

Long-Term Survival of African Americans in the Coronary Artery Surgery Study (CASS)

HERMAN A. TAYLOR, JR., MD, FACC,* MARY C. MICKEL, MS,*
BERNARD R. CHAITMAN, MD, FACC,† GEORGE SOPKO, MD,‡ GARY R. CUTTER, PhD,§
WILLIAM J. ROGERS, MD, FACC

Birmingham, Alabama; Saint Louis, Missouri; Bethesda, Maryland; and Seattle, Washington

Objectives. This study sought to determine the long-term (>15 years) outcome of a clinically well characterized cohort of African Americans with known or suspected coronary artery disease (CAD).

Background. The mortality rate from CAD is higher in African Americans than in whites. An earlier analysis of data from the Coronary Artery Surgery Study (CASS) registry suggested that African American and white patients treated surgically had equal 5-year survival rates.

Methods. Survival data from the CASS registry were analyzed to determine whether 1) African American race is an independent predictor of mortality; and 2) initial therapy is predictive of mortality among African American patients.

Results. Overall, 60% of white and 52% of African American patients survived 16 years ($p < 0.00001$). Multivariate Cox models confirmed that African American race was independently associ-

ated with higher mortality in both the medical group (hazard ratio [HR] 1.34, 95% confidence interval [CI] 1.11 to 1.63) and the surgical group (HR 1.63, 95% CI 1.19 to 2.23). Initial therapy was not predictive of survival among African American patients ($p = 0.81$). However, smoking status significantly influenced survival: African Americans who did not smoke experienced significantly improved survival (60% vs. 48% for smokers), which equaled survival for white nonsmokers (61%, $p = NS$).

Conclusions. In contrast to results from shorter term studies, African Americans experienced higher overall mortality rates than whites over the long term, regardless of the type of initial treatment. Survival among nonsmoking African Americans at 16 years equaled survival among nonsmoking whites.

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Higher mortality from coronary artery disease (CAD) occurs among African Americans than white Americans, especially in the younger age groups (1-3). One potential contributing cause is lower utilization of invasive care in management of CAD in African Americans (4-7). Using data from the Thrombolysis in Myocardial Infarction Phase II (TIMI II) trial, we reported (8) that equal access to urgent interventions and revascularization (including operation) resulted in equal survival rates 1 year after acute myocardial infarction, the leading cause of death from CAD. Furthermore, others, including the Coronary Artery Surgery Study (CASS) investigators, have reported (9,10) that surgical therapy produced equal survival in African American and white patients with CAD up to 5

years after operation. To examine the long-term survival of African Americans with known or suspected CAD, we analyzed data from the CASS registry 16 years after patient enrollment.

Methods

Patient population. Details of the CASS design, methods, definition of terms and baseline data have been reported previously (11). Fifteen clinical centers enrolled patients undergoing coronary angiography between 1974 and 1979. The study was approved by each center's institutional review board, and all patients gave written informed consent. Patients who had undergone cardiac surgery (except for pacemaker surgery) before enrollment and those of races other than African American or white were excluded from this analysis. The sample included 571 African Americans and 22,754 whites.

Follow-up. The CASS registry participants were contacted annually through 1982. To obtain data at least 10 years after enrollment, a follow-up questionnaire was administered by mail between 1988 and 1991, with vital status determined in 94% participants. Vital status through 1992 was also determined by searching the National Death Index. Patients with no death record were considered alive as of December 31, 1992. The mean follow-up period was 12.0 ± 5.2 years for African

From the Department of Medicine, Division of Cardiovascular Disease, University of Alabama at Birmingham, Birmingham, Alabama; *University of Washington, Seattle, Washington; †Department of Medicine, Division of Cardiology, Saint Louis University, Saint Louis, Missouri; ‡National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health, Bethesda, Maryland; and §Pythagoras, Inc., Birmingham, Alabama. The Coronary Artery Surgery Study (CASS) was funded by the NHLBI. Dr. Taylor is a recipient of the Preventive Cardiology Academic Award from the NHLBI.

