

## RACIAL DIFFERENCES IN THE OUTCOME OF LEFT VENTRICULAR DYSFUNCTION

DANIEL L. DRIES, M.D., M.P.H., DEREK V. EXNER, M.D., BERNARD J. GERSH, M.B., CH.B., D.PHIL.,  
HOWARD A. COOPER, M.D., PETER E. CARSON, M.D., AND MICHAEL J. DOMANSKI, M.D.

**ABSTRACT**

**Background** Population-based studies have found that black patients with congestive heart failure have a higher mortality rate than white patients with the same condition. This finding has been attributed to differences in the severity, causes, and management of heart failure, the prevalence of coexisting conditions, and socioeconomic factors. Although these factors probably account for some of the higher mortality due to congestive heart failure among blacks, we hypothesized that racial differences in the natural history of left ventricular dysfunction might also have a role.

**Methods** Using data from the Studies of Left Ventricular Dysfunction (SOLVD) prevention and treatment trials, in which all patients received standardized therapy and follow-up, we conducted a retrospective analysis of the outcomes of asymptomatic and symptomatic left ventricular systolic dysfunction among black and white participants. The mean ( $\pm$ SD) follow-up was  $34.2 \pm 14.0$  months in the prevention trial and  $32.3 \pm 14.8$  months in the treatment trial among the black and white participants.

**Results** The overall mortality rates in the prevention trial were 8.1 per 100 person-years for blacks and 5.1 per 100 person-years for whites. In the treatment trial, the rates were 16.7 per 100 person-years and 13.4 per 100 person-years, respectively. After adjustment for age, coexisting conditions, severity and causes of heart failure, and use of medications, blacks had a higher risk of death from all causes in both the SOLVD prevention trial (relative risk, 1.36; 95 percent confidence interval, 1.06 to 1.74;  $P=0.02$ ) and the treatment trial (relative risk, 1.25; 95 percent confidence interval, 1.04 to 1.50;  $P=0.02$ ). In both trials blacks were also at higher risk for death due to pump failure and for the combined end point of death from any cause or hospitalization for heart failure, our two predefined indicators of the progression of left ventricular systolic dysfunction.

**Conclusions** Blacks with mild-to-moderate left ventricular systolic dysfunction appear to be at higher risk for progression of heart failure and death from any cause than similarly treated whites. These results suggest that there may be racial differences in the outcome of asymptomatic and symptomatic left ventricular systolic dysfunction. (N Engl J Med 1999;340:609-16.)

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**T**HERE are approximately 2 million Americans with congestive heart failure, and about 400,000 new cases are diagnosed each year.<sup>1</sup> The population-based mortality rate from congestive heart failure is 1.8 times as high for black men as for white men and 2.4 times as high for black women as for white women.<sup>2,3</sup> The higher mortality among blacks has been attributed to differences between blacks and whites in the severity and causes of heart failure, the prevalence of coexisting conditions, socioeconomic and cultural factors, and access to high-quality medical care.<sup>4-6</sup> Not all studies, however, have found a higher mortality among blacks than among whites with heart failure. For example, in a recent statewide study of hospital-discharge data on patients with congestive heart failure, the case fatality rate was lower for blacks than for whites.<sup>7</sup>

A randomized clinical trial has advantages for studying differences between blacks and whites in the outcome of heart failure, because the management and follow-up of the condition of interest are standardized, thereby reducing potential confounding by factors that might explain the findings of previous population-based studies. We therefore conducted a retrospective analysis of the rates of progression of heart failure and mortality from heart failure among the white and black participants in the Studies of Left Ventricular Dysfunction (SOLVD) prevention and treatment trials.<sup>8,9</sup>

**METHODS**

The SOLVD prevention and treatment trials assessed the effect of the angiotensin-converting-enzyme inhibitor enalapril on survival in patients with asymptomatic left ventricular systolic dysfunction (in the prevention trial) and symptomatic left ventricular systolic dysfunction (in the treatment trial). The primary end point in both trials was overall mortality. There were 4228 patients in the prevention trial and 2569 patients in the treatment trial. The participants in each trial were randomly assigned to treatment with enalapril or placebo. The exclusion criteria were active angina pectoris requiring surgical intervention, unstable angina, myocardial infarction within one month before the start of the study, a serum creatinine concentration above 2.0 mg per deciliter ( $177 \mu\text{mol}$  per liter), and severe pulmonary disease. The rationale, design, and methods of these trials have been described previously.<sup>10</sup>

From the Clinical Trials Scientific Research Group, Division of Epidemiology and Clinical Application, National Heart, Lung, and Blood Institute, Bethesda, Md. (D.L.D., D.V.E., H.A.C., M.J.D.); the Division of Cardiology, Georgetown University Hospital, Washington, D.C. (B.J.G.); and the Department of Veterans Affairs, Washington, D.C. (P.E.C.). Address reprint requests to Dr. Dries at Clinical Trials Scientific Research Group, NHLBI, 2 Rockledge Ctr., 6701 Rockledge Dr., Rm. 8149, Bethesda, MD 20892-7936, or at ddries@aol.com.

