
<td>1.50</td>
<td>0.136</td>
<td>37.81 (8/18)</td>
</tr>
<tr>
<td>Whites</td>
<td>0.65</td>
<td>12.17</td>
<td>37.59 (10/25)</td>
</tr>
<tr>
<td></td>
<td>Age ≥60 y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blacks</td>
<td>3.07</td>
<td>0.0125†</td>
<td>37.59 (10/25)</td>
</tr>
<tr>
<td>Whites</td>
<td>7.16</td>
<td>50.30</td>
<td>50.30 (50/98)</td>
</tr>
</tbody>
</table>

*Numbers in parentheses are fatal/incident MIs.
†Blacks vs whites: highly significant.
different hospitals. It is also possible that detection bias might have affected the incidence of acute nonfatal MI events differently in blacks and whites because of variations in access to and use of diagnostic techniques. Moreover, treatment of the acute MI, because of either a delay in reaching medical attention or differences in hospital care, such as the use of acute interventions, may have influenced outcomes. Because this study was not designed to assess the impact of hospitalization on outcome, we did not have access to the data needed for relevant analyses. However, we do have accurate records of revascularization experience. In both young and old patients, revascularization was 2 to 3 times more commonly performed in whites than in blacks.28–29 These race differences in the use of diagnostic and therapeutic services have been previously reported.30–32

Although causality cannot be inferred from this single study, the available data suggest several plausible hypotheses. Perhaps smoking, diabetes, and cholesterol as risk factors or use of acute revascularization may help to explain the gap in mortality that currently separates young black and white men.

The inability to explore the course of patients during the acute experience of a cardiac event is a significant limitation of this study. In addition, because this study was limited to men, it is necessary to extrapolate to women with caution. Indeed, because there was only 1 fatal event in young white women and none in black women, it is not possible to comment in regard to young women. However, in older women, the trend in MI incidence and fatality was similar to that of older men. The important study strengths include its prospective nature, the systematic ascertainment of known cardiovascular risk factors both before and during treatment, inclusion of patients drawn from socioeconomically homogeneous unions with equal health benefits, and the fact that all study subjects received equivalent antihypertensive treatment with clinically similar results. All end points of interest were systematically and uniformly captured.

In summary, young black men, achieving good BP control in this multiracial hypertensive treatment program, still suffered greater coronary mortality than did young white men despite a lower incidence of MI. This apparent paradox, seen only among younger subjects, is due to the sharply higher case fatality rate of young black men. Although the available data cannot account for these findings, very different use of revascularization and a more frequent history of diabetes and smoking in young black men point to possible clinical explanations, as well as opportunities for corrective intervention.

References


### Table 4. Proportional Hazards Cox Regression Model: Risk Factors Associated With MI Deaths in Hypertensive Men With Incident MI by Age and Race

<table>
<thead>
<tr>
<th>Variable*</th>
<th>Age &lt;60 y</th>
<th>Age ≥60 y</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Blacks (n=954)</td>
<td>Whites (n=1389)</td>
</tr>
<tr>
<td></td>
<td>(MI Deaths=8)</td>
<td>(MI Deaths=5)</td>
</tr>
<tr>
<td>Age</td>
<td>0.043</td>
<td>0.003</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>0.016</td>
<td>0.111</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>0.004</td>
<td>0.018</td>
</tr>
<tr>
<td>Smoker</td>
<td>0.006</td>
<td>0.035</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>0.006</td>
<td>0.021</td>
</tr>
</tbody>
</table>

*Other variables not found to be predictive in all models were body mass index, history of cardiovascular disease, and left ventricular hypertrophy.
Myocardial Infarction in Treated Hypertensive Patients: The Paradox of Lower Incidence but Higher Mortality in Young Blacks Compared With Whites
Michael H. Alderman, Hillel W. Cohen and Shantha Madhavan

_Circulation._ 2000;101:1109-1114
doi: 10.1161/01.CIR.101.10.1109

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2000 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/101/10/1109

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/