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Address for correspondence: Dr. Herman A. Taylor, Jr., Division of Cardiovascular Disease, 318 LHRB, 701 South 19th Street, UAB Station, Birmingham, Alabama 35294-0007.

Abbreviations and Acronyms

CABG = coronary artery bypass graft surgery
 CAD = coronary artery disease
 CASS = Coronary Artery Surgery Study
 CCS = Canadian Cardiovascular Society
 CI = confidence interval
 HR = hazard ratio
 PTCA = percutaneous transluminal coronary angioplasty

Americans and 12.7 ± 4.9 years for whites, with a maximum of 18 years for both groups.

Data analysis. The clinical characteristics of patients surviving ≥ 10 years with complete follow-up data were compared by the Pearson chi-square test and, where appropriate, the chi-square test for trend. Patients who died before the 1988 follow-up contact or did not complete a questionnaire were necessarily excluded from this analysis.

Survival curves were estimated by the Kaplan-Meier method and compared by the log-rank statistic. Stratified analyses were used to adjust for important baseline characteristics.

Cox proportional hazards models were used to determine the independent effect of race on survival in patients treated with medicine or operation and to assess the effect of type of therapy on survival in African Americans. First, all covariates except the variable of interest were considered in a stepwise Cox regression analysis. After this model was constructed, the variable of interest (race or therapy) was allowed to enter if it offered additional predictive power. Validity of the proportional hazards assumption was confirmed by stratified models.

Variables considered in the multivariate models are shown in Table 1. Initial therapy and survival times for medical and surgical group patients were defined as follows: Patients were considered to be *surgically treated* if they underwent coronary artery bypass graft surgery (CABG) within the time period at each center within which 95% of the CABG procedures in the first year occurred; all others were assigned to the medical group. The data of CABG was the starting point for calculation of survival time in the surgical group. For medical patients, survival time was calculated from the date of enrollment plus the average time to operation at each center. This calculation adjusts for the discrepancy in exposure time between the medical and surgical groups. Patients who died before reaching the average time to operation at that center were excluded. Medical group patients who subsequently underwent CABG remained in the medical group.

Results

Baseline characteristics. Descriptive data for African Americans and whites in the CASS registry at enrollment have been published previously (12). That initial survey of baseline features revealed that more African Americans had hypertension and diabetes and were current smokers than was true for

Table 1. Variables Considered for Entry Into Cox Proportional Hazards Models

Variable	Definition
Age	Age at angiography
Gender	Male/female
Smoking at baseline	Never, former, current
Smoking at anytime (including follow-up)	Yes/no
Hypertension	Yes/no
Diabetes	Yes/no
No. of associated medical conditions	0-13
Previous MI	None, single, multiple
History of CHF	Yes/no
CHF score	0-4 (no-severe CHF)
Functional impairment due to CHF	0-4 (no CHF-severe impairment)
Recreational activity	1-4 (strenuous-sedentary)
CCS class	0-4 (0 = no angina; 1-4 = class I-IV)
Unstable angina	0-2 (0 = no angina; 1 = stable angina; 2 = unstable angina)
Normal arteriogram	Yes/no (yes = entire coronary vasculature normal)
No. of diseased vessels	0-3
No. of diseased proximal vessels	0-3
Myocardial jeopardy index	0-3 (0 = no jeopardized LV segments; 1 = inferior wall jeopardy; 2 = anterior wall jeopardy; 3 = both segments jeopardized)
LV wall motion score	5-30 (5 = normal left ventricle)
LMCA disease	Percent obstruction at baseline
Ejection fraction	At baseline
LV end-diastolic pressure	At baseline
Nitroglycerin	Yes/no
Beta-blockers	Yes/no
Digitalis	Yes/no
Diuretic drugs	Yes/no
Employment	Laborer/clerical/professional/homemaker
Race	White/black
Initial therapy	Medical/surgical

CCS = Canadian Cardiovascular Society; CHF = congestive heart failure; LMCA = left main coronary artery; LV = left ventricular; MI = myocardial infarction.

the whites; however, whites were more likely to be heavy smokers (>2 packs/day). Also, white men more frequently had a history of a documented myocardial infarction. With respect to symptomatology, significantly more African Americans fell into the "no angina" category and significantly fewer African Americans who had angina pectoris reported Canadian Cardiovascular Society (CCS) class III or IV symptoms. Also, substantially more African American than white patients had no "significant" coronary stenoses (at least 70% narrowing of any of the three main epicardial arteries or their branches or at least 50% stenoses of the left main coronary artery). Forty-seven percent of African American men and 67% of African American women fell into the "no CAD" category compared with 20% and 55% of white men and women, respectively.