### Collection of Data

Base-line data regarding patients' demographic characteristics, medical history, and current use of medications were obtained at the time of enrollment. Data on race and ethnic background were obtained from the SOLVD eligibility form, on which investigators identified participants by choosing among the ethnic and racial categories American Indian, Asian, black, white, Hispanic, and other. Participants identified as black or white constitute the comparison groups for this analysis.

### Definition of End Points

The causes of death were determined by the principal investigators at each clinical site. Deaths from cardiac causes were classified by the SOLVD investigators as due to pump failure, probable arrhythmia with some antecedent worsening of heart failure, or probable arrhythmia with no antecedent worsening of heart failure. In our analysis, we classified all deaths in the first two categories as deaths due to pump failure, since in our opinion a death from arrhythmia related to decompensated heart failure is best classified as a death due to worsening pump failure. We included as deaths from arrhythmia only deaths classified by the SOLVD investigators as due to probable arrhythmia with no antecedent worsening of heart failure. We reasoned that the progression of left ventricular dysfunction would lead eventually to death from pump failure or hospitalization for worsening heart failure. Therefore, our two predefined indicators of the progression of left ventricular dysfunction were death from pump failure and the combined end point of death from any cause or hospitalization for heart failure.

### Statistical Analysis

Age, left ventricular ejection fraction, and systolic and diastolic blood pressure were analyzed as continuous variables. The following were analyzed as dichotomous variables: diabetes (yes or no), prior hypertension (yes or no), prior stroke (yes or no), base-line serum creatinine concentration (1.5 to 2.0 mg per deciliter [133 to 177  $\mu$ mol per liter] or <1.5 mg per deciliter), cause of left ventricular dysfunction (ischemic or nonischemic), New York Heart Association (NYHA) functional class (II vs. I in the prevention trial; III or IV vs. I or II in the treatment trial), and race (black or white). Base-line use of medications was analyzed as a series of dichotomous variables according to use or nonuse of antiplatelet agents, diuretics, antiarrhythmic drugs, digoxin, and beta-blockers, and according to random assignment in the trial to enalapril or placebo.

Comparisons of continuous data between the groups were performed with use of Student's *t*-test, and comparisons of categorical data with use of the chi-square statistic. A two-sided *P* value of 0.05 or less was considered to indicate statistical significance. Univariate and multivariate relations were investigated by Cox proportional-hazards models. Statistical analyses were conducted with the Statistical Analysis System software, version 6.12 (SAS Institute, Cary, N.C.).

## RESULTS

### Base-Line Characteristics

The base-line characteristics of the white and black participants in the prevention and treatment trials are shown in Table 1. In both trials the black participants were younger, on average, than the whites. Measures of the severity of heart failure, such as NYHA functional class and the left ventricular ejection fraction, were similar for blacks and whites. Blacks had a higher prevalence of diabetes, prior hypertension, prior stroke, and left ventricular dysfunction of nonischemic cause and a lower prevalence of prior myocardial infarction. In both trials blacks had significantly higher average diastolic blood pressure

and serum creatinine concentrations, but there was no significant difference between blacks and whites in average systolic blood pressure. Use of beta-blockers and antiarrhythmic drugs was less common and the use of diuretics was more common among blacks. In both trials, similar proportions of white and black participants were randomly assigned to receive enalapril. Black participants were enrolled from all 23 SOLVD clinical sites. The average ( $\pm$ SD) follow-up time was  $34.2 \pm 14.0$  months in the prevention trial and  $32.3 \pm 14.8$  months in the treatment trial.

### Univariate Analysis

According to univariate analysis, black participants in the SOLVD prevention trial were at significantly higher risk than whites for death from all causes (relative risk, 1.62; 95 percent confidence interval, 1.30 to 2.03;  $P < 0.001$ ), death from pump failure (relative risk, 1.79; 95 percent confidence interval, 1.21 to 2.67;  $P = 0.004$ ), and the combined end point of death from any cause or hospitalization for heart failure (relative risk, 1.91; 95 percent confidence interval, 1.60 to 2.28;  $P < 0.001$ ), but not for death from arrhythmia (relative risk, 1.21; 95 percent confidence interval, 0.78 to 1.88;  $P = 0.4$ ). In the treatment trial, blacks were at higher risk for death from all causes (relative risk, 1.22; 95 percent confidence interval, 1.03 to 1.44;  $P = 0.02$ ), death from pump failure (relative risk, 1.35; 95 percent confidence interval, 1.07 to 1.70;  $P = 0.01$ ), and the combined end point of death from any cause or hospitalization for heart failure (relative risk, 1.36; 95 percent confidence interval, 1.18 to 1.56;  $P < 0.001$ ), but not for death from arrhythmia (relative risk, 0.91; 95 percent confidence interval, 0.63 to 1.34;  $P = 0.6$ ).

In both trials, the variables associated with an increased risk of death from all causes according to univariate analysis were older age, a lower ejection fraction at base line, a higher NYHA functional class, a serum creatinine concentration of 1.5 to 2.0 mg per deciliter as opposed to less than 1.5 mg per deciliter, diabetes, and the use of digoxin, diuretics, or antiarrhythmic drugs. The variables in both trials that were associated with a decreased risk of death from all causes were the use of beta-blockers and the use of antiplatelet agents. In the prevention trial only, a nonischemic cause of left ventricular dysfunction was associated with a decreased risk of death from all causes, and a history of hypertension was associated with an increased risk. In the treatment trial only, random assignment to receive enalapril was associated with a decreased risk of death from all causes. Sex was not associated with the risk of death from all causes in either trial.

### Causes of Death

Tables 2 and 3 show the causes of death among blacks and whites in the prevention and treatment

**TABLE 1.** BASE-LINE CHARACTERISTICS OF PARTICIPANTS IN THE STUDIES OF LEFT VENTRICULAR DYSFUNCTION.\*

CHARACTERISTIC	PREVENTION TRIAL		TREATMENT TRIAL	
	BLACKS (N=404)	WHITES (N=3658)	BLACKS (N=396)	WHITES (N=2061)
Age (yr)	57±10.9	59.5±10.3†	57.3±11.2	61.7±9.5†
Left ventricular ejection fraction	27.5±6.0	28.4±5.6‡	24.5±7.0	25.0±6.7
Serum creatinine (mg/dl)§	1.26±0.4	1.14±0.3†	1.31±0.4	1.22±0.3†
Blood pressure (mm Hg)				
Systolic	126.9±19.3	125.3±16.2	125.1±18.8	124.7±17.4
Diastolic	80.1±10.1	77.7±9.4†	79.4±11.1	76.3±10.0†
NYHA functional class (%)				
III or IV	29.8	33.6	0	0
II	70.2	66.4	31.3	31.8
I	0	0	68.7	68.2
Cause of left ventricular dysfunction (%)				
Ischemic	58.7	86.2†	48.0	75.8†
Nonischemic	41.3	13.8†	52.0	24.2†
Sex (%)				
Male	79	90†	68	83†
Female	21	10†	32	17†
Other conditions (%)				
Diabetes	25.3	13.5†	31.8	24.2†
Prior stroke	10.9	5.3	8.8	7.6
Prior myocardial infarction	52.5	83.5†	46.2	69.4†
Prior hypertension	59.6	34.5†	64.7	37.5†
Drug use (%)				
Beta-blocker	15.9	25.0¶	3.3	8.7†
Diuretic	39.1	14.2†	92.7	83.8†
Digoxin	9.2	12.9	65.9	68.1
Antiarrhythmic drug	11.2	15.9‡	13.4	24.1†
Antiplatelet agent	9.9	9.3	11.4	14.2
Assigned treatment (%)				
Enalapril	48.5	49.9	52.8	49.4
Placebo	51.5	50.1	47.2	50.6

\*Plus-minus values are means ±SD. NYHA denotes New York Heart Association.

†P≤0.001 for the comparison with blacks.

‡P≤0.01 for the comparison with blacks.

§To convert values to micromoles per liter, multiply by 88.4.

¶P≤0.10 for the comparison with blacks.

||P≤0.05 for the comparison with blacks.

trials, respectively. Death from pump failure and the composite of death from stroke or pulmonary embolism were the two categories of death that were significantly more frequent among blacks in both trials. Pump failure was the cause of death associated with the greatest absolute risk among both blacks and whites in the treatment trial and among blacks in the prevention trial. Among whites in the prevention trial, death from arrhythmia was associated with the greatest absolute risk, but the absolute risk associated with death from pump failure was only slightly smaller. Although the risk of death from the composite of fatal stroke or pulmonary embolism was significantly greater among blacks than whites in both trials, the absolute risk of death from this cause was much lower than that of death from pump failure, which accounted for 32.6 percent of

total deaths among blacks and 29.5 percent of total deaths among whites in the prevention trial and 52.7 percent of total deaths among blacks and 47.9 percent of total deaths among whites in the treatment trial.