Ten-year survivors. The key features of CASS registry patients who were alive and available for follow-up 10 years

Table 2. Comparison of Follow-Up Variables in African Americans and Whites

10-Yr F/U Variable	Whites [no. (%)]	African Americans [no. (%)]	p Value
Chest pain	8,575 (61%)	180 (69%)	0.01
Use of nitroglycerin in past year	5,194 (62%)	129 (73%)	0.003
CCS class			0.0006
No angina	5,522 (43%)	84 (38%)	
I	1,546 (12%)	20 (9%)	
II	3,008 (23%)	48 (21%)	
III	930 (7%)	15 (7%)	
IV	1,934 (15%)	57 (25%)	
Limitation of activities			0.41
None	4,541 (33%)	75 (32%)	
Intermittent	1,633 (12%)	23 (10%)	
Mild	2,582 (19%)	49 (21%)	
Moderate	3,126 (23%)	63 (27%)	
Severe	1,667 (12%)	27 (11%)	
Hypertension	5,120 (40%)	174 (69%)	<0.0001
Diabetes	1,926 (17%)	74 (35%)	<0.0001
Cerebrovascular disease	749 (7%)	24 (12%)	0.003
Aspirin for heart disease	7,068 (50%)	100 (38%)	0.0002
Diet to lower cholesterol	6,498 (49%)	100 (42%)	0.03
Cholesterol medications	2,081 (16%)	27 (12%)	0.11
Smoked cigarettes in last year	2,886 (21%)	73 (28%)	0.003
Use of estrogen (women only)	1,380 (41%)	21 (23%)	0.0006

CCS = Canadian Cardiovascular Society; F/U = follow-up.

after enrollment are shown in Table 2. African Americans had a higher prevalence of hypertension (69% vs. 40%, $p < 0.0001$), diabetes mellitus (35% vs. 17%, $p < 0.0001$) and current smoking (28% vs. 21%, $p = 0.003$) than whites. In contrast to the findings at baseline, more African Americans than whites complained of chest pain (69% vs. 61%, $p = 0.01$) and reported use of nitroglycerin (73% vs. 62%, $p = 0.003$). Furthermore, proportionately more African Americans reported CCS class III or IV angina pectoris than did their white counterparts.

Risk factor modification. Table 2 also shows the frequency of certain risk factor reduction strategies among African American and white survivors at 10 years. Whites more frequently than African Americans were taking aspirin (50% vs. 38%, $p = 0.0002$) and actively dieting to lower cholesterol (49% vs. 42%, $p = 0.03$). The use of estrogen replacement therapy was significantly more common among white women than among African American women (41% vs. 23%, $p = 0.0006$).

Cause of death. The cause of death was determined for 8,428 CASS registry patients who died during the first 16 years (94% of all deaths). The cause was cardiac related in 6,403 deaths (76% of classifiable deaths). The proportion of deaths due to cardiac-related causes was similar between the two racial groups (75% among African Americans vs. 76% among whites).

Predictors of survival in African Americans. Age, left ventricular wall motion score, smoking at baseline and number of diseased vessels were the strongest predictors of mortality

Table 3. Multivariate Predictors of Survival for 530 African Americans in the CASS Registry