**Multivariate Analysis**

According to multivariate analysis, black participants in the prevention trial were at significantly higher risk than whites for death from all causes (relative risk, 1.36; 95 percent confidence interval, 1.06 to 1.74; P=0.02), death from pump failure (relative risk, 1.57; 95 percent confidence interval, 1.01 to 2.44; P=0.05), and the composite end point of death from any cause or hospitalization for heart failure (relative risk, 1.54; 95 percent confidence interval, 1.27 to 1.88; P<0.001) (Table 4), but not for

**TABLE 2. CAUSES OF DEATH IN THE PREVENTION TRIAL.**

CAUSE OF DEATH	BLACKS (N=404)		WHITES (N=3658)		P VALUE*
	NO. OF DEATHS (%)	INCIDENCE/100 PERSON-YR†	NO. OF DEATHS (%)	INCIDENCE/100 PERSON-YR†	
All causes	89 (22.0)	8.1	532 (14.5)	5.1	<0.001
Pump failure	29 (7.2)	2.6	157 (4.3)	1.5	0.003
Arrhythmia	22 (5.4)	2.0	176 (4.8)	1.7	0.40
Myocardial infarction	13 (3.2)	1.2	84 (2.3)	0.8	0.20
Stroke or pulmonary embolism	10 (2.5)	0.9	25 (0.7)	0.2	<0.001
Other	15 (3.7)	1.5	90 (2.5)	0.9	0.08

\*Two-sided P values for the comparison between blacks and whites were derived with the log-rank statistic.

†The unadjusted incidence is expressed as the rate per 100 person-years of follow-up.

**TABLE 3. CAUSES OF DEATH IN THE TREATMENT TRIAL.**

CAUSE OF DEATH	BLACKS (N=396)		WHITES (N=2061)		P VALUE*
	NO. OF DEATHS (%)	INCIDENCE/100 PERSON-YR†	NO. OF DEATHS (%)	INCIDENCE/100 PERSON-YR†	
All causes	167 (42.2)	16.7	748 (36.3)	13.4	0.02
Pump failure	88 (22.2)	8.8	358 (17.4)	6.4	0.01
Arrhythmia	31 (7.8)	3.1	182 (8.8)	3.3	0.64
Myocardial infarction	14 (3.5)	1.4	88 (4.3)	1.6	0.65
Stroke or pulmonary embolism	10 (2.5)	0.9	23 (1.1)	0.4	0.02
Other	24 (6.1)	2.3	97 (4.7)	1.7	0.17

\*Two-sided P values for the comparison between blacks and whites were derived with the log-rank statistic.

†The unadjusted incidence is expressed as the rate per 100 person-years of follow-up.

death from arrhythmia (relative risk, 1.05; 95 percent confidence interval, 0.65 to 1.70; P=0.85).

In the treatment trial, blacks were at higher risk than whites for death from all causes (relative risk, 1.25; 95 percent confidence interval, 1.04 to 1.50; P=0.02), death from pump failure (relative risk, 1.32; 95 percent confidence interval, 1.02 to 1.70; P=0.03), and the composite end point of death from any cause or hospitalization for heart failure (relative risk, 1.28; 95 percent confidence interval, 1.10 to 1.49; P=0.002) (Table 5), but not for death from arrhythmia (relative risk, 0.97; 95 percent confidence interval, 0.64 to 1.45; P=0.86).

**Differences in Education and Socioeconomic Status**

Base-line data on educational level and the percentage of participants reporting “major financial distress” (yes vs. no) at any time during the 12 months

before enrollment were available for 2427 participants (208 blacks and 2219 whites) in the prevention trial and 2239 participants (341 blacks and 1898 whites) in the treatment trial. Fewer black than white participants had 12 or more years of education in both the prevention trial (13.3 percent vs. 28.4 percent, P<0.001) and the treatment trial (11.1 percent vs. 22.3 percent, P<0.001). More blacks than whites had eight or fewer years of education in both the prevention trial (34.5 percent vs. 21.9 percent, P<0.001) and the treatment trial (42.4 percent vs. 25.2 percent, P<0.001). More blacks than whites reported that they had experienced major financial distress in both the prevention trial (35.6 percent vs. 22.8 percent, P=0.001) and the treatment trial (38.4 percent vs. 23.1 percent, P=0.001).

According to univariate analysis, a lower educational level was associated with an increased risk of

TABLE 4. RESULTS OF THE MULTIVARIATE ANALYSIS OF DATA FROM THE PREVENTION TRIAL.

VARIABLE	DEATH FROM ALL CAUSES	DEATH FROM PUMP FAILURE	DEATH FROM ANY CAUSE OR HOSPITALIZATION FOR HEART FAILURE
	relative risk (95 percent confidence interval)		
Race (black vs. white)	1.36 (1.06–1.74)*	1.57 (1.01–2.44)*	1.54 (1.27–1.88)†
Age (per 5-yr increase)	1.12 (1.08–1.16)†	1.19 (1.11–1.28)†	1.11 (1.07–1.14)†
Left ventricular ejection fraction (per 10% decrease)	1.45 (1.26–1.66)†	1.49 (1.22–1.81)†	1.48 (1.34–1.62)†
Sex (male vs. female)	1.12 (0.86–1.45)	1.06 (0.67–1.69)	0.99 (0.80–1.21)
Creatinine‡	1.43 (1.16–1.77)†	1.67 (1.15–2.41)§	1.42 (1.19–1.70)†
Diastolic blood pressure (per 5 mm Hg increase)	0.96 (0.92–0.99)	0.95 (0.88–1.02)	0.98 (0.94–1.02)
NYHA functional class (II vs. I)¶	1.09 (0.93–1.29)	1.31 (0.97–1.76)	1.22 (1.07–1.40)§
Cause of ventricular dysfunction (ischemic vs. nonischemic)	0.96 (0.77–1.19)	0.84 (0.57–1.23)	0.86 (0.72–1.02)
History of stroke	1.63 (1.25–2.13)†	1.28 (0.76–2.16)	1.52 (1.21–1.91)†
History of hypertension	1.22 (0.93–1.35)	1.22 (0.87–1.71)	1.02 (0.88–1.19)
Diabetes	1.39 (1.13–1.70)§	1.60 (1.12–2.28)§	1.58 (1.34–1.87)†
Drug use			
Beta-blocker	0.84 (0.69–1.03)	0.78 (0.53–1.15)	0.79 (0.66–0.94)§
Diuretic	1.18 (0.96–1.45)	1.05 (0.72–1.53)	1.17 (0.99–1.39)
Antiarrhythmic drug	1.08 (0.88–1.34)	1.11 (0.76–1.62)	1.12 (0.94–1.33)
Antiplatelet agent	0.83 (0.70–0.98)*	0.97 (0.71–1.31)	0.81 (0.71–0.94)§
Digoxin	1.24 (1.00–1.54)*	1.36 (0.93–1.98)	1.13 (0.95–1.36)
Random assignment (enalapril vs. placebo)	0.93 (0.79–1.74)	0.81 (0.61–1.08)	0.82 (0.72–0.94)§

\*P≤0.05.

†P≤0.001.

‡The comparison is between patients with base-line serum creatinine concentrations of 1.5 to 2.0 mg per deciliter as compared with those with concentrations of <1.5 mg per deciliter.

§P≤0.01.

¶NYHA denotes New York Heart Association.

||P≤0.10.

death. For example, as compared with participants with 12 or more years of education, those with 8 or fewer years of education were at increased risk (relative risk of death, 1.59; 95 percent confidence interval, 1.37 to 1.85; P<0.001), as were those with 9, 10, or 11 years of education (relative risk, 1.34; 95 percent confidence interval, 1.16 to 1.56; P<0.001). An affirmative response to the question of whether the participant had experienced major financial distress during the 12 months before randomization was not associated with an increased risk of death according to univariate analysis.

Combining participants in both the prevention and the treatment trials, we performed multivariate analyses in which we adjusted for these socioeconomic differences in addition to the variables in the main analyses (Table 6). After adjustment the black participants remained at higher risk for death from all causes (relative risk, 1.28; 95 percent confidence interval, 1.08 to 1.51; P=0.004), death from pump failure (relative risk, 1.38; 95 percent confidence in-

terval, 1.08 to 1.76; P=0.009), and the combined end point of death from any cause or hospitalization for heart failure (relative risk, 1.37; 95 percent confidence interval, 1.20 to 1.57; P<0.001), but not for death from arrhythmia (P=0.36). When we analyzed each trial individually, adjusting for differences in socioeconomic status in addition to the variables in the main analyses, the black patients remained at increased risk for death from all causes in both the prevention trial (relative risk, 1.46; 95 percent confidence interval, 1.07 to 1.97; P=0.02) and the treatment trial (relative risk, 1.22; 95 percent confidence interval, 1.00 to 1.49; P=0.05).

**Consistency within Subgroups**

The increased mortality among the black as compared with the white participants remained the same when the participants from both trials were combined and the multivariate analyses, which included the same variables, were conducted within subgroups. In particular, overall mortality remained higher for