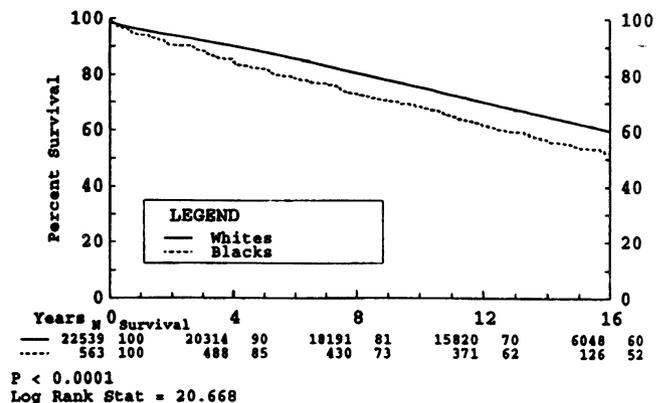
Variable	Chi-Square	p Value
Age	29.56	<0.0001
LV wall motion score	23.69	<0.0001
Smoking at baseline	18.85	<0.0001
No. of diseased vessels	16.04	0.0001
Diabetes	10.48	0.0012
CHF score	9.23	0.0024
Clerical worker (reduced risk)	5.08	0.0242
Therapy	0.06	0.81

Abbreviations as in Table 1.

for African American patients. Univariate analyses illustrate the effects of these variables. Only 42% of African American patients >55 years old at enrollment survived 16 years, compared with 72% for those who were ≤45 years old at enrollment. Impaired left ventricular function, as indicated by wall motion score, also had a profound effect on 16-year survival in African American patients, with the survival rate being 29% for those with severely abnormal wall motion, 67% for those with normal left ventricular function and 61% for those with moderate impairment. Only 48% of smokers survived 16 years compared with >60% for nonsmokers. Seventy-four percent of patients without any diseased coronary vessels survived 16 years compared with only 24% of those with three-vessel disease. However, the form of initial therapy had no impact on 16-year survival after adjusting for significant covariates (Table 3).

Effect of race on survival. Overall age-adjusted 16-year survival was better in whites than in African Americans (Fig. 1). After adjusting for significant clinical and treatment variables, African American race was still a strong independent predictor of mortality in both treatment groups. During 16 years of follow-up, African Americans treated medically were 34% more likely to die than whites (hazard ratio [HR] 1.34, 95% confidence interval [CI] 1.11 to 1.63); those treated surgically were 63% more likely to die than whites (HR 1.63, 95% CI 1.19 to 2.23), (Fig. 2, Table 4).

Figure 1. Age-adjusted survival in African Americans and whites in the CASS registry. Numbers below x-axis = number of patients at risk and the percentages surviving at years after entry indicated.



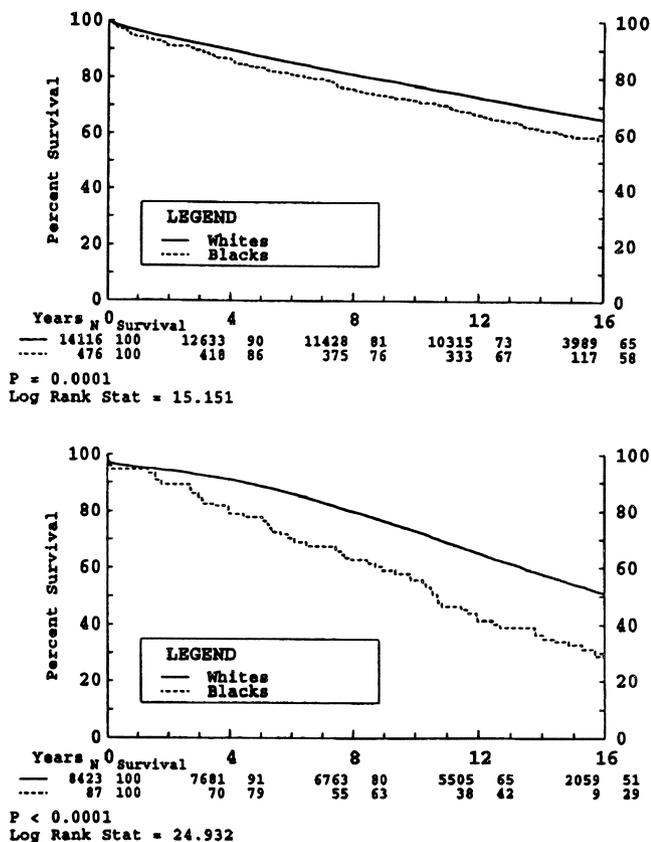


Figure 2. Age-adjusted survival in African Americans and whites. **Top,** medical treatment strategy. **Bottom,** Surgical treatment strategy. **Numbers below x-axis =** numbers and percentages of patients at years after entry indicated.

Stratified survival analyses (Table 5). Stratified survival function analyses were performed to further examine the impact of key predictors of mortality in patients in the two racial groups in the CASS registry. African American patient survival was worse in the younger age categories. Long-term survival for women did not differ between the races, whereas African American men had significantly worse survival than their white counterparts.

African American smokers had significantly worse survival than their white counterparts. There was no difference in survival between African American and white patients who either never smoked or who had quit smoking before entering the study. The Kaplan-Meier survival curves shown in Figure 3 illustrate the impact of smoking on survival in the two racial groups over the 16 years of follow-up.

Hypertensive status affected survival in both groups. However, the survival rate of hypertensive African Americans was not significantly different from that of hypertensive whites. Diabetes mellitus worsened survival for both African American and white patients.

African American and white patients without angina had equally good survival rates. However, African American patients with angina of any severity had poorer survival than whites in the corresponding CCS class.

Differences in survival between African American and white CASS registry patients were also evident in a variety of angiographically defined subgroups. African American patient mortality exceeded white patient mortality in the one-, two- or three-vessel coronary artery disease categories. African American patients with no CAD also had worse survival than their white counterparts. Left ventricular wall motion score results suggest that among patients with the mildest left ventricular dysfunction, proportionally more African Americans died over the 16 years after study entry ($p < 0.0005$). No significant differences emerged between African American and white patients with similar ejection fractions. Among patients with the most severe congestive heart failure, African American survival was better than that of the white patient group.

Discussion

Our analysis of follow-up data from the CASS registry suggests that despite similar survival rates for African American and white patients 5 years after operation (10), profound differences in survival emerge between the two groups by 16 years after operation. Furthermore, surgical therapy was not associated with improved survival for African American patients at 16 years after operation as it had been at the earlier follow-up evaluation. The higher African American patient mortality in both the medical and surgical treatment groups is disappointing and raises questions about factors that influence long-term survival of African American patients.

The significantly higher prevalence of classical risk factors among African Americans in the CASS registry reflects rates seen in the general African American population. These characteristics are not only risk factors for CAD in native vessels, but also hasten the occlusion of coronary artery bypass grafts, thus placing the African American group at risk for a poorer long-term outcome regardless of treatment. In our analysis, these factors did not account for all of the disparity in survival rates; however, their influence on African American patient survival is evident.

Smoking, in particular, had a disproportionately profound effect on survival of African American patients. In the absence of smoking, survival rates are relatively high and equivalent for African Americans and whites. However, African Americans who were smokers at entry have a much reduced chance of long-term survival than their white counterparts. This finding suggests that smoking is a particularly lethal practice for African Americans. Interestingly, others have noted disproportionately high mortality among African American smokers from other diseases as well (13,14). These differences in tobacco-related mortality are poorly understood; however, racial differences in the details of the smoking habit (i.e., brand selection, nuances of inhaling, amount of tobacco smoked per cigarette, less success of African Americans in smoking cessation, as well as possible differences in metabolism of toxins found in cigarette smoke) may play a role in the excess mortality found among African American smokers in the CASS registry (15). Neither serum cotinine levels nor detailed

Table 4. Multivariate Predictors of Survival for Medical and Surgical Group Patients in the CASS Registry