**TABLE 5.** RESULTS OF THE MULTIVARIATE ANALYSIS OF DATA FROM THE TREATMENT TRIAL.

VARIABLE	DEATH FROM ALL CAUSES	DEATH FROM PUMP FAILURE	DEATH FROM ANY CAUSE OR HOSPITALIZATION FOR HEART FAILURE
	relative risk (95 percent confidence interval)		
Race (black vs. white)	1.25 (1.04–1.50)*	1.32 (1.02–1.70)*	1.28 (1.10–1.49)†
Age (per 5-yr increase)	1.07 (1.03–1.11)‡	1.07 (1.02–1.13)†	1.00 (0.93–1.07)
Left ventricular ejection fraction (per 10% decrease)	1.39 (1.26–1.54)‡	1.55 (1.35–1.78)‡	1.54 (1.26–1.87)‡
Sex (male vs. female)	1.15 (0.97–1.37)	1.03 (0.81–1.31)	1.16 (1.00–1.34)§
Creatinine¶	1.36 (1.17–1.59)‡	1.45 (1.17–1.81)‡	1.31 (1.15–1.50)‡
Diastolic blood pressure (per 5 mm Hg increase)	0.94 (0.91–0.97)‡	0.90 (0.86–0.95)‡	0.97 (0.90–1.04)
NYHA functional class (III or IV vs. I or II)	1.56 (1.36–1.78)‡	1.96 (1.62–2.38)‡	1.66 (1.48–1.86)‡
Cause of ventricular dysfunction (ischemic vs. nonischemic)	1.07 (0.92–1.25)	0.87 (0.71–1.08)	0.97 (0.86–1.11)
History of stroke	1.23 (0.98–1.55)§	1.28 (0.92–1.77)	1.18 (0.97–1.44)§
History of hypertension	1.02 (0.89–1.18)	1.02 (0.83–1.25)	1.03 (0.92–1.17)
Diabetes	1.21 (1.04–1.40)*	1.25 (1.01–1.54)*	1.34 (1.18–1.52)‡
Drug use			
Beta-blocker	0.88 (0.66–1.16)	0.91 (0.59–1.40)	0.90 (0.74–1.17)
Diuretic	1.24 (1.01–1.53)*	1.26 (0.93–1.72)	1.38 (1.16–1.65)‡
Antiarrhythmic drug	1.25 (1.08–1.46)†	1.34 (1.08–1.66)†	1.19 (1.04–1.35)†
Antiplatelet agent	0.83 (0.71–0.97)*	0.86 (0.68–1.07)	0.84 (0.74–0.96)†
Digoxin	1.33 (1.14–1.54)‡	1.59 (1.26–2.00)‡	1.17 (1.03–1.32)*
Random assignment (enalapril vs. placebo)	0.87 (0.77–0.99)*	0.86 (0.71–1.04)	0.72 (0.65–0.81)‡

\*P≤0.05.

†P≤0.01.

‡P≤0.001.

§P≤0.10.

¶The comparison is between patients with base-line serum creatinine concentrations of 1.5 to 2.0 mg per deciliter as compared with those with concentrations of &lt;1.5 mg per deciliter.

||NYHA denotes New York Heart Association.

blacks than for whites among patients with nonischemic left ventricular dysfunction (relative risk of death from all causes, 1.29; 95 percent confidence interval, 1.00 to 1.66; P=0.05), those with ischemic left ventricular dysfunction (relative risk, 1.28; 95 percent confidence interval, 1.06 to 1.53; P=0.009), those without a history of hypertension (relative risk, 1.28; 95 percent confidence interval, 1.03 to 1.60; P=0.03), those without diabetes (relative risk, 1.37; 95 percent confidence interval, 1.16 to 1.64; P<0.001), those randomly assigned to receive placebo (relative risk, 1.15; 95 percent confidence interval, 1.02 to 1.53; P=0.03), and those randomly assigned to receive enalapril (relative risk, 1.34; 95 percent confidence interval, 1.08 to 1.66; P=0.007).

## DISCUSSION

These data demonstrate that black patients with asymptomatic or symptomatic mild-to-moderate left ventricular systolic dysfunction have higher overall mortality than white patients. The black participants

were also at higher risk for our two predefined indicators of the progression of disease, death from pump failure and the composite end point of death from any cause or hospitalization for heart failure. This was true even in the prevention trial, which enrolled mostly patients with asymptomatic left ventricular dysfunction. This result further suggests that black patients are at increased risk for progression of left ventricular systolic dysfunction, whether asymptomatic or symptomatic, as compared with similarly treated white patients.

The higher mortality among the black patients was evident even after adjustment for differences in age, sex, the severity and cause of left ventricular dysfunction, coexisting illnesses, use of medications, and socioeconomic status. Differences in socioeconomic status, including differences in educational levels, have been clearly demonstrated to be related to the increasing disparity in health among socioeconomic groups in the United States.<sup>11-13</sup> The black participants were equally distributed among the clin-

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**TABLE 6.** RESULTS OF THE MULTIVARIATE ANALYSIS OF COMBINED DATA FROM THE PREVENTION AND TREATMENT TRIALS, WITH ADJUSTMENT FOR SOCIOECONOMIC DIFFERENCES.