Variable	Medical Group (n = 9,724)		Surgical Group (n = 5,977)	
	Chi-Square	p Value	Chi-Square	p Value
Age	440.50	<0.0001	227.67	<0.0001
No. of diseased vessels	89.57	<0.0001	40.87	<0.0001
Smoking at baseline	106.04	<0.0001	40.93	<0.0001
LV wall motion score	88.09	<0.0001	36.64	<0.0001
Ejection fraction	51.55	<0.0001	23.64	<0.0001
Diabetes	90.66	<0.0001	42.53	<0.0001
LV end-diastolic pressure	38.18	<0.0001	19.30	<0.0001
CHF score	51.19	<0.0001	20.87	<0.0001
Gender	29.81	<0.0001	*	*
Recreational activity	20.57	<0.0001	*	*
Normal arteriogram	22.08	<0.0001	*	*
Functional impairment	17.46	<0.0001	*	*
LMCA disease	21.20	0.0001	8.16	0.004
Hypertension	31.76	<0.0001	29.23	<0.0001
Smoking at F/U	13.87	0.0002	*	*
Diseased proximal vessels	4.89	0.03	*	*
CHF	5.36	0.02	*	*
Black race	8.87	0.003	9.17	0.003
No. of illnesses	†	†	25.70	<0.0001
Laborer	†	†	25.93	<0.0001
Digitalis	†	†	6.39	0.01
HR (95% CI) for black vs. white mortality	1.34 (1.11-1.63)	1.63 (1.19-2.23)		

*Variable not a significant predictor of survival for surgical group patients. †Variable not a significant predictor of survival for medical group patients. CI = confidence interval; HR = hazard ratio; other abbreviations as in Tables 1 and 2.

quantification of cigarettes smoked were obtained in the present study.

Differences in the effectiveness of the CABG procedure in African Americans and whites appear unlikely; however, recent data suggest that the highly effective left internal mammary artery bypass graft may be used less frequently among African Americans undergoing CABG (16). If such a difference in the specifics of the bypass procedure occurred for black and white patients in the CASS registry, long-term survival among black patients could have suffered as a result.

Access to care. Despite access to coronary angiography and surgical therapy at the time of enrollment into the CASS registry, African American patients may have experienced impaired access to longitudinal care for CAD. Although the CASS design provided for periodic monitoring of a variety of patient clinical and treatment variables, ongoing care was left to the patient's usual resources and behavior. Barriers to primary care (17) and invasive care (4,6,7,18) for African Americans have been documented previously by many investigators. That less comprehensive care was given to the African American patients enrolled in the CASS registry is suggested by the lower rates of secondary prevention efforts reported by African American 10-year survivors. The 10-year survivor data suggest a race-associated disparity in utilization of secondary prevention strategies. However, these data must be interpreted with caution. The results may be biased by the fact that data are available from survivors only, giving us no insight into the

level of care provided those patients who died before 10 years in the study. Furthermore, response rates to the survey may differ by race. Nevertheless, a pattern of responses consistent with other reports documenting poor access to care for African American patients emerges from the 10-year survivor data. Fewer African Americans reported using daily aspirin or modifying their diets to lower cholesterol, and more were smoking. Estrogen-replacement therapy was used sparingly among African American women. The findings are particularly worrisome given that more African Americans had clinically obvious ischemia, as indicated by a heavier dependence on nitroglycerin for angina pectoris. Also, the higher prevalence of CAD risk factors (diabetes, hypertension, smoking and evidence of cerebrovascular disease) among African American survivors suggests that they should have been receiving more, rather than less, secondary prevention therapy.

Limitations of the study. Some limitations of the study have been mentioned. Additionally, it should be recalled that the number of African American patients in the CASS registry is relatively small, especially 16 years after enrollment. However, this series is unique in that it offers the advantage of long-term follow-up of a group of African American patients with CAD for whom a substantial amount of clinical information is available.

Another possible limitation is that the initial data for CASS were obtained in the era preceding the wide availability and utilization of thrombolytic therapy and percutaneous translu-

Table 5. Stratified Survival Analyses in African Americans and Whites

Variable and Subgroup	16-Year Survival Rates		P Value
	Whites	African Americans	
Age (yr)			
<45	77%	72%	0.05
45-55	66%	54%	<0.0001
>55	46%	42%	0.13
Gender			
Women	69%	66%	0.23
Men	57%	52%	0.02
Hypertension			
No	64%	65%	0.91
Yes	52%	53%	0.67
Diabetes			
No	62%	61%	0.40
Yes	40%	38%	0.38
Smoker			
Never	66%	68%	0.61
Former	58%	61%	0.72
Current	57%	48%	0.0004
CCS class			
No angina	69%	72%	0.55
I/II	63%	46%	<0.0001
III/IV	51%	43%	0.008
No. of diseased vessels			
0	83%	74%	<0.0001
1	65%	51%	0.0005
2	53%	38%	0.0025
3	39%	24%	0.0001
Ejection fraction			
≤50%	39%	36%	0.36
>50%	68%	65%	0.09
LV wall motion score			
5	75%	67%	0.0005
6-9	59%	61%	0.89
≥10	35%	29%	0.06
CHF score			
None	68%	67%	0.47
Mild	54%	48%	0.07
Mod/severe	27%	42%	0.01