VARIABLE	OVERALL MORTALITY	DEATH FROM PUMP FAILURE	DEATH FROM ANY CAUSE OR HOSPITALIZATION FOR HEART FAILURE
		relative risk (95 percent confidence interval)	
Race (black vs. white)	1.28 (1.08–1.51)*	1.38 (1.08–1.76)*	1.37 (1.20–1.57)†
Education (yr)			
<8 vs. >12	1.22 (1.03–1.44)‡	1.11 (0.86–1.43)	1.24 (1.08–1.43)*
9–12 vs. >12	1.26 (1.09–1.45)*	1.19 (0.95–1.47)	1.28 (1.13–1.44)†
Financial distress (yes vs. no)	1.00 (0.88–1.14)	1.11 (0.91–1.35)	1.04 (0.93–1.16)
Age (per 5-yr increase)	1.09 (1.06–1.13)†	1.10 (1.06–1.14)†	1.06 (1.03–1.09)†
Left ventricular ejection fraction (per 10% decrease)	1.43 (1.32–1.55)†	1.58 (1.38–1.82)†	1.34 (1.26–1.45)†
Sex (male vs. female)	1.20 (1.02–1.41)‡	1.02 (0.81–1.28)	1.21 (1.06–1.39)*
Creatinine§	1.39 (1.21–1.59)†	1.51 (1.24–1.85)†	1.37 (1.22–1.54)†
Diastolic blood pressure (per 5 mm Hg increase)	0.95 (0.93–0.98)†	0.92 (0.88–0.96)†	0.96 (0.93–0.99)
NYHA functional class (III or IV vs. I or II)¶	1.58 (1.39–1.81)†	1.90 (1.56–2.32)†	1.59 (1.41–1.78)†
Cause of ventricular dysfunction (ischemic vs. nonischemic)	1.02 (0.89–1.16)	0.80 (0.66–0.97)‡	0.90 (0.80–1.01)
History of stroke	1.34 (1.10–1.63)*	1.27 (0.94–1.71)	1.30 (1.10–1.54)*
History of hypertension	1.05 (0.93–1.19)	1.02 (0.84–1.22)	1.08 (0.97–1.19)
Diabetes	1.27 (1.11–1.44)†	1.32 (1.10–1.61)*	1.41 (1.26–1.57)†
Drug use			
Beta-blocker	0.87 (0.72–1.04)	0.82 (0.59–1.12)	0.85 (0.72–0.99)‡
Diuretic	1.28 (1.09–1.49)*	1.21 (0.95–1.55)†	1.35 (1.19–1.54)†
Antiplatelet agent	0.85 (0.75–0.97)‡	0.95 (0.78–1.16)	0.85 (0.77–0.95)*
Antiarrhythmic drug	1.21 (1.06–1.38)*	1.30 (1.07–1.58)*	1.15 (1.03–1.29)‡
Digoxin	1.36 (1.19–1.55)†	1.54 (1.25–1.89)†	1.19 (1.06–1.33)†
Random assignment (enalapril vs. placebo)	0.87 (0.78–0.98)‡	0.85 (0.72–1.01)	0.73 (0.67–0.80)†
Trial (treatment vs. prevention)	1.18 (0.99–1.41)‡	1.47 (1.10–1.94)*	1.34 (1.16–1.55)†

\*P≤0.01.

†P≤0.001.

‡P≤0.05.

§The comparison is between patients with base-line serum creatinine concentrations of 1.5 to 2.0 mg per deciliter as compared with those with concentrations of <1.5 mg per deciliter.

¶NYHA denotes New York Heart Association.

||P≤0.10.

ical centers participating in the trials, and follow-up was standardized according to the SOLVD protocols. Therefore, as compared with the findings of earlier population-based studies, these results are less likely to be explained by racial differences in the treatment and follow-up of patients with heart failure. There may have been differences in the management of coexisting medical conditions, despite the patients' involvement in the SOLVD trials. However, this factor is unlikely to explain our results, given the consistency of the findings among subgroups — notably among patients without diabetes, those with no history of hypertension, and those with different causes of left ventricular dysfunction. Finally, follow-up was complete for more than 99 percent of participants. The percentage of patients who discontin-

ued treatment was similar for blacks and whites in the treatment trial but was slightly higher for blacks than for whites in the prevention trial (28 percent vs. 21 percent, P<0.001). However, when multivariate analyses were performed on data from only the participants in the prevention trial who continued to receive the assigned therapy, the differences between blacks and whites remained, indicating that the differences were not due to differences in the frequency of discontinuation of therapy.

The limitations of this retrospective analysis must be emphasized. Although we adjusted for potentially confounding differences between the groups, we cannot exclude the possibility that these findings could be explained by other important differences that we did not account for or by residual confound-

ing from the covariates for which we did adjust. With these limitations kept in mind, the data suggest that there may be differences in the natural history of ischemic and nonischemic left ventricular dysfunction between black and white patients. These differences may be related to differences in the physiologic response to left ventricular dysfunction. For example, blacks may have a greater degree of activation of neuroendocrine compensatory mechanisms than whites with a similar degree of left ventricular systolic impairment. Such differences might have important prognostic implications.<sup>14</sup> There may also be racial differences in the magnitude of benefit derived from the use of angiotensin-converting-enzyme inhibitors to treat left ventricular systolic dysfunction. Some data suggest that black patients with hypertension have an attenuated response to angiotensin-converting-enzyme inhibitors.<sup>15,16</sup> The small number of black participants in the SOLVD trials precludes meaningful comparisons of the efficacy of angiotensin-converting-enzyme inhibition in blacks and whites. However, racial differences in the response to angiotensin-converting-enzyme inhibitors would seem to be an unlikely explanation for the results of our analysis, since there was no evidence of interaction between race and random assignment to treatment with enalapril or placebo with respect to outcomes, since random assignment to enalapril or placebo was adjusted for in the multivariate analyses, and since the black participants still had higher mortality when the analyses were stratified according to whether the patient was assigned to receive placebo or the angiotensin-converting-enzyme inhibitor.