Mod = moderate; other abbreviations as in Table 1.

minimal coronary angioplasty (PTCA). We consider this concern to be a minor one in that CABG is still a prominent modality for the management of CAD, and examination of its long-term results in African Americans and whites is appropriate and timely. Also, the key advantage of the present study (i.e., long-term survival analysis) requires that we evaluate interventions made before PTCA and thrombolysis were commonly used. The impact of PTCA or thrombolysis, or both, on the divergent long-term mortality data for African Americans and whites in the CASS registry was not assessed directly by this analysis. However, given the acknowledged lower utilization of these interventions among African American patients with CAD (4,6), it is possible that uneven utilization of these revascularization techniques contributed to the disparate 16-year outcome.

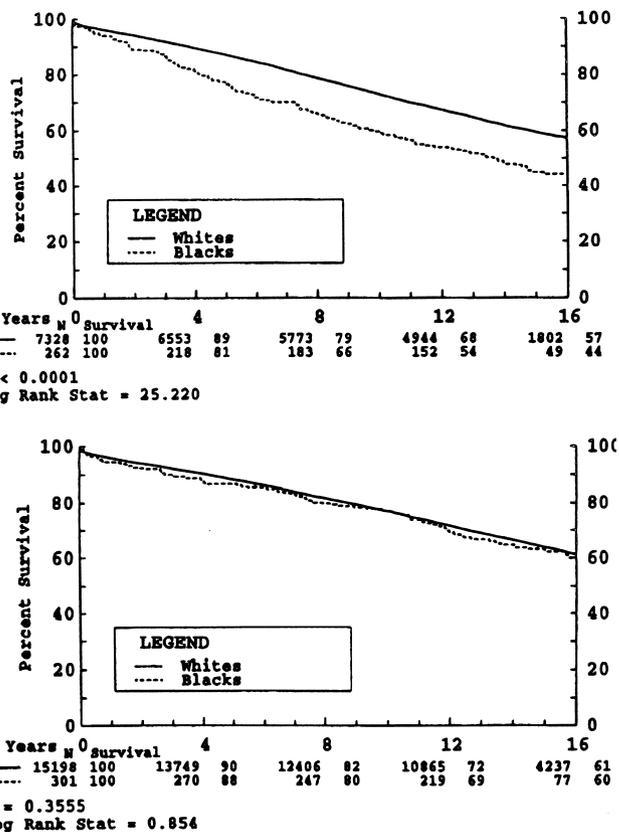


Figure 3. Age-adjusted survival in African Americans and whites. **Top**, Current smokers at baseline. **Bottom**, Never/former smokers at baseline. **Numbers below x-axis** = numbers and percentages of patients at years after entry indicated.

Summary. Coronary artery disease is the most frequent cause of death among African American and white Americans. Access to major cardiovascular interventions for all patients who need them is an important goal in our health care system's efforts to optimize CAD care. However, although surgical intervention provides encouragingly similar survival patterns between African American and white patients for a few years, 16-year follow-up data from the CASS registry suggest that operation alone does not produce a sustainable improvement in survival rates among African American patients. Significant racial differences in risk factor modification were suggested by these data. The smoking habit profoundly worsened mortality among African American patients; in the absence of smoking, there was no difference in survival between the racial groups. Access to comprehensive long-term care with special emphasis on smoking cessation is critically important in efforts to improve the prognosis for African American patients at risk for death from CAD. Without such services, the potential long-term survival benefits that access to CABG or other invasive procedures provide will most likely be lost.

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