It will be important to understand the mechanisms underlying the differences in outcomes, since these may have therapeutic implications that will improve the survival of black patients with left ventricular dysfunction. For example, if black patients with left ventricular systolic dysfunction, as compared with white patients with similar degrees of left ventricular dysfunction, have an exaggerated neuroendocrine compensatory response, they may be ideal candidates for the early use of third-generation beta-blockers, which have been demonstrated to decrease the risk of progression in mild-to-moderate heart failure when used in conjunction with an angiotensin-converting-enzyme inhibitor.<sup>17-19</sup>

In conclusion, black patients with asymptomatic or symptomatic left ventricular systolic dysfunction appear to be at higher risk for progression of heart failure and for death than similarly treated white patients, even when adjustment is made for differences

in the severity and cause of heart failure, the management of heart failure, coexisting illnesses, and socioeconomic status. The reason for these observations is not known, but when elucidated it may have therapeutic implications.

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## REFERENCES

- Heart failure: management of patients with left-ventricular systolic dysfunction. Quick reference guide for clinicians. No. 11. Rockville, Md.: Agency for Health Care Policy and Research, June 1994. (AHCPR publication no. 94-0613.)
- Gillum RE. Heart failure in the United States 1970-1985. *Am Heart J* 1987;113:1043-5.
- Idem*. The epidemiology of cardiovascular disease in black Americans. *N Engl J Med* 1996;335:1597-9.
- Mortality from congestive heart failure — United States, 1980-1990. *MMWR Morb Mortal Wkly Rep* 1994;43:77-81.
- Council on Ethical and Judicial Affairs. Black-white disparities in health care. *JAMA* 1990;263:2344-6.
- Alexander M, Grumbach K, Selby J, Brown AF, Washington E. Hospitalization for congestive heart failure: explaining racial differences. *JAMA* 1995;274:1037-42.
- Philbin EF, DiSalvo TG. Influence of race and gender on care process, resource use, and hospital-based outcomes in congestive heart failure. *Am J Cardiol* 1998;82:76-81.
- The SOLVD Investigators. Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fractions. *N Engl J Med* 1992;327:685-91.
- Idem*. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. *N Engl J Med* 1991;325:293-302.
- Idem*. Studies of Left Ventricular Dysfunction (SOLVD) — rationale, design and methods: two trials that evaluate the effect of enalapril in patients with reduced ejection fraction. *Am J Cardiol* 1990;66:315-22. [Erratum, *Am J Cardiol* 1990;66:1026.]
- Ghali JK, Kadakia S, Cooper R, Ferlinz J. Precipitating factors leading to decompensation of heart failure: traits among urban blacks. *Arch Intern Med* 1988;148:2013-6.
- Williams DR. Socioeconomic differentials in health: a review and redirection. *Soc Psychol Q* 1990;53:81-99.
- Pappas G, Queen S, Hadden W, Fisher G. The increasing disparity in mortality between socioeconomic groups in the United States, 1960 and 1986. *N Engl J Med* 1993;329:103-9. [Erratum, *N Engl J Med* 1993;329:1139.]
- Benedict CR, Shelton B, Johnstone DE, et al. Prognostic significance of plasma norepinephrine in patients with asymptomatic left ventricular dysfunction: SOLVD Investigators. *Circulation* 1996;94:690-7.
- Weir MR, Gray JM, Paster R, Saunders E. Differing mechanisms of action of angiotensin-converting enzyme inhibition in black and white hypertensive patients. *Hypertension* 1995;25:124-30.
- Materson BJ, Reda DJ, Cushman WC, et al. Single-drug therapy for hypertension in men: a comparison of six antihypertensive agents with placebo. *N Engl J Med* 1993;328:914-21. [Erratum, *N Engl J Med* 1994;330:1689.]
- Packer M, Colucci WS, Sackner-Bernstein JD, et al. Double-blind, placebo-controlled study of the effects of carvedilol in patients with moderate to severe heart failure: the PRECISE Trial: Prospective Randomized Evaluation of Carvedilol on Symptoms and Exercise. *Circulation* 1996;94:2793-9.
- Colucci WS, Packer M, Bristow MR, et al. Carvedilol inhibits clinical progression in patients with mild symptoms of heart failure. *Circulation* 1996;94:2800-6.
- Chatterjee K. Heart failure therapy in evolution. *Circulation* 1996;94:2689-93.

**CORRECTION****Racial Differences in the Outcome of Left Ventricular Dysfunction**

Racial Differences in the Outcome of Left Ventricular Dysfunction . On page 611, in Table 1, the NYHA functional class values should have read as follows:

Corrected NYHA Functional Class Values.

CHARACTERISTIC	PREVENTION TRIAL		TREATMENT TRIAL	
	BLACKS (N=404)	WHITES (N=3658)	BLACKS (N=396)	WHITES (N=2061)
NYHA functional class (%)				
III or IV	0	0	31.3	31.8
II	29.8	33.6	68.7	68.2
I	70.2	66.4	0	0